Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health technology assessment of COVID-19 vaccination in Ireland

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Foreword

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since its discovery, multiple variant strains of SARS-CoV-2 have been identified. Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment due to increasing immunity from past infections and or vaccination but some (for example, those with underlying health conditions and those living with immunocompromise) are at a higher risk of severe illness. Others may continue to experience symptoms long after the infectious period has ended, this is known as long COVID or post COVID condition.

The National Immunisation Advisory Committee (NIAC) provides independent evidence-based recommendations and advice to the Minister for Health on immunisation and related health matters to inform health policy in Ireland. NIAC first issued recommendations in relation to COVID-19 vaccination in 2020. These recommendations have changed over time in response to the evolving epidemiological situation, evidence updates and the products available. On 6 May 2025, NIAC published updated recommendations on vaccination against COVID-19 to reflect the evolution of the COVID-19 pandemic to an endemic phase.

The Health Service Executive (HSE) COVID-19 vaccination programme provides access to COVID-19 vaccination, in line with NIAC guidance and the Department of Health policy, which is free at the point of care. In the context of the updated COVID-19 vaccination recommendations published by NIAC, the aim of this health technology assessment (HTA) was to support the work of the Department of Health and provide advice to the Minister for Health and HSE in relation to the groups for whom COVID-19 vaccination is funded by the HSE for the 2027/2028 vaccination campaign onwards.

Work on the HTA was undertaken by an Evaluation Team from the HTA Directorate in the Health Information and Quality Authority (HIQA). A multidisciplinary Expert Advisory Group was convened to advise the Evaluation Team during the course of the HTA. HIQA would like to thank the Evaluation Team, the members of the Expert Advisory Group and all who contributed to the preparation of this report.

Dr Máirín Ryan

Deputy Chief Executive & Director of Health Technology Assessment

Health Information and Quality Authority

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Healthcare Pricing Office, HSE

National Immunisation Office, HSE

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Conflicts of Interest

It is noted that the Irish Pharmacy Union (IPU) receives advertising revenue from the pharmaceutical industry through its publication, the IPU review. The IPU also receives funding for educational activities from the pharmaceutical industry.

General practices and pharmacies derive a small portion of their income from administration of vaccines.

There were no other reported potential conflicts of interest for members of the Expert Advisory Group or Evaluation Team.

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Key findings and Advice to the Minister for Health and Health Service Executive

At the request of the Department of Health, the Health Information and Quality Authority (HIQA) agreed to undertake a health technology assessment (HTA) to inform a policy decision by the Minister for Health on Coronavirus Disease 2019 (COVID-19) vaccination in Ireland, specifically in relation to the groups for whom COVID-19 vaccination is funded by the HSE for the 2027/2028 vaccination campaign onwards. This HTA aimed to summarise the clinical effectiveness and safety of COVID-19 vaccines, assess the cost effectiveness and budget impact of COVID-19 vaccination, and consider any additional implications relating to a potential change in COVID-19 vaccination policy (including organisational, ethical, patient and social considerations).

The key findings of this HTA, which informed HIQA's advice to the Minister for Health and the Health Service Executive (HSE), were:

- COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Symptom severity of acute COVID-19 can range from asymptomatic to life threatening. Older adults, those with underlying health conditions and those living with immunocompromise are at a higher risk of severe illness compared to the general population. Some people continue to experience symptoms long after the infectious period has ended, this is known as long COVID.
- The World Health Organization (WHO) declared that the outbreak of COVID-19 disease constituted a global pandemic on 11 March 2020. The severity of COVID-19 has declined over time (due to virus evolution and the establishment of population immunity through vaccination and natural infection). While the SARS-CoV-2 virus continues to circulate, on 5 May 2023, the WHO declared that COVID-19 no longer constituted a public health emergency of international concern, signalling its evolution from a pandemic to an endemic phase.
- Antigenically updated vaccines currently authorised by the European Medicines Agency for the prevention of COVID-19 include mRNA vaccines and protein subunit vaccines.
    - The mRNA vaccines include:
        - mNexspike® (authorised for use in people aged 12 years and older), Spikevax® and Comirnaty® (both authorised for use in those aged six months and older)

    - the combined vaccine, mCOMBRIAX® (authorised for use in people aged 50 years and older against COVID-19 and seasonal influenza).

  - The protein subunit vaccines include:
    - Nuvaxovid® and Bimervax® (authorised for the prevention of COVID-19 in individuals aged 12 years and older).

- In May 2025, the National Immunisation Advisory Committee (NIAC) issued updated COVID-19 vaccination recommendations for Ireland. Based on the evidence considered, vaccination is recommended for those who continue to be at increased risk of severe outcomes, to be given:

  - twice yearly for all those in whom immunity wanes more quickly, that is those aged:
    - 80 years and older
    - 18 to 79 years and living in long-term care facilities (LTCFs) for older adults
    - six months and older with immunocompromise associated with a suboptimal response to vaccination.

  - once a year for those aged:
    - 60 to 79 years
    - six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death.

- NIAC also recommends that access to vaccination is available for additional individuals not included above (health and care workers, pregnant women, those aged 18 to 59 years without additional risk factors for severe disease) for whom vaccination is no longer specifically recommended, but who wish to receive the vaccine.

- To date, availability of a particular COVID-19 vaccine in Ireland has typically been dependent on whether a particular vaccine product has been preferentially recommended by NIAC and opting into a joint procurement framework contract negotiated between manufactures and the European Commission's Health Emergency Preparedness and Response Authority (HERA).

- Currently, the HSE COVID-19 vaccination programme provides access to COVID-19 vaccination in line with NIAC guidance and the Department of Health policy, which is free at the point of care. The preferentially recommended vaccine is an antigenically updated mRNA vaccine, which is available year-round; however, campaigns are run twice yearly, in the autumn/winter (to align with the seasonal influenza campaign) and again in the spring to promote and support uptake in those for whom vaccination is recommended. During the autumn/winter

2025/2026 campaign, COVID-19 vaccination was available to all groups outlined in the May 2025 NIAC recommendations, including those for whom NIAC advised access should be made available.

- As of August 2026, COVID-19 vaccines are not currently available for private purchase in Ireland.
- All European countries provided broad population level access to publicly funded COVID-19 vaccination during the emergency phase of the pandemic. However, national policies continue to be updated in line with epidemiological developments, including restricting access to those considered to be at higher risk of severe disease. Further updates are expected as purchase agreements through centrally negotiated HERA contracts end, with the potential for policy decisions to also take consideration of broader issues including cost effectiveness.
    - Since 2025, following consideration of cost effectiveness, the national COVID-19 vaccination programme in England was limited to adults aged 75 years and over (with this cohort being further limited to those aged 80 years and older in autumn 2027); residents of care homes for older adults; and individuals aged six months and older who are living with immunocompromise.
- Health Protection and Surveillance Centre (HPSC) incidence data indicate that for the period 2023 to 2025 the burden of COVID-19:
    - has declined over time in the total population aged six months and older with reductions in the notified case rates (from 699.1 to 248.3 per 100,000), emergency department (ED) visit rates (from 109.9 to 93.7 per 100,000), hospital admission rates (from 303.6 to 94.0 per 100,000), intensive care unit (ICU) admission rates (from 3.1 to 1.4 per 100,000) and mortality rates (from 16.6 to 5.1 per 100,000, equating to a reduction from 848 notified COVID-19-related deaths in 2023 to 260 notified deaths in 2025).
    - generally increases with age, with a disproportionate burden among the oldest adults. Specifically, those aged:
        - 80 years and older accounted for 27% of notified cases; 22% of notified ED visits; 36% of notified hospitalisations; 17% of notified ICU admissions; and 64% of notified deaths, while representing less than 4% of the total population.
        - 75 years and older accounted for 38% of notified cases; 33% of notified ED visits; 50% of notified hospitalisations; 32% of notified ICU

admissions; and 79% of notified deaths, while representing only 7% of the total population.

- Limited data are available with respect to the vaccination status of notified cases and in relation to the presence of underlying conditions in those experiencing severe disease.
    - Vaccination status of notified hospital cases (from 2023 to 2025) was known for, on average, 68% of those aged 80 years and older and 67% of those aged 60 to 79 years. In 2025, considering those aged:
        - 80 years and older for whom twice yearly vaccination is recommended, 85% of notified hospital admissions and 88% of notified ICU admissions in this age group were in those who had not been vaccinated within the previous 180 days.
        - 60 to 79 years for whom once yearly vaccination is recommended, 63% of notified hospital admissions and 77% of notified ICU admissions in this age groups were in those who had not been vaccinated within the previous 365 days.
    - Comorbidity data were limited to those admitted to ICU. In all years, more than 90% of notified ICU admissions were in those with one or more underlying medical condition.
- While recognising that long COVID can have a considerable impact on an individual's quality of life, their ability to work and daily functioning, data are lacking (in Ireland and internationally) in relation to both the prevalence and burden associated with long COVID.
- A number of COVID clinics have been established by the HSE nationally to provide post-acute and long COVID care. Data indicate that the number of new patients being referred to these clinics has decreased from 2023 to 2025 (which is broadly consistent with the trend observed for notified COVID-19 cases in Ireland), with return patients comprising most patients being assessed at these clinics. While reported new referrals to the clinics may be decreasing, given the lack of national level data it is unclear whether there is also a decrease in the incidence and prevalence of long COVID in Ireland.
- Irish public acute hospital data for 2023 and 2024 highlight the substantial burden associated with COVID-19 on the secondary healthcare system. These data are not directly comparable as prior to 2024, COVID-19 could only be coded as an additional diagnosis, even if it was the primary reason the patient presented to the healthcare system. Considering the total population (all ages):

- In 2023, there were 17,828 discharges with an additional diagnosis of COVID-19. The mean length of stay was 23 days, and the total number of bed days was 409,621 days.
- In 2024 there were:
  - 2,876 discharges (42 of which included an ICU admission) with a principal diagnosis of COVID-19. The mean length of stay was six days, and the total number of bed days was 18,039 days.
  - 11,533 discharges with an additional diagnosis of COVID-19. The mean length of stay was 25 days, and the total number of bed days was 292,315 days.
- These data also indicate that the burden generally increases with age, with a disproportionate burden among the oldest adults. In considering the total discharges in those with a principal diagnosis of COVID-19 in 2024, those aged:
  - 80 years and older accounted for 34% of discharges, 51% of the total bed days, and had the longest average length of stay per patient at 10 days.
  - 75 years and older accounted for 45% of discharges, 67% of the total bed days and had an average length of stay of nine days per patient.

- Using 2024 data, the average cost associated with a hospital stay for a patient with a principal diagnosis of COVID-19 was €6,870, and the total annual cost associated with all discharges with a principal diagnosis of COVID-19 was approximately €19.8 million.
  - Additional costs may accrue for patients who require post-discharge rehabilitation and care, and in relation to long COVID, both from the healthcare and societal perspective.
- The COVID-19-related morbidity and mortality observed are in the context of an ongoing COVID-19 vaccination programme that continues to offer funded COVID-19 vaccination to certain at-risk groups.
  - During the 2025/2026 autumn/winter campaign, reported uptake was 73.6% in residents of LTCFs for older adults, 60.8% in those aged 80 years and older, 33.2% in those aged 60 to 79 years, and 18.2% in those identified as living with immunocompromise. These rates are lower than the HSE targets that 75% of those aged 65 years and older and 50% of those living with immunocompromise receive their booster doses.

  - When comparing vaccination campaigns from autumn 2023 onwards, there has been a gradual decrease in uptake, with substantially lower uptake in the spring campaigns for those in whom twice yearly vaccination is recommended (for example, for those aged 80 years and older, uptake was 32.3% in the spring 2025 campaign versus 60.8% in the autumn/winter 2025/2026 campaign).

- Evidence from a systematic review published in October 2025 was used to inform the assessment of the effectiveness and safety of antigenically updated COVID-19 vaccines for the populations of interest to this HTA. Where data for subgroups of interest were lacking in the systematic review, evidence was supplemented by a search of European, UK and US platforms. In total, the review included vaccine effectiveness (VE) data from 22 observational studies. The review included safety findings from 19 studies, all of which were limited to ancestral strain COVID-19 vaccines.

- In general, Omicron-adapted vaccines were associated with a significant reduction in severe COVID-19 disease outcomes across several of the population groups. While some estimates of vaccine effectiveness (VE) may appear to be modest, it is important that these effects are viewed in the context of the considerable burden associated with COVID-19, particularly for those at increased risk of severe disease.

- In terms of the evidence for the effectiveness of Omicron-adapted COVID-19 vaccines:
  - Estimates of effect were typically higher for outcomes related to severe disease compared with medically attended or symptomatic infection outcomes.
  - Protection against hospitalisation and mortality was observed up to five to six months post-vaccination among older adults, those living with immunocompromise, those living with underlying medical conditions, and those aged 18 to 59 years in the general population.
  - There was evidence of waning protection, particularly over longer follow-up periods.
  - Where effectiveness estimates were disaggregated by age, there was no consistent pattern and confidence intervals typically overlapped.
  - Only one study reported on VE against post-acute sequelae associated with long COVID; there was no evidence of protection reported for those aged 60 years and older, while a VE of 49% was reported for those aged 18 to 59 years.

- The majority of the evidence related to Omicron-adapted mRNA COVID-19 vaccines. Where studies included other vaccine types (for example, protein subunit vaccines), only a small number of participants received these other types and studies typically did not report findings disaggregated by vaccine type. No evidence was identified for newer COVID-19 formulations or technologies licensed since 2025.
- No evidence was identified in this chapter regarding the effectiveness of Omicron-adapted vaccines for:
    - those living in LTCFs; however, high levels of protection against severe COVID-19, using original COVID-19 vaccines, were previously documented for this population during the early years of the pandemic
    - pregnant individuals; however, previous evidence of effectiveness supports COVID-19 vaccination during pregnancy to prevent severe disease and adverse maternal and child outcomes.
- The findings reported in this chapter are consistent with the existing literature base as it pertains to the safety profile of COVID-19 vaccines, which is largely favourable. One study noted an increased risk of myocarditis (in those aged 50 years and older) with COVID-19 vaccination, and another reported an increased risk of myopericarditis (in those aged 66 years and older). Post-marketing surveillance has noted the frequency of myocarditis or pericarditis, where known, occurs in fewer than 1 in 10,000 vaccinations and would be considered very rare.
- An economic model was developed to characterise the incidence of notified cases of COVID-19 in Ireland and estimate the cost effectiveness and budget impact of COVID-19 vaccination programmes for the general population of adults aged 60 years and older in Ireland. The five-year budget impact of COVID-19 vaccination for specific population groups, as defined by NIAC recommendations for COVID-19 vaccination, was also estimated.
- The economic evaluation for the general population aged 60 years and older assess the following two vaccination strategies:
    - Strategy 1 (S1) – a vaccine offered twice each year for those aged 80 years and older
    - Strategy 2 (S2) – a vaccine offered twice each year for those aged 80 years and older (S1) and once each year for those aged 60 to 79 years.
- For the economic model, average annual VE against COVID-19 by age and outcome was estimated based on the data reported in the review of the

effectiveness of Omicron-adapted vaccines. Model parameter estimates (notified cases) were:

  - 80 years and older: medically attended visits - 18%; ED visits - 29%; hospitalisations - 36%; deaths - 55% (assuming twice yearly vaccination)
  - 60 to 79 years: medically attended visits - 12%; ED visits - 22%; hospitalisations - 27%; deaths - 52% (assuming once yearly vaccination).

- From the payer perspective, at a vaccine cost of €75 per dose (ex VAT), that was estimated based on published international prices, and assuming 2025 incidence of notified COVID-19, the analysis that considered the incremental cost effectiveness ratio (ICER) per quality-adjusted life year (QALY) gained found that:
  - the ICER for S1 compared with no vaccination was €56,500
  - the ICER for S2 compared with S1 was €202,000
  - both ICERs exceeded a willingness-to-pay threshold of €45,000
  - in a scenario analysis assessing a strategy of vaccination from aged 75 years, the ICER was €80,000 when compared with S1.
- Based on assumptions in the model, the vaccine cost would need to be less than €60 per dose for S1 to be cost effective at a WTP threshold of €45,000 per QALY gained. A scenario analysis, where incidence of notified COVID-19 was varied, demonstrated that using:
  - 2024 incidence data in the model, the ICER for S1 compared with no vaccination fell to €15,500 per QALY.
  - 2023 incidence data in the model, S1 was cost-saving (that is, less costly and more effective) compared with no vaccination.
- The five-year incremental budget impact versus no vaccination was €111.5 million for S1 and €307.0 million for S2.
  - Vaccine procurement accounted for the majority of costs incurred for both strategies over the five-year time horizon (approximately 71% to 75%).
  - Total cost offsets (largely relating to hospitalisation and long-term care post COVID-19) as a percentage of total costs incurred, were 28% and 15% for S1 and S2, respectively.

- The budget impact model for other populations outlined in the NIAC recommendations only considered the costs incurred over a five-year period. Due to a lack of relevant epidemiological data for Ireland, costs averted were not estimated. At current uptake rates, and recommended vaccination intervals (yearly or twice yearly), the five-year budget impact versus no vaccination was:
    - €37.4 million for those aged 18 to 79 years living in a long-term care facility for older adults (twice yearly)
    - €18.0 million for those aged six months and older with immunocompromise associated with a suboptimal response to vaccination (twice yearly)
    - €21.1 million for those aged six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death (once yearly)
    - €18.1 million for health and care workers who choose to receive a vaccine (once yearly)
    - €6.8 million for pregnant adolescents and adults (once in each pregnancy)
    - €63.8 million for all others aged 18 to 59 years not included in other specific population groups (once yearly).
- While this analysis demonstrated that vaccination against COVID-19 is associated with reductions in outcomes related to COVID-19, the strategies assessed in the base-case economic analysis would be considered not cost effective at the modelled vaccine price at a WTP threshold of €45,000 per QALY. However, as demonstrated in the results of the sensitivity and threshold analysis, the outcome of this economic evaluation is highly sensitive to both the assumed price of the vaccine and the incidence of COVID-19 going forward. As such, both parameters require careful consideration in informing decision-making regarding future COVID-19 vaccination policy.
- General organisational issues relating to the COVID-19 vaccination programme include:
    - Challenges associated with an existing model based on use of a multidose vial formulation, packaged in boxes of 10, that are delivered from the manufacturer frozen and which must be thawed and relabelled with a new, shorter "use by" date before transportation to primary vaccination sites. This results in additional operational complexity, greater potential for dosing errors, and greater wastage compared with other vaccines provided through the HSE National Cold Chain Service (NCCS).

- Efficiencies may be realised by moving to a refrigerated (never frozen), single dose, pre-filled syringe product when procurement contracts are retendered. This would be consistent with how most other vaccines are supplied, would reduce wastage, and provide efficiencies for NCCS staff in terms of vaccine storage and management, and healthcare staff in terms of vaccine administration.

- Although a programme comprising a range of vaccine products may increase choice and potentially improve resilience, these benefits would need to be considered in the context of the cost difference (if any) between products and the additional logistical burden associated with making a range of products available.

- Given the lack of seasonality with COVID-19 and evidence of waning vaccine effectiveness over time, more frequent campaigns may be required to promote uptake when national and international data suggest periods of higher circulation. Consideration could also be given to expanding access outside defined seasonal campaigns to anyone whose vaccination status is not considered to be current (within the preceding 180 or 365 days, as appropriate).

- There are potential ethical, patient and social issues associated with a decision to change or restrict access to funded COVID-19 vaccination, including a potential:

  - increase in the burden of COVID-19 among individuals for whom vaccination is no longer funded, particularly if eligibility is based solely on age-based criteria, rather than also considering other groups known to be at increased risk of severe disease, (for example, those residing in LTCFs for older adults or those living with immunocompromise)

  - increased level of long-term disability among non-eligible groups who may go on to experience long COVID and an associated reduced participation in the labour market, or potential worsening of symptoms for those already living with long COVID

  - reduction in the workload for healthcare staff due to a reduction in the number of individuals requiring vaccination. This efficiency is particularly relevant when considering subgroups for whom the current benefits of vaccination are limited given the decline in severity of COVID-19.

  - perceived curtailment of an individual's autonomy in those for whom access to funded COVID-19 vaccination is no longer available. However, decisions about healthcare distribution should ensure that resources are allocated or reallocated fairly and that the opportunity costs of investments are

considered. Funding interventions that are not cost effective could create issues of justice and equity with respect to a fair distribution of benefits and burdens. This is particularly important in the context of a finite healthcare budget and increasing demands for services provided.

- In acknowledging the overall decline in the burden associated with COVID-19, a decision to change the groups eligible for COVID-19 vaccination should still be considered in the context of the overall resilience of a healthcare system that exhibits high bed occupancy rates. While COVID-19 lacks seasonality, the potential for vaccination to support reductions in winter overcrowding could strengthen resilience in the health service.
- The assessment of cost effectiveness in this HTA was limited to age-based cohorts (that is, vaccination of older adults). Due to a lack of Irish epidemiological data, it was not feasible to evaluate the cost effectiveness of vaccinating other cohorts at high risk of severe disease (such as those residing in LTCFs for older adults and those living with immunocompromise) and those at increased risk of exposure (such as, health and care workers). However, this does not preclude a decision on whether to continue to provide COVID-19 vaccination for such individuals, given that policy decisions are informed by multiple domains and not just cost effectiveness.
- Given the continuing uncertainty regarding future disease patterns, variant emergence and long-term health impacts, it will be important to continue the use of national and international surveillance data as well as recommendations from the National Immunisation Advisory Committee (NIAC) to inform national COVID-19 vaccination policy.
- Any change to the national COVID-19 vaccination programme needs to be appropriately communicated to the public and healthcare providers. This would include:
    - timely information for those no longer eligible to funded vaccination who may have concerns about their risk of infection and severe disease
    - targeted outreach in relation to the population groups who remain eligible to optimise uptake and avoid wastage. This information should support an understanding of their ongoing risk of severe disease due to COVID-19 and the potential for this to be mitigated by remaining up-to-date with their vaccine recommendations.

Arising from the findings of this HTA, and in the context of an established HSE COVID-19 vaccination programme that has provided free (at the point of care)

access in line with Department of Health policy, HIQA's advice to the Minister for Health and the HSE with respect to COVID-19 vaccination is as follows:

- COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Health Protection and Surveillance Centre (HPSC) data for the period 2023 to 2025 indicate that the absolute risk of severe COVID-19 disease has continued to decline in all age groups since the end of the emergency phase of the pandemic. Older adults, those with underlying health conditions and those living with immunocompromise are at a higher relative risk of severe illness compared with the general population. Some people continue to experience symptoms long after the infectious period has ended, this is known as long COVID.
- While the overall burden has decreased, the available data indicate that older adults continue to be disproportionately affected:
    - between 2023 and 2025, those aged 80 years and older represented less than 4% of the total population but accounted for 36% of notified hospitalisations and 64% of notified deaths
    - where vaccination status was known, in 2025, 85% of notified hospital admissions in those aged 80 years and older were in those who had not been vaccinated as recommended within the preceding 180 days.
- Antigenically updated COVID-19 vaccines are safe and effective. Effectiveness is greater against severe disease; however, there is a consistent trend of waning protection over time.
    - Based on the evidence reviewed, the vaccine effectiveness estimates used in the economic model assumed that vaccination would prevent approximately one third of notified hospitalisations and over half of all notified deaths each year among those aged 80 years and older (based on twice yearly vaccination).
- The economic evaluation considered vaccination of the general population aged 60 years and older. It assumed the vaccine is offered once each year to those aged 60 to 79 years and twice yearly to those aged 80 years and older. In the absence of indicated vaccine prices for Ireland, a vaccine cost of €75 per dose (ex VAT) was used. Assuming 2025 incidence of notified COVID-19, the analysis that considered the incremental cost effectiveness ratio (ICER) per quality-adjusted life year (QALY) found:

  - an ICER of €56,000 per QALY for adults aged 80 years and older compared with no vaccination
  - an ICER of €201,000 per QALY for those aged 60 years and older compared with offering vaccination to just those aged 80 years and older
  - both ICERs exceeded a willingness-to-pay (WTP) threshold of €45,000 per QALY gained
  - in a scenario analysis assessing a strategy of vaccination from age 75 years, the ICER was €80,000 per QALY when compared with vaccination of those aged 80 years and older.
- Based on the assumptions in the model, the vaccine cost would need to be less than €60 per dose for vaccination of those aged 80 years and older to be cost effective at a WTP threshold of €45,000 per QALY.
- At current uptake rates, the five-year incremental budget impact versus no vaccination was €112.0 million for those aged 80 years and older and €307.6 million for those aged 60 years and older. Vaccine procurement accounted for approximately 71% to 75% of costs for both strategies.
- At current uptake rates and recommended vaccination intervals (once yearly or twice yearly), the total five-year cost of providing vaccination for other population groups was:
  - €37.4 million for those aged 18 to 79 years living in a long-term care facility for older adults (twice yearly)
  - €18.0 million for those aged six months and older with immunocompromise associated with a suboptimal response to vaccination (twice yearly)
  - €21.1 million for those aged six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death (once yearly)
  - €18.1 million for health and care workers who choose to receive a vaccine (once yearly)
  - €6.8 million for pregnant adolescents and adults (once each pregnancy)
  - €63.8 million for all others aged 18 to 59 years not included in other specific population groups (once yearly).

- The results of the economic evaluation are highly sensitive to both the assumed price of the vaccine and the incidence of COVID-19. These should be key considerations in any decision-making and in procurement negotiations with vaccine manufacturers.
- Any changes to the national COVID-19 vaccination programme should:
  - continue to be informed by national and international surveillance data and recommendations from NIAC
  - include timely communication to those who may be impacted, as well as targeted outreach to eligible population groups to optimise uptake.

Executive Summary

A health technology assessment (HTA) is intended to support evidence-based decision-making in regard to the optimum use of resources in healthcare services. Measured investment and disinvestment decisions are essential to ensure that overall population health gain is maximised, particularly given finite healthcare budgets and increasing demands for services provided. The aim of this HTA was to provide advice to the Minister for Health and Health Service Executive (HSE), to inform a decision on potential changes to the groups for whom coronavirus disease 2019 (COVID-19) vaccination is funded by the HSE for the 2027/2028 vaccination campaign onwards. This HTA considered the following domains:

- description of the technology
- epidemiology and burden of disease
- clinical effectiveness and safety
- economic evaluation
- organisational, ethical, patient and social considerations.

Background

COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However, some people (for example, older people, those with underlying health conditions and those living with immunocompromise) are at higher risk of severe illness compared to the general population. Some people may continue to experience symptoms long after the infectious period has ended, this is known as long COVID.

The World Health Organization (WHO) declared that the outbreak of COVID-19 disease constituted a global pandemic on 11 March 2020. The severity of COVID-19 has declined over time (due to virus evolution and the establishment of population immunity through vaccination and natural infection). While the SARS-CoV-2 virus continues to circulate, on 5 May 2023, the WHO declared that COVID-19 no longer constituted a public health emergency of international concern, signalling its evolution from a pandemic to an endemic phase.

In May 2025, the National Immunisation Advisory Committee (NIAC) updated its recommendations on COVID-19 vaccination as follows:

- A COVID-19 vaccine is recommended twice each year for those aged 80 years and older; those aged 18 to 79 years and living in long-term care facilities

(LTCFs) for older adults; and those aged six months and older with immunocompromise associated with a suboptimal response to vaccination.
- A COVID-19 vaccine is recommended once each year for those aged 60 to 79 years and for those aged six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death.
- A COVID-19 vaccine should be available to healthcare workers who choose to receive a vaccine; pregnant adolescents and adults, who following discussion with a healthcare provider, choose to receive a vaccine; and other adults aged 18 to 59 years who, following discussion with a healthcare provider, choose to receive a vaccine.

Following a request from the Department of Health, the Health Information and Quality Authority (HIQA) agreed to undertake a HTA of COVID-19 vaccination in Ireland to provide advice in relation to the groups for whom COVID-19 vaccination is funded for the 2027/2028 vaccination campaign onwards.

Description of technology

Antigenically updated vaccines currently authorised by the European Medicines Agency for the prevention of COVID-19 include messenger ribonucleic acid (mRNA) vaccines and protein subunit vaccines.

- The mRNA vaccines include:
  - mNexspike® (authorised for use in individuals aged 12 years and older), and Spikevax® and Comirnaty® (both authorised for use in individuals aged six months and older)
  - the combined vaccine, mCOMBRIAX®, indicated for the protection of people aged 50 years and older against COVID-19 and seasonal influenza.

- The protein subunit vaccines include:
  - Nuvaxovid® and Bimervax® (authorised for the prevention of COVID-19 in individuals aged 12 years and older).

Currently authorised COVID-19 vaccines are available in various forms, which include multidose vials, single dose vials and single dose pre-filled syringes. Depending on the form, the vaccine may require reconstitution prior to use and may be supplied frozen (and thawed before use) or supplied ready to use at refrigerated temperatures. To date, availability of a particular COVID-19 vaccine in Ireland has typically been dependent on whether a particular vaccine product has been preferentially recommended by NIAC and on opting into a joint procurement

framework contract negotiated between manufacturers and the European Commission's Health Emergency Preparedness and Response Authority (HERA).

Currently, the HSE COVID-19 vaccination programme provides access to COVID-19 vaccination in line with NIAC guidance and the Department of Health policy, which is free at the point of care. The preferentially recommended vaccine is an antigenically updated mRNA vaccine which is available year-round; however, campaigns are run twice yearly, in the autumn/winter (to align with the seasonal influenza campaign) and again in the spring to promote and support uptake in those for whom vaccination is recommended. During the autumn/winter 2025/2026 campaign, COVID-19 vaccination was available to all groups outlined in the May 2025 NIAC recommendations, including to those for whom NIAC have advised access should be made available. As of August 2026, COVID-19 vaccines are not currently available for private purchase in Ireland.

All European countries provided broad population level access to publicly funded COVID-19 vaccination during the emergency phase of the pandemic. However, national policies continue to be updated in line with epidemiological developments, including restricting funded access to subgroups of the population considered to be at higher risk of severe disease. Further updates are expected as purchase agreements through centrally negotiated HERA contracts end, with the potential for policy decisions to also take consideration of broader issues including cost effectiveness. For example, since 2025, following consideration of cost effectiveness, the national COVID-19 vaccination programme in England has been limited to adults aged 75 years and over (with this cohort being further limited to those aged 80 years and older in autumn 2027); residents in care homes for older adults; and individuals aged six months and older who are living with immunocompromise. It is also noted that a number of COVID-19 vaccines are now available for private purchase in the UK following a consultation with a healthcare provider.

Epidemiology and burden of disease

COVID-19 incidence data and hospital utilisation data were sourced from the Health Protection Surveillance Centre (HPSC) and Hospital In-Patient Enquiry (HIPE) system, respectively. Data were reported by calendar year and limited to the period 2023 to 2025 (HPSC) and 2023 and 2024 (HIPE) to facilitate the inclusion of the latest available data most relevant to the current epidemiological situation (that is, data specific to currently circulating variants in a population exhibiting high levels of immunity, and recognising the differences in current testing practices compared to those implemented during the early years of the COVID-19 pandemic).

HPSC data indicate that the burden of COVID-19 in the total population aged six months and older has declined over time (from 2023 to 2025), specifically the notified:

- case rate decreased from 699.1 to 248.3 per 100,000
- emergency department (ED) visit rate decreased from 109.9 to 93.7 per 100,000
- hospital admission rate decreased from 303.6 to 94.0 per 100,000
- intensive care unit (ICU) admission rate decreased from 3.1 to 1.4 per 100,000
- mortality rate decreased from 16.6 to 5.1 per 100,000 (equating to a reduction from 848 notified COVID-19-related deaths in 2023 to 260 notified deaths in 2025).

When disaggregated by age group, HPSC data for the three-year period indicate that the burden generally increases with age, with a disproportionate burden among the oldest adults. Specifically, those aged:

- 80 years and older accounted for 27% of notified cases; 22% of notified ED visits; 36% of notified hospitalisations; 17% of notified ICU admissions; and 64% of notified deaths, while representing less than 4% of the total population.
- 75 years and older accounted for 38% of notified cases; 33% of notified ED visits; 50% of notified hospitalisations; 32% of notified ICU admissions; and 79% of notified deaths, while representing only 7% of the total population.

Limited data are available with respect to the vaccination status of notified cases and in relation to the presence of underlying conditions in those experiencing severe disease.

- Vaccination status of notified hospital cases (from 2023 to 2025) was known for, on average, 68% of those aged 80 years and older and 67% of those aged 60 to 79 years. In 2025, considering those aged:
    - 80 years and older for whom twice yearly vaccination is recommended, 85% of notified COVID-19-related hospital admissions were in those who had not been vaccinated within the previous 180 days.

  - 60 to 79 years for whom once yearly vaccination is recommended, 63% of notified COVID-19-related hospital admissions were in those who had not been vaccinated within the previous 365 days.

- Comorbidity data for this HTA were limited to those admitted to ICU. In all years, more than 90% of notified ICU admissions were in those with one or more underlying medical condition.

- While recognising that long COVID can have a considerable impact on an individual's quality of life, their ability to work and daily functioning, data are lacking (in Ireland and internationally) in relation to both the prevalence and burden associated with long COVID.

HIPE data for 2023 and 2024 highlight the substantial burden associated with COVID-19 on the secondary healthcare system. These data are not directly comparable as prior to 2024, COVID-19 could only be coded as an additional diagnosis, even if it was the primary reason the patient presented to the healthcare system. Considering the total population (all ages):

- In 2023, there were 17,828 discharges with an additional diagnosis of COVID-19. The mean length of stay was 23 days and the total number of bed days was 409,621 days.

- In 2024, there were:
  - 2,876 discharges (42 of which included an ICU admission) with a principal diagnosis of COVID-19. The mean length of stay was six days and the total number of bed days was 18,039 days.
  - 11,533 discharges with an additional diagnosis of COVID-19. The mean length of stay was 25 days and the total number of bed days was 292,315 days.

When disaggregated by age group, HIPE data also indicated that burden generally increases with age, with a disproportionate burden among the oldest adults. In considering the total discharges in those with a principal diagnosis of COVID-19 in 2024, those aged:

- 80 years and older accounted for 34% (n=966) of discharges, 51% (n=9,232 days) of the total bed days, and had the longest average length of stay per patient (n=10 days).

- 75 years and older accounted for 45% (n=1,307) of discharges, 67% (n=12,156 days) of the total bed days and had an average length of stay of nine days per patient.

Using 2024 data, the average cost associated with a hospital stay for a patient with a principal diagnosis of COVID-19 was approximately €6,870, and the total annual cost associated with all discharges with a principal diagnosis of COVID-19 in 2024 was approximately €19.8 million.

- Additional costs may accrue for patients who require post-discharge rehabilitation and care. For discharges for whom the discharge destination was known, approximately 6% of those with a primary diagnosis of COVID-19 and approximately 14% of those with an additional diagnosis of COVID-19 were newly discharged to a post-acute care setting, with a disproportionate requirement for post-discharge support in older adults.

- Additional costs may also accrue in relation to long COVID both from the healthcare and societal perspective. In the absence of definitively effective treatments, much of this burden may arise from reduced labour participation and productivity losses rather than medical expenditure alone.

The COVID-19-related morbidity and mortality observed are in the context of an ongoing COVID-19 vaccination programme that continues to offer funded COVID-19 vaccination to certain at-risk groups. Considering specifically uptake in selected at-risk groups:

- During the 2025/2026 autumn/winter campaign, reported uptake was 33.2% in those aged 60 to 79 years, 60.8% in those aged 80 years and older, 73.6% in residents of long-term care facilities for older adults, and 18.2% in those identified as living with immunocompromise. These rates are lower than the HSE targets that 75% of those aged 65 years and older and 50% of those who are immunocompromised receive their booster doses.

- When comparing vaccination campaigns from autumn 2023 onwards, there has been a gradual decrease in uptake, with substantially lower uptake in the spring campaigns for those in whom twice yearly vaccination is recommended (for example, for those aged 80 years and older, uptake was 32.3% in the spring 2025 campaign versus 60.8% in the autumn/winter 2025/2026 campaign.

In summary, while there is evidence that the overall burden associated with COVID-19 has decreased in recent years, there continues to be a disproportionate burden in older adults and a general trend of decreasing COVID-19 vaccination uptake since September 2023.

Clinical effectiveness and safety

Evidence from a systematic review (index review) published in October 2025 was used to inform this assessment of the effectiveness and safety of antigenically updated COVID-19 vaccines for seven distinct populations. Where data for subgroups of interest were lacking in the systematic review, evidence was supplemented by a search of European, UK and US platforms. The seven population groups of interest were:

- older adults (adults aged 65 years and older)
- individuals residing in LTCFs
- those with immunocompromising conditions
- those with underlying medical conditions
- pregnant individuals
- healthcare workers
- those in the general population aged between 18 and 59 years.

Of the 20 observational studies from the index review that reported vaccine effectiveness (VE) findings, 16 included XBB.1.5 vaccines exclusively, one included a combination of XBB.1.5, JN.1 and KP.2 vaccines, one included KP.2 vaccines exclusively, one included a combination of KP.2 and JN.1 vaccines and one study reporting on long COVID outcomes included bivalent booster vaccines. Of the 21 studies identified as part of the supplemental search, two provided evidence that addressed gaps in the evidence provided by the index review; one included XBB.1.5 vaccines exclusively and one included XBB.1.5 and non-XBB.1.5 adapted vaccines. The 19 studies from the index review that reported safety findings covered the period 2020 to 2023 and were limited to ancestral strain COVID-19 vaccines.

In general, Omicron-adapted vaccines were associated with a significant reduction in severe COVID-19 disease outcomes across several of the population groups considered relevant to this HTA. However, there was evidence of waning effectiveness over time, particularly in studies that reported over longer incremental follow-up periods. While some estimates of VE may appear to be modest, it is important that these effects are viewed in the context of the considerable burden associated with COVID-19, particularly among those at increased risk of severe disease.

Estimates of effect were typically higher for outcomes related to severe disease compared to medically attended or symptomatic infection outcomes. Protection against hospitalisation and mortality was observed up to five to six months post-vaccination among older adults, those living with immunocompromise, those living

with underlying medical conditions, and those aged 18 to 59 years in the general population. However, as noted, there was evidence of waning protection, particularly over longer follow-up periods. Where effectiveness estimates were disaggregated by age, there was no consistent pattern and confidence intervals typically overlapped.

The majority of the included evidence relates to Omicron-adapted mRNA COVID-19 vaccines. While some studies included other vaccine types (for example, protein subunit COVID-19 vaccines), only small numbers of participants received these vaccine types. Studies typically did not report findings disaggregated by vaccine type, so it is not possible to determine if effectiveness differs by vaccine type based on the evidence included in this chapter. Only one study included in this chapter reported on the effectiveness of Omicron-adapted vaccines against post-acute sequelae associated with long COVID; there was no evidence of protection reported for those aged 60 years and older, while a VE of 49% was reported for those aged 18 to 59 years. No evidence was identified for newer COVID-19 formulations or technologies licensed since 2025.

No evidence was identified in this chapter regarding the effectiveness of Omicron-adapted vaccines for:

- those living in LTCFs; however, high levels of protection against severe COVID-19, using original COVID-19 vaccines, were previously documented for this population during the early years of the pandemic.
- pregnant individuals; however, previous evidence of effectiveness supports COVID-19 vaccination during pregnancy to prevent severe disease and adverse maternal and child outcomes.

The findings reported in this chapter are consistent with the existing literature base as it pertains to the safety profile of COVID-19 vaccines, which is largely favourable. One study noted an increased risk of myocarditis (in those aged 50 years and older) with COVID-19 vaccination, and another reported an increased risk of myopericarditis (in those aged 66 years and older). Post-marketing surveillance has noted that the frequency of myocarditis or pericarditis, where known, occurs in fewer than 1 in 10,000 vaccinations and would be considered very rare.

Most of the primary studies included in the index review were judged by the index review authors to be at low risk of bias (37/39 studies). Specific weaknesses identified in the quality appraisal of the index review (relating to a lack of grey literature searching, list of excluded studies and assessments of publication bias) were partially mitigated by the supplemental search conducted by the Evaluation Team; the findings from these studies largely aligned with the index review.

Economic evaluation

An economic model was developed to characterise the incidence of notified cases of COVID-19 in Ireland and estimate the cost effectiveness and budget impact of COVID-19 vaccination programmes for the general population of adults aged 60 years and above in Ireland. The budget impact of COVID-19 vaccination for specific population groups was also estimated.

The economic evaluation for the general population aged 60 years and above assessed the following two vaccination strategies:

- Strategy 1 (S1) - a vaccine offered twice each year for those aged 80 years and above
- Strategy 2 (S2) - a vaccine offered twice each year for those aged 80 years and above (S1) and once each year for those aged 60 to 79 years.

The five-year budget impact was estimated for a range of strategies as defined by the NIAC recommendations for COVID-19 vaccination. Model parameters including but not limited to disease incidence, hospitalisation and mortality rates, vaccine effectiveness, costs, utility values and quality-adjusted life year losses were estimated from a variety of published sources and national datasets for Ireland.

Results from the epidemiological analysis using 2025 notified case data indicate that in a single year, vaccination is associated with a decrease in notified COVID-19 cases. Reductions associated with S1 (those aged 80 years and above), compared with no vaccination, ranged from 11% for notified cases of COVID-19 to 33% for notified deaths with COVID-19. Overall reductions for S2 (those aged 60 years and above), compared with no vaccination, ranged from 8% for notified cases of COVID-19 to 29% for notified deaths with COVID-19.

From the payer perspective, at a vaccine cost of €75 per dose (ex VAT) and assuming 2025 incidence of notified COVID-19, the incremental cost effectiveness ratio (ICER) for S1 compared with no vaccination was €56,500 per quality-adjusted life year (QALY) and the ICER for S2 compared with S1 was €202,000 per QALY. Both ICERs exceeded a willingness-to-pay (WTP) threshold of €45,000 per QALY gained. In a scenario analysis assessing a strategy of vaccination from age 75 years, the ICER was €80,000 per QALY when compared with S1.

Based on the assumptions in the model, the vaccine cost would need to be less than €60 per dose for S1 to be cost effective at a WTP threshold of €45,000 per QALY gained. A scenario analysis, where incidence of notified COVID-19 was varied, demonstrated that using:

- 2024 incidence data in the model, the ICER for S1 compared with no vaccination fell to €15,000 per QALY.
- 2023 incidence data in the model, S1 was cost-saving (less costly and more effective) compared with no vaccination.

The five-year incremental budget impact versus no vaccination was €111.5 million for S1 and €307.0 million for S2. The majority of costs incurred for both vaccination strategies over the five-year time horizon related to vaccine procurement (approximately 71% to 75%). Cost offsets (largely relating to hospitalisation and long-term care post COVID-19) as a percentage of total costs incurred, were 28% and 15% for S1 and S2, respectively.

The budget impact model for other populations outlined in the NIAC recommendations only considered the costs incurred over a five-year period. Due to a lack of relevant epidemiological data for Ireland, costs averted were not estimated. At current uptake rates, and recommended vaccination intervals (yearly or twice yearly), the five-year budget impact versus no vaccination was:

- €37.4 million for Strategy 3 – a vaccine offered twice each year for those aged 18 to 79 years living in a long-term care facility for older adults
- €18.0 million for Strategy 4 – a vaccine offered twice each year for those aged six months and older with immunocompromise associated with a suboptimal response to vaccination
- €21.1 million for Strategy 5 – a vaccine offered once each year for those aged six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death
- €18.1 million for Strategy 6 – a vaccine offered once each year for health and care workers who choose to receive a vaccine
- €6.8 million for Strategy 7 – a vaccine offered once each year for pregnant adolescents and adults
- €63.8 million for Strategy 8 – a vaccine offered once each year for all others aged 18 to 59 years not included in other specific population groups.

While this analysis demonstrates that vaccination against COVID-19 is associated with reductions in outcomes associated with COVID-19, the strategies assessed in the base-case economic analysis would be considered not cost effective at the modelled vaccine price at a WTP threshold of €45,000 per QALY. However, as demonstrated in the results of the sensitivity and threshold analyses, the outcome of this economic evaluation is highly sensitive to both the assumed price of the vaccine

and the incidence of COVID-19 going forward. As such, both parameters require careful consideration in informing decision-making regarding future COVID-19 vaccination policy.

Organisational, ethical, patient and social considerations

There are several organisational, ethical, patient and social considerations that are relevant to this HTA both in the context of general considerations for the programme and in the context of a decision being made to restrict the cohorts for which COVID-19 vaccination is funded (compared to those funded during the 2025/2026 COVID-19 vaccination campaign).

The HSE COVID-19 vaccination programme provides access to COVID-19 vaccination, in line with the National Immunisation Advisory Committee recommendations and the Department of Health policy, which is free at the point of care. In line with these recommendations, the programme:

- preferentially provides an antigenically updated mRNA vaccine (Comirnaty®), with access provided through usual primary care vaccination sites (GP practices and pharmacies) and by HSE mobile vaccination teams.
- provides access to the antigenically updated protein subunit vaccine Nuvaxovid® to the small number of individuals for whom an mRNA COVID-19 vaccine is clinically unsuitable. Nuvaxovid® is not routinely available through GP clinics and pharmacies, and instead is accessible through HSE vaccine clinics by appointment. These additional steps can represent a logistical barrier for some patients.

Twice yearly vaccination campaigns have been run by the HSE in recent years, whereby the autumn/winter programme aligns with the seasonal influenza vaccination campaign. This aims to improve uptake rates and provide efficiencies for patients and providers where individuals are eligible to receive both vaccines. A second campaign is run approximately six months later in the spring for those for whom twice yearly vaccination is recommended with the aim of providing year-round protection. Access outside the seasonal campaigns is available, where clinically indicated.

General organisational issues relating to the COVID-19 vaccination programme include:

- Challenges associated with an existing model based on use of a multidose vial formulation, packaged in boxes of 10, that are delivered from the manufacturer frozen and which must be thawed and relabelled with a new,

shorter "use by" date before transportation to primary vaccination sites. This results in additional operational complexity, greater potential for dosing errors, and greater wastage compared with other vaccines provided through the HSE National Cold Chain Service (NCCS).

- Efficiencies may be realised by moving to a refrigerated (never frozen), single dose, pre-filled syringe product when procurement contracts are retendered. This would be consistent with how most other vaccines are supplied, would reduce wastage, and provide efficiencies for NCCS staff in terms of vaccine storage and management, and healthcare staff in terms of vaccine administration.

- Although a programme comprising a range of vaccine products may increase choice and potentially improve resilience, these benefits would need to be considered in the context of the cost difference (if any) between products and the additional logistical burden associated with making a range of products available.

- Given the lack of seasonality with COVID and evidence of waning vaccine effectiveness over time, more frequent campaigns may be required to promote uptake when national and international data suggest periods of higher circulation. Consideration could also be given to expanding access outside defined seasonal campaigns to anyone whose vaccination status is not considered to be current (within the preceding 180 or 365 days, as appropriate).

Potential ethical, patient and social issues associated with a decision to restrict access to funded COVID-19 vaccination to those at the highest risk of severe disease and or on the basis of cost effectiveness include a potential:

- increase in the incidence of notified cases, notified hospital admissions and mortality among non-eligible individuals. This is particularly the case if eligibility is based solely on age-based criteria, rather than also considering other groups known to be at increased risk of severe disease (such as those residing in LTCFs for older adults or those living with immunocompromise) and those at increased risk of exposure (such as, health and care workers).

- increased level of long-term disability among non-eligible groups who may go on to experience long COVID (if such illness could have been prevented by vaccination) and an associated reduced participation in the labour market or potential worsening of symptoms for those already living with long COVID.

- reduction in the workload for healthcare staff due to a reduction in the number of individuals requiring vaccination. This efficiency is particularly relevant when considering subgroups for whom the current benefits of vaccination are limited given the decline in severity of COVID-19.

In acknowledging the overall decline in the burden associated with COVID-19, a decision to change the groups eligible for COVID-19 vaccination should still be considered in the context of the overall resilience of a healthcare system that exhibits high bed occupancy rates. While COVID-19 lacks seasonality, the potential for vaccination to support reductions in winter overcrowding could strengthen resilience in the health service.

Restricting access to funded COVID-19 vaccination could be perceived as curtailment of an individual's autonomy in those for whom it is no longer available. However, decisions about healthcare distribution should ensure that resources are allocated or reallocated fairly and that the opportunity costs (the value of the next best alternative forgone) of investments are considered. Funding interventions that are not cost effective could create issues of justice and equity with respect to a fair distribution of benefits and burdens. This is particularly important in the context of a finite healthcare budget and increasing demands for services provided. While ordinarily there may be potential to pay for a vaccine privately if access is not funded as part of a national programme, COVID-19 vaccines are not currently (as of August 2026) available for private purchase in Ireland. For authorised vaccines, such availability is at the discretion of the individual manufacturer.

The assessment of cost effectiveness in this HTA was limited to age-based cohorts (that is, vaccination of older adults). Due to a lack of Irish epidemiological data, it was not feasible to evaluate the cost effectiveness of vaccinating other individuals at high risk of severe disease, such as those residing in LTCFs for older adults and those living with immunocompromise. However, this does not preclude a decision on whether to continue to provide COVID-19 vaccination for such individuals, given that policy decisions are informed by multiple domains and not just cost effectiveness. As with any modelling exercise, the applicability of the findings is dependent on the underlying assumptions that underpin the model structure and the chosen parameter values. Evidence included in this HTA relating to the burden of disease and effectiveness and safety of COVID-19 vaccination were collected at a specific point in time and the conclusions could change over time as the evidence base evolves. This is particularly important given that the sensitivity and scenario analyses conducted as part of this assessment demonstrated that the economic evaluation is highly sensitive to both the assumed price of the vaccine and the incidence of COVID-19 going forward.

Given the continuing uncertainty regarding future disease patterns, variant emergence and long-term health impacts, it will be important to continue the use of national and international surveillance data as well as recommendations from NIAC to inform national COVID-19 vaccination policy.

Any change to the national COVID-19 vaccination programme needs to be appropriately communicated to the public and healthcare providers. This would include:

- timely information for those no longer eligible for funded vaccination who may have concerns about their risk of infection and severe disease.
- targeted outreach in relation to the population groups who remain eligible to optimise uptake and avoid wastage. This information should support an understanding of their ongoing risk of severe disease due to COVID-19 and the potential for this to be mitigated by remaining up-to-date with their vaccine recommendations.

Conclusion

The aim of this HTA was to provide advice in relation to the groups for whom COVID-19 vaccination is funded by the HSE for the 2027/2028 vaccination campaign onwards. The HSE COVID-19 vaccination programme provides access to COVID-19 vaccination, in line with NIAC guidance and the Department of Health policy, which is free at the point of care. While the overall burden associated with COVID-19 has decreased in recent years, there is still a disproportionate burden observed in older adults. The economic evaluation suggests that the COVID-19 vaccination strategies assessed in the base-case analysis would be considered not cost effective at a WTP threshold of €45,000 per QALY. However, these results are highly sensitive to the unit cost of the vaccine and incidence of COVID-19 going forward, both of which are key considerations in any decision-making and in procurement negotiations with vaccine manufacturers.

Plain language summary

What is COVID-19?

Coronavirus disease 2019 (COVID-19) is a disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. It is very contagious and can spread quickly. In most people, it can usually be managed without needing treatment. However, it can cause severe infections in some people, and they may need special treatment or hospital care. Older adults, people with other health problems and people with a weak immune system are at a higher risk of severe illness due to COVID-19. For some people, COVID-19 can cause symptoms that last weeks or months after the infection has gone. This is sometimes called long COVID.

What did we look at?

We looked at the vaccines that can be used to protect against COVID-19. We described the burden of COVID-19 and the uptake of COVID-19 vaccination in Ireland. We looked at whether COVID-19 vaccination is safe and effective in specific population groups (such as, older people and those with other health problems) and we assessed the cost associated with vaccinating these population groups. We also summarised other factors (such as, the organisational, ethical, patient and social issues) that should be considered when making changes to the COVID-19 vaccination programme in Ireland.

This assessment will help the Department of Health make a decision on the groups of people that should be prioritised for a COVID-19 vaccination in Ireland in 2027/2028 onwards.

Do similar vaccination programmes exist in other countries?

During the emergency phase of the pandemic, all European countries offered COVID-19 vaccination to most people. Many countries are now offering it to specific groups only. Countries are also beginning to use cost-effectiveness data to inform their vaccination programmes. For example, England has updated its COVID-19 vaccination programme, and it now limits free COVID-19 vaccination to adults aged 75 years and over, residents in care homes for older adults, and individuals aged six months and older who have a weak immune system.

What did we find?

Burden of COVID-19 in Ireland

Unlike flu, COVID-19 is not a seasonal disease and the number of new cases of COVID-19 has peaked at different times throughout 2023 to 2025. Burden of disease

refers to the negative health impacts and number of deaths caused by a particular disease. The overall burden associated with COVID-19 has continued to decrease in all age groups since 2023. However, some groups such as older adults remain at higher risk of severe disease. In 2025, there were over 12,000 cases of COVID-19 recorded in Ireland and almost 4,000 of these cases were in people aged 80 years and older, with this group accounting for more than a third of the recorded hospital admissions. In 2025, almost all patients admitted to the intensive care unit (ICU) with COVID-19 had other health problems. Some hospitalised patients also needed rehabilitation support after they were discharged. There were 260 COVID-19-related deaths in 2025 and more than two thirds of these were in people aged 80 years and older.

COVID-19 vaccination uptake in Ireland

Ireland already has a COVID-19 vaccination programme that offers a free COVID-19 vaccine to several groups of people considered to be at a higher risk of severe disease. However, the uptake of COVID-19 vaccination has decreased since September 2023.

COVID-19 vaccination effectiveness and safety

We found that COVID-19 vaccination can reduce the chances of people requiring medical care or admission to hospital, but the protection decreases over time. We also found that COVID-19 vaccination is safe and serious side effects are rare. However, minor reactions are common. These include pain where the injection is given, headache and fever, but these are usually mild and short-lived.

Cost effectiveness of COVID-19 vaccination

At a vaccine price of €75 per dose, offering COVID-19 vaccination to adults aged 80 years and older twice a year would cost the HSE €111.5 million over five years. Although vaccination would reduce the burden of COVID-19 (by reducing the number of COVID-19 cases, emergency department visits, hospital and ICU visits, and deaths), it would not be cost effective at that price. If the price paid for the vaccine was reduced to €60 per dose, offering vaccination to adults aged 80 years and older twice a year would be considered cost effective. The best value option would depend on the price the HSE has to pay for the vaccine, but these prices are confidential. The cost-effectiveness estimates are based on the current rates of COVID-19 disease. Vaccination would be more cost effective if rates were to increase to those seen prior to 2025, so it will be important to continue to monitor COVID-19 activity.

Other factors to be considered

If there are any changes to the groups of people prioritised for a free COVID-19 vaccine, it would be important to inform the public and healthcare professionals about these changes. Clear information on the benefits of COVID-19 vaccination should be provided to those who remain eligible for a free COVID-19 vaccine to improve COVID-19 vaccination uptake. It would also be important to provide specific information to those no longer eligible for a free COVID-19 vaccine and address any concerns they may have about their risk of infection and severe disease. This information would support healthcare professionals in providing trustworthy advice and ultimately help people to make informed decisions about vaccination.

Conclusion

In summary, COVID-19 vaccination is safe and effective and reduces the risk of severe outcomes such as hospital admission. The overall burden associated with COVID-19 has decreased over time. However, there continues to be a higher burden in some groups, such as older adults. Whether vaccination of these groups represents a good use of HSE resources will depend on the price the HSE has to pay for the vaccine and future levels of COVID-19 activity.

List of abbreviations used in this report

ACER	average cost-effectiveness ratio
AESI	adverse event of special interest
aHR	adjusted hazard ratio
AMSTAR 2	A MeaSurement Tool to Assess Systematic Reviews, version 2
aOR	adjusted odds ratio
aRR	adjusted risk ratio
aVE	adjusted vaccine effectiveness
BIA	budget impact analysis
CDC	Centers for Disease Control and Prevention
CDM	chronic disease management
CEAC	cost-effectiveness acceptability curve
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CI	confidence interval
CIDR	Computerised Infectious Disease Reporting system
COPD	chronic obstructive pulmonary disease
COVAX	National COVID-19 Immunisation system
COVID-19	coronavirus disease 2019
CSO	Central Statistics Office

CUA	cost-utility analysis
DPS	Drug Payment Scheme
DRG	Diagnosis Related Group
DSA	deterministic sensitivity analyses
EAG	expert advisory group
ECDC	European Centre for Disease Prevention and Control
ED	emergency department
EEA	European Economic Area
EMA	European Medicines Agency
EQ-5D	EuroQol five-dimension
ESKD	end-stage kidney disease
ESRI	Economic and Social Research Institute
ETF	Emergency Task Force
EU	European Union
EUROCAT	European Surveillance of Congenital Anomalies classification
FADA	Follow-up After Disease Acquisition
GBS	Guillain-Barré syndrome
GMS	General Medical Service
GP	general practitioner

HERA	Health Emergency Preparedness and Response Authority
HIPE	Hospital In-Patient Enquiry
HIQA	Health Information and Quality Authority
HPO	Healthcare Pricing Office
HPSC	Health Protection Surveillance Centre
HR	hazard ratio
HRQoL	health-related quality of life
HSE	Health Service Executive
HSUV	health state utility value
HTA	health technology assessment
ICATT	Increasing Community Access To Testing
ICER	incremental cost-effectiveness ratio
ICD-10	International Classification of Diseases, Tenth Revision
ICD-10-AM	International Classification of Diseases, Tenth Revision, Australian Modification
ICU	intensive care unit
IDS-TILDA	Intellectual Disability Supplement to TILDA
ILI	influenza-like illness
IPU	Irish Pharmacy Union
IQR	interquartile range

IRR	incidence rate ratio
IVY	Investigating Respiratory Viruses in the Acutely Ill
JCVI	Joint Committee on Vaccination and Immunisation (UK)
LTCF	long-term care facilities
LTI	Long-Term Illness
mRNA	messenger ribonucleic acid
NCCS	National Cold Chain Service
NHIS	National Health Interview Survey
NHS	National Health Service
NHSN	National Healthcare Safety Network
NICU	neonatal intensive care unit
NIAC	National Immunisation Advisory Committee
NIIS	National Immunisation Information System
NIO	National Immunisation Office
NITAG	National Immunisation Technical Advisory Group
NVRL	National Virus Reference Laboratory
OR	odds ratio
OWSA	one-way sensitivity analysis
PCRS	Primary Care Reimbursement Service

PICO	Population, Intervention, Comparator, Outcomes
PICOS	population, intervention, comparator, outcome, study design
PRECISE	Prevalence of COVID-19 in Irish Healthcare Workers
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PSA	probabilistic sensitivity analyses
QALY	quality-adjusted life year
R0	basic reproductive number
RCT	randomised controlled trial
RI	relative incidence
RNA	ribonucleic acid
RR	risk ratio / relative risk
RSV	respiratory syncytial virus
SARI	severe acute respiratory infection
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SIREN	Sarscov2 Immunity & REinfection EvaluatioN
SmPC	Summary of Product Characteristics
TAG-CO-VAC	Technical Advisory Group on COVID-19 Vaccine Composition
TIA	transient ischaemic attack

TILDA	The Irish Longitudinal Study on Ageing
UC	urgent care
UKHSA	UK Health Security Agency
UKHSA IIS	UK Health Security Agency Immunisation Information System
VE	vaccine effectiveness
VEBIS	Vaccine Effectiveness, Burden and Impact Studies
VEBIS-EHR	Vaccine Effectiveness, Burden and Impact Studies Electronic Health Record
VISION	Virtual SARS-CoV-2, Influenza and Other respiratory viruses Network
VOC	variant of concern
wGA	weeks' gestational age
WHO	World Health Organization
WTE	whole-time equivalent
WTP	willingness to pay

1 Introduction

1.1 Background to the request

Coronavirus disease 2019 (COVID-19) is an infectious disease which, as of June 2026, has caused over 7.1 million deaths globally.[1] COVID-19 is caused by the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) — one of five *Betacoronaviruses,* belonging to the *Orthocoronavirinae* sub-family, which have been found to infect humans. Other *Betacoronaviruses* which have been found to infect humans include the Middle East respiratory syndrome-related coronavirus and SARS-CoV. The *Orthocoronavirinae* sub-family belongs to the *Coronaviridae* family, which are enveloped, positive-strand ribonucleic acid (RNA) viruses.[2]

When viruses replicate in the host cell, mutations in the genetic coding can occur. While some of these mutations have no impact on the characteristics of the virus, others can result in significant changes, such as enhanced transmissibility, severity of resultant infection and ability to evade an immune response (whether that be an innate or adaptive immune response).[3] Since its discovery in 2019, SARS-CoV-2 has spread and evolved globally, leading to the detection of SARS-CoV-2 variants. These variants are monitored by the World Health Organization and the Technical Advisory Group on Virus Evolution. The more significant variants are categorised into one of three groups:

- Variants under monitoring: variants with genetic changes that may affect the characteristics of the virus, but for which enhanced monitoring is required to determine if these genetic changes have a phenotypic or epidemiological impact.
- Variants of interest: variants with genetic changes that are known to affect how the virus behaves or its potential impact on human health. These variants are referred to using established scientific nomenclature systems, such as those used by Nextstrain and Pango.
- Variants of concern (VOCs): variants with genetic changes that are known to affect how the virus behaves or its potential impact on human health and can cause a detrimental change in disease severity, have a substantial impact on healthcare systems or cause a significant decrease in the effectiveness of available vaccines in protecting against severe disease.[4] These variants are referred to using Greek letters. VOCs identified to date include Alpha, Beta, Gamma, Delta, and Omicron.

The first COVID-19 vaccines that were developed used messenger RNA (mRNA) from the ancestral virus, identified in December 2019. Since then, other COVID-19 vaccine technologies have been developed and include viral vector and protein

subunit vaccines. While these vaccines elicit high levels of virus-specific antibodies in the vaccinated individual, over time, waning immunity increases the likelihood of breakthrough infections. This is further complicated by genomic mutations and the emergence of variants that decrease the effectiveness of these original vaccines.[5] One of the most notable variants has been Omicron, specifically the subvariant Omicron BA.1, which emerged in November 2021. This subvariant, with its 53 mutations, was phylogenetically distinct from prior lineages, showed enhanced transmissibility, was associated with a significant decrease in vaccine effectiveness and had a substantial impact on healthcare systems globally.[6] As such, variant-adapted bivalent vaccines were developed. The first of these adapted vaccines, which contained mRNA from the ancestral SARS-CoV-2 strain and Omicron BA.1 variant, was approved by the European Medicines Agency in September 2022.[7] Throughout this health technology assessment (HTA), the terms 'variant-adapted', 'antigenically updated' and 'Omicron-adapted' are used interchangeably when referring to the COVID-19 vaccines of interest to this HTA.

In May 2025, the National Immunisation Advisory Committee (NIAC) in Ireland published updated recommendations on vaccination against COVID-19.[8] The updated recommendations, with respect to the groups eligible for a COVID-19 vaccination, are outlined in Table 1.1.

Table 1.1 Updated National Immunisation Advisory Committee recommendations on vaccination against COVID-19 (May 2025)

1. A COVID-19 vaccine is recommended twice each year for:	▪ those aged 80 years and above ▪ those aged 18-79 years living in long term care facilities for older adults ▪ those aged 6 months and older with immunocompromise associated with a suboptimal response to vaccination.
2. A COVID-19 vaccine is recommended once each year for:	▪ those aged 60-79 years ▪ those aged 6 months to 59 years with medical conditions~ associated with a higher risk of COVID-19 hospitalisation, severe disease or death.
3. Access to a COVID-19 vaccine once each year should be available for:	▪ health and care workers* who choose to receive a vaccine ▪ pregnant adolescents and adults* who, following discussion with a healthcare provider, choose to receive a vaccine ▪ adults aged 18-59 not included in the groups listed in points 1 or 2 who, following discussion with a healthcare provider, choose to receive a vaccine.

~Medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death include: cancer, chronic heart disease, chronic kidney disease, chronic liver disease, chronic neurological disease, chronic respiratory disease, diabetes and other metabolic disorders including inherited metabolic disorders, haemoglobinopathies, immunocompromise due to disease or treatment, body mass index ≥40kg/m^2, serious mental health conditions, children and adults with Down syndrome, children with moderate to severe neurodevelopmental disorders. This list is not exhaustive, and the medical practitioner should apply clinical judgment to consider the risk of COVID-19 infection exacerbating any medical condition that a patient may have as well as the risk of serious illness from COVID-19 infection.

*Pregnant adolescents and adults and or health and care workers who also fall into the risk groups outlined in points 1 and 2 should follow the corresponding recommendations.

The overarching aim of this HTA was to support the work of the Department of Health and provide advice to the Minister for Health and Health Service Executive (HSE) to inform COVID-19 vaccination policy in Ireland. Specifically, and in the context of the updated COVID-19 vaccination recommendations published by NIAC, the aim of this HTA was to provide advice in relation to the groups for whom COVID-19 vaccination is funded by the HSE for the 2027/2028 vaccination campaign onwards.

1.2 Terms of reference

The HTA will be submitted to the Department of Health and provide advice to the Minister for Health and HSE to inform COVID-19 vaccination policy in Ireland. In consultation with the Department of Health, the Health Information and Quality Authority (HIQA) Evaluation Team developed a set of objectives with consideration to the evidence needs of the decision-maker.

The following were the terms of reference for this HTA:

- describe the COVID-19 vaccines authorised for use in Ireland
- describe the epidemiology and burden of COVID-19
- summarise the clinical effectiveness and safety of COVID-19 vaccines
- assess the cost effectiveness of COVID-19 vaccination with respect to the subgroups outlined in the NIAC recommendations, where the data allow
- assess the budget impact of COVID-19 vaccination with respect to the subgroups outlined in the NIAC recommendations
- consider any additional implications relating to a potential change in COVID-19 vaccination policy
- based on the evidence in this assessment, provide advice to support a decision regarding potential changes to the COVID-19 vaccination programme in Ireland.

1.3 Overall approach

Following an initial scoping of the available evidence, the terms of reference for this assessment were agreed between HIQA and the Department of Health. HIQA appointed an evaluation team comprising staff from the HTA Directorate to carry out the assessment.

HIQA convened an expert advisory group (EAG) comprising representation from relevant stakeholders, including patient representation, decision-makers, clinical experts, public health experts and methodological expertise. The role of the EAG was to inform and guide the process, provide expert advice and information, and to provide access to data where appropriate. A full list of the membership of the EAG is available in the EAG membership section of this report.

The terms of reference for the EAG were to:

- Contribute to the provision of high-quality research and considered advice by HIQA to the Department of Health.
- Contribute to the work of the group by providing expert guidance, as appropriate.
- Be prepared to provide expert advice on relevant issues, outside of group meetings as requested.
- Provide advice to HIQA regarding the scope of the report.

- Review the project plan outline and advise on priorities, as required.
- Support the Evaluation Team during the process by providing expert opinion and access to pertinent data, as appropriate.
- Review the draft report from the Evaluation Team and recommend amendments, as appropriate.
- Contribute to HIQA's development of its approach to evidence synthesis by participating in an evaluation of the process on the conclusion of the project.
- Notify the project lead if a nominee can no longer participate or contribute to the process as non-participation may require alternative EAG membership to be sought.

The terms of reference for the HTA were reviewed by the EAG at its first meeting. The draft protocol was also circulated to the EAG and discussed at that meeting. Draft chapters of the report were circulated for review by the EAG and discussed at the second meeting of the EAG. These chapters were amended as appropriate before a final draft report was prepared for public consultation. After the public consultation, a final draft version of the report and advice to the Minister for Health and HSE were circulated for review by the EAG. The updated report was submitted to the Board of HIQA for approval. Following its approval, the completed assessment was submitted to the Department of Health, Minister for Health and HSE as advice and published on the HIQA website.

2 Description of the technology

Key Points

- COVID-19 is an infectious disease caused by SARS-CoV-2. Symptom severity of acute COVID-19 can range from asymptomatic to life threatening. Older adults, those with underlying health conditions and those living with immunocompromise are at higher risk of severe illness compared to the general population. Some people continue to experience symptoms long after the infectious period has ended, this is known as long COVID.
- Antigenically updated vaccines currently authorised by the European Medicines Agency for the prevention of COVID-19 include mRNA vaccines and protein subunit vaccines.
    - The mRNA vaccines include:
        - mNexspike® (authorised for use in individuals aged 12 years and older), and Spikevax® and Comirnaty® (both authorised for use in individuals aged six months and older)
        - the combined vaccine, mCOMBRIAX®, indicated for the protection of people aged 50 years and older against COVID-19 and seasonal influenza.
    - The protein subunit vaccines include:
        - Nuvaxovid® and Bimervax® (authorised for the prevention of COVID-19 in individuals aged 12 years and older).
- Currently authorised COVID-19 vaccines are available in various forms, which include multidose vials, single dose vials and single dose pre-filled syringes. Depending on the form, the vaccine may require reconstitution prior to use and may be supplied frozen (and thawed before use) or supplied ready to use at refrigerated temperatures.
- In May 2025, the National Immunisation Advisory Committee (NIAC) issued updated COVID-19 vaccination recommendations for Ireland. Based on the evidence considered:
    - vaccination is recommended for those who continue to be at increased risk of severe outcomes, to be given
        - twice yearly for all those in whom immunity wanes more quickly, that is, those aged:
            - 80 years and older

        - 18 to 79 years and living in long-term care facilities for older adults
        - six months and older with immunocompromise associated with a suboptimal response to vaccination.
    - once a year for those aged:
        - 60 to 79 years
        - six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death.

- access to vaccination is recommended for additional individuals not included above (health and care workers, pregnant women, those aged 18 to 59 years without additional risk factors for severe disease) for whom vaccination is no longer specifically recommended, but who wish to receive the vaccine. Pregnant adolescents and adults and or health and care workers who fall into the risk groups outlined above should follow the corresponding recommendations.

- To date, availability of a particular COVID-19 vaccine in Ireland has typically been dependent on whether a particular vaccine product has been preferentially recommended by NIAC and opting into a joint procurement framework contract negotiated between manufacturers and the European Commission's Health Emergency Preparedness and Response Authority (HERA).
- The HSE COVID-19 vaccination programme provides access to COVID-19 vaccination in line with NIAC guidance and the Department of Health policy, which is free at the point of care. The preferentially recommended vaccine is an antigenically updated mRNA vaccine, which is available year-round; however, campaigns are run twice yearly, in the autumn/winter (to align with the seasonal influenza campaign) and again in the spring to promote and support uptake in those for whom vaccination is recommended. During the autumn/winter 2025/2026 campaign, COVID-19 vaccination was available to all groups outlined in the May 2025 NIAC recommendations, including to those for whom NIAC have advised access should be made available.
- As of August 2026, COVID-19 vaccines are not currently available for private purchase in Ireland.
- All European countries provided broad population level access to publicly funded COVID-19 vaccination during the emergency phase of the pandemic. However, national policies continue to be updated in line with epidemiological developments, including restricting funded access to subsets considered to be at higher risk of severe disease. Further updates are expected as purchase agreements through centrally negotiated HERA contracts end, with the

potential for policy decisions to also take consideration of broader issues including cost effectiveness.

- For example, since 2025, following consideration of cost effectiveness, the national COVID-19 vaccination programme in England has been limited to adults aged 75 years and over (with this cohort being further limited to those aged 80 years and older in autumn 2027); residents of care homes for older adults; and individuals aged six months and older who are living with immunocompromise.
- A number of COVID-19 vaccines are now available for private purchase in the UK following a consultation with a healthcare provider.

2.1 Introduction

The purpose of this chapter is to describe the antigenically updated COVID-19 vaccines authorised by the European Medicines Agency (EMA) through the centralised procedure for use in the EU. These vaccines serve as a tool to protect against SARS-CoV-2, the virus responsible for causing COVID-19. This chapter provides a brief background on the transmission of SARS-CoV-2 and the signs and symptoms associated with resultant COVID-19. A description of the publicly funded COVID-19 immunisation programme in Ireland as well as changes in international COVID-19 vaccination policy is also provided.

2.2 Pathogen and disease

SARS-CoV-2 is one of five Betacoronaviruses, belonging to the *Orthocoronavirinae* sub-family, which have been found to infect humans.[2] The *Orthocoronavirinae* sub-family belongs to the *Coronaviridae* family, which are enveloped, positive-strand RNA viruses.[2]

As with most RNA viruses, mutations occur and as such multiple variant strains of SARS-CoV-2 have been identified.[9, 10] Variants, as described in Chapter 1, are subject to monitoring with regard to their growth potential or mutation profile, which could impact vaccine effectiveness.[9] These variants are monitored by the World Health Organization (WHO) and the Technical Advisory Group on Virus Evolution .[11]

COVID-19, is caused by SARS-CoV-2.[12] COVID-19 is an infectious disease which, as of June 2026, has caused over 7.1 million deaths globally, and over 9,800 deaths in Ireland.[13] SARS-CoV-2 has not yet exhibited a clear seasonal trend for transmission.[9, 14]

2.2.1 Transmission

Before the widespread use of vaccines, masks and social distancing, estimates for the basic reproductive number (R0) of SARS-CoV-2 ranged from two to eight.[15-17] The R0 may be higher in confined settings[18, 19] and varies depending on the circulating strain.[20, 21] Transmission occurs mainly between those within conversational distance or indoors in closed rooms that are poorly ventilated.[22]

SARS-CoV-2 virus spreads through the air via infectious respiratory particles that are released when an infected person breathes, sings, talks, coughs, or sneezes. A person can then become infected with the virus when these infectious respiratory particles are inhaled or if they are directly deposited on the mucous membranes of the eyes, nose, or mouth.[22] Staying at least one metre away from infected people lowers the risk of transmission.[23] However, in crowded indoor places with poor ventilation, the virus can spread over greater distances.[22] The virus can also survive on surfaces for multiple days[24] and this provides an alternative route of infection when an individual touches that surface and then touches their eyes, nose or mouth.[22] Individuals may also become infected by touching their eyes, nose, or mouth after direct contact (such as shaking hands) with a person with SARS-CoV 2 infection.[22]

The average duration of the SARS-CoV-2 incubation period ranges from three to seven days, depending on the strain.[25] The infectious period begins a few days before and usually peaks around symptom onset, with large individual variation.[26]

2.2.2 Signs and symptoms

There are a range of signs and symptoms associated with COVID-19, but the most commonly reported for currently-circulating variants (that is, BA.3.2 and XFG)[27] include fever, chills and sore throat.[12] Other less common symptoms may include nasal congestion, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, sore eyes, dizziness, cough, chest tightness or chest pain, hoarse voice, numbness or tingling, difficulty sleeping, appetite loss, gastrointestinal issues and new loss of taste or smell.[12]

Symptom severity of acute COVID-19 can range from asymptomatic to very serious. Severe COVID-19 is defined as oxygen saturation levels of less than 90% in room air, severe pneumonia, or signs of severe respiratory distress.[28] Critical COVID-19 is defined by acute respiratory distress syndrome, sepsis, septic shock, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation or vasopressor therapy.[28]

Most people recover from COVID-19 without treatment due to increasing immunity from past infections and or vaccination.[12] However, older adults, people with

certain underlying health conditions and those living with immunocompromise are at higher risk of severe illness compared to the general population.

Some people who have had acute COVID-19 continue to experience symptoms (such as fatigue, shortness of breath, post-exertional malaise and cognitive issues) which impact on everyday functioning long after the infectious period has ended.[12] Known as long COVID or post COVID-19 condition, this has been defined by the WHO as persistent symptoms occurring three months after the onset of acute COVID-19, which have persisted or re-occurred for at least two months and cannot be explained by alternative diagnoses.[29] In addition to the symptoms and functional impairment related to long COVID, other illnesses can be triggered following an acute COVID-19 illness. These include, but are not limited to, cardiovascular and neurological events (such as stroke), and kidney and lung impairments. Subsequent reinfections with SARS-CoV-2 are associated with an increased severity and excess burden of these conditions.[30, 31] There is some evidence to suggest that SARS-CoV-2 infection is linked to an increased risk of developing new-onset autoimmune diseases after the acute phase of SARS-CoV-2 infection.[32, 33] However, a causal link has not been established.[34]

2.3 Vaccines authorised by the EMA for the prevention of COVID-19

2.3.1 Centralised authorisation procedure

The centralised authorisation procedure is compulsory for medicines such as antigenically updated COVID-19 vaccines as they are derived from biotechnology processes.[35] Under this procedure, pharmaceutical companies submit a single marketing authorisation application to the EMA.[35] Upon receipt of a favourable opinion from the EMA's Committee for Medicinal products for Human Use, the European Commission (as the authorising body) makes a legally binding decision based on this recommendation. Once granted, a centralised marketing authorisation is valid in all EU Member States as well as in European Economic Area (EEA) countries.[35]

It should be noted that not all EMA-authorised COVID-19 vaccines are available in Ireland. To date, availability typically depended on whether a particular vaccine product has been preferentially recommended by the National Immunisation Advisory Committee (NIAC), and on whether Ireland opted into one of the joint procurement framework contracts issued for the different COVID-19 vaccines, negotiated between the manufacturer and the European Commission's Health Emergency Preparedness and Response Authority.[36] These contracts are facilitated through the Joint Procurement Agreement, a mechanism at the EU level to jointly

procure medical countermeasures, and in particular pandemic vaccines, on a voluntary and flexible basis.[37] This mechanism contributes to EU-level preparedness for public health crises and or pandemics. Ireland, through its continued participation in these EU-led procurement processes, has gained access to COVID-19 vaccines at a cost negotiated collectively by the EU.[38]

2.3.2 Antigenic update of vaccines

The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) monitors the genetic and antigenic evolution of SARS-CoV-2 variants and the effectiveness of COVID-19 vaccines against circulating variants.[39] Based on these data the WHO advises vaccine manufacturers and regulatory authorities on required updates to COVID-19 vaccine antigen composition.[39] On 16 May 2026, the WHO TAG-CO-VAC advised vaccine manufacturers that monovalent LP.8.1 is the currently recommended vaccine antigen but clarified that other antigens (for example, XFG) could also be used.[40]

In Europe, the EMA's Emergency Task Force (ETF) is the permanent advisory and support body that handles regulatory activities in preparation for and during a public health emergency, such as a pandemic. As part of its remit, the ETF makes recommendations to market authorisation holders regarding updates to vaccine composition.[41] The ETF consults with the WHO, international partners and marketing authorisation holders when considering such recommendations.[42] In May 2025, the ETF advised that COVID-19 vaccines adapted to target the LP.8.1 variant of the JN.1 family of Omicron sub-variants were preferentially recommended.[43] In October 2025, the National Immunisation Office in Ireland issued a statement advising that the antigenically-adapted COVID-19 vaccine, Comirnaty® LP.8.1, was available for all ages and that all older variant-adapted COVID-19 vaccines used for previous campaigns should be removed.[44] As of 29 May 2026, the ETF recommended updating COVID-19 vaccines to target the new SARS-CoV-2 variant XFG for the 2026/2027 vaccination campaign.[42]

2.3.3 mRNA vaccines

When used in vaccines, mRNA delivers instructions for making a piece of protein identical to one found in the cells of a particular virus or bacterium. The genetic code in conventional COVID-19 mRNA vaccines instructs the recipient to produce all, or selected parts, of the spike protein found on the surface of SARS-CoV-2 virus.[45] Spike proteins are viral membrane proteins that facilitate target cell recognition and viral entry into the host cell via fusion of the viral and cellular membranes.[46] This results in the release of the viral RNA genome into the cytoplasm.[47] After vaccination, the mRNA from the COVID-19 vaccine is translated into antigenic proteins by the ribosomes within the host's cells. Antigen presenting cells display

fragments of these proteins on their surface and trigger the adaptive immune response which includes stimulation of B cells by helper T cells to produce neutralising antibodies, thus offering the host protection against SARS-CoV-2.[45, 48] Table 2.1 provides an overview of the key characteristics of antigenically updated mRNA vaccines authorised, by the EMA for the prevention of COVID-19. It includes mCOMBRIAX®, which is the first seasonal influenza plus COVID-19 combination vaccine indicated for the protection of people aged 50 years and older against COVID-19 and seasonal influenza, which was authorised on 20 April 2026.[49]

Table 2.1 Summary of the key characteristics of antigenically updated mRNA vaccines authorised by the European Medicines Agency for prevention of COVID-19, as of August 2026

Trade name	mCOMBRIAX®*[49, 50]	mNexspike®[51, 52]	Spikevax®†[53]	Comirnaty®[7, 54]
Marketing authorisation holder	Moderna Biotech, Spain S.L.	Moderna Biotech, Spain, S.L.	Moderna Biotech, Spain, S.L.	BioNTech Manufacturing GmbH
Date marketing authorisation issued	20 April 2026	12 February 2026	06 January 2021	21 December 2020
Strain of SARS-CoV-2 targeted	XBB.1.5	XBB.1.5	XFG	XFG
SARS-CoV-2 protein encoded	The linked N-terminal domain and receptor-binding domain of the viral spike protein of SARS-CoV-2.‡	The linked N-terminal domain and receptor-binding domain of the viral spike protein of SARS-CoV-2.	The viral spike protein of SARS-CoV-2.	The viral spike protein of SARS-CoV-2.
Therapeutic indication	Active immunisation to prevent influenza and COVID-19 in adults aged ≥50 years.	Active immunisation to prevent COVID-19 in individuals aged ≥12 years.	Active immunisation to prevent COVID-19 in individuals aged ≥6 months.	Active immunisation to prevent COVID-19 in individuals aged ≥6 months.
Pharmaceutical form	Dispersion for injection ▪ 31.7mcg/dose (PFS)	Dispersion for injection ▪ 10mcg/dose (PFS)	Dispersion for injection ▪ 25mcg/dose (PFS; MDV) ▪ 50mcg/dose (PFS; MDV)	Dispersion for injection ▪ 10 mcg/dose (SDV; MDV) ▪ 30 mcg/dose (PFS; MDV)
Administration	All administered via intramuscular injection.			
Additional monitoring	These vaccines are subject to additional monitoring as new biological medicines.			

Key: mRNA – messenger ribonucleic acid; MDV – multidose vial; N/A – not applicable; PFS – pre-filled syringe; SDV – single dose vial.
†Previously called COVID-19 Vaccine Moderna.
‡This combination vaccine also encodes the seasonal influenza haemagglutinin glycoproteins A/H1N1, A/H3N2 and B/Victoria.

A comparison of current containers and storage types for authorised COVID-19 mRNA vaccine products for those aged 12 years and older is provided in Table 2.2, while details for products authorised for use in those aged less than 12 years is provided in Table 2.3. Availability of these products may vary across EU countries.

Table 2.2 Authorised COVID-19 mRNA vaccine products for those aged 12 years and older, by container and storage type

Container	Storage	Trade name			
		mCOMBRIAX®[49, 50]	mNexspike® [51, 52]	Spikevax® [53]	Comirnaty® [7]
Single dose pre-filled syringe	Refrigerated only				✓
	Supplied frozen*	✓	✓	✓	
Multidose vial	Refrigerated only				✓
	Supplied frozen*			✓	✓

*Across the authorised vaccine products, there are differences in the specific requirements in relation to storage when supplied frozen, with temperatures ranging from between -90°C to -60°C and -40°C to -15°C. Products also differ in their shelf-life once thawed.

The mNexspike® pre-filled syringe and the Spikevax® multidose vials and pre-filled syringes are supplied frozen from the manufacturer and must be thawed before use[51, 53] while mCOMBRIAX® is shipped and supplied either as a frozen or thawed pre-filled syringe.[50] Comirnaty® multidose vials can be supplied frozen (to be thawed before use) or refrigerated only. Comirnaty® is also available as refrigerated only pre-filled syringes.[7]

Table 2.3 Authorised COVID-19 mRNA vaccine products for those aged less than 12 years by container and storage type

		Spikevax®[53]		Comirnaty®[7, 54]
Storage	**Container**	6 months to 4 years	5 to 11 years	6 months to 11 years
Supplied frozen	Single dose pre-filled syringe	✓	✓	
	Single dose vial			✓
	Multidose vial	✓	✓	✓

As per Table 2.3, there are only two mRNA COVID-19 vaccines (Spikevax® and Comirnaty®) authorised for use in children aged less than 12 years. These are variably offered as either single dose pre-filled syringes or vials or as multidose vials; all forms are supplied frozen.

Across the authorised product forms, there are differences in the specific requirements in relation to storage when supplied frozen (temperatures range from between -90°C to -60°C and -40°C to -15°C), the shelf life when stored frozen (range 9 to 18 months), the shelf life when refrigerated for products previously stored frozen (range 30 days to 10 weeks) and the length of time at which the product may be stored at room temperature after removal from refrigeration prior to its use (range 12 to 24 hours). Moreover, multidose vials differ in terms of the number of doses per vial (range: 5 to 10, depending on the product and dose). Vaccines from a number of manufacturers are currently available both as single dose (pre-filled syringe or single dose vial) and multidose vial forms for selected paediatric and adult populations. It has been suggested that in time, these product lines may be simplified to include single dose forms only. Moreover, while technological advances have enabled the development of refrigeration-only products, some vaccines are only authorised to be supplied frozen. More detailed information regarding the posology, pharmaceutical form and containers, shelf life and storage for each mRNA vaccine is provided in Appendix A Table A.1.

2.3.4 Protein subunit vaccines

Protein subunit vaccines contain one or more antigens that correspond to proteins found on or within a pathogen, such as a virus. Currently authorised COVID-19 protein subunit vaccines in the EU contain a copy of all, or selected parts, of the SARS-CoV-2 spike protein produced by recombinant DNA technology.[55, 56] They also contain an adjuvant which strengthens the immune response to the vaccine. Following administration, an immune response is generated, both at a humoral and cellular level, against the SARS-CoV-2 antigen which contributes to protection against COVID-19.[55, 56] See Table 2.4 for a summary of the key characteristics of protein subunit vaccines authorised by the EMA for prevention of COVID-19.

Table 2.4 Summary of the key characteristics of protein subunit vaccines authorised by the European Medicines Agency for prevention of COVID-19, as of August 2026

Trade name	Nuvaxovid®[56]	Bimervax®[55]
Marketing authorisation holder	Sanofi Winthrop Industrie	Hipra Human Health S.L.
Date marketing authorisation was issued	20 December 2021	30 March 2023
Strain of SARS-CoV-2 targeted	XFG	XFG.1.1
Recombinant SARS-CoV-2 protein included	SARS-CoV-2 recombinant spike protein.	SARS-CoV-2 virus recombinant spike protein receptor-binding domain fusion homodimer.
Therapeutic indication	Active immunisation to prevent COVID-19 in individuals aged ≥12 years.	Active immunisation to prevent COVID-19 in individuals aged ≥12 years.
Pharmaceutical form	Dispersion for injection ▪ 5mcg/dose (PFS)†	Emulsion for injection ▪ 40mcg/dose (PFS; SDV)‡
Administration	Administered via intramuscular injection.	
Additional monitoring	These vaccines are subject to additional monitoring as new biological medicines.	

Key: PFS – pre-filled syringe; SDV – single dose vial.
†Adjuvanted with Matrix-M containing per 0.5 mL dose: Fraction-A (42.5 micrograms) and Fraction-C (7.5 micrograms) of Quillaja saponaria Molina extract.
‡Adjuvanted with SQBA containing per 0.5 mL dose: squalene (9.75 mg), polysorbate 80 (1.18 mg), sorbitan trioleate (1.18 mg), sodium citrate (0.66 mg), citric acid (0.04 mg) and water for injections.

There is no COVID-19 protein subunit vaccine authorised for use in children aged less than 12 years. A comparison of containers and storage types for authorised COVID-19 protein subunit vaccine products is provided in Table 2.5

Table 2.5 Authorised COVID-19 protein subunit vaccine containers by product and storage type

Storage	Container	Trade name	
		Nuvaxovid®[56]	Bimervax®[55]
Refrigerated only	Single dose pre-filled syringe	✓	✓
	Single dose vial	✓	✓

Note that both authorised protein subunit vaccines are supplied from the manufacturer ready to use at refrigerated temperatures and should be stored at 2°C to 8°C. Unopened Nuvaxovid® syringes and vials can be stored at this temperature for nine months, while unopened Bimervax® syringes and vials can be stored at this temperature for one year from the date of manufacture.[55, 56] More detailed information regarding the posology, pharmaceutical form and containers, shelf life and storage for each protein subunit vaccine is provided in Appendix A Table A.2.

2.3.5 Co-administration with other vaccines

A systematic review of updated evidence for COVID-19, respiratory syncytial virus (RSV) and influenza vaccines for 2025/2026 included evidence in relation to the co-administration of these vaccines. The review included 17 studies relating to the co-administration of COVID-19 and influenza vaccines with evidence of similar immunogenicity and safety to that of sequential administration. It also reported, based on evidence from a single randomised trial in adults aged 65 years and older, that triple co-administration of COVID-19, RSV and influenza vaccines, as well as co-administration with non-respiratory vaccines, showed acceptable immunogenicity and safety profiles.[57] However, there is some evidence from a Danish prospective cohort study that systemic adverse events are more frequent in individuals receiving three vaccines (namely, COVID-19, influenza and pneumococcal) together when compared with a COVID-19 vaccine only group.[58] This was attributed to the multiple pneumococcal antigens included in the pneumococcal vaccine and was an issue highlighted in the study as potentially impacting patient acceptability.

In adults, the Immunisation Guidelines for Ireland advise that COVID-19 vaccines may be administered at the same time as other adult vaccines.[9] The guidelines also note that where practicable, COVID-19 and seasonal influenza vaccines should be co-administered to adults during the same appointment to maximise uptake by reducing the number of vaccination appointments needed. Co-administered vaccines should be given in different limbs if possible, or, if administered in the same limb, be separated by at least 2.5cm. Due to the unknown risk of myocarditis, the guidelines

advise there should be an interval of at least four weeks between the mpox vaccine and a subsequent COVID-19 vaccine; however, no interval is required between administration of a COVID-19 vaccine and a subsequent mpox vaccine.[9]

The Immunisation Guidelines for Ireland note that no interaction studies have been performed on the co-administration of COVID-19 vaccines with routine childhood vaccines.[9] As such, the guidelines recommend that priority should be given to other routine childhood immunisations and that it would be prudent to separate COVID-19 vaccination in children aged six months to four years from other vaccines for a period of 14 days.[9]

2.3.6 Contraindications to authorised COVID-19 vaccines

Contraindications for all authorised COVID-19 vaccines include hypersensitivity to the active substance or any of the excipients. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.[7, 51, 53, 55, 56]

2.4 National COVID-19 immunisation policy

NIAC is Ireland's National Immunisation Technical Advisory Group (NITAG). NIAC provides independent evidence-based recommendations and advice to the Minister for Health on immunisation and related health matters to inform health policy in Ireland. The Immunisation Guidelines for Ireland are also updated to reflect current NIAC recommendations. The recommendations are considered by the Chief Medical Officer who then makes a recommendation to the Minister of Health.[59] After deliberation, the Minister of Health makes policy decisions on any changes to the National Immunisation Programme, such as changes in the funding of particular vaccines.[59]

2.4.1 NIAC COVID-19 vaccination recommendations

NIAC first issued recommendations in relation to COVID-19 vaccination in 2020. These recommendations have changed over time in response to the evolving epidemiological situation, evidence updates and the products available. On 6 May 2025, NIAC published updated recommendations on vaccination against COVID-19 to reflect the evolution of the SARS-CoV-2 pandemic to an endemic phase.[8] These are intended as a set of standing COVID-19 vaccination recommendations for Ireland going forward and are outlined in Table 2.6. The aim of the COVID-19 vaccine recommendations is to offer year-round protection to those groups identified to be at increased risk of severe outcomes from COVID-19 (that is, hospital admission, intensive care unit admission and death). To achieve this, vaccination once per year is recommended for most at-risk individuals, with twice-yearly

vaccination recommended for those in whom immunity wanes more quickly. An individualised approach (which considers the patient's underlying medical conditions and medications) is necessary when determining if a patient is considered immunocompromised and, in some cases, consultation with a specialist may be appropriate. This is because the degree of immunocompromise due to disease and or treatment can vary significantly between patients.[60]

Health and care workers aged less than 60 years and without additional risk factors are now considered to be at low risk of severe COVID-19. Additionally, the effectiveness of COVID-19 vaccination against infection and onwards transmission is modest and short lived, and timing of SARS-CoV-2 peaks is unpredictable. Therefore, as of May 2025, NIAC no longer recommends annual COVID-19 vaccination for all health and care workers, but instead supports continued access for such individuals who prefer to receive a COVID-19 vaccination.[8] COVID-19 severity in pregnancy has declined and severe COVID-19 in pregnant women is rare. This is due to an increased level of population immunity from previous infection and or vaccination, and evolution of the virus itself. As such, NIAC no longer recommends a COVID-19 vaccine in pregnant women without additional risk factors. However, NIAC supports continued access to COVID-19 vaccination for pregnant women who, following discussion with a healthcare provider, choose to receive a vaccine.[8]

Table 2.6 National Immunisation Advisory Committee recommendations on vaccination against COVID-19 (updated 6 May 2025)

1. A COVID-19 vaccine is recommended twice each year for:	▪ those aged 80 years and above ▪ those aged 18-79 years living in long term care facilities for older adults ▪ those aged 6 months and older with immunocompromise associated with a suboptimal response to vaccination.
2. A COVID-19 vaccine is recommended once each year for:	▪ those aged 60-79 years ▪ those aged 6 months to 59 years with medical conditions~ associated with a higher risk of COVID-19 hospitalisation, severe disease or death.
3. Access to a COVID-19 vaccine once each year should be available for:	▪ health and care workers* who choose to receive a vaccine ▪ pregnant adolescents and adults* who, following discussion with a healthcare provider, choose to receive a vaccine ▪ adults aged 18-59 not included in the groups listed in points 1 or 2 who, following discussion with a healthcare provider, choose to receive a vaccine.

~Medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death include: cancer, chronic heart disease, chronic kidney disease, chronic liver disease, chronic neurological disease, chronic respiratory disease, diabetes and other metabolic disorders including inherited metabolic disorders, haemoglobinopathies, immunocompromise due to disease or treatment, body mass index ≥40kg/m^2, serious mental health conditions, children and adults with Down syndrome, children with moderate to severe neurodevelopmental disorders. This list is not exhaustive, and the medical practitioner should apply clinical judgment to consider the risk of COVID-19 infection exacerbating any medical condition that a patient may have as well as the risk of serious illness from COVID-19 infection.

*Pregnant adolescents and adults and or health and care workers who also fall into the risk groups outlined in points 1 and 2 should follow the corresponding recommendations.

On the basis of the evidence considered, NIAC preferentially recommended an antigenically updated mRNA vaccine where available. For those with a contraindication or precaution to mRNA vaccines, it was noted that consideration may be given to a protein subunit vaccine, and in such cases, Nuvaxovid® (antigenically updated) was the preferred alternate.[8]

2.4.2 COVID-19 immunisation programme

In Ireland, COVID-19 vaccination is provided free at the point of care and is available at any time of year for those who have not previously received a COVID-19 vaccine. The COVID-19 immunisation programme commenced in Ireland in 2020 with updates to the programme over time to reflect changes to the NIAC recommendations. During the autumn and winter 2025/2026 campaign, a COVID-19 vaccination was available and specifically recommended by the HSE for all those:

- aged 60 years and older
- aged 18 years and older and living in a long-term care facility

- living with immunocompromise associated with a suboptimal response to vaccination
- living with a health condition associated with a higher risk of serious illness from COVID-19.[61]

Health and care workers who did not fall into one of the above risk groups could get a COVID-19 vaccine in autumn or winter 2025/2026, if they chose to.[62] Additionally, pregnant women who did not fall into one of these risk groups could also receive a COVID-19 vaccine following discussion with their general practitioner or healthcare provider.[63] During the autumn and winter 2025/2026 vaccination campaign, any adult aged 18 years and older who did not fall into one of the groups for which the vaccine was recommended could still receive one for free at the point of care after discussion with their healthcare provider.[61] As of August 2026, COVID-19 vaccines are not currently available for private purchase in Ireland. For authorised vaccines, such availability is at the discretion of the individual manufacturer.

2.5 Changes in international COVID-19 vaccination policy

In the context of increasing population baseline immunity to COVID-19 (due to vaccination and or previous infection) and the evolving epidemiological situation, a number of European countries have revised their policy regarding the groups for which COVID-19 vaccination is publicly funded. Due to the time constraints associated with this project, it was not possible to undertake an exhaustive search of the changes in COVID-19 vaccination policies across all European countries. Moreover, as outlined in Section 2.3.1, many countries, including Ireland, had committed to the procurement of defined amounts of vaccine stock through the Joint Procurement Agreements negotiated between the manufacturer and the European Commission. As these agreements expire, there will be an opportunity to retender for vaccine supplies. As such, it is expected that funding policy will be reviewed in many European countries during 2026 and 2027. Therefore, a description of the relationship between NITAG vaccination recommendations (where applicable) and funding decisions, and a summary of recent changes in COVID-19 vaccination policy is described below for Denmark and the UK only. These countries were selected as they were known by the Evaluation Team to have made recent changes to their COVID-19 vaccination funding policy.

2.5.1 Denmark

Funding of COVID-19 vaccinations

In Denmark, the Vaccination Council within the Danish Health Authority advises the Authority with regard to the use of vaccines against infectious diseases.[64] The Minister for the Interior and Health uses this advice to decide on the inclusion of

vaccines within publicly funded immunisation programmes, which provide vaccination free at the point of care.[65] The Danish Health Authority then publishes the advice on who should be vaccinated as part of the funded national vaccination programme.

Vaccination is provided once yearly between October and December. In 2025, COVID-19 vaccination (Comirnaty® LP8.1 adapted) was funded for those aged 65 years and older and for those aged under 65 years with specified chronic diseases or conditions.[66]

Health and care workers

In Denmark, health and care workers, and those working in certain social services, were a target group of the autumn/winter 2022/2023 COVID-19 vaccination campaign.[67] However, they have not been included among the target groups for funded COVID-19 vaccination since 2023.[68-70]

Pregnant women

As of 2025, the Danish Health Authority no longer recommend funded COVID-19 vaccination in healthy pregnant women. Hospital admission due to COVID-19 is rare in pregnant women, and overall, the severity of COVID-19 has decreased in young, healthy people in Denmark.[70]

Other changes to COVID-19 vaccine policy

In 2025, only those in a particular age or risk category themselves were offered a publicly funded COVID-19 vaccine.[70] In previous campaigns, relatives and or household contacts of those in certain risk groups were offered a publicly funded COVID-19 vaccine.[67-69] In 2025, "early retirees" defined by age and duration of service, and determined by Udbetaling Danmark[71] (the Danish public authority responsible for certain public benefits such as the state pension), were also no longer eligible for a publicly funded COVID-19 vaccine.[69, 70]

2.5.2 United Kingdom

Funding of COVID-19 vaccinations

In England and Wales, vaccinations recommended by the Joint Committee on Vaccination and Immunisation (JCVI) as part of national immunisation programmes are typically government funded as there is a statutory requirement for ministers to implement advice from the JCVI, as far as is reasonably practicable.[72]

In 2025, twice-yearly COVID-19 vaccination was recommended and funded for the following groups:

- adults aged 75 years and over
- residents in a care home for older adults
- individuals aged six months and over who are living with immunocompromise.

In Scotland and Northern Ireland, JCVI advice is not statutory and implementation is decided by their respective governments.[73] To date, JCVI recommendations on COVID-19 vaccination have been adopted in all UK countries and vaccines provided free at the point of care within the National Health Service for the groups specified within national immunisation programmes. However, governments may expand eligibility to groups beyond those included in the JCVI recommendations. For example, the Welsh government chose to fund COVID-19 vaccination for frontline health and social care workers, unpaid carers and household contacts of those living with immunocompromise during autumn 2024 even though the JCVI no longer recommended it for these groups.[74, 75] The JCVI note that the risk of severe disease (that is, hospitalisation and mortality) continues to be highest in those aged over 85 years. Of note, despite restricting to cohort eligible for vaccination in 2025, COVID-19 hospitalisations have not increased in individuals that were previously vaccinated according to clinical risk group status. As such, in July 2026, the JCVI advised that in autumn 2027, vaccination should be offered to adults aged 80 years and older, residents in a care home for older adults and individuals aged six months and over who are immunosuppressed. They noted that, while there is still uncertainty regarding the future epidemiology of COVID-19, the year-round baseline activity of COVID-19 has been decreasing over time. The potential for a single peak of activity (as observed in 2025), together with a potential increase in the durability of vaccine protection, could mean that only one vaccine dose per year may be needed to protect these higher risk populations.[76]

Health and care workers

For autumn 2024, COVID-19 vaccine doses were no longer routinely available for all health and care workers, household contacts of those living with immunocompromise or those in receipt of a carer's allowance.[77] This was in part due to the high levels of population immunity and evidence of moderate protection and limited duration of protection provided by such doses.

Pregnant women

In 2025, the JCVI noted that the risk of hospitalisation and or mortality in pregnant individuals had significantly reduced. As such, additional doses of the COVID-19 vaccine in healthy pregnancies were no longer routinely funded.[78]

Other changes to COVID-19 vaccine recommendations

Several changes have been made to COVID-19 vaccination recommendations in the UK in recent years. In autumn 2024, in addition to the groups listed above, vaccination was still also recommended and funded for adults aged 65 to 74 years, and for those aged six months to 64 years in a clinical risk group. This was despite evidence from a cost effectiveness analysis that it was unlikely to be cost effective for these cohorts, assuming a combined cost of vaccine and delivery of £25. However, the policy decision considered the unique situation that sufficient COVID-19 vaccines had already been pre-procured as part of the pandemic emergency response to allow the vaccine to be provided to these groups at no additional cost to the programme.[77] From 2025, funding for these groups is no longer provided in the national COVID-19 vaccination programme. The JCVI advised that the focus of the programme was shifting towards targeted vaccination of the oldest adults and individuals who are immunosuppressed, as these groups were at higher risk of severe disease.[79] However a number of COVID-19 vaccines are now separately marketed in the UK and available for private purchase following a consultation with a healthcare provider. While noting that the JCVI has no role in the procurement or delivery of COVID-19 vaccines or any other vaccine, in general, adult vaccine eligibility is subject to procurement and delivery at a cost-effective price.[78]

The JCVI has not issued a preference for a specific COVID-19 vaccine in the adult population. However, it has indicated a preference for having vaccine products based on more than one vaccine platform (such as, mRNA and protein-based vaccines) available in the programme. For children and young people who are immunosuppressed, the JCVI continues to advise that the appropriate dose of the Comirnaty® vaccine be used.[78]

2.6 Discussion

The COVID-19 pandemic resulted in the development of several vaccines against SARS-CoV-2 with multiple platform types investigated. Currently, both mRNA and protein subunit COVID-19 vaccines are authorised by the EMA. The use of mRNA, which can be manufactured in a cell-free manner, represented an advance in vaccine technology through facilitation of rapid and scalable production.[45] The more conventional protein subunit vaccine platform has been used previously to protect against other diseases such as shingles. However, currently (antigenically updated) mRNA COVID-19 vaccines are preferentially recommended by NIAC over COVID-19 protein subunit vaccines due to the extensive safety and effectiveness data available.[80]

While this chapter has outlined the main characteristics of antigenically updated COVID-19 vaccines currently authorised by the EMA, it should be acknowledged that additional types of COVID-19 vaccines were previously available. A whole virus inactivated COVID-19 vaccine Valneva®,[81] viral vector vaccines Vaxzevria® (previously COVID-19 Vaccine AstraZeneca)[82] and Jcovden® (previously COVID-19 Vaccine Janssen)[83] have since been withdrawn for commercial reasons. Furthermore, while all COVID-19 vaccines currently authorised by the EMA are administered via intramuscular injection, as of February 2025, five mucosal COVID-19 vaccines have received approval for human use in China (Convidecia Air®, Pneucolin®), Indonesia (Convidecia Air®), India (iNCOVACC®), Iran (RAZI-COV PARS®), Morocco (Convidecia Air®) and Russia (Sputnik V®).[84] Convidecia Air® is inhaled via a nebulizer while Pneucolin®, iNCOVACC® and Sputnik V® are administered intranasally as nasal sprays. RAZI-COV PARS® is initially administered as an intramuscular injection with a booster dose formulated as a nasal spray to be administered intranasally. It is also worth noting that Kostaive® (based on the original strain of SARS-CoV-2)[83] is the first self-amplifying mRNA COVID-19 vaccine authorised in the EU and this platform may offer additional advantages such as sustained antigen production which may enhance the immune response's magnitude and duration at lower doses and potentially reduce the need for additional doses.[48] Although an antigenically updated version of Kostaive® is not available in the EU currently, an updated version of this vaccine targeting the JN.1 lineage of Omicron sub-variants has been approved and marketed in Japan.[85] Additionally, as highlighted in Section 2.3.3, in April 2026 the EMA authorised mCOMBRIAX®, the first seasonal influenza plus COVID-19 combination vaccine.[86] It is therefore likely that new COVID-19 vaccine technologies will continue to become available in the EU.

In the initial stages of the COVID-19 pandemic, there was an urgent requirement to rapidly develop and scale up production of vaccines, in order to facilitate mass vaccination across the globe. A substantial challenge of mRNA vaccines is their inherent instability. Initial supply in the early stages of the pandemic was in the context of stringent, ultracold storage requirements (storage at -20^{0}C to -80^{0}C), but products still had limited shelf life (up to six months). This contrasts with traditional cold chain storage and delivery systems of 2 to 8^{0}C for other vaccines and refrigeration only medicines. Ultracold storage requirements and limited shelf life significantly increased the cost and operational complexity of mRNA vaccine distribution and storage, and limited accessibility of these vaccines in resource-poor countries.[87] Factors affecting mRNA vaccine stability include the mRNA molecular structure, the type of mRNA vaccine delivery system and extrinsic factors such as environmental and storage conditions. Freeze-drying technology can improve their stability and extend shelf life, but the product then requires reconstitution prior to administration.[88] Provision of COVID-19 vaccines as multidose vials provided

efficiencies during these mass vaccination campaigns. In recent years, technological advances and increased stability data have supported the availability of refrigeration only, clinically effective mRNA vaccines, which can be stored for longer periods.[89] As such, companies have expanded their product range, with some products available in both single dose and multidose format for the same population and as both refrigeration only and supplied frozen product. As SARS-CoV-2 moves to an endemic stage, and supported by ongoing technological developments, it is likely that mRNA vaccine product lines will be simplified in time, with an ultimate goal of ready-to-use, refrigeration only, single dose forms that do not require reconstitution — an approach that would be consistent with how most other vaccines are supplied.

As the SARS-CoV-2 pandemic evolves to an endemic phase there is an increased level of immunity due to past infections and or vaccinations among the Irish population. This, along with evolution of the virus, has resulted in a decline in rates of COVID-19 related morbidity and mortality. As such, NITAGs (including NIAC) have updated their recommendations over time. Most recently, this has included updated recommendations in relation to healthy pregnant women and for health and care workers without additional risk factors for severe disease.[80] In line with these changing clinical recommendations, some European countries have also updated the groups for which COVID-19 vaccination is publicly funded. Cost effectiveness and budget impact are important domains in vaccine policy decisions in many countries, including Ireland. Depending on the remit of the NITAG, this evidence may be considered as part of the NITAG recommendation (such as in the UK and Germany) or subsequent to the NITAG recommendation, such as in Ireland when the policy decision may additionally be informed by a HTA. For example, having considered evidence of cost effectiveness in their COVID-19 vaccination policy, access to publicly funded vaccination is now limited to subgroups at highest risk of severe disease in England.

During the 2025/2026 campaign, free (at the point of care) COVID-19 vaccination was available in Ireland through the HSE's COVID-19 vaccination programme for all groups outlined in the May 2025 NIAC recommendations and for all the groups for which NIAC have advised access should be made available. In addition, any adults aged 18 years and older who did not fall into one of the groups for which the vaccine was recommended could still access vaccination through the programme. With the impending end of the EU agreement with Pfizer and BioNTech to deliver COVID-19 vaccines through 2026,[90] and as existing vaccine stock expires or updated vaccines become available that target newly recommended antigens, there will be requirement for Ireland to retender for its vaccine supplies. This provides an opportunity to consider a wide range of issues, including cost effectiveness. It is

acknowledged, however, that as more variants of SARS-COV-2 emerge in future, any policy decision based on current epidemiological data may have to be reviewed.

The burden of COVID-19 in Ireland is explored in detail in Chapter 3, evidence relating to the clinical effectiveness and safety of these interventions are discussed in Chapter 4, and the cost effectiveness is explored in Chapter 5.

3 Epidemiology and burden of disease

Key points

- COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. While the severity of COVID-19 has declined over time (due to virus evolution and the establishment of population immunity through vaccination and natural infection), older adults, those with underlying medical conditions and those who are immunocompromised are at increased risk of developing severe COVID-19. Some people continue to experience symptoms long after the infectious period has ended, this is known as long COVID.
- COVID-19 incidence data and hospital utilisation data were sourced from the Health Protection Surveillance Centre (HPSC) and Hospital In-Patient Enquiry (HIPE) system, respectively. Data were reported by calendar year and limited to the period 2023 to 2025 (HPSC) and 2023 and 2024 (HIPE) to facilitate the inclusion of data most relevant to the current epidemiological situation (that is, data specific to currently circulating variants in a population exhibiting high levels of immunity, recognising the differences in current testing practices compared to those implemented during the early years of the COVID-19 pandemic).
- HPSC data indicate that the burden of COVID-19 in the total population aged six months and older has declined over time (from 2023 to 2025), specifically the notified:
  - case rate decreased from 699.1 to 248.3 per 100,000
  - emergency department (ED) visit rate decreased from 109.9 to 93.7 per 100,000
  - hospital admission rate decreased from 303.6 to 94.0 per 100,000
  - intensive care unit (ICU) admission rate decreased from 3.1 to 1.4 per 100,000
  - mortality rate decreased from 16.6 to 5.1 per 100,000 (equating to a reduction from 848 notified COVID-19-related deaths in 2023 to 260 notified deaths in 2025).
- When disaggregated by age group, HPSC data for the three-year period indicate that the burden generally increased with age, with a disproportionate burden among the oldest adults. Specifically, those aged:
  - 80 years and older accounted for on average 27% of notified cases; 22% of notified ED visits; 36% of notified hospitalisations; 17% of notified ICU admissions; and 64% of notified deaths, while representing less than 4% of the total population.

- 75 years and older accounted for 38% of notified cases; 33% of notified ED visits; 50% of notified hospitalisations; 32% of notified ICU admissions; and 79% of notified deaths, while representing only 7% of the total population.

- Limited data are available with respect to the vaccination status of notified cases, in relation to the presence of underlying conditions in those experiencing severe disease, and in relation to long COVID.
  - Vaccination status of notified hospital cases (from 2023 to 2025) was known for, on average, 68% of those aged 80 years and older and 67% of those aged 60 to 79 years. In 2025, considering those aged:
    - 80 years and older for whom twice yearly vaccination is recommended, 85% of notified hospital admissions and 88% of notified ICU admissions in this age group were in those who had not been vaccinated within the previous 180 days.
    - 60 to 79 years for whom once yearly vaccination is recommended, 63% of notified hospital admissions and 77% of notified ICU admissions in this age group were in those who had not been vaccinated within the previous 365 days.
  - Comorbidity data for this HTA were limited to those admitted to ICU. In all years, more than 90% of all notified ICU admissions were in those with one or more underlying medical condition.
  - While recognising that long COVID can have a considerable impact on an individual's quality of life, their ability to work and daily functioning, data are lacking (in Ireland and internationally) in relation to both the prevalence and burden associated with long COVID.

- HIPE data for 2023 and 2024 highlight the substantial burden associated with COVID-19 on the secondary healthcare system. These data are not directly comparable as prior to 2024, COVID-19 could only be coded as an additional diagnosis, even if it was the primary reason the patient presented to the healthcare system. Considering the total population (all ages):
  - In 2023, there were 17,828 discharges with an additional diagnosis of COVID-19. The mean length of stay was 23 days and the total number of bed days was 409,621 days.
  - In 2024, there were:
    - 2,876 discharges (42 of which included an ICU admission) with a principal diagnosis of COVID-19. The mean length of stay was six days and the total number of bed days was 18,039 days.

    - 11,533 discharges with an additional diagnosis of COVID-19. The mean length of stay was 25 days and the total number of bed days was 292,315 days.

- When disaggregated by age group, HIPE data also indicate that burden generally increased with age, with a disproportionate burden among the oldest adults. In considering the total discharges in those with a principal diagnosis of COVID-19 in 2024, those aged:
    - 80 years and older accounted for 34% (n=966) of discharges, 51% (n=9,232 days) of the total bed days, and had the longest average length of stay per patient (n=10 days).
    - 75 years and older accounted for 45% (n=1,307) of discharges, 67% (n=12,156 days) of the total bed days and had an average length of stay of nine days per patient.

- Using 2024 data, the average cost associated with a hospital stay for a patient with a principal diagnosis of COVID-19 was approximately €6,870, and the total annual cost associated with all discharges with a principal diagnosis of COVID-19 in 2024 was approximately €19.8 million.
    - Additional costs may accrue for patients who require post-discharge rehabilitation and care. For discharges for whom the discharge destination was known, approximately 6% of those with a primary diagnosis of COVID-19 and approximately 14% of those with an additional diagnosis of COVID-19 were newly discharged to a post-acute care setting, with a disproportionate requirement for post-discharge support in older adults.
    - Additional costs may also accrue in relation to long COVID both from the healthcare and societal perspective. In the absence of definitively effective treatments, much of this burden may arise from reduced labour participation and productivity losses rather than medical expenditure alone.

- The COVID-19-related morbidity and mortality observed are in the context of an ongoing COVID-19 vaccination programme that continues to offer funded COVID-19 vaccination to certain at-risk groups. Considering specifically uptake in selected at-risk groups:

    - During the 2025/2026 autumn/winter campaign, reported uptake was 73.6% in residents of LTCFs for older adults, 60.8% in those aged 80 years and older, 33.2% in those aged 60 to 79 years, and 18.2% in those identified as living with immunocompromise. These rates are lower than the HSE targets that 75% of those aged 65 years and older

and 50% of those living with immunocompromise receive their booster doses.
    - When comparing vaccination campaigns from autumn 2023 onwards, there has been a gradual decrease in uptake, with substantially lower uptake in the spring campaigns for those in whom twice yearly vaccination is recommended (for example, for those aged 80 years and older, uptake was 32.3% in the spring 2025 campaign versus 60.8% in the autumn/winter 2025/2026 campaign.
- In summary, while there is evidence that the overall burden associated with COVID-19 has decreased in recent years, there continues to be a disproportionate burden in older adults and a general trend of decreasing COVID-19 vaccination uptake since September 2023.

3.1 Introduction

This chapter describes the epidemiology and the burden of disease of COVID-19 in Ireland, EU/EEA countries, the UK and the USA.

COVID-19 is an infectious illness caused by the SARS-CoV-2 virus. Since its identification in 2019, the severity of COVID-19 has declined over time due to virus evolution and the establishment of population immunity through vaccination and natural infection.[9] The most common symptoms associated with currently circulating variants are fever, chills, and a sore throat, while symptoms associated with more severe disease including difficulty breathing, confusion, drowsiness, persistent pain or pressure in the chest and loss of speech. Older adults, those with underlying medical conditions and those who are immunocompromised are at increased risk of developing severe COVID-19.[12] Some people continue to experience symptoms long after the infectious period has ended, this is known as long COVID.[12]

Replication of SARS-CoV-2 in the host cell has resulted in genetic mutations in the virus' genetic coding which in turn has led to the evolution and detection of SARS-CoV-2 variants. The basic reproductive number (R0) of the SARS-CoV-2 virus varies depending on the circulating strain but, prior to the widespread use of vaccines, the R0 for SARS-CoV-2 ranged from two to eight.[9] The incubation period of COVID-19is typically three to seven days,[25] and the infectious period usually begins a few days before symptom onset and peaks around symptom onset.[26]

As reported in Chapter 1, genomic mutations and the emergence of variants decreased the effectiveness of the COVID-19 vaccines originally developed using the ancestral strain of SARS-CoV-2. One of the most notable variants has been Omicron,

specifically the subvariant Omicron BA.1, which emerged in November 2021. Since then, Omicron has displaced Delta as the globally predominant variant, with further shifts between Omicron sub-lineages throughout 2023 onwards.

3.2 Data sources

The focus of this HTA is on COVID-19, which can be acquired at any time of year, and currently does not exhibit seasonality. Surveillance of COVID-19 refers to the collection, aggregation and analysis of COVID-19 activity information for a defined population for a specified period of time. COVID-19 surveillance involves collection of both clinical and virological data. Clinical surveillance monitors the impact of the illness on the health service and the community, while the purpose of virological surveillance is to identify when COVID-19 is circulating and the current strain.[91] The Health Protection Surveillance Centre (HPSC) reports COVID-19, influenza and respiratory syncytial virus (RSV) surveillance data in its Integrated Respiratory Virus Bulletin.[92] Unlike COVID-19, influenza and RSV exhibit seasonality, with epidemics occurring during the winter months in temperate regions. As such, where seasonal data are referred to within this chapter, this does not infer that COVID-19 also exhibits seasonality, but rather it refers to COVID-19 data reported as part of the respiratory virus season in general.

COVID-19 has been a notifiable disease in Ireland since 2020 under the Infectious Disease Regulations. Surveillance of all confirmed COVID-19 notifications, including emergency department (ED) visits who were not subsequently admitted as hospital inpatients, hospitalisations, intensive care unit (ICU) admissions, deaths and outbreaks, are reported through the Irish Computerised Infectious Disease Reporting system (CIDR) notification system.[27] Confirmed cases are defined as those who have had SARS-CoV-2 nucleic acid or antigen detected in a clinical specimen.[93]

For this HTA, notified COVID-19 surveillance data reported by week were obtained from the HPSC for the period 2023 to 2025. Data were restricted to this time period to facilitate the inclusion of data most relevant to the current epidemiological situation, that is, data specific to currently circulating variants in a population exhibiting high levels of immunity (through exposure to previous infection and or vaccination).[94] Limiting the data to 2023 onwards also recognises differences in testing practices during the emergency phase of the COVID-19 pandemic compared with current policies. One specific example was removal of the recommendation to test all asymptomatic patients and asymptomatic contacts in 2022.[95]

Data were extracted from the CIDR system on Monday 3 February 2026 and it is noted that all data are provisional and subject to ongoing review, validation and update. Data for 2025 specifically should be interpreted with caution due to delays in

the registration of deaths. Rates were calculated using Central Statistics Office (CSO) census denominator data for the total and associated age-stratified population of Ireland. Census data from 2022 were used for these analyses.[96]

Data from the Hospital In-Patient Enquiry (HIPE) system in Ireland were also gathered to understand the nature of COVID-19 hospitalisations (for example, complications of the disease and length of stay). These data were gathered for 2023 and 2024 and reported by calendar year (data for 2025 were not available at the time of writing this report). HIPE data were used to examine hospital discharges with and without an ICU stay.

From 2020 to 2023, the International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM) was used by HIPE to capture COVID-19 related activity. The following codes were applied:

- B97.2 Coronavirus as the cause of disease classified elsewhere or
- B34.2 Coronavirus infection, unspecified site

and either:

- U07.1 Emergency use of U07.1 (COVID-19, virus identified) or
- U07.2 Emergency use of U07.2 (COVID-19, virus not identified).

In other words, all COVID-19-related activity had two codes assigned to it (a "B" code and a "U" code) with COVID-19 always assigned as an additional diagnosis, even if it was the primary reason the patient presented to the healthcare system.

Since January 2024, the ICD-10-AM Twelfth Revision has been used. In contrast to the 2020 to 2023 data, there is now an option to assign COVID-19 as a principal or as an additional diagnosis. COVID-19 is now coded using one of the following "U" codes (and no longer requires the assignment of a "B" code):

- U07.1 Emergency use of U07.1 (COVID-19, virus identified) or
- U07.2 Emergency use of U07.2 (COVID-19, virus not identified).

As such, HIPE data for those with an additional diagnosis of COVID-19 (with ICD-10 codes B97.2 or B34.2 and either U07.1 or U07.2) were extracted for 2023. For 2024, HIPE data for those with either a principal or an additional diagnosis of COVID-19 (with ICD-10 codes U07.1 or U07.2) were extracted. Discharge data for those with an additional diagnosis of COVID-19 (in 2023 and 2024) will include patients who were hospitalised for a variety of reasons unrelated to COVID-19, but were subsequently diagnosed with COVID-19 during the course of their admission.

Differences can arise between hospitalisations among notified COVID-19 cases (as reported by the HPSC) and COVID-19 discharges as reported by HIPE for several reasons. HPSC data include all reports of hospitalisation among notified cases (primary or additional diagnosis), with notified cases limited to confirmed cases, that is, laboratory confirmed cases. HIPE data may include cases where a diagnosis of COVID-19 was made based on clinical and epidemiological criteria, and laboratory confirmation was deemed unnecessary by the clinician.

A HIPE discharge record is created when a patient is discharged from, or dies in, hospital. This record contains information for a discrete episode of care. An episode of care begins at admission to hospital, as a day or inpatient, and ends at discharge from (or death in) that hospital.[97] HIPE data are used to create Diagnosis Related Groups to inform Activity Based Funding,[98] which is a funding model for hospital care for inpatient and day-case services. Using this model, a specified price is paid to each hospital for each weighted unit of inpatient and day-case work undertaken. HIPE data for this assessment also included the total cost of discharges, reported separately for those with and without an ICU stay, for those with a primary diagnosis of COVID-19 in 2024.

The SARS-CoV-2 genomic sequencing sampling framework currently focuses on notified COVID-19 cases with severe disease (that is, hospitalisation and ICU admission) and deaths, COVID-19 outbreaks in health and care settings, sentinel surveillance programmes in the community and acute hospitals, as well as targeted sequencing based on public health risk assessment and or clinical requests and virological changes (for example, a new variant of concern). There is typically a lag time of one to three weeks between a COVID-19 case being notified, selected for sequencing and SARS-CoV-2 sequencing being completed. The HPSC link sequencing results received from laboratories to epidemiological data on COVID-19 cases reported on the CIDR system.[99, 100]

3.3 Incidence of COVID-19 in Ireland

Notified COVID-19 cases for 2023 to 2025 are reported in Table 3.1. Note that different predominant SARS-CoV-2 variants were circulating at different time points during this period. From week 40 to 47 2023, the highest proportion of sequenced SARS-CoV-2 specimens in Ireland were categorised as the XBB.1.5-like lineage.[101] By December 2023, the JN.1 variant began to dominate the circulating SARS-CoV-2 variants in Ireland.[101] From week 35 2024, circulation of the XEC variant (KS.1.1 and KP.3.3 recombinant) steadily rose, becoming dominant between December 2024 and January 2025. Circulation of other variants, particularly LP.8.1, began to rise by week 17 (2025).[101] From week 34 to week 53 2025, the XFG variant was reported as the predominant SARS-CoV-2 variant.[102-104] The European Centre for Disease

Prevention and Control (ECDC) has not reported the circulation of any SARS-CoV-2 Variants of Concern in Europe since 3 March 2023.[10] Moreover, none of the currently reported circulating variants are considered by the ECDC or WHO likely to be associated with any increase in transmissibility, severity or immunity, compared with previously circulating variants.[10, 105]

Over the three-year period from 2023 to 2025, the notified case rate in the total population aged six months and older decreased from 699.1 cases per 100,000 in 2023 (n=35,798) to 248.3 cases per 100,000 (n=12,714) in 2025. This decrease in notified case rates was observed in all age groups.

The notified case rate consistently increased with increasing age, with a disproportionate burden seen among the oldest adults. On average, 27% of all notified cases occurred in those aged 80 years and older, while 38% occurred in those aged 75 years and older.

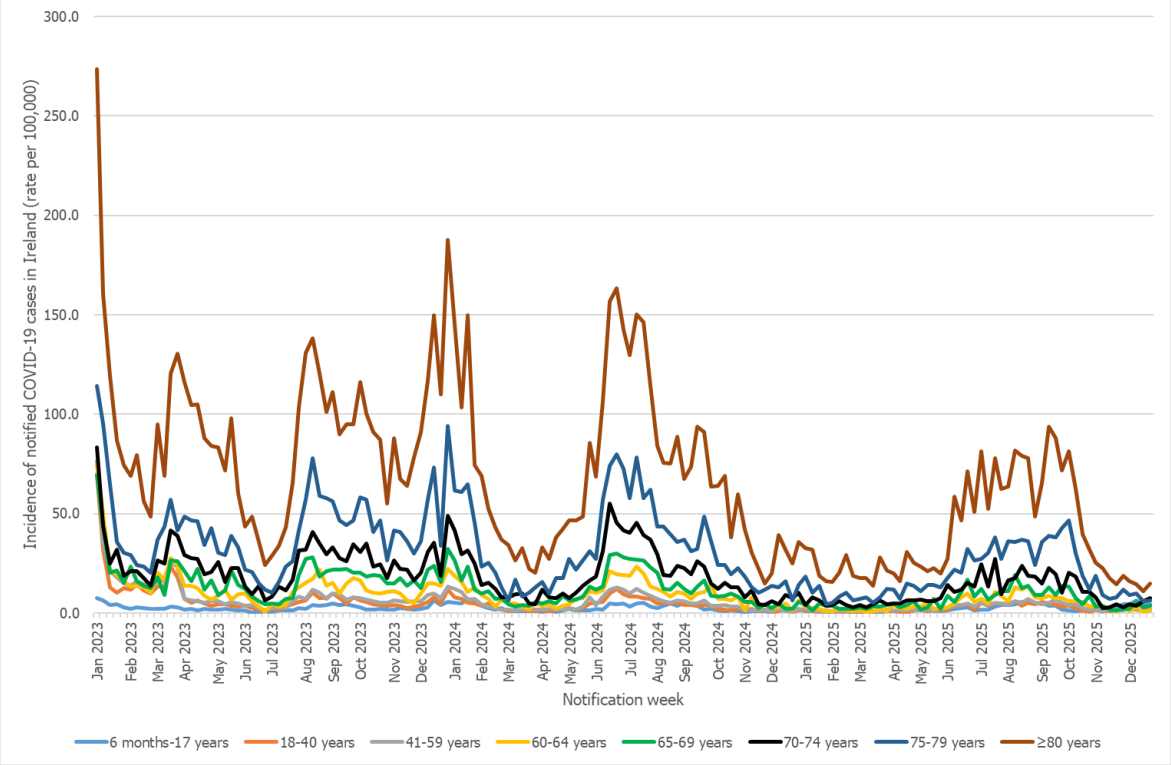
Table 3.1 Notified COVID-19 cases in Ireland (2023 to 2025), reported by age band

Age band	2023		2024		2025	
	n	Rate per 100,000	n	Rate per 100,000	n	Rate per 100,000
6 months to 17 years	1,690	142.1	1,540	129.4	1,365	114.7
18 to 40 years	7,005	457.0	2,979	194.3	1,788	116.6
41 to 59 years	7,539	559.0	3,332	247.0	1,902	141.0
60 to 64 years	2,071	759.5	1,258	461.4	641	235.1
65 to 69 years	2,322	975.0	1,430	600.5	795	333.8
70 to 74 years	2,789	1,374.7	1,963	967.5	1,042	513.6
75 to 79 years	3,501	2,269.5	2,557	1,657.6	1,506	976.3
≥80 years	8,881	4,905.9	6,449	3,562.5	3,675	2,030.1
Total	**35,798**	**699.1**	**21,508**	**420.1**	**12,714**	**248.3**

Source: Health Protection Surveillance Centre.

Figure 3.1 provides an overview of the notified COVID-19 case rate per 100,000 across the three years (2023, 2024 and 2025), reported by notification week. In general, the notified case rate has decreased over time for the total population and for each distinct age group. Across the three years, the notified case rate has been consistently highest in those aged 80 years and older, and lowest in those aged six months to 17 years. While COVID-19 still does not exhibit seasonality, peaks in the notified case rate were seen in April, August and December 2023, as well as in June 2024 and September 2025.

Figure 3.1 Notified COVID-19 cases per 100,000 in Ireland (2023 to 2025), reported by age band and notification week



Source: Health Protection Surveillance Centre.

3.4 Burden of disease

3.4.1 Complications and hospitalisations in Ireland

COVID-19-related ED visits

Notified COVID-19-related ED visits for 2023 to 2025 are reported in Table 3.2. Notified ED visits are defined as ED attendances in those with confirmed COVID-19 who were not subsequently admitted as hospital inpatients. In the total population aged six months and older, the notified ED visit rate ranged from 93.7 (n=4,800) to 139.2 (n=7,129) ED visits per 100,000, with the highest rate observed in 2024.

In general, the notified ED visit rate increased with increasing age, with a disproportionate burden in the oldest adults. On average, 22% (range 22% to 23%) of all notified ED visits occurred in those aged 80 years and older, while 33% (range 32% to 34%) occurred in those aged 75 years and older.

Table 3.2 Notified COVID-19-related emergency department visits in Ireland (2023 to 2025), reported by age band

Age band	2023		2024		2025	
	n	Rate per 100,000	n	Rate per 100,000	n	Rate per 100,000
6 months to 17 years	427	35.9	619	52.0	661	55.6
18 to 40 years	1,171	76.4	1,337	87.2	931	60.7
41 to 59 years	1,067	79.1	1,203	89.2	813	60.3
60 to 64 years	320	117.4	421	154.4	233	85.5
65 to 69 years	379	159.1	480	201.6	286	120.1
70 to 74 years	486	239.5	620	305.6	357	176.0
75 to 79 years	556	360.4	781	506.3	484	313.8
≥80 years	1,222	675.0	1,668	921.4	1,035	571.7
Total	**5,628**	**109.9**	**7,129**	**139.2**	**4,800**	**93.7**

Note: Emergency department visits are defined as those with laboratory-confirmed COVID-19 who were not subsequently admitted as hospital inpatients.
Source: Health Protection Surveillance Centre.

COVID-19-related hospital admissions

Notified COVID-19-related hospital admissions for 2023 to 2025 are reported in Table 3.3. Over this three-year period, the notified hospital admission rate in the total population decreased year on year from 303.6 (n=15,545) to 94.0 (n=4,811) hospital admissions per 100,000 in 2023 and 2025, respectively. This decrease in notified COVID-19 hospital admission rates was observed in all age groups.

Among adults aged 18 years and older, the notified hospital admission rate increased with increasing age, with a disproportionate burden in the oldest adults. On average, 36% (range 35% to 36%) of all notified hospital admissions occurred in those aged 80 years and older, while 50% occurred in those aged 75 years and older.

Table 3.3 Notified COVID-19-related hospital admissions in Ireland (2023 to 2025), reported by age band

Age band	2023		2024		2025	
	n (%)	Rate per 100,000	n (%)	Rate per 100,000	n (%)	Rate per 100,000
6 months to 17 years	768	64.6	644	54.1	510	42.9
18 to 40 years	1,255	81.9	706	46.1	378	24.7
41 to 59 years	1,832	135.8	989	73.3	504	37.4
60 to 64 years	886	324.9	524	192.2	255	93.5
65 to 69 years	1,303	547.1	658	276.3	322	135.2
70 to 74 years	1,704	839.9	953	469.7	450	221.8
75 to 79 years	2,209	1,432.0	1,237	801.9	699	453.1
≥80 years	5,588	3,086.8	3,265	1,803.6	1,693	935.2
Total	**15,545**	**303.6**	**8,976**	**175.3**	**4,811**	**94.0**

Source: Health Protection Surveillance Centre.

Data on the COVID-19 vaccination status of notified COVID-19-related hospital admissions (excluding those admitted to the ICU) and notified COVID-19-related ICU admissions were also provided by the HPSC. COVID-19 vaccination status was verified using the National Immunisation Register for COVID-19.

Table 3.4 summarises data relating to the COVID-19 vaccination status of notified COVID-19-related hospital admissions (excluding those admitted to the ICU). Of these notifications, the COVID-19 vaccination status was known for an average of 67% of those aged 60 to 79 years, and 68% of those aged 80 years and older across the three years. In those for whom COVID-19 vaccination status was known, the proportion that were not vaccinated prior to infection increased over the period from 2023 to 2025. This increase was seen in both age groups and when considering both the 180 and 365 days prior to infection.

In line with NIAC recommendations, those aged 80 years and older are eligible to receive a free COVID-19 vaccine twice yearly. Notified COVID-19 hospital admission data for 2025 show that 85% of this age group had not received a COVID-19 vaccine within the previous 180 days. Those aged 60 to 79 years are eligible to receive a free COVID-19 vaccine once each year (unless they are living in a long-term care facility or living with immunocompromise associated with a suboptimal response to vaccination, in which case they can also receive two COVID-19 vaccine doses per year). Notified COVID-19 hospital admission data for 2025 show that 63% of this age group had not received a COVID-19 vaccine within the previous 365 days.

Table 3.4 COVID-19 vaccination status of notified COVID-19-related hospital admissions (excluding those admitted to the intensive care unit)

	2023		2024		2025	
Age group (years)	**60-79**	**≥80**	**60-79**	**≥80**	**60-79**	**≥80**
Known vaccination status (%)	70.9	72.9	70.0	71.3	60.3	60.1
Not vaccinated <180 days prior (%)*	67.0	60.0	80.7	65.8	89.8	85.0
Not vaccinated <365 days prior (%)*	36.8	29.5	53.2	39.2	62.6	57.4
Vaccinated 0-14 days prior to infection	0.8	1.9	0.4	0.9	0.5	0.1

*Percentages calculated based on those for whom COVID-19 vaccination status is known.

COVID-19-related ICU admissions

Notified COVID-19 ICU-related admissions for 2023 to 2025 are reported in Table 3.5. Over this three-year period, the notified ICU admission rate in the total population decreased year on year from 3.1 (n=161) to 1.4 (n=72) ICU admissions per 100,000, with a decrease in admission rates observed in all age groups aged 40 years and older.

The presence of underlying medical conditions is recorded by the ICU clinician and, although not cross checked against any other records, the expectation is that these data are gathered by reviewing the patient's notes (this includes documentation from the GP referral and hospital and or ICU admission, as well as daily clinical notes). Data on the presence of underlying medical conditions were considered complete for all notified ICU admissions. In all years, more than 90% of all notified ICU admissions (average 91.8%) were in those with one or more underlying medical conditions. Differences were noted for the cohort aged six months to 17 years, where a lower proportion (range 38.5% to 72.7%) of notified ICU admissions were in those with underlying medical conditions.

In general, the notified ICU admission rate increased with increasing age, albeit with the highest rate observed in those aged 75 to 79 years in two of the three years. On average, 17% (range 15% to 19%) of all notified ICU admissions occurred in those aged 80 years and older, while 32% (range 31% to 33%) occurred in those aged 75 years and older.

Table 3.5 Notified COVID-19-related intensive care unit admissions in Ireland (2023 to 2025), reported by age band and the presence of underlying medical conditions

Age band	2023			2024			2025		
	n	Rate per 100,000	Has ≥1 underlying medical condition n (%)	n	Rate per 100,000	Has ≥1 underlying medical condition n (%)	n	Rate per 100,000	Has ≥1 underlying medical condition n (%)
6 months to 17 years	9	0.8	5 (55.6)	13	1.1	5 (38.5)	11	0.9	8 (72.7)
18 to 40 years	3	0.2	2 (66.7)	7	0.5	7 (100.0)	9	0.6	7 (77.8)
41 to 59 years	26	1.9	24 (92.3)	11	0.8	11 (100.0)	7	0.5	7 (100.0)
60 to 64 years	15	5.5	15 (100.0)	11	4.0	10 (90.9)	5	1.8	5 (100.0)
65 to 69 years	29	12.2	26 (89.7)	14	5.9	13 (92.9)	10	4.2	9 (90.0)
70 to 74 years	28	13.8	27 (96.4)	18	8.9	18 (100.0)	6	3.0	6 (100.0)
75 to 79 years	24	15.6	23 (95.8)	17	11.0	17 (100.0)	10	6.5	10 (100.0)
≥80 years	27	14.9	27 (100.0)	16	8.8	16 (100.0)	14	7.7	14 (100.0)
Total	**161**	**3.1**	**149 (92.5)**	**107**	**2.1**	**97 (90.7)**	**72**	**1.4**	**66 (91.7)**

Note: COVID-19 intensive care unit admissions refer to those admitted to intensive care where COVID-19 is the primary or contributory cause of admission.
Source: Health Protection Surveillance Centre.

Table 3.6 summarises data relating to the COVID-19 vaccination status of notified COVID-19-related ICU admissions. Of these notifications, the COVID-19 vaccination status was known for an average of 67% of those aged 60 to 79 years and 63% of those aged 80 years and older across the three years. From 2023 to 2025, in those for whom COVID-19 vaccination status was known, the proportion of those not vaccinated within the 180 and 365 days prior to infection increased in both age groups.

As noted previously, those aged 80 years and older are eligible to receive a free COVID-19 vaccine twice yearly while those aged 60 to 79 years can receive a free COVID-19 vaccine once each year (unless they are living in a long-term care facility or living with immunocompromise associated with a suboptimal response to vaccination, in which case they can also receive two COVID-19 vaccine doses per year). Notified COVID-19-related ICU admission data for 2025 show that 88% of those aged 80 years and older had not received a COVID-19 vaccine within the previous 180 days, while 77% of those aged 60 to 79 years had not received a COVID-19 vaccine within the previous 365 days.

Table 3.6 COVID-19 vaccination status of notified COVID-19-related intensive care unit admissions

	2023		2024		2025	
Age groups (years)	**60-79**	**≥80**	**60-79**	**≥80**	**60-79**	**≥80**
Known vaccination status (%)	60.9	50.0	68.8	82.4	71.0	57.1
Not vaccinated <180 days prior (%)*	67.9	30.8	79.5	50.0	90.5	87.5
Not vaccinated <365 days prior (%)*	25.0	23.1	54.5	42.9	77.3	75.0
Vaccinated 0-14 days prior to infection	1.8	15.4	0.0	0.0	0.0	0.0

*Percentages calculated based on those for whom COVID-19 vaccination status is known.

Hospital discharges and bed days

Data from the HIPE system in Ireland were used to examine hospital discharges with and without an ICU stay for the total population with an additional diagnosis of COVID-19 (with ICD-10 codes B97.2 or B34.2 and either U07.1 or U07.2) in 2023 and those with either a principal or an additional diagnosis of COVID-19 (with ICD-10 codes U07.1 or U07.2) in 2024. As noted in Section 4.2, a HIPE discharge record is created when a patient is discharged from, or dies in, hospital. This record contains information for a discrete episode of care. An episode of care begins at admission to hospital, as a day or inpatient, and ends at discharge from (or death in) that hospital.[97] Data extracted included information on the patient's age, length of stay, whether they were admitted to ICU during their inpatient stay, where they were admitted from and their discharge destination. Data were gathered by calendar year and are reported below. As highlighted in Section 3.2, COVID-19 was always

assigned as an additional diagnosis in 2023 even if it was the primary reason the patient presented to the healthcare system. In 2024, COVID-19 could be assigned as either a principal or an additional diagnosis. Therefore, COVID-19 discharge data for those with an additional diagnosis (in 2023 and 2024) will include patients who were hospitalised for a variety of reasons unrelated to COVID-19, but were subsequently diagnosed with COVID-19 during the course of their admission.

COVID-19 discharges and bed days (2023 data)

Table 3.7 provides an overview of total hospital discharges, number of bed days and average length of stay per patient in those with an additional diagnosis of COVID-19 in 2023, presented by age band. There was a total of 17,828 discharges related to an additional diagnosis of COVID-19 in 2023, this equated to a total of 409,621 bed days and an average length of stay of 23 bed days per patient. There was a disproportionate burden in the oldest age groups. Those aged 80 years and older accounted for 35.7% (n=6,359) of all discharges, 41.4% (n=168,464) of bed days and had an average length of stay of 26 bed days per patient. When considering those aged 75 years and older, this cohort accounted for 49.7% (n=8,866) of all discharges, 56.5% (n=231,396) of bed days and had an average length of stay of 26 days per patient.

In total, 9.0% of all discharges (1,599 out of 17,828) in 2023 included an ICU stay. These discharges had a longer average length of stay compared with discharges that did not include an ICU stay (44 versus 21 bed days per patient). The length of stay data represent the total length of stay related to the discharge — it is not possible to determine what proportion of the stay was in the ICU. A disproportionate burden was again observed in the oldest adults, with those aged 80 years and older accounting for 21.4% (n=342) of the discharges with an ICU stay and 37.1% (n=6,017) of the discharges without an ICU stay, while those aged 75 years and older accounted for 37.8% (n=605) of the discharges with an ICU stay and 50.9% (n=8,261) of the discharges without an ICU stay. Of note, the probability of having an ICU stay during inpatient care was highest in those aged 60 to 64 years, whereby approximately 1 in 7 discharges included an ICU stay in 2023. This age group also had the longest average length of stay (50 bed days per patient).

Of the 17,828 discharges for whom discharge destination data were available, 19.2% (n=3,430) were discharged to some form of post-acute care (namely, hospice, a nursing home, convalescent home or long stay accommodation, non-acute hospital, external rehabilitation facility or psychiatric hospital and or unit). Considering that 1,048 of these discharges were admitted to hospital from some form of non-acute care, this means that 13.4% (n=2,382) of all discharges were newly discharged to post-acute care. Of the 2,382 patients newly discharged to

post-acute care, those aged 80 years and older accounted for 58.5% of these discharges, while those aged 75 years and older accounted for 74.3%. While the proportion of those discharged to post-acute care generally increased with increased age, 107 of these new discharges to post-acute care were in those aged 41 to 59 years.

Table 3.7 Hospital discharges, length of stay and average length of stay per patient for those with an additional diagnosis of COVID-19 in 2023, reported by age band

Age band (years)	Total number of hospital discharges (% of total hospital discharges)	Total number of bed days (% of total bed days)	Average LOS (days) per patient	Total number of hospital discharges without an ICU stay (% of total hospital discharges without an ICU stay)	Total number of bed days for those without an ICU stay (% of total bed days without an ICU stay)	Average LOS (days) per patient for those without an ICU stay	Total number of hospital discharges with an ICU stay (% of total hospital discharges with an ICU stay)	Total number of bed days for those with an ICU stay (% of total bed days with an ICU stay)	Average LOS (days) per patient for those with an ICU stay
0 to 17	1,400 (7.9)	8,387 (2.0)	6	1,330 (8.2)	5,626 (1.7)	4	70 (4.4)	2,761 (4.0)	39
18 to 40	1,321 (7.4)	16,027 (3.9)	12	1,220 (7.5)	11,270 (3.3)	9	101 (6.3)	4,757 (6.8)	47
41 to 59	1,940 (10.9)	44,744 (10.9)	23	1,674 (10.3)	32,134 (9.5)	19	266 (16.6)	12,610 (18.1)	47
60 to 64	977 (5.5)	24,256 (5.9)	25	835 (5.1)	17,154 (5.0)	21	142 (8.9)	7,102 (10.2)	50
65 to 69	1,404 (7.9)	36,418 (8.9)	26	1,213 (7.5)	27,970 (8.2)	23	191 (11.9)	8,448 (12.1)	44
70 to 74	1,920 (10.8)	48,393 (11.8)	25	1,696 (10.5)	37,609 (11.1)	22	224 (14.0)	10,784 (15.5)	48
75 to 79	2,507 (14.1)	62,932 (15.4)	25	2,244 (13.8)	51,827 (15.3)	23	263 (16.4)	11,105 (15.9)	42
≥80	6,359 (35.7)	168,464 (41.4)	26	6,017 (37.1)	156,240 (46.0)	26	342 (21.4)	12,224 (17.5)	36
Total	**17,828**	**409,621**	**23**	**16,229**	**339,830**	**21**	**1,599**	**69,791**	**44**

Key: ICU – intensive care unit; LOS – length of stay.

Source: Hospital In-Patient Enquiry System.

COVID-19 discharges and bed days (2024 data)

As noted in Section 3.2, COVID-19 could be assigned as either a principal diagnosis or an additional diagnosis in 2024. Table 3.8 provides an overview of total hospital discharges, number of bed days and average length of stay per patient in those with a principal diagnosis of COVID-19 in 2024, presented by age band.

There was a total of 2,876 discharges related to a principal diagnosis of COVID-19 in 2024, this equated to a total of 18,039 bed days and an average length of stay of six bed days per patient. Using 2024 data, the average cost associated with a hospital stay for a patient with a principal diagnosis of COVID-19 was approximately €6,870, and the total annual cost associated with all principal diagnoses of COVID-19 in 2024 was approximately €19.8 million. There was a disproportionate burden in the oldest age groups. Those aged 80 years and older accounted for 33.6% (n=966) of all discharges, 51.2% (n=9,232) of bed days and had an average length of stay of 10 days per patient. When considering those aged 75 years and older, they accounted for 45.4% (n=1,307) of all discharges, 67.4% (n=12,156) of bed days and had an average length of stay of nine days per patient.

Only 1.5% of the discharges (42 out of 2,876) included an ICU stay. These discharges had a longer average length of stay compared with discharges that did not include an ICU stay (16 versus 6 bed days per patient). A disproportionate burden was again observed in the oldest adults, with those aged 80 years and older accounting for 47.6% (n=20) of the discharges with an ICU stay and 33.4% (n=946) of the discharges without an ICU stay, while those aged 75 years and older accounted for 59.5% (n=25) of the discharges with an ICU stay and 45.2% (n=1,282) of the discharges without an ICU stay. The probability of having an ICU stay during inpatient care was highest in the age group 41 to 59 years, whereby approximately 1 in 46 discharges included an ICU stay in 2024.

Of the 2,830 discharges for whom discharge destination data were available, 11.6% (n=327) were discharged to some form of post-acute care (namely, hospice, a nursing home, convalescent home or long stay accommodation, non-acute hospital, external rehabilitation facility or psychiatric hospital and or unit). Considering that 168 of these discharges were admitted to hospital from some form of non-acute care, this means that 5.6% (n=159) of all discharges with a principal diagnosis of COVID-19 were newly discharged to post-acute care. Of the 159 patients discharged to post-acute care, those aged 80 years and older accounted for 71.1% of these discharges while those aged 75 years and older accounted for 83.0%.

Table 3.8 Hospital discharges, length of stay and average length of stay per patient for those with a principal diagnosis of COVID-19 in 2024, reported by age band

Age band (years)	Total number of hospital discharges (% of total hospital discharges)	Total number of bed days (% of total bed days)	Average LOS (days) per patient	Total number of hospital discharges without an ICU stay (% of total hospital discharges without an ICU stay)	Total number of bed days for those without an ICU stay (% of total bed days without an ICU stay)	Average LOS (days) per patient for those without an ICU stay	Total number of hospital discharges with an ICU stay (% of total hospital discharges with an ICU stay)	Total number of bed days for those with an ICU stay (% of total bed days with an ICU stay)	Average LOS (days) per patient for those with an ICU stay
0 to 17	522 (18.2)	983 (5.4)	2	518 (18.3)	968 (5.6)	2	4 (9.5)	15 (2.2)	4
18 to 40	190 (6.6)	423 (2.3)	2	190 (6.7)	423 (2.4)	2	0 (0.0)	0 (0.0)	0
41 to 59	321 (11.2)	1,396 (7.7)	4	314 (11.1)	1,341 (7.7)	4	7 (16.7)	55 (8.2)	8
60 to 64	154 (5.4)	824 (4.6)	5	152 (5.4)	751 (4.3)	5	2 (4.8)	73 (10.9)	37
65 to 69	142 (4.9)	790 (4.4)	6	140 (4.9)	757 (4.4)	5	2 (4.8)	33 (4.9)	17
70 to 74	240 (8.3)	1,467 (8.1)	6	238 (8.4)	1,452 (8.4)	6	2 (4.8)	15 (2.2)	8
75 to 79	341 (11.9)	2,924 (16.2)	9	336 (11.9)	2,860 (16.5)	9	5 (11.9)	64 (9.5)	13
≥80	966 (33.6)	9,232 (51.2)	10	946 (33.4)	8,816 (50.8)	9	20 (47.6)	416 (62.0)	21
Total	**2,876**	**18,039**	**6**	**2,834**	**17,368**	**6**	**42**	**671**	**16**

Key: ICU – intensive care unit; LOS – length of stay.
Source: Hospital In-Patient Enquiry System.

Table 3.9 provides an overview of total hospital discharges, length of stay and average length of stay per patient in those with an additional diagnosis of COVID-19 in 2024, presented by age band. There was a total of 11,533 discharges related to an additional diagnosis of COVID-19 in 2024, this equated to a total of 292,315 bed days and an average length of stay of 25 bed days per patient. Those aged 65 to 69 years had the longest average length of stay at 30 days per patient. As with discharges for those with a primary diagnosis of COVID-19, there was a disproportionate burden in the oldest age groups. Those aged 80 years and older accounted for 36.9% (n=4,251) of all discharges and 40.8% (n=119,339) of bed days, while those aged 75 years and older accounted for 51.3% (n=5,913) of all discharges and 55.6% (n=162,637) of bed days.

In total, 10.8% of the discharges (1,250 out of 11,533) included an ICU stay. These discharges had a longer average length of stay compared with discharges that did not include an ICU stay (49 versus 23 bed days per patient). A disproportionate burden was again observed in the oldest adults, with those aged 80 years and older accounting for 20.6%% (n=257) of the discharges with an ICU stay and 38.8% (n=3,994) of the discharges without an ICU stay, while those aged 75 years and older accounted for 38.0% (n=475) of the discharges with an ICU stay and 52.9% (n=5,438) of the discharges without an ICU stay. Those aged 41 to 59 years had the highest probability of having an ICU stay during inpatient care, whereby approximately 1 in 6 discharges included an ICU stay in 2024, with this age group also having the longest average length of stay (67 days) for this discharge type.

Of the 11,533 discharges for whom discharge destination data were available, 19.8% (n=2,281) were discharged to some form of post-acute care (namely, hospice, a nursing home, convalescent home or long stay accommodation, non-acute hospital, external rehabilitation facility or psychiatric hospital and or unit). Considering that 640 of these discharges were admitted to hospital from some form of non-acute care, this means that 14.2% (n=1,641) of discharges with an additional diagnosis of COVID-19 were newly discharged to post-acute care. Of the 1,641 patients discharged to post-acute care, those aged 80 years and older and 75 years and older accounted for 57.6% and 74.0% of all such discharges, respectively.

Table 3.9 Hospital discharges, length of stay and average length of stay per patient for those with an additional diagnosis of COVID-19 in 2024, reported by age band

Age band (years)	Total number of hospital discharges (% of total hospital discharges)	Total number of bed days (% of total bed days)	Average LOS (days) per patient	Total number of hospital discharges without an ICU stay (% of total hospital discharges without an ICU stay)	Total number of bed days for those without an ICU stay (% of total bed days without an ICU stay)	Average LOS (days) per patient for those without an ICU stay	Total number of hospital discharges with an ICU stay (% of total hospital discharges with an ICU stay)	Total number of bed days for those with an ICU stay (% of total bed days with an ICU stay)	Average LOS (days) per patient for those with an ICU stay
0 to 17	781 (6.8)	6,774 (2.3)	9	725 (7.1)	3,716 (1.6)	5	56 (4.5)	3,058 (5.0)	55
18 to 40	867 (7.5)	10,962 (3.8)	13	780 (7.6)	7,605 (3.3)	10	87 (7.0)	3,357 (6.5)	39
41 to 59	1,200 (10.4)	34,803 (11.9)	29	991 (9.6)	20,871 (9.0)	21	209 (16.7)	13,932 (23.0)	67
60 to 64	655 (5.7)	17,523 (6.0)	27	545 (5.3)	12,115 (5.2)	22	110 (8.8)	5,408 (8.9)	49
65 to 69	900 (7.8)	27,448 (9.4)	30	745 (7.2)	18,183 (7.8)	24	155 (12.4)	9,265 (15.3)	60
70 to 74	1,217 (10.6)	32,168 (11.0)	26	1,059 (10.3)	25,161 (10.9)	24	158 (12.6)	7,007 (11.6)	44
75 to 79	1,662 (14.4)	43,298 (14.8)	26	1,444 (14.0)	34,699 (15.0)	24	218 (17.4)	8,599 (14.2)	39
≥80	4,251 (36.9)	119,339 (40.8)	28	3,994 (38.8)	109,323 (47.2)	27	257 (20.6)	10,016 (16.5)	39
Total	**11,533**	**292,315**	**25**	**10,283**	**231,673**	**23**	**1,250**	**60,642**	**49**

Key: ICU, intensive care unit; LOS, length of stay.
Source: Hospital In-Patient Enquiry System.

3.4.2 Mortality in Ireland

COVID-19-related mortality data were obtained from the HPSC and HIPE. Notified COVID-19-related deaths for 2023 to 2025 are reported in Table 3.10. Over this three-year period, the notified COVID-19 mortality rate in the total population decreased year on year from 16.6 (n=848) to 5.1 (n=260) deaths per 100,000.

The notified COVID-19 mortality rate consistently increased with increasing age, with a disproportionate burden among the oldest age groups. On average, 64% (range 63% to 68%) of all notified deaths were in those aged 80 years and older, while 79% (range 79% to 83%) were in those aged 75 years and older.

Table 3.10 Notified COVID-19 deaths in Ireland (2023-2025), reported by age band

Age band	2023		2024		2025	
	n	Rate per 100,000	n	Rate per 100,000	n	Rate per 100,000
6 months to 17 years	1	0.1	1	0.1	1	0.1
18 to 40 years	4	0.3	5	0.3	2	0.1
41 to 59 years	27	2.0	24	1.8	6	0.4
60 to 64 years	22	8.1	18	6.6	5	1.8
65 to 69 years	57	23.9	16	6.7	16	6.7
70 to 74 years	70	34.5	50	24.6	15	7.4
75 to 79 years	130	84.3	77	49.9	39	25.3
≥80 years	537	296.6	342	188.9	176	97.2
Total	**848**	**16.6**	**533**	**10.4**	**260**	**5.1**

Note: COVID-19 deaths are defined as a death in a person with laboratory-confirmed COVID-19 infection as per guidance on case definitions (this includes cases detected postmortem).[93]
Source: Health Protection Surveillance Centre.

HIPE data for deaths associated with COVID-19 were obtained for those with an additional diagnosis of COVID-19 (with ICD-10 codes B97.2 or B34.2 and either U07.1 or U07.2) in 2023 and those with either a principal or an additional diagnosis of COVID-19 (with ICD-10 codes U07.1 or U07.2) in 2024. COVID-19-related mortality data as reported by HIPE reflect all those coded with a diagnosis of COVID-19 for whom destination data were available. It should be noted that HPSC mortality data reflect deaths among notified COVID-19 cases. Since not all COVID-19 cases are notified (see Section 3.2), COVID-19-related mortality data as reported by the HPSC may differ to that reported by HIPE.

Table 3.11 reports the total number of deaths associated with an additional diagnosis of COVID-19 in 2023, and the total number of deaths associated with a principal or an additional diagnosis of COVID-19 in 2024. Across both years, those aged 80 years and older accounted for the greatest proportion of deaths associated with a principal and or an additional diagnosis of COVID-19. The observed number of deaths associated with an additional diagnosis of COVID-19 is markedly higher than that associated with a principal diagnosis of COVID-19. Data for 2023 and 2024 are not directly comparable since COVID-19 could only be assigned as an additional diagnosis in 2023.

In 2023 there were 1,343 deaths among discharges with an additional diagnosis of COVID-19, of which 56% (n=755) occurred in those aged 80 years and older and 73% (n=977) occurred in those aged 75 years and older. In 2024, there were 62 deaths among discharges with a principal diagnosis of COVID-19, and 967 deaths among discharges with an additional diagnosis of COVID-19. Those aged 80 years and older and those aged 75 years and older accounted for 65% (n=40) and 79% (n=49) of deaths among discharges with a principal diagnosis of COVID-19, respectively. Among discharges with an additional diagnosis of COVID-19, 55% (n=528) and 71% (n=683) of deaths were in those aged 80 years and older and those aged 75 years and older, respectively.

Table 3.11 Mortality for those with an additional diagnosis (2023) and a principal or an additional diagnosis (2024) of COVID-19, reported by age band

Age band (years)	Total deaths in 2023 (additional diagnosis) n (% of total deaths)	Total deaths in 2024 (principal diagnosis) n (% of total deaths)	Total deaths in 2024 (additional diagnosis) n (% of total deaths)
0 to 17	5 (0.4)	0 (0.0)	3 (0.3)
18 to 40	10 (0.7)	0 (0.0)	5 (0.5)
41 to 59	67 (5.0)	2 (3.2)	60 (6.2)
60 to 64	51 (3.8)	3 (4.8)	38 (3.9)
65 to 69	99 (7.4)	3 (4.8)	66 (6.8)
70 to 74	134 (10.0)	5 (8.1)	112 (11.6)
75 to 79	222 (16.5)	9 (14.5)	155 (16.0)
≥80	755 (56.2)	40 (64.5)	528 (54.6)
Total	**1,343**	**62**	**967**

Source: Hospital In-Patient Enquiry System.

3.4.3 Burden of disease in specific subgroups

Irish data for certain population groups of interest to this HTA were either incomplete or lacking. Specifically, the population groups of interest to this HTA (for which Irish data are lacking) are: those living in long-term care facilities (LTCFs), those living with immunocompromise, those living with underlying medical

conditions, pregnant adolescents or adults and healthcare workers. As such, international data for these groups have been summarised, where available. This HTA focuses on data specific to 2023 onwards and, therefore, the evaluation team aimed to identify international literature that was also specific to this time period. However, in instances where we found there to be a dearth of international literature relating to this specific time period, the evaluation team has summarised data available for as close to this time period as possible. It is worth noting that differences in the reported incidence of COVID-19 internationally may reflect actual differences in incidence or differences in policies within that jurisdiction (for example, differences in testing policies).

Long-term care facilities

While data on the epidemiology of COVID-19 in LTCFs, specifically relating to 2023 onwards, are limited, it has been well established in the international literature that those residing in these facilities are at increased risk of severe COVID-19 for a variety of reasons.[106-109] Residents of LTCFs are more likely to be of older age and, as reported in Sections 3.3 and 3.4, COVID-19 continues to be associated with a disproportionately higher morbidity and mortality in older adults.[110] Those living in LTCFs are also likely living with multiple chronic conditions such as cardiovascular disease, hypertension, and diabetes, thereby rendering them more susceptible to severe disease.[111] Additionally, there is an increased risk of disease transmission in these settings due to the congregation of residents and movement of health and social care professionals and visitors.[112] All of which can make the management of COVID-19 in such settings challenging.

During the 2023-2024 respiratory virus season in the US, the SARS-CoV-2 infection rate peaked at 133.8 per 10,000 nursing home residents. While this was lower than the peaks observed for the previous three seasons, it was reported that SARS-CoV-2 infection continued to cause substantial morbidity among these residents during this season. For example, COVID-19-related hospital admissions among this population group peaked at 7.1 per 10,000 residents versus a peak weekly rate of 0.87 per 10,000 among all US adults aged 70 years and older. While nursing home data cannot be directly compared with data for the general population (due to methodological and population differences), the increased risk of COVID-19-related hospital admission among nursing home residents in the US is still evident.[113] More recent data from the Nursing Home Data Dashboard show that, while there is still considerable burden in this population group, it has fallen. During the 2024-2025 and 2025-2026 seasons, the SARS-CoV-2 infection rate peaked at 717.8 and 448.6 per 100,000 nursing home residents, respectively, in the US.[114]

Immunocompromise

A systematic review of data published between January 2022 and March 2024 reported a significantly increased risk of mortality, hospital admission, ICU admission and any combination of these outcomes (termed the "combined outcome") in those with immunocompromising conditions (defined as autoimmune diseases, cancer, liver disease, renal diseases, unspecified immunocompromising conditions, or transplant patients) when compared with those who were not immunocompromised. The highest risk of mortality, hospital admission and the combined outcome was observed in transplant recipients (pooled relative risks (RR) were 6.78 (95% confidence interval (CI): 4.41 to 10.43), 6.75, (95% CI: 3.41 to 13.37) and 8.65, (95% CI: 4.01 to 18.65), respectively). However, it should be noted that, in relation to mortality data, statistical heterogeneity ranged from considerable to substantial for all immunocompromising conditions and publication bias was present in the renal disease and transplant groups. In relation to hospital admission data, statistical heterogeneity was considerable (that is, greater than 90%) across all immunocompromising conditions. While publication bias was not detected in any of the groups, its presence could not be assessed in the studies of people with autoimmune diseases or transplant recipients due to a small number of studies.[115]

Participants with unspecified immunocompromising conditions had the highest risk of ICU admission (RR 3.38, 95% CI: 2.37 to 4.83) when compared with participants without the respective immunocompromising conditions or the general population. Statistical heterogeneity ranged from substantial to considerable across all immunocompromising conditions, and while publication bias was not detected for the studies of people with renal disease, it could not be assessed for other conditions due to a small number of studies.[115]

Underlying medical conditions

While there were limited Irish data on the burden of COVID-19 in those with underlying medical conditions, HPSC data showed that on average, more than 90% of all notified ICU admissions were in those with one or more underlying medical condition (see Section 3.4.1). This is consistent with what has been reported internationally.

In the same 2025 systematic review referred to above,[115] the risk of severe COVID-19 outcomes was higher in individuals with underlying medical conditions compared with those without, during the Omicron era.[116] The authors reported that the risk of mortality, hospital admission and the "combined outcome" (defined as the presence of any of the following outcomes: mortality, hospital admission or ICU admission) was higher in those with cerebrovascular disease, chronic obstructive pulmonary disease, diabetes, respiratory diseases, heart disease, and heart failure. The pooled RR ranged from 1.27 (95% CI: 1.17 to 1.38), for heart disease and hospital

admission, to 1.78 (95% CI: 1.46 to 2.16), for heart failure and mortality. Additionally, the presence of diabetes and obesity were associated with an increased ICU admission risk (RR 1.20 (95% CI: 1.04 to 1.38) and RR 1.32 (95% CI: 1.11 to 1.57), respectively).[116] In relation to mortality data, statistical heterogeneity was considerable in all analyses except among those with heart failure and hypertension (which had substantial heterogeneity), and publication bias was only evident for studies of individuals with diabetes. In relation to hospital admission data, statistical heterogeneity was substantial or considerable for seven out of nine comorbidities. Publication bias could only be assessed in the studies of those with diabetes due to the small number of studies in the other groups; no publication bias was found. Results of all sensitivity analyses for mortality and hospital admission data had the same direction of effect and degree of significance as the main analysis. Statistical heterogeneity ranged from not important to considerable across the analyses for the outcome admission to ICU. Publication bias was only assessed in the groups with diabetes and heart disease due to the small number of studies in other groups; no publication bias was found. Although four sensitivity analyses resulted in loss or gain of significance when compared with the main analysis for risk of ICU admission, the direction of effect (that is, an increased risk of ICU admission) remained the same.[116]

A 2024 systematic review examined the risk of COVID-19-related morbidity and mortality in those with multimorbidity (the presence of two or more long-term conditions).[117] In this review, data published from 2022 to 2023 showed that multimorbidity was associated with increased mortality (RR: 2.61 (95% CI: 2.27 to 3.0)), hospital admission (RR: 2.4 (95% CI: 1.92 to 2.99)), severe disease (RR: 2.61 (95% CI 1.92 to 3.54)), ICU admission (RR: 1.22 (95% CI 1.07 to 1.39)) and mechanical ventilation (RR: 1.83 (95% CI 1.18 to 2.84)), compared with those without.[117] Of note, pooled RRs for adverse outcomes were higher in studies comprising children and young people with multimorbidity when compared to studies involving people of all age groups. The authors concluded that this finding may suggest that increased risk is more likely to be associated with extremes of age (that is, the very young and very old) in those with multimorbidity rather than increasing age.[117]

A large US observational cohort study of adults with laboratory-confirmed COVID-19 reported on the risks of severe clinical outcomes associated with the Omicron variant SARS-CoV-2 infection. Data from July to November 2021 and December 2021 to January 2022 showed that the mean number of SARS-CoV-2 infections per day was substantially higher during the Omicron period (48,101 infections in a 21-day period or 2,291.7 infections per day) versus the Delta period (69,977 infections during a 147-day period or 476.0 infections per day).[118] Despite this, data showed that

those infected during the Omicron era were less likely to experience severe clinical outcomes such as hospital admission and death compared to those affected during the Delta era. For those that were admitted to hospital with COVID-19 during the Omicron era, they were significantly less likely to require high-intensity oxygen support or inpatient treatment when compared to those admitted during the Delta period. The risk factors for developing severe COVID-19 were increasing age, overall comorbidity score, and certain comorbidities (such as diabetes, atherosclerotic cardiovascular disease and obesity), and these remained similar across both time periods.[118]

Pregnancy

SARS-CoV-2 infection has been associated with an increased risk of complications (such as, hospitalisation, ICU admission, and mechanical ventilation) in pregnant women. This was particularly evident during the Alpha and Delta phases of the pandemic, but has decreased in the post-Omicron era.[119] Surveillance data from the UK Health Security Agency (from August 2022 to February 2024) showed that, while the rate of COVID-related hospital admission during the third trimester was 120 per 100,000 pregnancies, the reported rate of severe hospital admissions was low (0.8 per 100,000; n=4) and there were no ICU admissions or deaths reported. Although admission rates were relatively high when compared to non-pregnant women, the mean length of stay was low (two days), with the suggestion that this may indicate a low threshold for hospital admission during pregnancy.[120]

In a systematic review (which included data up to March 2023) of the prevalence of pregnancy loss in pregnant women with confirmed SARS-CoV-2 infection compared to those without, the authors found no evidence of an association between SARS-CoV-2 infection and miscarriage (odds ratio (OR) 1.10, 95% CI: 0.81 to 1.48). Miscarriage occurred in 9.9% (95% CI: 6.2 to 14.0%) and 1.2% (95% CI: 0.3 to 2.4%) of women with SARS CoV-2 infection in their first and second trimesters, respectively. These rates corresponded to those expected in women without SARS-CoV-2 infection.[121]

In 2023, HPSC data (provided to NIAC to inform their updated recommendations on COVID-19 vaccination) showed that no pregnant or postpartum women were admitted to ICU due to COVID-19. In 2024, two pregnant women and one postpartum woman were admitted to ICU due to COVID-19 with relatively short lengths of stay (ranging from one to three days). Of the three women admitted to ICU in 2024, none had underlying medical conditions. Regarding COVID-19 vaccination status, two had no record of vaccination, and one had a last documented vaccination more than 2.5 years prior to admission.[8] The risk of severe COVID-19 outcomes in pregnant women appears to be reduced during the more recent phases

of the pandemic and while vaccination remains safe in pregnancy, the benefits are now less pronounced than they were previously. As such, NIAC no longer routinely recommends a COVID-19 vaccine dose once in each pregnancy. However, NIAC still recommends that pregnant adolescents and adults with immunocompromise and or other medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death should receive one COVID-19 vaccine dose in each pregnancy.[8]

Healthcare workers

Prevalence of COVID-19 in Irish Healthcare Workers (PRECISE) is a series of multicentre seroprevalence studies among healthcare workers in two Irish hospital sites (Galway and Dublin).[122] Adult healthcare workers were invited and enrolled in the study from November to December 2022 and followed until September 2023. In total, 1,260 participants enrolled in the study (equating to a participation rate of 13.8%), of which 4.3% (n=54) were unvaccinated. During the study period, 274 participants (21.7%) reported incident SARS-CoV-2 infections. There was a peak in the number of infections reported in December 2023, reflecting the national epidemiology of SARS-CoV-2 infection at that time. More than half (60.6%) of the incident infections were asymptomatic and no participant required admission to hospital or supplemental oxygen support during the study period. Having at least one underlying risk factor for developing severe SARS-CoV-2 infection was associated with an increased chance of incident infection (adjusted OR (aOR) 1.67, 95% CI: 1.04 to 2.65). The probability of incident infection was higher in those whose last infection was more than 180 days previously, compared with those who had been infected within 180 days (aOR 1.86, 95% CI: 1.24 to 2.84). However, there was no association between reporting an incident infection and time since last COVID-19 vaccination.[122]

Healthcare workers may experience an increased risk of SARS-CoV-2 infection due to their close proximity to infected patients and exposure to undiagnosed or subclinical infectious cases.[123] However, data relating to the epidemiology of COVID-19 in healthcare workers specific to the Omicron variant are lacking. For example, in a systematic review and meta-analysis of SARS-CoV-2 infection rates and associated risk factors in healthcare workers, eligible studies were published between December 2019 and February 2024 but included studies only included data published up to December 2021. The reported global SARS-CoV-2 infection rate was 11% (95% CI: 9% to 13%) among 283,932 healthcare workers. However, the majority of included studies (55/63) were conducted when the ancestral SARS-CoV-2 strain was circulating, and no data relating to the Omicron variant were included.[124]

More recent analyses have shown that SARS-CoV-2 has continued to constitute a considerable burden in healthcare workers. In a cohort study of 8,205 healthcare workers (followed from March 2020 through January 2023) in Italy, 64% incurred at least one SARS-CoV-2 infection. Almost all (99.1%) reinfections occurred after 30 November 2021. Of the 1,091 reinfections reported, 63% followed a pre-Omicron primary event versus 37% that followed an Omicron event. Regardless of when the primary SARS-CoV-2 infection occurred, the risk of reinfection decreased with increased doses of COVID-19 vaccines, being lowest after the second booster.[125] In a study of healthcare workers in Quebec, of the 37,732 presumed BA.2 cases (a subtype of the SARS-CoV-2 Omicron variant) included in the analysis, pre-Omicron primary infection was associated with a 38% reduction in BA.2 infection risk.[126]

3.4.4 Long COVID

While the focus of this HTA is not specifically long COVID (also known as post-COVID condition), it is acknowledged that long COVID may be an outcome of acute SARS-CoV-2 infection for some individuals, thus it contributes to the burden of COVID-19 in Ireland. As highlighted in Section 2.2.2, the World Health Organization (WHO) define post-COVID condition as "the continuation or development of new symptoms three months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least two months with no other explanation."[29] However, there continues to be a lack of consensus on the naming and definition of this condition internationally. Additionally, there is a diversity of symptoms associated with long COVID, with more than 200 symptoms reported across 10 organ systems.[127] Moreover, the severity of symptoms and whether they are continuous or relapsing-remitting in nature adds further to the uncertainty surrounding the pathology of long COVID.[128] For example, the definition of long COVID lacks a minimum level of symptom severity and therefore, someone with a single mild symptom contributes as much to an estimate of prevalence as someone with multiple severe symptoms. As such, the interpretation of long COVID epidemiological studies is complicated and it is difficult to ascertain the true prevalence of the condition since study populations exhibit differing inclusion criteria, participant demographics and diagnostic criteria.[129]

Reported estimates on the prevalence of long COVID following acute infection have ranged from 8% (in vaccinated individuals) to 85% (in unvaccinated individuals who were admitted to hospital).[129] In a 2023 systematic review of the prevalence and long-term health effects of long COVID, a pooled prevalence of 45% was reported among COVID-19 survivors experiencing at least one unresolved symptom, regardless of hospitalisation status.[130] The authors noted several limitations to their findings, (namely, a wide range of follow-up periods from 'more than 28 days' to 387 days, the lack of control and or comparator groups in the majority (89%) of included

studies, and the absence of an assessment of the impact of vaccination on long COVID). Consequently, this reported prevalence of long COVID has been contested,[131] especially in light of estimates from the WHO which suggest a long COVID prevalence of 10% to 22%.[29] Estimates from a 2022 systematic analysis that included data for 1.2 million individuals from 22 countries suggested that 6.2% (95% CI: 2.4%-13.3%) of individuals with symptomatic SARS-CoV-2 infection experienced at least one of three long COVID symptom clusters at three months post infection, with a significantly higher risk in those who required hospitalisation or admission to ICU during the acute phase of their illness.[132] Other factors associated with an increased risk of long COVID included presence of certain comorbidities, age over 40 years and female sex, while risk was noted to be lower in those who had received prior vaccination.[133] In an international review of the epidemiology of long COVID, published by HIQA in 2023, which included data from over 50 primary research studies and four international registry documents, HIQA found that prevalence rates varied considerably across the studies. It was noted that much of this variation may have been due to differences in reporting methods and population demographics within studies. In studies based on self-reported data, estimates for the prevalence of long COVID in the general population ranged from 15% to 53%. While prevalence estimates were highest in those with a history of severe COVID-19 illness, long COVID was reported across all populations and age groups.[134]

The Follow-up After Disease Acquisition (FADA) Survey was a retrospective cohort study of a community-based sample residing in the HSE Dublin and Midlands health region. The aim of the FADA survey was to estimate the prevalence of long COVID, describe the symptoms, severity and duration of long COVID, investigate potential factors that may predispose or protect against long COVID, and describe the healthcare utilisation and preferences of those with ongoing or resolved long COVID.[128] The prevalence of long COVID reported in the survey was 16%. However, the response rate on the survey was low (9.6%) and the published results of the survey were not limited to those who had received a clinical diagnosis of long COVID, but also included individuals who, having read a definition of long COVID, reported themselves as having long COVID. Additionally, the survey only included individuals who had a confirmed SARS-CoV-2 infection prior to February 2022. This is important because from late November 2021, Omicron began to emerge as the dominant COVID-19 variant globally, causing less severe disease on average than the previous Delta variant.[135] Given these limitations, it is considered that the FADA study does not provide a reliable estimate of the prevalence of long COVID in Ireland in the Omicron era. More recently, the UK Office of National Statistics estimated that the prevalence of long COVID symptoms 12 weeks or more after acute COVID-19 infection in a large sample of adults and children (from England and Scotland in February and March 2024) was 1.8%. This figure increased to 3.3%

when people with symptoms lasting from 4 to 12 weeks were included.[136] In the absence of a reliable estimate for Ireland, it was considered that the prevalence of long COVID in Ireland is likely similar to the 1.8% observed in the UK.[137]

It is acknowledged that long COVID can have a considerable impact on an individual's quality of life, their ability to work and daily functioning.[128] In an Irish cohort of 988 participants, 43% and 33% of participants reported that long COVID symptoms had a moderate or severe impact on their general well-being, respectively. More specifically, the disease caused a reported moderate or severe limitation in their ability to carry out their usual activities (as reported by 48% of participants), impaired mobility (as reported by 27% of participants), a moderate or higher level of pain (as reported by 44% of participants), and a moderate or higher level of anxiety or depression (as reported by 33% of participants) reporting.[138] These findings are also reflected in the international literature.[139, 140]

There is some evidence of a potential association between COVID-19 infection and the development of post-viral postural orthostatic tachycardia syndrome (POTS). An interrupted time series analysis on the incidence of POTS in US patients diagnosed from January 2018 to June 2024 demonstrated a significant increase in the incidence of such diagnoses following the COVID-19 pandemic.[141] Long COVID shares several overlapping symptoms with POTS, such as fatigue, exercise intolerance, and orthostatic intolerance; additionally, a significant number of long COVID patients exhibit POTS-like symptoms.[141] Further research is warranted to explore the mechanisms linking COVID-19 to POTS. It is noted that the RECOVER-AUTONOMIC study is currently ongoing, this study is examining the benefits and risks of three different interventions namely, pharmacotherapy with intravenous immunoglobulin, pharmacotherapy with ivabradine and non-pharmacologic care, for the treatment of POTS in long COVID.[142]

In a study that consisted of individuals with long COVID (recruited from a long COVID clinic at an Irish hospital) and individuals who did not develop long-term symptoms following COVID-19 infection, online survey results (for 122 participants) indicated a significant difference between groups relating to perceived immune status, perceived cognitive function, depression scores, and fatigue. Those within the long COVID group reported lower immune status (self-reported), more cognitive difficulties, and higher levels of depression and fatigue. Regression analysis in the same group indicated that immune status and depression significantly contributed to variance in subjective cognitive functioning. The association between self-reported immune status and cognitive functioning scores remained significant following adjustment for depression, fatigue, and other related covariates such as body mass index.[143]

3.5 Size of the target population in Ireland

As described in Chapter 2, in May 2025, NIAC updated its COVID-19 vaccination recommendations.[8]

The population groups identified in the NIAC recommendations and therefore of interest to this HTA are:

- twice yearly vaccination for those aged
  - 80 years and older
  - 18 to 79 years living in LTCFs for older adults
  - six months and older with immunocompromise associated with a suboptimal response to vaccination
- once yearly vaccination for those aged
  - 60 to 79 years
  - six months to 59 years with underlying medical conditions
- access to vaccination for
  - healthcare workers
  - pregnant adolescents and adults
  - those aged 18 to 59 years in the general population.

The estimated size of each population group of interest is described in this section and summarised in Table 3.13. Data sources included the CSO's reports and population projections, the HSE's Structured Chronic Disease Management (CDM)Treatment Programme in General Practice, the Healthcare Pricing Office's perinatal statistics report, communications received from expert advisors, the HSE's Primary Care Reimbursement Service (PCRS) and Economic and Social Research (ESRI) projections. Although an attempt has been made to estimate the size of each population group, it is noted that some individuals will fall into more than one category. For example, an 80-year-old living with immunocompromise associated with a suboptimal response to vaccination would technically fall into two of the specified population groups outlined above. Since it is not possible to account for all instances where this may be the case, the estimates below reflect each distinct population group, acknowledging that some individuals will fall into more than one group.

3.5.1 Target population estimates by age group

Population estimates from the CSO indicate that there were 208,500 people aged 80 years and older living in Ireland in 2025, representing a 5.2% increase on estimates from the previous year (when there were an estimated 198,100 people aged 80 years and older living in Ireland). The cohort aged 60 to 79 years has also increased from 2024 to 2025; reported CSO estimates for this population group were 930,400

and 954,300, respectively (representing a 2.6% increase). When considering the total cohort aged 60 years and older, those aged 60 to 64 years represent the largest subgroup, with CSO estimates indicating there were 301,600 people aged 60 to 64 years living in Ireland in 2025. However, when comparing the reported estimates for 2024 and 2025, data (disaggregated by five-year age band) showed that the highest increase observed among those aged 60 years and older was in the subgroup aged 85 years and older (5.3%), with the size of this subgroup increasing from 91,200 in 2024 to 96,000 in 2025.[144]

Based on Census 2022 data, population projections from the CSO indicate that there were 3,050,400 people aged 18 to 59 years living in Ireland in 2025.[145]

3.5.2 Target population estimates by risk group

Those aged 18 to 79 years living in long-term care facilities for older adults

According to the ESRI report published in 2025, there was a total of 33,324 beds (29,579 long-stay beds and 3,745 short-stay beds) in LTCFs in 2022. The report estimated that there were over 29,650 residents across these beds, with the majority (96%, n=28,394) aged 65 years and older.[146] The ESRI report does not report the proportion of residents that are aged 80 years and older, but in a survey of 100 registered private and voluntary nursing homes in Ireland, respondents reported that 81.6% of residents were aged 76 years and older. According to the ESRI report, the median age of nursing home care residents in Ireland is projected to rise from 85 years in 2022 to 88 years in 2040.[147] The ESRI report does not include disaggregated data for those aged less than 65 years; however, a 2024 Ombudsman report suggests that 85% of those aged less than 65 years and living in residential care are aged between 50 and 64 years.[148] The HPSC report annual COVID-19 vaccination uptake data for those living LTCFs (see Section 3.7.2). The denominators used in these reports were 40,000 (in the autumn/winter 2024-2025 report)[149] and 32,000 (in the spring 2025[150] and autumn 2025[151] reports). The denominator used in the autumn/winter 2024-2025 report was based on the maximum bed capacity of all LTCFs for older adults and people with disabilities as recorded in the HSE health service directory as of June 2024. In the spring and autumn 2025 reports, the denominator was revised based on the maximum bed capacity of all LTCFs for older adults (as recorded on the HSE health service directory in April 2025), that is to exclude the approximately 8,000 residents of disability-based facilities in the denominator count. This aligns with the cohort identified in the NIAC recommendations, which is specific to those living in a LTCF for older adults. Using the information reported above and UK data, an estimated 74% of LTCF residents are aged 80 years and older; this would mean that 26% of

the total 32,000 beds are occupied by those aged 18 to 79 years, equating to an estimated population of 8,320 residents .[152]

Those aged six months and older living with immunocompromise

There is no national registry in Ireland tracking those living with immunocompromise, and as such the size of this population is not explicitly reported. There are several difficulties associated with estimating the prevalence of immunocompromise internationally. For example, an individual's immunocompromised status is often a secondary clinical factor related to a reported primary diagnosis or medication. There is also widespread variation in what constitutes immunocompromise and clinical definitions can vary between different sources.[153] In their most recent COVID-19 vaccination uptake report[151] (see Section 3.7.3), the HPSC used a figure of 66,203 as an estimate of the size of the population living with immunocompromise in Ireland (obtained from the HSE National Vaccination Programmes – Access and Integration database on 10 October 2025). It is unclear if this figure is limited to those living with immunocompromise associated with a suboptimal response to vaccination (for whom twice yearly vaccination is recommended) or if it also includes those with less severe immunocompromise or who mount an adequate response to vaccination (for whom once yearly vaccination may be recommended). As such, this figure of 66,203 may be an overestimate.

Those aged six months to 59 years living with underlying medical conditions

Medical conditions associated with higher risk of severe COVID-19 include, but are not limited to, cancer, chronic heart disease, chronic kidney disease, chronic liver disease, chronic neurological disease, chronic respiratory disease, diabetes and other metabolic disorders, serious mental health conditions, children and adults with Down syndrome and children with moderate to severe neurodevelopmental disorders.[9]

The HSE's Structured CDM Treatment Programme in General Practice[137] may provide an indication of the size of the population aged 18 years and older with certain chronic conditions. The CDM Treatment Programme was launched in January 2020 and initially rolled out to patients aged 70 years and older. It was extended to those aged 65 years and older commencing from January 2021 and subsequently to all adults aged 18 years and older from January 2022. The CDM Treatment Programme is open to all adults who have a General Medical Services (GMS), GP Visit or Health Amendment Act card who are registered with a GP that accepts these cards and who have been diagnosed with at least one of the following chronic diseases: type 2 diabetes mellitus, ischaemic heart disease, atrial fibrillation, heart

failure, cerebrovascular accident, transient ischaemic attack, chronic obstructive pulmonary disease (COPD) or asthma. Of note, everyone aged 70 years and older is eligible to register for a GP Visit card, whereas for other age groups, eligibility for both GMS and GP Visit cards is based on meeting certain criteria and or means-testing.

Table 3.12 presents the number of unique individuals aged 18 years and older that enrolled in the programme from 1 January 2020 to 31 December 2025.[137] As of 31 December 2025, there were an estimated 501,793 unique individuals enrolled in the programme.[137]

Table 3.12 Population enrolled in the HSE's Structured Chronic Disease Management Treatment Programme in General Practice from 1 January 2020 to 31 December 2025*

Age group (years)	Enrolled (n)
Total ≥18	501,793
18-24	6,246
25-34	9,808
35-44	19,875
45-54	42,189
55-64	68,744
65-69	46,282
70-74	87,815
75-79	93,718
80-84	69,640
85-89	40,098
≥90	17,378

*Figures provided by personal communication.
Source: The Structured Chronic Disease Management Treatment Programme in General Practice

While these data provide some information on the number of adults in Ireland living with underlying medical conditions, there are a number of caveats that are worth highlighting. Firstly, it is noted that individuals are not eligible for the programme if they reside in LTCFs. Secondly, once enrolled in the programme, individuals are currently not removed from programme records upon death or entering long-term care. Thirdly, these data are limited to individuals diagnosed with at least one of the specified chronic diseases (namely, type 2 diabetes mellitus, ischaemic heart disease, atrial fibrillation, heart failure, cerebrovascular accident, transient ischaemic attack, chronic obstructive pulmonary disease and asthma) and who have a GMS or a GP Visit card and are registered with a participating GP service. As such, they underrepresent the total number of individuals aged 18 years and older with one of these chronic diseases. Fourthly, there is incomplete overlap between the medical conditions that put individuals at increased risk of severe COVID-19 outlined in the NIAC recommendations and those included in the CDM Treatment Programme.

Specifically, these include cancer, chronic kidney disease, chronic liver disease, chronic neurological disease, serious mental health conditions and Down syndrome. These individuals are not currently eligible for the HSE's CDM Treatment Programme unless they have also been diagnosed with at least one of the specified conditions.

As part of its primary care schemes, the HSE also operates a non-means tested Long-Term Illness (LTI) Scheme, which provides free access to certain drugs, medicines and medical appliances for 16 specific conditions.[154] PCRS data for December 2025 indicate that there were 204,497 eligible individuals for the LTI Scheme.[155] Disaggregated data are not reported by condition or by age, so while these data would include individuals with relevant conditions not otherwise identified, such as certain chronic neurological conditions (cerebral palsy, epilepsy, muscular dystrophy, parkinsonism and spina bifida), and certain cancers (acute leukaemia), there would also be overlap with the CDM scheme (for example, diabetes mellitus) and also data relating to individuals not identified as being at increased risk (haemophilia, hydrocephalus, intellectual disability). However, a 2021 review of the LTI scheme suggests that claimants with diabetes and epilepsy account for 90% of all claimants, with diabetes claimants alone accounting for approximately 150,000 of the 195,000 scheme claimants in that year.[156] Parkinsonism and multiple sclerosis were noted as the next two largest patient cohorts. Fifty per cent of LTI claimants additionally had medical card eligibility. These data illustrate the complexity of accurately estimating the size of this population.

Pregnant adolescents and adults

There is no national maternity register, so it is not possible to directly estimate the annual number of pregnant adolescents and adults. Data are available in relation to the number of registered live births each year, which are reported quarterly by the CSO for Vital Statistics. These data may provide a reasonable proxy for the annual number of pregnancies. The number of registered births in 2024 was 54,062. The number of births has declined in recent decades, with a 19.9% decrease noted in the 10 years since 2014 (67,462). It is noted that yearly summary Vital Statistics reports provide figures on the number of births and registered in a calendar year. However, not all life events registered in a year occurred in that particular year. For example, of the 54,062 births registered in 2024, 91.3% (approximately n=49,400) occurred in 2024 and the remainder occurred in 2023.[157] Data are also available from the National Perinatal Reporting System (NPRS), which collects and reports data on perinatal events in Ireland. These data also include details of the number of maternities reported to the NPRS. In 2023, a total of 53,732 maternities were reported to NPRS resulting in 54,469 births (live, stillbirths and early neonatal

deaths).[158] This compares with the 54,526 registered births in 2023 reported in the CSO's vital statistics annual report.[159]

Healthcare workers

According to the CSO's Labour Force Survey, there were approximately 382,500 people working in Human Health and Social Work Activities in Q4, 2024.[160] According to National Healthcare Statistics data, it was estimated that, in 2024, there were 145,103 practicing healthcare professionals in Ireland (that is, 20,961 physicians, 4,389 midwives, 76,558 nurses, 27,995 carers, 2,560 dentists, 6,250 pharmacists and 6,390 physiotherapists).[161] In 2025, the Department of Health published a paper on Ireland's Future Health and Social Care Workforce. According to regulator data, there were 157,666 people in the health and social care workforce in 2024.[162]

In their COVID-19 vaccination uptake reports[149] (see Section 3.7.6), the HPSC used a denominator of 250,000 as an estimate of the size of the population who are health and care workers (citing the National Immunisation Information System (NIIS) and the Department of Health as the source for this estimate).

Table 3.13 Estimated size of the populations eligible for COVID-19 vaccination

Population eligible for vaccination~	Estimated size (n)	Source
Aged ≥80 years	208,500	Central Statistics Office[144]
Aged 60 to 79 years	954,300	Central Statistics Office[144]
Aged 18 to 79 years living in long-term care facilities for older adults#	8,320	HSE health service directory[150, 151] Office for National Statistics[152]
Aged ≥6 months with immunocompromise associated with a suboptimal immune response	66,203	HSE National Vaccination Programmes – Access and Integration database[151]
Aged 6 months to 59 years with underlying medical conditions*	112,490	Structured Chronic Disease Management Treatment Programme in General Practice[137]
Pregnant adolescents and adults	54,062	Central Statistics Office[157]
Healthcare workers	250,000	NIIS and the Department of Health[149]
Aged 18-59 years in the general population+	2,633,848	Central Statistics Office[145]

Key: NIIS – National Immunisation Information System.
~It is acknowledged that individuals may fall into one or more risk groups eligible for COVID-19 vaccination in Ireland. As such, the figures reported in this table are an overestimate of the size of the total population that could avail of a COVID-19 vaccination either once or twice annually.
#Estimate of the proportion aged 18 to 79 years living in long-term care facilities based on data from the Office for National Statistics, UK.
*Estimate is based on the number of individuals enrolled in the Structured Chronic Disease Management (CDM) Treatment Programme in General Practice up to 31 December 2025 (provided by personal communication). It is acknowledged that the CDM figure does not reflect those aged six months to 17 years and that once enrolled in the programme, individuals are currently not removed from programme records upon death or entering long-term care, so the provided figure may not be accurate.
+Estimate is based on the number of people aged 18 to 59 years living in Ireland in 2025 minus those present in other risk groups.

3.6 Management of COVID-19

SARS-CoV-2 infection is characterised by respiratory and systemic symptoms including fever, cough, wheezing, decreased appetite, sore throat and nasal congestion. In most healthy individuals, symptoms of SARS-CoV-2 infection are mild, self-limiting and typically resolve fully in two weeks.[163] Individuals with mild symptoms may not require treatment or need to see their GP. However, certain individuals have an increased risk of severe disease and may require hospitalisation. These high-risk groups include those living in LTCFs, those with a weakened immune system and those with underlying medical conditions.

For all ages, treatment for COVID-19 is mainly supportive, aiming to ensure adequate oxygenation, ventilation, nutrition, and hydration. Approaches to treatment vary and depend on illness severity.

3.6.1 Treatment of acute COVID-19

Symptom relief

Analgesics such as paracetamol and (if appropriate ibuprofen) are recommended for symptoms with associated pain (such as, acute cough, sinusitis or sore throat).[164-166] The symptoms of cough or bronchitis in those aged one year and older may be relieved by honey for a soothing effect.[164, 165] In adults with an acute cough, over the counter products containing dextromethorphan or guaifenesin may alleviate symptoms.[164] Short-term use of systemic decongestants, topical decongestants or saline preparations for local irrigation may help with symptoms of a blocked nose.[167] Medicated lozenges or anaesthetic sprays can help relieve the pain of a sore throat.[166]

Prescription medicines to treat COVID-19

Medications that have been authorised in the EU for the treatment of COVID-19 are detailed on the EMA website.[168] The following sections describe medications described in the HSE's interim guidance for the management of patients with COVID-19.[169]

Antivirals

Paxlovid® (that is, nirmatrelvir and ritonavir) is an oral antiviral indicated for the treatment of COVID-19 in adults and paediatric patients (aged six years of age and older weighing at least 20 kg) who do not require supplemental oxygen and who are at increased risk for progressing to severe COVID-19.[170] HSE clinical guidance recommends that its use is limited to selected seriously immunocompromised COVID-19 patients,[171] with reimbursement under publicly-funded community drug schemes approved for this purpose.

In Ireland, the PCRS collate data on medications dispensed by community pharmacists through a range of publicly-funded community drug schemes (for example, General Medical Service (GMS), Drugs Payment Scheme (DPS), Long-Term Illness (LTI) and High-Tech). Eligibility and co-payments for these schemes differ. The PCRS data do not capture prescriptions that are paid for privately, nor do they include claims which are under the DPS monthly threshold amount (May 2026: €80 per calendar month per family). Between April 2022 and February 2025, eligible patients could access Paxlovid® free at-the-point of care under a unique arrangement; stock was procured and paid for by the HSE, while a High-Tech

patient care fee was paid to the dispensing pharmacy. In February 2025, Paxlovid® was added to the reimbursement list[172] (€952.92 per 30-tablet pack) and made available to eligible individuals through the HSE community drug schemes.

PCRS usage and expenditure data relating to Paxlovid® (that is, J05AE30) for adults aged 18 years and older were obtained for 2023, 2024 and 2025. Summary data by calendar year across all schemes (GMS, DPS, LTI and High-Tech) are presented in Table 3.14. The annual number of claims has declined from 3,086 in 2023 to 1,319 in 2025. Reported cost data for 2023 and 2024 are limited to patient care fees and exclude the cost of stock. In 2025, the total cost (fees and stock) was almost €1.2 million across 1,316 unique individuals.

Table 3.14 Estimated Paxlovid® usage for adults aged 18 years and older through the HSE community drug schemes, by calendar year

Calendar year	Number of claims* (n)	Cost~ (€)
2023	3,086	68,325
2024	2,834	48,756
2025	1,319	1,192,039

*Claims include all claims to the PCRS through the GMS, DPS, LTI and High-Tech schemes, comprising 1,319 claims for 1,316 unique individuals in 2025.
~Costs for 2023 and 2024 are limited to the patient care fee paid to dispensing pharmacy (that is, exclude stock cost); cost for 2025 includes cost of stock and all fees paid through the PCRS under the GMS, LTI, DPS and High-Tech Schemes.
Source: HSE Primary care Reimbursement Service (PCRS).

Alternative antiviral treatments included remdesivir (Veklury®) and sotrovimab (Xevudy®), both of which were authorised for administration by intravenous infusion in a hospital setting to those for whom Paxlovid® is contraindicated or unsuitable.[173] The HSE has issued guidance for remdesivir, detailing the priority groups for whom treatment is reimbursed.[174] Of note, the marketing authorisation for sotrovimab was withdrawn on 18 February 2026 (by the European Commission) at the request of the marketing authorisation holder who cited commercial reasons for its decision to permanently discontinue the marketing of the product.[175]

Corticosteroids

Corticosteroids such as dexamethasone (or hydrocortisone or prednisolone if dexamethasone is contraindicated) may be used to treat COVID-19 in patients who need supplemental oxygen or have a level of hypoxia that needs supplemental oxygen but who are unable to receive or tolerate it.[176]

Venous thromboembolism prophylaxis

Being hospitalised with COVID-19 is associated with a high risk of venous thromboembolism. Unless contraindicated, the HSE guidelines recommend provision of appropriate prophylaxis for all patients with COVID-19 admitted to hospital.

Other medications

Tocilizumab (RoActemra®) is a monoclonal antibody used to treat rheumatoid arthritis which is also indicated for the treatment COVID-19 in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation.[177] It is an immunosuppressant that works by inhibiting the pro-inflammatory cytokine interleukin-6.[177] Baricitinib (Olumiant®) is another immunosuppressant medication[178] that has been used off-label in the UK in those with COVID-19 who need supplemental oxygen and are having, or have completed, a course of corticosteroids;[176] however, it is unclear if has also been used in Ireland purpose. Both of these agents should only be used when there is no evidence of infection (other than SARS-CoV-2) that might be worsened by their use.[176]

In considering long COVID specifically, there are currently no treatments authorised for long COVID. Instead, management is typically tailored to the symptoms experienced by that individual. For example, clinicians may use a combination of pharmacological and non-pharmacological interventions for which there is an evidence base to support evidence of effectiveness and safety for patients experiencing COVID-19-associated fatigue and post-exertional dyspnoea, postural orthostatic tachycardia syndrome and mast cell disorder.[30] While it has been reported that the off-label use of metformin (when taken during or shortly after acute COVID-19 infection) may reduce the risk of developing long COVID, causality has not been confirmed.[179-181] Moreover, data supporting the use of metformin as a treatment for those already diagnosed with long COVID are lacking.

Antibiotics

Antibiotics should only be used for those with COVID-19 when there is a clinical suspicion of additional bacterial co-infection.[28, 176]

Respiratory support in secondary care

If COVID-19-related hypoxia is the cause of breathlessness, supplemental oxygen therapy in secondary care may be required.[28, 166] For severe cases, advanced respiratory support, that is, continuous positive airway pressure, high-flow nasal oxygen or mechanical ventilation, may be necessary.[176]

3.6.2 Rehabilitation following acute COVID-19-related hospital admission

Access to post-acute inpatient rehabilitation is an essential component of a functional health system. When patients are delayed in accessing such care it can result in poorer outcomes and increased disability for the patient, as well as inefficiencies in terms of health service provision.[182] A systematic review published in 2023 concluded that comprehensive pulmonary rehabilitation approaches may benefit shortness of breath and exercise tolerance in adults following COVID-19. It noted that impairment of functioning (as a result of COVID-19) can be diverse and the involvement of a multidisciplinary team and an individualised rehabilitation plan is desirable.[183]

Following acute COVID-19-related hospital admission, some individuals exhibit functional loss at the time of discharge compared to their pre-admission status. This is particularly noted in older adults and among those with prolonged admission to ICUs. Considering specifically older adults, some may require new or additional home support services, residential care or access to rehabilitation as a result of this functional impairment. Functional impairment is not specific to COVID-19-related hospital admission, as evidenced by the 2012 HSE's Specialist Geriatric Services Model of Care report, wherein 35% of those aged 70 years showed some functional loss at the time of discharge compared to their pre-admission status; this figure increased to 65% in those aged 90 years.[184]

There are no national data in terms of the number of individuals provided with post-discharge rehabilitation care or who newly required additional support with activities of daily living and or residential care following an acute COVID-19 related hospital admission. However, as highlighted in Section 3.4.1, HIPE data for 2024 suggest that when considering discharges for which the discharge destination is known, approximately 6% those with a primary diagnosis of COVID-19 and approximately 14% of those with an additional diagnosis of COVID-19 are newly discharged to a post-acute care setting (namely, hospice, a nursing home, convalescent home or long stay accommodation, non-acute hospital, external rehabilitation facility or psychiatric hospital and or unit), with a disproportionate requirement in older adults. In a multicentre European observational cohort study of 831 patients admitted to hospital with COVID-19 (between 27 February and 10 June 2020), 23% of patients had increased care needs at discharge. Pre-admission frailty was strongly associated with the need for an increased level of care at discharge.[185] A 2023 systematic review of clinical outcomes of older adults with COVID-19 (who received multidisciplinary team rehabilitation in the inpatient acute or post-acute hospital setting) found that older adults stayed in rehabilitation units for an average of 19 days (95% confidence interval (CI) 15.88 to 21.79 days).[186]

Inadequate availability of rehabilitation services can result in delayed transfers of care within acute hospitals. The Office of the Comptroller and Auditor General

reported that in 2018, 44% of applicants for the Nursing Home Support Scheme (Fair Deal) were being cared for in acute hospitals.[187] Moreover, in a HSE report of post-acute inpatient rehabilitation service provision, the reported national average number of non-tertiary beds per Community Health Organisation (CHO) was 23.7 beds per 100,000 population (n=136 beds). Disparity in the distribution of rehabilitation beds across CHOs was also reported, ranging from 6.3 beds per 100,000 population in CHO 8 to 45.2 beds per 100,000 population in CHO 9. The report concluded that its findings on availability of and access to rehabilitation supported the need for further investment in post-acute rehabilitation.[182]

3.6.3 Long COVID management

As noted in Section 2.2.2, COVID-19 may result in a range of persistent symptoms that develop during or after SARS-CoV-2 infection.[188] Known as post-acute COVID-19 or long COVID, it can result in significant cognitive, physical and psychological impairments, which may persist despite resolution of the infection. International data indicate that patients living with long COVID often experience difficulties in accessing appropriate medical care,[189] with diagnostic delays and perceived dismissal by healthcare professionals being commonly reported.[190] While the complexity of long COVID may make it difficult for healthcare professionals and the general public to understand its prognosis, recognition of the patient's lived experience is important so as to avoid further isolation of this patient group.[191] Qualitative research conducted within Irish general practices has indicated that there is strong agreement among GPs and patients on the complexity of managing long COVID and the necessity for holistic and integrated multidisciplinary supports. However, there is a lack of consensus regarding the optimal supports that GPs can refer patients to, with authors advocating for continued research investigating the management of long COVID in general practice.[192]

The HSE established an interim model of care for a national long COVID service, which was first published in September 2021. This model of care proposed a three-pillar approach to care, with support provided across three settings, as appropriate:

- patient-led rehabilitation and support (online support and education platform to support self-management of symptoms at home)
- general assessment, support and rehabilitation (GP and primary care rehabilitation)
- specialist assessment support and rehabilitation (specialist acute hospital clinics supported by primary care health and social care professionals).[163]

Consistent with this approach, a number of COVID clinics have been established by the HSE nationally to provide post-acute and long COVID care. The post-acute clinics are designed to support people in their recovery 4 to 12 weeks after the acute phase of their COVID-19 illness, when the main issues are cardiopulmonary in nature. The long COVID clinics support people beyond 12 weeks, while a number of clinics are established as combination clinics, providing support both to those in the post-acute 4 to 12-week period and the post-12-week period. Additionally, there is a neurology clinic for long COVID located at St James's Hospital which receives referrals from all other clinics. The model of care suggests that all patients admitted to hospital with COVID-19 should be reviewed post discharge, with early review (four to six weeks post discharge) recommended for those with severe disease or who required ICU admission. Patients may also be referred from primary care. At these clinics, patients undergo a comprehensive assessment and a specific care plan is developed for the patient. In some cases, the patient may be discharged following this assessment. Those requiring ongoing specialist service support usually attend the clinic every six months, although a shorter follow-up may occur when necessary and contingent on there being sufficient capacity within the clinic. It is noted that the HSE's model of care for long COVID is under review. UK guidance on the management of long COVID advocates for the use of a multidisciplinary approach to guide rehabilitation. This should include physical, psychological and psychiatric aspects of management.[193] In Ireland, it has been noted that not all post-acute and long COVID care clinics have access to this type of multidisciplinary support.[137]

No centrally collated data are available in relation to the number of patients referred to or who have accessed the HSE long COVID clinics. Data were provided by a number of the clinics to the evaluation team for the purpose of this HTA. An overview of the number of patients using the service in the long COVID clinic at St Vincent's University Hospital, Dublin is provided in Table 3.15 for the period 2023 to 2025. In total, 376 new patients were referred to the clinic over this three-year period, with the number of new referrals decreasing over time. The majority of those attending the clinic each year were returning patients, who comprised over 90% of all patients (new plus returning patients) accessing the clinic in 2025. The median age of those accessing the service was reported to be 47 years and approximately 70% of the population was female.

Table 3.15 Number of patients accessing the HSE long COVID clinic at St Vincent's University Hospital (Dublin), reported by year

Year	New patients (n)	Returning patients (n)	Discharged patients (n)	Waiting list in January (n)	Waiting list in December (n)
2023	219	527	151	149	21
2024	116	669	132	25	2
2025	41	631	107	3	20*

Note: Patients who were discharged might have been referred to the service again by the GP if their symptoms worsened.
*The service was reduced from once weekly to twice monthly during 2025 due a declining number of patients requiring access to the service; however, a once weekly service was resumed in January 2026.

Other long COVID clinics in Ireland have also provided data reflective of a six-month period from August 2025 to February 2026. In Cork, 157 patients are attending the clinic, 44 patients are on the clinic waiting list and 38 patients have been discharged back to their primary care provider. Of those patients attending the clinic, approximately 70% are female and over half are aged between 40 and 60 years. In the long COVID clinic at St James's Hospital (Dublin), 22 new patients have been reviewed at the clinic along with 96 return patients and 14 patients were discharged back to primary care. There was no waiting list at the time and patients could expect to get an appointment within approximately four weeks. In Limerick, 39 new patients were reviewed at the long COVID clinic over the six-month period to February 2026, 10 of which were discharged back to primary care. There are currently 40 patients enrolled at the clinic (of which approximately 83% are female), and there were 26 patients on the waiting list.

As highlighted in Section 3.4.4, one of the aims of the FADA study was to describe the healthcare utilisation and preferences of those with ongoing or resolved long COVID. While the results of the survey supported the overall design of the HSE's Interim Model of Care for long COVID, there was indication of a potential unmet need at the time within primary care services. Of those with long COVID, 42% and 31% reported accessing GP services and information on a website, respectively. While few reported accessing specialist care, some perceived that access to more specialist care would be beneficial.[128]

As each acute SARS-CoV-2 infection carries the risk of developing long COVID, additional SARS-CoV-2 infections may increase the cumulative risk of developing long COVID. However, the evidence of this is not conclusive. One retrospective cohort study in the US of 465,717 eligible children and adolescents from 1 January 2022 to 13 October 2023 found that reinfection was associated with a significantly increased risk of an overall post-acute sequelae of SARS-CoV-2 infection diagnosis (RR 2.08, 95% CI: 1.68 to 2.59) and a range of potentially associated symptoms and

conditions.[194] In comparison, a study which included UK COVID-19 Infection Survey participants who tested positive for SARS-CoV-2 between 1 November 2021 and 8 October 2022 reported that while there remains some risk of new-onset long COVID after a second infection, the per-infection risk was lower than after a first infection for persons aged 16 years and older.[195] In addition a US electronic health record study cohort of over 3 million patients from 1 March 2020 to 1 March 2023 reported that long COVID diagnoses appear to occur more often following initial infection than reinfection in the context of the same COVID-19 variant.[196]

Evidence of COVID-19 vaccines as a treatment for long COVID is lacking.[197] However, as highlighted above, each acute SARS-CoV-2 infection carries the risk of developing long COVID. As such, by reducing the risk of infection, COVID-19 vaccination may reduce the risk of an individual developing long COVID. A rapid review commissioned by the ECDC concluded that in general adult populations of mixed disease severity, vaccination offered an estimated 27% reduction in the risk of developing a post-COVID condition compared to no vaccination. Due to a lack of data, it was not possible to assess this relationship in immunocompromised populations, or children and adolescents. The review also highlighted the ongoing need for further studies that evaluate post-COVID conditions and consistently apply the WHO case definitions.[198] The effectiveness and safety of COVID-19 vaccination in reducing the risk of reinfection and COVID-19 related disease in those with long COVID is discussed in Chapter 4.

In 2023, HIQA published a systematic review of randomised controlled trials of pharmaceutical and non-pharmaceutical interventions to improve long COVID symptoms. Across the included trials, the evidence was found to be limited, with no definitively effective treatments identified. There was evidence of potential short-term improvements from personalised exercise interventions for shortness of breath, fatigue and physical function among some people with long COVID, although it was noted that there is potential for exercise to worsen symptoms in individuals with post-exertional malaise.[199] The evidence for physiotherapy and rehabilitation programmes also suggested potential short-term benefits.[199] Long-term outcomes were not assessed for the interventions in the included studies.

3.7 COVID-19 vaccination uptake rates

In this section, an overview of Irish and international COVID-19 vaccination uptake data is presented. These data are reported by risk group, where available.

The HPSC in Ireland reports COVID-19 vaccination uptake rates by week and respiratory virus season. As noted in Section 4.2, COVID-19 does not exhibit seasonality, but COVID-19 activity and vaccination uptake are reported with

influenza, which does. Vaccination uptake data reported below for Ireland were sourced from the HPSC and supplemented by Irish COVID-19 vaccination uptake data included in reports from the European Centre for Disease Prevention and Control (ECDC). COVID-19 vaccination uptake data (prior to November 2025) reported by the HPSC are based on the National COVID-19 Immunisation System (COVAX), used previously for recording COVID-19 vaccination data for Irish residents. As of November 2025, this system has been renamed the National Immunisation Information System (NIIS), with this system representing the HSE's long-term national system for recording all publicly offered immunisations.[200]

While data are presented as proportions of the total population, it is noted that not all people within these populations were eligible for COVID-19 vaccination at all times (for example, if they have recently had SARS-CoV-2 infection) and when comparing spring and autumn campaigns.[201] Specifically, the target population of older adults for whom vaccination was encouraged in the spring campaign was limited to those aged 80 years and older, those who were immunocompromised or living in a LTCF for older adults, and those aged 70 to 79 years who had not received a COVID-19 vaccine in the preceding 12 months). Recording of variables (such as, risk factors that rendered a person eligible for vaccination through the HSE's COVID-19 vaccination programme) was not always mandatory. Additionally, for individuals with more than one risk factor for a given vaccination event, not all relevant risk factors may not have been recorded.[201]

Under the HSE's COVID-19 vaccination programme, eligible individuals living in the community can access the COVID-19 vaccine either through their general practice or community pharmacy. For individuals residing in LTCFs, the vaccine may be administered by HSE mobile vaccination teams. Table 3.16 provides an overview of the proportion of COVID-19 vaccinations delivered by each vaccinator category, reported by vaccination campaign. Across all campaigns, the highest proportion of doses was delivered in general practice settings (range: 50 to 59%).

Table 3.16 Number and proportion of COVID-19 vaccinations delivered in general practices, community pharmacies and by HSE vaccination teams, reported by vaccination campaign (September 2023 to March 2026)

Vaccination campaign	General practice n (%)	Community pharmacy n (%)	HSE vaccination teams n (%)
Autumn/winter 2023/2024[202]	425,459 (55.8)	267,627 (35.1)	68,622 (9.0)
Spring 2024[203]	80,683 (52.4)	44,961 (29.2)	28,331 (18.4)
Autumn/winter 2024/2025[149]	328,012 (59.3)	174,792 (31.6)	50,336 (9.1)
Spring 2025[150]	44,357 (50.0)	18,098 (20.4)	26,171 (29.5)
Autumn/winter 2025/2026[204]	306,620 (58.8)	172,604 (33.1)	42,238 (8.1)

Source: Health Protection Surveillance Centre.

3.7.1 Older adults

Irish data

HPSC data on the number of COVID-19 vaccine doses and the percentage uptake among those aged 60 years and older are presented in Table 3.17, reported by vaccination campaign and age group.

As noted, certain age bands were not always the target population for the spring campaign, so it is not appropriate to compare uptake between the spring and autumn/winter campaigns when considering the general population aged 60 years and older. Uptake of COVID-19 vaccination has decreased over time. Comparing the three autumn/winter campaigns, uptake decreased from 50.1% to 37.9% in those aged 60 years and older, with the largest drop between the 2023/2024 and 2024/2025 campaigns. Comparing the two spring campaigns in 2024 and 2025, uptake was also noted to decrease from 13.7% to 7.9% in those aged 60 years and older.

Limited data were available by age band among those aged 60 years and older. Where reported, uptake increased with increasing age and was substantially higher in those aged 80 years and older (60.8% to 62.2%) compared with those aged 60 to 79 years (33.2% to 35.6%) based on data for the autumn/winter campaigns (vaccination recommended for everyone aged 60 and older).

Table 3.17 COVID-19 vaccination uptake among older age groups, reported by vaccination campaign (September 2023 to March 2026)

			Autumn/winter 2023-2024[202]		Spring 2024 [203]		Autumn/winter 2024-2025[149]		Spring 2025[150]		Autumn/winter 2025-2026[204]	
Age group (years)		Estimated population* (n)	Doses (n)	Uptake (%)	Doses (n)	Uptake (%)	Doses (n)	Uptake (%)	Doses (n)	Uptake (%)	Doses (n)	Uptake (%)
≥60		1,048,985	525,721	50.1	144,042	13.7	421,400	40.2	83,098	7.9	398,325	37.9
60 to 79		867,958	NR	NR	63,800	7.4†	308,741	35.6	24,715	2.8†	288,251	33.2
	60 to 64	272,670	86,866	31.9	4,358	1.6†	63,248	23.2	2,457	0.9†	NR	NR
	65 to 69	238,144	104,190	43.8	6,798	2.9†	77,704	32.6	3,393	1.4†	NR	NR
	70 to 74	202,884	NR	NR	NR‡	NR‡	85,097	41.9	NR	NR	NR	NR
	75 to 79	154,260	NR	NR	NR‡	NR‡	82,692	53.6	NR	NR	NR	NR
≥80		181,027	NR	NR	80,242	44.3	112,659	62.2	58,383	32.3	110,074	60.8

Key: NR – not reported.

*Census 2022 population used as estimated denominator except where specified otherwise.

†These age groups were not the primary target group of the spring 2024 or spring 2025 vaccination campaigns.

‡This age group were not the primary target group in the spring 2024 vaccination campaign but, following a discussion with a healthcare provider, they could choose to receive a vaccine.

Source: Health Protection Surveillance Centre.

EU/EEA data

The ECDC has published reports on COVID-19 vaccine coverage in EU/EEA countries during the 2023/2024[205] and the 2024/2025[206] vaccination campaigns, based on data reported by the Member States through The European Surveillance System. Table 3.18 provides an overview of the COVID-19 vaccination uptake rates in older adults, reported by age band and country. Reported COVID-19 vaccination uptake rates varied substantially across the included countries in both time periods. For example, the reported uptake rate varied from less than 0.1% to 93.9% in those aged 80 years and older in 2023/2024. In general, within countries, uptake consistently increased with increasing age. Uptake rates were lower in the 2024/2025 vaccination campaign compared with those reported for the 2023/2024 period, with reductions seen across all countries and almost all age groups. Data for Ireland were provided to the ECDC by the HPSC for these age bands and time periods, with a similar pattern of increasing uptake with increasing age and lower overall rates in 2024/2025 compared with 2023/2024.

Table 3.18 COVID-19 vaccination uptake rates (%), reported by age band and country for the 2023/2024 and 2024/2025 vaccination campaigns

	1 September 2023 – 31 July 2024			1 August 2024 - 28 February 2025		
Country	60 to 69 years	70 to 79 years	80 years and older	60 to 69 years	70 to 79 years	80 years and older
Austria	14.6	20.9	24.9	NR	NR	NR
Belgium*	35.6	55.9	64.6	12.6	43.6	47.4
Bulgaria	1.4	2.9	2.6	0.4	2.1	2.0
Cyprus	6.0	16.5	21.5	0.7	3.6	4.5
Czechia	7.0	13.9	16.5	2.3	10.7	13.6
Denmark*	43.8	80.7	88.6	12.8	59.8	64.1
Estonia	8.9	15.0	14.4	2.8	15.3	8.5
Finland*	32.9	64.2	64.1	11.9	60.3	69.7
France*	15.8	32.4	37.5	NR	NR	NR
Greece	7.1	11.7	8.9	0.5	1.7	1.4
Hungary	0.5	1.1	1.3	0.1	0.6	0.9
Iceland	26.6	44.4	46.6	NR	NR	NR
Ireland	38.7	63.7	80.3	13.2	46.1	61.8
Italy	6.0	11.7	15.8	1.1	4.8	7.0
Latvia*	NR	NR	NR	1.3	5.2	5.8
Liechtenstein*	3.4	6.9	11.5	NR	NR	NR
Lithuania*	3.4	6.8	7.6	0.5	1.8	2.3
Luxembourg	14.6	26.8	37.1	0.8	2.8	4.9
Malta	0.8	0.5	1.2	NR	NR	NR
Netherlands†	38.8	63.4	67.4	16.5	58.8	63.3
Norway*	30.3	61.3	61.9	12.1	55.1	60.1
Poland	4.0	8.4	5.7	1.2	1.2	4.2
Portugal	43.5	59.6	63.9	13.6	46.6	56.4
Romania	0.02	0.02	0.03	NR	NR	NR
Slovakia*	1.1	2.0	1.6	NR	NR	NR
Slovenia*	2.8	6.4	8.2	0.7	3.0	4.3
Spain	32.7	52.4	64.4	7.3	27.3	36.9
Sweden*	39.5	72.7	93.9	11.6	62.2	83.5

Key: NR – not reported.

Notes: Croatia and Germany are not listed in the table as no data were reported to the European Centre for Disease Prevention and Control during either time period.

*In some countries, the COVID-19 vaccine was only recommended in people aged 65 years and older (Belgium, Denmark, Finland, France, Latvia, Lithuania, Liechtenstein, Norway, Slovakia, Slovenia, Sweden, and possibly others). For these countries, the vaccination coverage reported under 60 to 69 years should be interpreted with caution.

Source: European Centre for Disease Prevention and Control.

3.7.2 Residents of long-term care facilities

Irish data

The number of COVID-19 vaccine doses and the percentage uptake rates among all residents of LTCFs are presented by age group and vaccination campaign in Table 3.19. During the autumn/winter 2024/2025 vaccination campaign,[149] the estimated uptake was 62.9% (25,156 doses administered to an eligible population of 40,000). During the spring 2025 vaccination campaign, although the reported number of administered doses decreased (24,454 doses), there was an increase in the reported uptake rate (76.4%). This apparent increase in uptake rate was a consequence of a decreased denominator (that is, the eligible population was estimated to be 32,000) as it was no longer considered appropriate to include the approximately 8,000 residents of disability-based facilities, as had been included in the previous campaign.[150]

Those ordinarily resident in Ireland and in need of accommodation in a LTCF can apply to the Nursing Homes Support Scheme (Fair Deal).[207] The scheme is managed by the HSE and those participating pay a certain amount towards the cost of their care and the HSE pays the balance. This care is provided by approved private, voluntary or public LTCFs for older adults.[207] In January 2025, the HPSC reported that the COVID-19 vaccination uptake among those living in LTCFs was 80% for the spring 2024 vaccination campaign based on 23,268 residents who availed of the Fair Deal Scheme across 528 LTCFs.[208] During the autumn/winter 2024-2025 vaccination campaign,[149] the percentage uptake of COVID-19 vaccination among Fair Deal residents was 77.1% (18,167 doses administered to an eligible population of 23,554), this decreased slightly to 75.8% during the spring 2025 vaccination campaign.[150] From 15 September 2025 to 8 March 2026 (autumn/winter 2025-2026 vaccination campaign), there have been 17,453 COVID-19 vaccine doses administered to Fair Deal Residents, this equates to a percentage uptake of 73.6%.[204]

Table 3.19 COVID-19 vaccination uptake rate for residents of long-term care facilities in Ireland, reported by age group and vaccination campaign

Age (years)	Autumn/winter 2024-2025[149]			Spring 2025[150]		
	Doses (n)	Estimated population (n)	Uptake (%)	Doses (n)	Estimated population (n)	Uptake (%)
18 to 59	2,156	NR	NR	1,147**	NR	NR
≥60	22,996	NR	NR	23,294**	NR	NR
All ages	25,156	40,000*	62.9	24,454	32,000†	76.4

Key: NR – not reported.
*Based on the maximum bed capacity of all long-term care facilities for older adults and people with disabilities as recorded on the HSE Service Directory for all active residential care facilities (as of June 2024).
**Up to 1 June 2025.
†Based on the maximum bed capacity of all long-term care facilities for older adults as recorded on the HSE Service Directory for all active residential care facilities (as of April 2025).
Source: Health Protection Surveillance Centre.

United States data

Since 2021, nursing homes in the United States are required by the Centers for Medicare and Medicaid Services to report weekly aggregate COVID-19 vaccination uptake data among nursing home residents to the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN).[209] As of 8 January 2023, 48.9% of residents were up-to-date with their COVID-19 vaccinations,[210] this had fallen to 33.1% by 10 December 2023;[209] by 11 February 2024 the reported uptake had increased to 40.5%.[113] As of the 5 April 2026, the reported cumulative uptake rate of COVID-19 vaccination in nursing home residents was 35%, according to the NHSN Nursing Home Data Dashboard on the CDC website.[114]

3.7.3 Those living with immunocompromise

Irish data

The HPSC reports COVID-19 vaccination uptake rates among those aged six months and older living with immunocompromise.

During the autumn/winter 2024-2025 vaccination campaign,[149] the reported uptake was 44.7% (28,188 doses administered to an eligible population of 63,000). This decreased to 14.6% during the spring 2025 vaccination campaign (9,225 doses administered to an eligible population of 63,000).[150] The eligible population was estimated as the number of individuals recorded on COVAX and or NIIS as living with immunocompromise and who had been assessed as immunocompromised at both the account level and vaccination record levels. Data for the autumn/winter 2025-2026 vaccination campaign[151] (which are incomplete – data to 8 February

2026) suggest an uptake of 18.2% based on 12,067 COVID-19 vaccine doses administered to an eligible population of 66,203 people living with immunocompromise. The estimated denominator for the autumn/winter 2025-2026 vaccination campaign was updated based on a HSE National Vaccination Programmes – Access and Integration source (dated 10 October 2025).

A breakdown of the number of COVID-19 vaccine doses administered by age band to those living with immunocompromise is presented in Table 3.20. Approximately 8% (n=931) of the 12,067 doses were administered to those aged 80 years and older.

Table 3.20 Number of COVID-19 vaccine doses administered to those aged six months and older living with immunocompromise, reported by age band for the autumn/winter 2025-2026 vaccination campaign

Age	Autumn/winter 2025-2026[211]
	Doses (n)
6 months to 4 years	0
5 to 9 years	4
10 to 14 years	35
10 to 11 years	NR
12 to 15 years	NR
16 to 17 years	NR
18 to 19 years	NR
15 to 19 years	107
20 to 24 years	183
25 to 29 years	210
30 to 34 years	296
35 to 39 years	515
40 to 44 years	739
45 to 49 years	932
50 to 54 years	1,219
55 to 59 years	1,478
60 to 64 years	1,658
65 to 69 years	1,591
70 to 74 years	1,231
75 to 79 years	938
80 to 84 years	593
≥85 years	338
Total	12,067

Key: NR – not reported.
Source: Health Protection Surveillance Centre.

United Kingdom data

The COVID-19 surveillance report from the UK Health Security Agency (19 June 2025) reports that 24.3% of all people aged less than 75 years living with immunocompromise and resident in England had been vaccinated during the spring 2025 vaccination campaign.[212]

3.7.4 Those living with underlying medical conditions

Irish data

COVID-19 vaccination uptake in this group is not reported by the HPSC as it is currently not possible to accurately summarise the number of individuals with underlying medical conditions from COVAX and or NIIS data.[201]

EU/EEA data

The ECDC report, which is based on survey data for EU/EEA member countries, included data from only two countries (Czechia and Spain) on the uptake of COVID-19 vaccination among people living with underlying medical conditions. For the autumn/winter 2023/2024[205] and 2024/2025[206] vaccination campaigns, the uptake rate was 2.0% and 1.8% in Czechia, respectively and for Spain it was 6.7% and 4.0%, respectively.

United Kingdom data

The UK Health Security Agency COVID-19 surveillance report from 6 February 2025 reported that between 3 October 2024 and 2 February 2025, 23.6% of all people aged less than 65 years and in a clinical risk group (living in England) had been vaccinated with an autumn 2024 booster.[213] An additional surveillance report from 17 April 2025 reported that between 1 April 2025 and 13 April 2025, 2.2% of all people aged less than 75 years and in a clinical risk group (living in England) had been vaccinated with a spring 2025 dose.[214]

3.7.5 Pregnancy

Irish data

The reported COVID-19 vaccination uptake rate during the autumn/winter 2024/2025 vaccination campaign was 6.5% (1,487 doses administered to an eligible population of 22,790).[149] The reported COVID-19 vaccination uptake rate during the spring 2025 vaccination campaign was 1.5% (134 doses administered to an eligible population of 9,002).[150] The eligible populations were estimated based on the number of live births recorded by the General Register Office.

EU/EEA data

The ECDC report limited data on the uptake of COVID-19 vaccination among pregnant women with survey data provided by two countries only (Ireland and Spain). For the autumn/winter 2023/2024[205] and 2024/2025[206] vaccination campaigns, the uptake rate was 19.6% and 6.9% in Ireland, respectively, and for Spain it was 7.9% and 5.7%, respectively. The slight difference in Irish uptake data for 2024/2025 to that reported by the HPSC (6.9% versus 6.5%) as listed above, is likely attributable to differences in the data collection period (1 August 2024 to 28 March 2025 versus 16 September 2024 to 9 March 2025).

United Kingdom data

In the November 2024 UK surveillance report,[120] of 388,195 women aged 15 to 54 years who gave birth from September 2023 to May 2024 (and who could be linked to vaccination records), 12.2% (47,397) received a COVID-19 vaccine during pregnancy. Coverage by month peaked at 16.5% in those giving birth in March 2024. Coverage varied by age, deprivation level and ethnicity. It increased with increasing maternal age. The highest uptake was in the most affluent areas and lowest in those living in the most deprived areas. The highest uptake levels were recorded in those of Chinese ethnicity, followed by those who were white Irish and of mixed Asian and white ethnicity or who were white British.[120]

United States data

A CDC survey of COVID-19 vaccination uptake was conducted from 28 March to 16 April 2023 of women aged 18 to 49 years who reported being pregnant at any time since 1 August 2022 through the date of the survey.[215] Among 1,252 women who were pregnant at the time of the survey, 27.3% reported having received a COVID-19 booster dose.

3.7.6 Health and care workers

Irish data

All health and care workers

There were 22,884 COVID-19 vaccine doses administered to health and care workers in the 2024/2025 autumn/winter campaign, equating to a 9.2% uptake rate based on an eligible population of 250,000, as reported by the Department of Health.[149] Of the COVID-19 vaccines administered to health and care workers, 22.4% were administered to Health and Social Care Professionals, and 21.4% to Nursing and Midwifery staff.[149] With the exception of retired staff, the majority of doses in each staff category were administered to those aged 18 to 59 years.[149]

HSE health and care workers

Although health and care workers were no longer a primary target group of the autumn/winter 2025/2026 vaccination campaign, it was reported that 9,570 doses were administered to HSE health and care workers, representing an uptake of 8.7%.[204] During the previous autumn/winter 2024/2025 vaccination campaign (when health and care workers were a primary target group), uptake was 11.6% (equating to 12,485 doses).[204]

EU/EEA data

The ECDC report limited data on the uptake of COVID-19 vaccination among health and care workers (n=7 countries); see Table 3.21. For both the autumn/winter 2023/2024[205] and 2024/2025[206] vaccination campaigns, uptake was noted to vary across the countries for which data were available (n=7), with the highest uptake rates reported by Belgium (20.7% and 13.7%, respectively); the corresponding rates in Ireland were 15.2% and 9.2%, respectively. While based on limited data, in general, uptake rates for the 2024-2025 vaccination campaign were lower than those reported for the previous year.

Table 3.21 COVID-19 vaccination uptake rates among health and care workers, reported by country and vaccination campaign

Country	Uptake for 2023-2024 (%)	Uptake for 2024-2025 (%)
Belgium	20.7	13.7
Bulgaria	0.6	0.6~
Czechia	7.1	6.0
France	12.2*	NR
Greece	4.4	1.2
Ireland	15.2	9.2
Spain	13.9	6.1**

Key: NR – not reported.
Notes: 2023-2024: 1 September 2023 to 31 July 2024; 2024-2025: 1 August 2024 to 28 February 2025.
~1 August 2024 to 31 December 2024
*1 September 2023 to 31 March 2024
**1 August 2024 to 31 March 2025
Source: European Centre for Disease Prevention and Control.

United States data

Acute care hospitals and nursing homes report data to the CDC NHSN according to surveillance protocols for COVID-19 vaccination. Among approximately 7.7 million health and care workers in 4,057 acute care hospitals, COVID-19 vaccination coverage was 17.2%, and among approximately 1.6 million health and care workers at 13,794 nursing homes, COVID-19 vaccination coverage was 22.8%, for the period 1 October 2022 to 26 March 2023.[216] The Nursing Home Data Dashboard reports

that, as of 12 April 2026, the weekly cumulative proportion of nursing home healthcare personnel vaccinated with a COVID-19 vaccine was approximately 7%.[114]

3.8 Economic burden of COVID-19

The COVID-19 pandemic resulted in a significant economic burden globally. The first confirmed COVID-19 case in Ireland was recorded on 29 February 2020[217] and by the end of 2020 the estimated direct COVID-19 expenditure by the Irish government amounted to €14.8 billion.[218] By the end of February 2022, the reported direct expenditure due to COVID-19 had reached an estimated €29.5 billion.[219]

The initial direct costs to the Irish government included the healthcare costs resulting from acute illness, personal protective equipment costs, the cost of test and trace programmes and acquisition of private hospital capacity, as well as wider spending on income supports. During the emergency phase of the pandemic, almost 1.5 million people received COVID-19 income supports with the highest number receiving such supports in April 2020.[220]

The COVID-19 vaccination programme in Ireland commenced in 2021 at a total cost to the government of €530 million that year.[221] In 2022, the COVID-19 vaccination programme cost an additional €425 million (inclusive of a write down of €33.7 million in relation to expired stock and €60.7 million for stock due to expire).[221] For 2023, the annual expenditure for the COVID-19 vaccination programme was €221 million (inclusive of a write down of €64.5 million in relation to expired stock and €22 million for stock due to expire).[222]

The COVID-19 pandemic also resulted in indirect costs such as productivity losses due to acute illness, long-term disability or premature death. One population-based retrospective cohort study analysed data from the German Statutory Health Insurance database.[223] It included employed individuals of working-age with either COVID-19-related outpatient visits (from April 2020 to December 2021) or COVID-19-related hospitalisations (from April 2020 to October 2022). The study concluded that important drivers of work absenteeism were, being older; being at increased risk of severe COVID-19; being admitted to hospital; and disease severity. The associated costs, contributed to a substantial economic burden in Germany. The median absenteeism duration and associated cost was 10 days and €1,061 in the outpatient (n=369,220) and 15 days and €1,591 in the hospitalised (n=20,687) cohort; with greater absenteeism in those who were older, those at increased risk of severe disease and those with severe disease.[223]

An observational longitudinal study of 206,299 adults of working-age in the UK (from 3 February 2021 to 30 September 2022) examined the association between long COVID and employment outcomes.[224] It reported that labour market inactivity was higher in those who reported having long COVID and the authors concluded that long COVID contributed to reduced participation in the UK labour market.

In May 2023 the WHO declared that COVID-19 was no longer a Public Health Emergency of International Concern.[217] Five years after the onset of the pandemic, employment levels in Ireland had recovered to pre-pandemic levels.[220] As the COVID-19 pandemic evolved to an endemic stage, the overall direct and indirect costs attributed to the disease have reduced. While the level of COVID-19 vaccine procurement substantially reduced in 2024, there was an additional write down of €8.78 million in relation to expired vaccine stocks and €2.36 million in respect of stock due to expire.[225] Overall, the direct healthcare spending on COVID-19 related programmes has also declined in recent years. The 2023 and 2024 HSE National Service Plans outlined that €564.5 million[226] and €148 million,[227] respectively, were allocated to the annual operating budgets for COVID-19 related costs, this was reduced to €18 million for both 2025 and 2026.[228, 229]

There will continue to be an ongoing economic burden associated with COVID-19. Indirect productivity losses are expected for those with acute infection and long COVID due to an inability to work and or take part in social activities. The current HSE advice for adults with COVID-19 symptoms who feel unwell is to stay at home for at least forty-eight hours after symptoms have abated and to avoid contact with other people.[230] If an individual has a positive COVID-19 test, it is advised that they stay home for at least five days and avoid contact with other people.[230] Those with long COVID in particular may experience an extended period of productivity loss. However, the increased level of population immunity and the changing characteristics of the circulating virus mean the year-to-year economic impact is expected to vary going forward.

3.9 Discussion

This chapter describes the epidemiology of COVID-19 and the burden of disease in Ireland and internationally. In summary, COVID-19 surveillance data (2023 to 2025) for Ireland show that the burden of COVID-19 has declined over time, both in the total population and within each of the age groups examined in this chapter. COVID-19 does not yet exhibit seasonality and the incidence of notified COVID-19 cases have peaked at various timepoints throughout the years included in this assessment. In 2023, the incidence of COVID-19 cases peaked in April, August and December, with further peaks observed in June 2024 and September 2025. Considering the total population, the rate of notified COVID-19 cases per 100,000 has decreased from

699.1 to 248.3 cases per 100,000 over the three-year period. The observed decrease over time is likely due to a combination of virus evolution, reduced transmission and improved immunity (through previous infection and or vaccination). As the SARS-CoV-2 virus continues to evolve and mutate, future emerging variants may result in a disease of increased severity. As such, it is important that any future policy decisions are made based on the epidemiological situation at that time.

As highlighted, to date, COVID-19 lacks seasonality. However, it may be useful to consider its burden relative to that of other notified respiratory viruses, specifically the seasonal respiratory viruses, influenza and RSV. In the following section, the relative burden of these viruses are considered by calendar year, for the years 2023 to 2025.[231] In 2023, the notified COVID-19 case rate per 100,000 in the total population was 699.1 cases (n=35,798) compared with 229.4 cases (n=11,744) for influenza and 152.4 cases (n=7,803) for RSV. However, it should be noted that up to the 30 March 2023 there was widespread community testing for SARS-CoV-2. Following revision of the testing criteria, the HSE community testing centres for SARS-CoV-2 closed, with a consistent testing approach adopted for those presenting with symptoms of acute respiratory infection. In 2024, the notification rates per 100,000 in the total population were: COVID-19: 420.1 cases (n=21,508); influenza: 415.6 cases (n=21,282); and RSV: 93.6 cases (n=4,795). In 2025, the notification rates per 100,000 in the total population were: COVID-19: 248.3 cases (n=12,714); influenza: 756.4 cases (n=38,731); and RSV: 151.8 cases (n=7,773). These data suggest that the burden of COVID-19 has declined relative to influenza. On average, across the three years, 30% and 24% of notified influenza and RSV cases were observed in those aged 65 years and older, respectively, compared to an average of 54% for COVID-19. It is acknowledged that there is less nuance when presenting influenza and RSV data by calendar year given the clear seasonality these viruses exhibit, with infection levels peaking during the autumn and winter months in the northern hemisphere. This can present challenges for the safe and effective provision of care when large numbers of patients present to primary and secondary healthcare services during periods of peak influenza and or RSV circulation. This is particularly an issue with influenza where the burden can vary substantially from season to season, due to differences in the transmissibility, virulence and degree of vaccine mismatch.

The 2025 NIAC COVID-19 vaccination recommendations prioritise a number of at-risk groups for either six-monthly or annual vaccination, with a view to providing them with year-round protection. Surveillance data on the burden of COVID-19 in Ireland are readily available for the age groups considered to be at risk of severe disease, but there is a dearth of information for other at-risk groups, for example, those aged 18 to 79 years living in LTCFs and those aged six months and older living

with immunocompromise. As such, this chapter largely focused on reporting the epidemiology of COVID-19 across various age groups in Ireland, with international data used to inform the epidemiological estimates for other at-risk groups.

From 2023 to 2025, the incidence of notified COVID-19 cases has decreased across all age groups. Across the three years, the notified case rate consistently increased with increasing age, with the highest rates in those aged 80 years and older. The notified case rate per annum ranged from 2,030.1 to 4,905.9 cases per 100,000 in those aged 80 years and older, while rates ranged from 1,545.2 to 3,693.0 cases per 100,000 in those aged 75 years and older. Despite representing less than 4% of the total population,[144] those aged 80 years and older accounted for between 25% and 30% of the total number of notified cases each year, while those aged 75 years and older accounted for between 35% and 42% of the total annual burden, despite representing only 7% of the total population. It is worth noting that the incidence data reflect medically attended notified cases, and as such, to be identified as a case, an individual must present to a healthcare setting, be tested and in the event of confirmed case, the data notified to the HPSC. While the reported incidence of COVID-19 varies by age group, some of this variation may be due to differences in testing practices, which may be influenced by the age and or clinical presentation of the patient.

From 2023 to 2025, the rate of notified COVID-19-related ED visits in those aged six months to 17 years increased from 35.9 (n=427) to 55.6 (n=661) per 100,000, representing an increase of approximately 55%. This rate decreased across all other age groups during this three-year period. In general, the notified ED visit rate increased with increasing age, with the highest rates observed in those aged 80 years and older, ranging from 571.7 to 921.4 ED visits per 100,000. Again, a disproportionate burden was observed in the oldest adults, with 22% to 23% of the total annual number of notified ED visits occurring in those aged 80 years and older while between 32% to 34% of all visits were in those aged 75 years and older. It is also worth noting that these data represent ED visits that were not subsequently admitted to hospital and, as such, the burden of COVID-19 on EDs in Ireland is underestimated.

From 2023 to 2025, there has been a marked decrease in the rate of notified COVID-19-related hospital admissions in the total population. However, while the absolute number of notified hospital admissions has decreased over time, the proportion of notified cases requiring an admission to hospital has remained similar. In 2023, 43% (n=15,545) of all notified COVID-19 cases were hospitalised, while in 2024 and 2025, the proportion hospitalised was 42% (n=8,976) and 38% (n=4,811), respectively. Across all three years, the notified hospital admission rate was highest in those aged 80 years and older, ranging from 935.2 (n=1,693) to

3,086.8 (n=5,588) admissions per 100,000. With regards to the absolute number of notified hospital admissions in the total population each year, over one third occurred in those aged 80 years and older while approximately 50% occurred in those aged 75 years and older.

Similar to the pattern observed for notified hospital admissions, while the absolute number of ICU admissions has decreased over time, the proportion of notified COVID-19 cases requiring an admission to ICU due to COVID-19 remained similar at less than 1%. In general, the notified ICU admission rate increased with increasing age, although in 2023 and 2024 the highest notified ICU admission rate was in those aged 75 to 79 years. However, this may reflect ICU admission policies rather than differences in COVID-19 severity.[232] With regards to the absolute number of notified ICU admissions in the total population each year, the proportion that occurred in those aged 80 years and older ranged from 15% to 19% and from 31% to 33% in those aged 75 years and older. Data for all three years indicated that over 90% of notified ICU admissions each year were in those with one or more underlying medical condition. This observed COVID-19-related morbidity in those with underlying medical conditions is reflected in the international literature.[233] It has been estimated that approximately 22% of the global population (1.7 billion people) are living with at least one underlying medical condition that increases their risk of developing severe COVID-19, though increased age remains the strongest risk factor.[234]

The reported rates of notified COVID-19-related deaths in the total population have also declined over the years included in this assessment, but like the other indicators of the burden of COVID-19 in Ireland, the proportion of notified COVID-19 cases that died has remained similar, at around 2%. With regards to the absolute number of notified deaths in the total population each year, the proportion that occurred in those aged 80 years and older ranged from 63% to 68% and from 79% to 83% in those aged 75 years and older.

The number of people living in Ireland aged 60 years and older has increased over the last decade from just over 840,000 in 2015 to almost 1.2 million in 2025, representing an increase of approximately 38%.[144] This proportion is set to continue to increase, with population projections predicting that the proportion of the total population aged 60 years and older will reach 27% (equating to just over 1.5 million people) in 2035 and 31% (equating to just over 1.8 million people) in 2042.[145] Moreover, the population group aged 80 years and older (who, in this assessment, accounted for 34% of hospital discharges and 51% of bed days per year with a principal diagnosis of COVID-19 in 2024) is set to rise to a greater degree, with projections estimating a greater than 50% increase in the number of individuals aged 80 years and older (to over 300,000 people) by 2042.[145] This will

likely have a significant knock-on effect on the healthcare system in terms of the healthcare utilisation associated with COVID-19 and other vaccine-preventable diseases given the disproportionate burden in this age group.

Testing capacity for respiratory viruses in acute hospital settings in Ireland (published in 2023),[235] expanded rapidly in the context of the COVID-19 pandemic. This greatly improved access to testing, particularly for those requiring admission to hospital, with 93% of hospital laboratories reporting that testing specimens were from hospital inpatients and ICU patients, making these the most common source of specimens; only 30% of laboratory-tested specimens were submitted from primary care practices. However, this expansion in testing capacity should be viewed in light of the changes to COVID-19 testing practices that were implemented in 2022 which included removal of the recommendation to test all asymptomatic patients and asymptomatic contacts.[236] Moreover, it is worth noting that not all COVID-19 cases are notified. Testing in primary care in particular is likely limited to that required as part of sentinel surveillance and testing of subgroups at high risk of severe outcomes whereby knowledge of the specific pathogen would support clinical decision making (including for example, the need for antiviral therapy).[27] As such, the true burden of COVID-19 in primary care is likely higher than that reported.

The burden associated with COVID-19 in Ireland is in the context of an existing HSE COVID-19 Vaccination Programme that continues to offer free-at-the-point-of-care COVID-19 vaccination to certain at-risk groups. The data for Ireland are also in the context of a highly effective vaccination campaign in the early stages of the pandemic, with 97% uptake in those aged 60 years and older, over 90% uptake in those aged 18 years and older, and 76% uptake in the total population by 30 September 2021.[237] Consistent with international data,[205, 206] HPSC COVID-19 vaccination uptake data show variability in uptake depending on the age group, whereby uptake is almost twice as high in those aged 80 years and older compared to those aged 60 to 79 years. However, it is noted that even in those aged 80 years and older, uptake is less that the target rate of 75% in those aged 65 years and older, as outlined in the National Immunisation Office Strategic Plan 2024-2027.[238] Of note, uptake rates are higher among residents of LTCFs for older adults, where vaccination campaigns are supported by HSE mobile vaccination teams, with uptake rates exceeding the 75% target in most campaigns. It is also noted that uptake rates have declined somewhat in recent years when comparing the three autumn/winter campaigns for which data were analysed (for example, from 50.1% to 37.9% in those aged 60 years and older), with reductions also noted when comparing the spring campaigns in 2024 and 2025. This may reflect growing complacency or a lack of understanding of the continued burden associated with COVID-19, particularly among those at higher risk of severe disease compared to the

general population. Vaccine hesitancy (that is, delay in acceptance or refusal of vaccines), while not a new issue, is complex and the COVID-19 pandemic exposed new levels of volatility around this phenomenon. Cited reasons for this include the evolving nature of the COVID-19 pandemic and subsequent protective measures, as well as emerging variants, the expedited introduction of new vaccines, the polarised political climate, social media and other digital platforms.[239, 240] Improvement of vaccine acceptance requires an acknowledgement of the individual's concerns and a considered response. Healthcare professionals have a unique opportunity in this, given they are still viewed as being some of the most trusted people in relation to healthcare advice. As such, it is important they understand the nature of vaccine hesitancy locally to inform conversations with patients in their sphere of influence and alleviate any concerns they may have about vaccinations and potential side effects.[241, 242]

While a COVID-19 vaccine can offer protection to the individual receiving the vaccine, and possibly against onward transmission, this protection is modest and short-lived. Factors that influence the effectiveness of COVID-19 vaccination include waning immunity, the emergence of variants and the recipient's age or health status.[243, 244] Data relating to the effectiveness and safety of antigenically updated COVID-19 vaccines (authorised by the EMA) will be assessed in detail in Chapter 4. In addition to vaccine effectiveness, vaccination coverage rates also influence the level of protection garnered. Vaccination is voluntary and typically is only systematically offered to selected groups (for example, based on clinical care plans for those identified to be at elevated risk of severe disease or through employer occupational health schemes for healthcare workers). Therefore, programmes often rely on individuals seeking vaccination, knowing it is available and being encouraged to avail of it. Given the scale of the COVID-19 pandemic and subsequent messaging around the availability of COVID-19 vaccinations, it is less likely that people are unaware of its availability.

The HSE information system NIIS captures information relating to the administration of all publicly funded COVID-19, influenza and pneumococcal vaccinations.[245] This technology collects information such as risk status and whether the individual is a healthcare worker. While there have been improvements in terms of the completeness of these vaccination uptake data, documentation of a person's risk status may be limited to capturing a single criterion. For example, a 60-year-old with diabetes and heart failure who is currently eligible for vaccination through the programme based on both their age and having documented medical risks that increase the risk of severe disease, may only have age captured as their risk category. In this HTA, notified ICU case data were stratified based on the presence or absence of one or more underlying medical conditions, with evidence, as noted

above, that over 90% of such discharges in all years were in those with one or more underlying conditions. Notified hospital admission and ICU admission data were stratified based on receipt of a COVID-19 vaccine within the previous 180 and 365 days, providing important additional insights into the morbidity associated with COVID-19. Most notably, of the notified COVID-19-related hospital admissions reported in 2025, 85% of such admissions in those aged 80 years and older were in individuals who had not received a COVID-19 vaccine within the previous 180 days, while 63% of such admissions in those age aged 60 to 79 years were in those who had not received a COVID-19 vaccine within the previous 365 days. These data highlight the important beneficial effect of vaccination in older adults and in those with underlying conditions and represent important information for providers and patients as part of any COVID-19 vaccination programme awareness campaign.

Severe acute respiratory illness (SARI) surveillance in Ireland is part of a wider European network of SARI hospitals, E-SARI-NET.[246] There are four SARI sentinel hospital sites in Ireland (St Vincent's University Hospital, St James's Hospital, University Hospital Limerick and Children's Health Ireland at Crumlin). SARI cases are identified from new admissions, based on clinical symptoms. Patients that develop SARI during their admission are not included. Patients are tested for SARS-CoV-2, influenza and RSV. The HPSC publish SARI epidemiological reports on a weekly basis,[247] these reports detail the incidence of persons hospitalised with SARI and include epidemiological, clinical and virological data as well as influenza and COVID-19 vaccination status and outcomes. It is worth noting that data from the SARI surveillance programme (which includes data on risk factors) was not used in this assessment due to small numbers and the time constraints associated with this project. However, publicly available SARI reports support the findings reported in this chapter, highlighting that there is a disproportionate burden in those with underlying medical conditions and in those who are unvaccinated or have not been vaccinated at the recommended intervals. Future expansion of the SARI surveillance programme to additional hospital sites would add to the evidence base available to future HTAs, as will Individual Health Identifier linkage to NIIS.

Adults living in LTCFs, and those living with immunocompromise associated with a suboptimal response to vaccination, are two groups identified by NIAC as being at high risk of severe COVID-19 disease, in whom twice yearly vaccination is recommended. Older adults residing in LTCFs may have increased susceptibility to infection and severe disease outcomes due to a combination of risk factors such as advanced age (with associated immunosenescence), frailty, multimorbidity and close living quarters that can contribute to the spread of infection.[248] Frailty at the time of hospital admission is associated with adverse outcomes; the HSE's Specialist Geriatric Services Model of Care notes that 35% of 70-year-olds show functional loss

at time of discharge compared with their pre-admission status, with this figure increasing to 65% for 90-year-olds.[249] Hospital avoidance in this cohort is therefore noted to be beneficial, with the Model of Care emphasising the importance of interventions that enhance healthy ageing and prevent disease.[249, 250] Considering those living with immunocompromise, there is a lack of Irish data in relation to both the size of this cohort and in terms of COVID-19 related morbidity and mortality. HPSC data for the autumn/winter 2025-2026 vaccination campaign suggest an uptake of 18.2% in those who are immunocompromised, which is substantially lower than the 50% target identified in the National Immunisation Office 2024-2027 strategic plan. Using international data, a large population-based study in the UK found that immunocompromised individuals accounted for 3.9% of the population living in England in 2022.[251] Using 2021 National Health Interview Survey (NHIS) data, the proportion of adults living with immunocompromise in the US was an estimated 6.6%;[252] this was more than double the rate estimated using 2013 NHIS data.[253] However, it is worth noting that these data were based on self-reported immunocompromise and lacked specific information on the cause of immunocompromise.[252, 253] The authors surmised that the increase in self-reported immunocompromise over this eight-year period may have been due to the increased use of immunosuppressive medications or an increased awareness about one's immunocompromised status following the COVID-19 pandemic.[252] While the number of people living with immunocompromise in Ireland has been estimated in this assessment, there are a number of limitations around this estimate. As outlined above, capturing risk factors, including that of immunocompromised status, on NIIS is a complicated and technical matter, not least because of how it is recorded on the different data streams that feed into this database. Among the different data streams are the GP and pharmacy-based systems. Considering specifically immunocompromised status, that information can be recorded on the patient's vaccination account record and or on each of their vaccination records. However, the immunocompromised status is not always a permanent condition and even though a patient may have been immunocompromised at the time that their account was first created on NIIS, they may not have been immunocompromised at each subsequent occasion that they were vaccinated. The reverse is also true, in that the record of a patient who was previously eligible for vaccination based on another criterion (for example, age or medical condition) may not get updated to reflect that they are immunocompromised at a subsequent vaccination visit.

HIPE data were gathered to understand the nature of COVID-19 hospitalisations (for example, complications of the disease and length of stay). Data analysed were limited to 2023 and 2024, and as noted in Section 3.2, prior to 2024, COVID-19 could only be assigned as an additional diagnosis, which means that data for the two years are not directly comparable. For example, in 2023, 9.0% of the discharges

related to an additional diagnosis of COVID-19 included an ICU stay. In 2024, 1.5% and 10.8% of the discharges related to a principal and an additional diagnosis of COVID-19 included an ICU stay, respectively. Discharges that included an ICU stay had a longer average length of stay compared with discharges that did not include an ICU stay. It is worth noting that the length of stay data represent the total length of stay related to the discharge and it is not possible to determine what proportion of the stay was in the ICU. There may be differences in those admitted to hospital as a result of COVID-19 and those for whom it is assigned as an additional diagnosis, with the latter including those for whom the principal reason was due to an exacerbation of an underlying condition, such as COPD or heart failure and those who were infected subsequent to their admission, potentially complicating their clinical care. These differences may have contributed to the observed differences in the length of stay for those with a principal or additional diagnosis of COVID-19. For example, in 2024, in those aged 80 years and older, the average length of stay for those with a principal and an additional diagnosis of COVID-19 was 10 days and 28 days per patient, respectively. Of note, the length of stay for those (aged 80 years and older) with a principal diagnosis of COVID-19 was similar to that reported in previous HTAs for other acute respiratory infections. For example, the average length of stay in those with a principal diagnosis of seasonal influenza was nine days in those aged 80 years and older.[254] In those with a principal diagnosis of RSV (from 2018 to 2024), the average length of stay ranged from 8 days to 16 days in those aged 80 years and older.[255]

Using HIPE data, the average cost associated with a hospital stay for a patient with a principal diagnosis of COVID-19 was approximately €6,870, and the total annual cost associated with all principal diagnoses of COVID-19 in 2024 was approximately €19.8 million. However, it is acknowledged that this is likely an underestimate as some discharges may not be coded and this only reflects patients with a principal diagnosis of COVID-19 (not those where COVID-19 is present along with other diagnoses). Again, it is noted that this cost of care in acute hospitals is in the context of an existing immunisation programme. The economic burden associated with COVID-19 includes direct costs resulting from providing care to the patient, such as primary care visits and medical costs, and indirect costs resulting from productivity loss due to illness, disability related to disease complications, or premature death. Considering specifically older adults and those with prolonged ICU stays, it is recognised that additional costs may accrue for patients who require post-discharge rehabilitation and care. Data are limited in relation to the extent and duration of such care; however, it was noted that approximately 6% of those with a primary diagnosis of COVID-19 and approximately 14% of those with an additional diagnosis of COVID-19 were newly discharged to a post-acute care setting, with again a disproportionate requirement in older adults. Although limited research has been

published on the total economic burden of COVID-19 in Ireland, international estimates suggest that the burden, including both direct and indirect costs, is likely to be considerable.[223] This will be explored further in Chapter 5.

There is a lack of national level data in relation to the prevalence and burden associated with long COVID in Ireland. As highlighted in Section 3.4.1, challenges include the diversity of symptoms and range of organ systems that may be impacted, the severity of symptoms, and whether they are continuous or relapsing-remitting in nature. Moreover, it is not known if the risk of long COVID has changed over time given virus evolution and changes in population-level immunity. As reported in Section 3.6.3, the number of new patients being referred to the long COVID clinics has decreased from 2023 to 2025 (which is broadly consistent with the trend observed for notified COVID-19 cases in Ireland), with return patients comprising most patients being assessed at these clinics. While reported new referrals to the long COVID clinics may be decreasing, given the lack of national level data it is unclear whether there is also a decrease in the incidence and prevalence of long COVID in Ireland. That said, it is recognised that long COVID can have a considerable impact on an individual's quality of life, ability to work and daily functioning, thus it contributes to the burden of COVID-19 in Ireland. In the absence of definitively effective treatments for long COVID, from the healthcare and societal perspective, it is possible that much of this continued burden may arise from reduced labour participation and productivity losses rather than medical expenditure alone.

In summary, while there is evidence that the overall burden associated with COVID-19 has decreased in recent years, there continues to be a disproportionate burden in older adults. This burden is in the context of an existing HSE COVID-19 Vaccination Programme that offers free at the point of care vaccination to this cohort.

4 Clinical effectiveness and safety

Key points

- Evidence from a systematic review (index review) published in October 2025 was used to inform this assessment of the effectiveness and safety of antigenically updated COVID-19 vaccines for seven distinct populations. Where data for subgroups of interest were lacking in the systematic review, evidence was supplemented by a search of European, UK and US platforms. The seven population groups of interest were:
    - older adults (adults aged 65 years and older)
    - individuals residing in long-term care facilities (LTCF)
    - those with immunocompromising conditions
    - those with underlying medical conditions
    - pregnant individuals
    - healthcare workers
    - those in the general population aged between 18 and 59 years.
- Evidence from the observational studies included in the index review was summarised in the write up of this chapter. Evidence from supplemental observational studies was only reported when it addressed a gap in the evidence base or reported findings contrary to those of the index review.
- Of the 20 observational studies from the index review that reported vaccine effectiveness (VE) findings, 16 included XBB.1.5 vaccines exclusively, one included a combination of XBB.1.5, JN.1 and KP.2 vaccines, one included KP.2 vaccines exclusively, one included a combination of KP.2 and JN.1 vaccines and one study reporting on long COVID outcomes included bivalent booster vaccines. Of the 21 studies identified as part of the supplemental search, two provided evidence that addressed gaps in the evidence provided by the index review; one included XBB.1.5 vaccines exclusively and one included XBB.1.5 and non-XBB.1.5 adapted vaccines. The 19 studies from the index review that reported safety findings covered the period 2020 to 2023 and were limited to ancestral strain COVID-19 vaccines.
- In general, Omicron-adapted vaccines were associated with a significant reduction in severe COVID-19 across several of the population groups considered relevant to this HTA. However, there was evidence of waning effectiveness over time, particularly in studies that reported over longer incremental follow-up periods. While some estimates of VE may appear to be modest, it is important that these effects are viewed in the context of the

considerable burden associated with COVID-19, particularly for those at increased risk of severe disease.

- Estimates of effect were typically higher for outcomes related to severe disease compared with medically attended or symptomatic infection outcomes. Protection against hospitalisation and mortality was observed up to five to six months post-vaccination among older adults, those living with immunocompromise, those living with underlying medical conditions, and those aged 18 to 59 years in the general population. However, as noted, there was evidence of waning protection, particularly over longer follow-up periods.
- Where effectiveness estimates were disaggregated by age, there was no consistent pattern and confidence intervals typically overlapped.
- The majority of the included evidence relates to Omicron-adapted mRNA COVID-19 vaccines. While some studies included other vaccine types (for example, protein subunit COVID-19 vaccines), only small numbers of participants received these vaccine types. Studies typically did not report findings disaggregated by vaccine type, so it is not possible to determine if effectiveness differs by vaccine type based on the evidence included in this chapter.
- Only one study included in this chapter reported on the effectiveness of Omicron-adapted vaccines against post-acute sequelae associated with long COVID; there was no evidence of protection reported for those aged 60 years and older while a VE of 49% was reported for those aged 18 to 59 years.
- No evidence was identified in this chapter regarding the effectiveness of Omicron-adapted vaccines for:
    - those living in LTCFs but high levels of protection against severe COVID-19, using original COVID-19 vaccines, were previously documented for this population during the early years of the pandemic
    - pregnant individuals but previous evidence of effectiveness supports COVID-19 vaccination during pregnancy to prevent severe disease and adverse maternal and child outcomes
    - newer COVID-19 formulations or technologies licensed since 2025.
- The findings reported in this chapter are consistent with the existing literature base as it pertains to the safety profile of COVID-19 vaccines, which is largely favourable. One study noted an increased risk of myocarditis (in those aged 50 years and older), and another reported an increased risk of myopericarditis (in

those aged 66 years and older). Post-marketing surveillance has noted that the frequency of myocarditis or pericarditis, where known, occurs in fewer than 1 in 10,000 vaccinations and would be considered very rare.

- Most of the primary studies included in the index review were judged by the index review authors to be at low risk of bias (37/39 studies). Specific weaknesses identified in the quality appraisal of the index review (relating to a lack of grey literature searching, list of excluded studies and assessments of publication bias) were partially mitigated by the supplemental search, the results of which largely aligned with the index review.

4.1 Introduction

This chapter summarises the clinical effectiveness and safety of COVID-19 vaccines authorised by the European Medicines Agency (EMA) for the populations of interest to this HTA (that is, the population groups prioritised in the updated COVID-19 vaccination recommendations published by the National Immunisation Advisory Committee (NIAC), see Table 1.1 in Chapter 1).

As outlined in Chapter 1, the emergence of SARS-CoV-2 virus variants, most notably Omicron in 2021 and its resulting subvariants, was associated with a significant decrease in vaccine effectiveness. Since 2022, Omicron variant-adapted vaccines have been developed and regularly updated based on advice by the World Health Organization (WHO) regarding appropriate COVID-19 vaccine antigen composition, with the first of these adapted vaccines approved by the EMA in September 2022. Chapter 2 provides a description of the antigenically updated COVID-19 vaccines currently authorised for use by the EMA as of May 2026. Chapter 3 notes that Omicron displaced Delta as the globally predominant variant during 2022, with further shifts between Omicron sub-lineages throughout 2023 and onwards. More broadly, since 2022 there have been policy changes in terms of the infection protection and control measures and testing,[95], while in May 2023, the WHO declared that COVID-19 was no longer a public health emergency of international concern.[256] Given the distinct differences in the landscape of COVID-19 pre- and post-2023, the focus of this chapter is limited to evidence relating to COVID-19 vaccine effectiveness and safety from 2023 to present, where available.

4.2 Methods

4.2.1 Research question

As outlined above, the aim of this chapter was to summarise the evidence of the clinical effectiveness and safety of antigenically updated COVID-19 vaccines authorised by the EMA for the populations of interest to this HTA. In the interests of

efficiency (and as outlined in the protocol), evidence from a high-quality, recently published systematic review of the clinical effectiveness and safety of COVID-19 vaccines was used to inform this HTA, where available. This was supplemented by evidence from primary data sources, as required. The PICO (Population, Intervention, Comparator, Outcomes) framework to identify the systematic review is outlined in Table B.1.

4.2.2 Search strategy

A comprehensive electronic search was performed in Embase (Elsevier), Medline Complete (EBSCO), and the Cochrane Library on 22 December 2025. Results were limited to those published within the previous 12 months (from 21 December 2024 to 22 December 2025).

4.2.3 Review selection, data extraction and management

Titles and abstracts of potentially eligible reviews were screened using Covidence software. Full text reviews were independently assessed for eligibility by two reviewers according to the pre-specified inclusion and exclusion criteria outlined in Table B.1. In this HTA, a systematic review was only considered eligible if it comprised the following characteristics:

- published within the last 12 months (from 21 December 2024 to 22 December 2025)
- included data from EU/EEA countries, the UK and the US (data from additional countries would also be included)
- included disaggregated data for 2023 onwards (to facilitate the inclusion of data relevant to the current situation, that is, data specific to currently circulating variants)
- had a clearly stated set of objectives with an explicit, reproducible methodology
- had a systematic search of at least two databases, which attempted to identify all studies that would meet the eligibility criteria
- had a systematic presentation and synthesis of the characteristics and findings of the included studies
- had a critical appraisal of the available evidence.

Data extraction was conducted by one reviewer (and checked by a second) using a standardised, electronic data extraction form. Disagreements in screening, eligibility and data extraction were resolved through discussion and with third-party arbitration, when required.

4.2.4 Assessment of methodological quality of identified review

Two reviewers independently assessed the quality of the review using the AMSTAR 2 tool, "A MeaSurement Tool to Assess systematic Reviews, version 2".[257] Disagreements were resolved by discussion and with third-party arbitration, when required.

4.2.5 Data synthesis

Summary characteristics of the identified review and overall findings were presented in table format, along with summary figures for vaccine effectiveness (VE) outcomes, and synthesised narratively. The findings were presented by population of interest and outcome.

4.2.6 Identification of supplementary data

As noted in section 4.2.1, it was agreed that evidence from a high-quality, recently published systematic review of the clinical effectiveness and safety of COVID-19 vaccines would be used to inform the HTA, where available. Where data for the subgroups of interest were lacking, these data were sought from the following platforms:

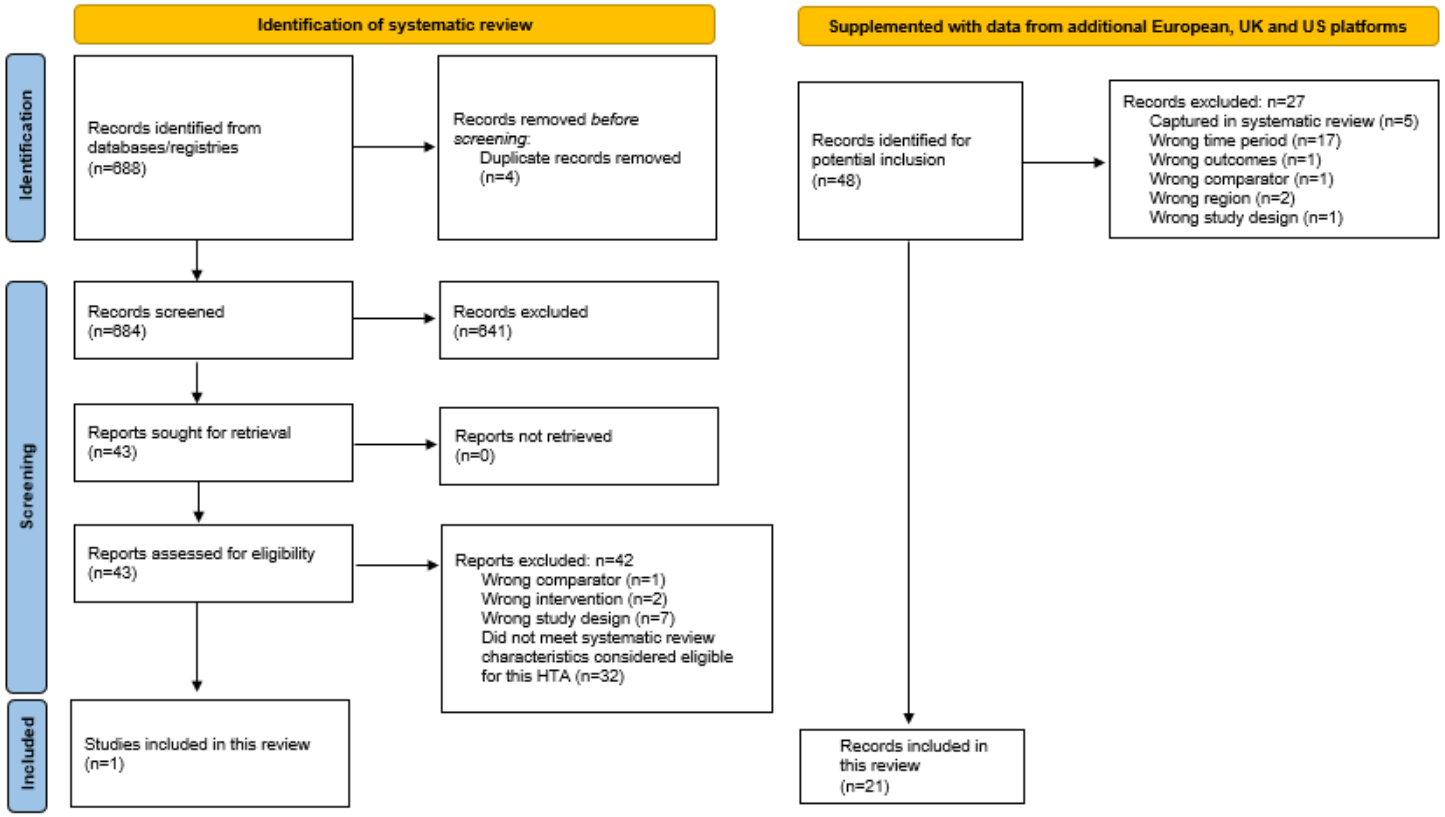
- Europe: Vaccine Effectiveness, Burden and Impact Studies (VEBIS) [258]
- UK: UK Health Security Agency (UKHSA) monitoring reports from the COVID-19 vaccine surveillance strategy[259]
- US: Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION)[260]
- US: Investigating Respiratory Viruses in the Acutely Ill (IVY) network.[261]

Data from the four platforms outlined above were only eligible for inclusion if they were collected in 2023, 2024 or 2025.

4.3 Results

After removing duplicates, the initial electronic database search identified a total of 684 articles. After excluding articles based on title and abstract review, a total of 43 articles remained for full text review. Following full text review and subsequent exclusion, one systematic review remained (hereafter referred to as the index review or Scott et al.)[57]; see Figure 4.1.

Figure 4.1 PRISMA flow diagram of review selection



Source: The PRISMA 2020 statement: an updated guidelines for reporting systematic reviews.[262]

4.3.1 Characteristics of included data sources

The index review (that is, Scott et al.), identified through the methods outlined in Sections 4.2.2 and 4.2.3 above, was published on 29 October 2025 and evaluated the efficacy, effectiveness, and safety of COVID-19 vaccines (licensed for use in the US).[57] In this index review, the search for COVID-19 vaccine effectiveness data was restricted to studies published from June 2024 to 31 July 2025. Eligible study designs for the index review included randomised controlled trials (RCTs), observational vaccine effectiveness studies with laboratory confirmation, immunogenicity or safety studies, and epidemiologic burden or surveillance studies. COVID-19 specific primary studies were only eligible for inclusion if they reported on outcomes from a study period that ended on 1 January 2024 or later (to reflect COVID-19 vaccine effectiveness data for more recent and currently circulating variants). The review included 334 COVID-19 specific primary studies. COVID-19 vaccine effectiveness data specific to adults, paediatrics, those living with immunocompromise and pregnant women were reported in 258, 121, 30 and 12 of the included primary studies, respectively. The index review stratified the results according to the populations of interest, defined as: infants who were aged 24 months or younger, children who were aged 2 to 17 years, younger adults who were aged 18 to 64 years, and older adults who were aged 65 years or older. Studies that reported age ranges that could not be disaggregated into prespecified populations were summarised separately. The index review authors summarised a total of 29 studies reporting on vaccine effectiveness outcomes – refer to supplementary tables S6 and S7 in the supplementary appendix. These 29 studies were checked by the evaluation team for relevant outcomes (as specified in Table B.1) within populations of interest to this HTA. From these lists, there were 20 studies identified that reported at least one relevant effectiveness outcome for at least one population group of interest to this HTA.

In addition, supplementary data were identified from VEBIS related publications on the ECDC and Eurosurveillance websites, monitoring reports from the COVID-19 vaccine surveillance strategy in the UK, and the VISION and IVY vaccine effectiveness networks in the US. Overall, this supplemental search identified an additional 21 relevant studies.

In total therefore, the index review (n=20) and supplemental search (n=21) identified a total of 41 studies reporting at least one relevant effectiveness outcome for one or more population groups of interest to this HTA. The number of included studies by population group of interest was as follows:

- Older adults n=38
    - Index review n=18
    - Supplemental search n=20

- Adults with immunocompromising conditions n=7
  - Index review n=7
  - Supplemental search n=0
- Adults with underlying medical conditions n=5
  - Index review n=4
  - Supplemental search n=1
- Pregnant women n=0
- Healthcare workers n=2
  - Index review n=1
  - Supplemental search n=1
- General population aged 18 to 59 years n=13
  - Index review n=8
  - Supplemental search n=5.

Twenty studies were included from the index review, this included 10 case-control and 10 cohort studies. Eleven studies used US data, three used multi-country European data, and two used Canadian data. One study each used data from England and Scotland, the UK, Italy, and Singapore. Of the 20 studies included from the index review, 14 were funded through agency, government or non-commercial grants and six were industry funded. The population and outcomes included varied across the studies, as discussed in section 4.3.2. While the studies differed in terms of the variant strain and type of COVID-19 vaccines administered during the study period, all studies included mRNA vaccines or either mRNA or protein-subunit based vaccines. Of the 20 studies included from the index review, 19 reported on vaccine effectiveness outcomes specific to the acute infection period, while one study reported on vaccine effectiveness against long COVID. The study periods for studies reporting on outcomes specific to the acute infection period were as follows:

- anytime between September 2024 and January 2025 (three studies)[263-265]
- anytime between September 2023 and January 2024 (three studies)[266-268]
- anytime between September 2023 and August 2024 (13 studies).[269-281]

The one study that reported on vaccine effectiveness against long COVID covered the period January 2022 to December 2023.[282]

The strain formulation of antigenically updated vaccines differed by study period; the three studies that covered September 2024 and January 2025 included JN.1, KP.2 and or XBB.1.5 vaccine formulations, while the studies that covered 2023 to 2024 predominantly included XBB.1.5 vaccine formulations or XBB.1.5 and or bivalent Original/Omicron BA.4-5 vaccine formulations.

The supplemental search identified 14 case-control studies, six cohort studies, and one screening method ecological study. Eleven studies used multi-country data from

European countries, two used US data, five used data from England, two used data from Netherlands and one used Canadian data. All studies identified from the supplemental search reported on vaccine effectiveness outcomes limited to the acute infection period.

4.3.2 Clinical effectiveness of COVID-19 vaccines

This section outlines the clinical effectiveness of COVID-19 vaccines in seven subgroups of interest: older adults, residents of long-term care facilities (LTCFs), those with immunocompromising conditions, those with underlying medical conditions, pregnant women, healthcare workers, and in the general population aged 18 to 59 years.

Older adults

The findings from the 18 studies from the index review and one study from the supplemental search reporting VE estimates for the various outcomes among older adults are presented in Tables B.2 to B.8.

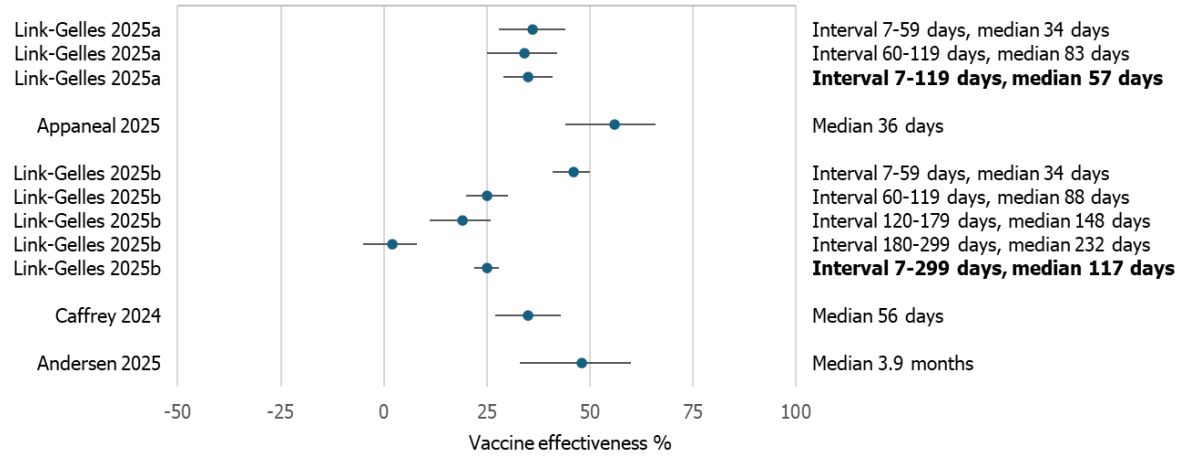
Symptomatic or medically attended infection

Table B.2 summarises the 10 studies included in the index review that reported on one or more of the following COVID-19-related outcomes: emergency department (ED) or urgent care (UC) visits (five studies);[263, 264, 266, 269, 270] outpatient visits (two studies);[263, 266] and symptomatic or medically attended infection (five studies).[265, 267, 271-273] Eight of these studies presented results for all adults aged 65 years and older (of which, one study focused on adults with end stage kidney disease (ESKD))[272], one study reported on those aged 60 years and older,[265] and one study stratified the results for those aged 65 to 74 years and 75 years and older.[271] Studies ranged in size from 1,840 to 428,654 individuals, and follow-up duration ranged from a median of 19 days to a median of 232 days post-vaccination. Studies included differing vaccine types (all studies included mRNA vaccines while seven additionally included protein subunit vaccines) and strain formulations (15 studies included only XBB.1.5 formulations). Across the outcomes, estimates of VE varied between studies, with no consistent difference in VE between studies reporting shorter follow-up duration and those reporting follow-up to six months or more post-vaccination. While three studies reported incremental follow-up periods, only one provided follow-up beyond four months. This study provided evidence of waning effectiveness over time from a median 34 days post-vaccination up to 232 days post-vaccination.[269] There was no evidence of a difference in VE when disaggregated by age sub-groups.

Of the five studies that reported on ED or UC visits, three (two case-control studies and one cohort study) included a combination of mRNA and or protein subunit XBB.1.5 vaccines (referred to in this chapter as mixed XBB.1.5 vaccines) and two case-control studies included mRNA KP.2 vaccines,[263, 264] one of which also included protein subunit JN.1 vaccines.[264] The median follow-up post-vaccination differed across the studies, three studies reported VE estimates for a single overall follow-up period,[263, 266, 270] and two provided estimates for both overall and incremental follow-ups.[264, 269] Unless otherwise stated, all VE estimates reported in the text will be those reported for the overall follow-up period, even if estimates were also reported for incremental follow-up time-points.

Across two case-control studies, the VE of mixed XBB.1.5 vaccines against ED or UC visits ranged from 25% (95% CI: 22% to 28%)[269] at a median 117 days post-vaccination to 35% (95% CI: 27% to 43%)[266] at a median 56 days post-vaccination. One cohort study of mixed XBB.1.5 vaccines reported a VE of 48% (95% CI: 33% to 60%) against ED visits at a median 3.9 months post-vaccination.[270] The two case-control studies of mRNA KP.2 and or protein subunit JN.1 vaccines reported VE estimates against ED or UC visits, these ranged from 35% (95% CI: 29% to 41%)[264] at a median 57 days post-vaccination to 56% (95% CI: 44% to 66%)[263] at a median 36 days post-vaccination. A summary of the vaccine effectiveness estimates against ED or UC visits is provided in Figure 4.2.

Figure 4.2 Vaccine effectiveness against emergency department or urgent care visits among older adults from the index review



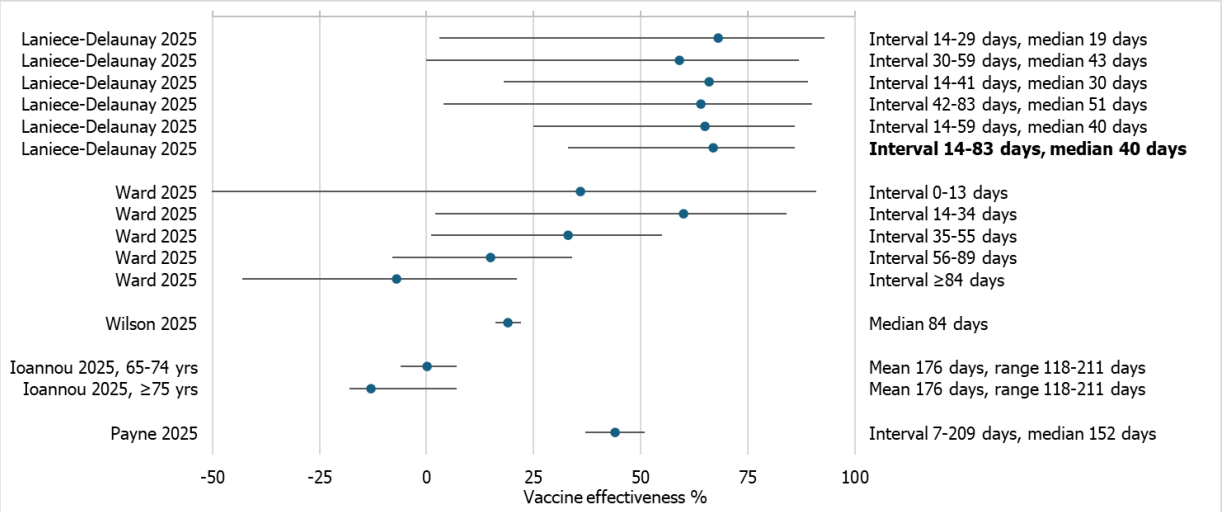
Notes: Four studies were case-control studies and the other study (Andersen 2025) was a cohort study. All studies reported on adults aged 65 years and older. Link-Gelles 2025a included mRNA KP.2 and protein subunit JN.1 vaccines and Appaneal 2025 included mRNA KP.2. The remaining three studies included XBB.1.5 vaccines (Caffrey 2024 and Andersen 2025 included mRNA XBB.1.5 vaccines and Link-Gelles 2025b included mixed XBB.1.5 vaccines). Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

The two case-control studies that reported on outpatient visits among those aged 65 years and older differed by study period and vaccine formulation.[263, 266] The study of autumn/winter 2023/2024 reported a VE of 24% (95% CI: 9% to 36%) for mRNA XBB.1.5 vaccines compared with no vaccination during that period (median 53 days post-vaccination).[266] The study of autumn 2024 reported a VE of 58% (95% CI: 36% to 73%) for mRNA KP.2 vaccines compared with no vaccination during that period (median 31 days post-vaccination).[263]

Of the five studies that reported on symptomatic SARS-CoV-2 infection, three reported on medically attended infection,[265, 267, 272] and two on laboratory-confirmed symptomatic infection.[271, 273] One case-control study of mRNA JN.1, KP.2, XBB.1.5 and unspecified vaccines (for the time period October 2024 to January 2025), reported a VE of 67% (95% CI: 33% to 86%) against medically attended infection at a median 40 days post-vaccination.[265] Four cohort studies reported the VE of XBB.1.5 vaccines (mRNA only[271, 272] and mixed mRNA and or protein subunit[267, 273]) for the time period September 2023 to May 2024. Two of these four studies reported a VE (against medically attended infection) that ranged from 19% (95% CI: 16% to 22%)[267] at a median 84 days post-vaccination to 44% (95% CI: 37 to 51)[272] at a median 152 days post-vaccination. It is worth noting that the latter study was conducted in a population of patients aged 65 years and older with ESKD. Of the two studies that reported VE against symptomatic infection, one reported a VE of 0.2% (95% CI: -6% to 7%) among those aged 65 to 74 years and -13% (-

18% to 7%) among those aged 75 years and older (at a mean 176 days post-vaccination).[271] The other study reported VE at incremental follow-up periods, ranging from -7% (-43% to 21%) at 84 days or more post-vaccination to 36% (95% CI: -358% to 91%) during the first 13 days post-vaccination.[273] A summary of the vaccine effectiveness estimates against symptomatic or medically attended infection among older adults is provided in Figure 4.3.

Figure 4.3 Vaccine effectiveness against symptomatic or medically attended SARS-CoV-2 infection among older adults from the index review



Notes: The case-control study Laniece-Delaunay 2025 included mRNA JN.1, KP.2, XBB.1.5 and unspecified strains and unspecified vaccines among adults aged 60 years and older. The four cohort studies reported on adults aged 65 years and older; two (Ward 2025 and Wilson 2025) included mRNA XBB.1.5 vaccines and two (Ioannou 2025 and Payne 2025) included mixed XBB.1.5 vaccines. Ioannou 2025 included age stratified results. For Ward 2025 at an interval of 0-13 days post-vaccination, the 95% CI was too wide to display fully (-358, 91). Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Hospitalisation

Thirteen studies from the index review reported on VE against COVID-19-related hospitalisation among older adults.[263, 264, 266-272, 274-277] These comprised seven case-control studies and six cohort studies and their results are summarised in Table B.4. A summary of the vaccine effectiveness estimates against hospitalisation among older adults is provided in Figure 4.4 for case-control studies and Figure 4.5 for cohort studies. Studies ranged in size from 1,111 to 14,234,785 individuals, and follow-up duration ranged from a median of 30 days to 230 days post-vaccination. Studies included differing vaccine types (all studies included mRNA vaccines while five additionally included protein subunit vaccines) and strain formulations (11 studies included only XBB.1.5 formulations). In general, while estimates of VE varied

between studies, there was evidence of waning effectiveness over time among case-control studies; VE estimates tended to be higher within two to four months post-vaccination, while there was evidence of waning effectiveness in two case-control studies that reported incremental follow-up periods beyond six-months post-vaccination. For studies that reported VE estimates disaggregated by age, there was no consistent pattern; confidence intervals typically overlapped. There was some evidence of an association between effectiveness and matching the vaccine formulation with the circulating strain of SARS-CoV-2 from two case-control studies, with poorer effectiveness when the formulation did not match the predominant strain.

Eleven of these 13 studies investigated XBB.1.5 vaccines, of which seven investigated mRNA vaccines only[266-268, 270, 274-276] and four investigated mixed mRNA and or protein subunit vaccines.[269, 271, 272, 277] Five of these 11 studies were case-control studies[266, 268, 269, 274, 275] and six were cohort studies.[267, 270-272, 276, 277]

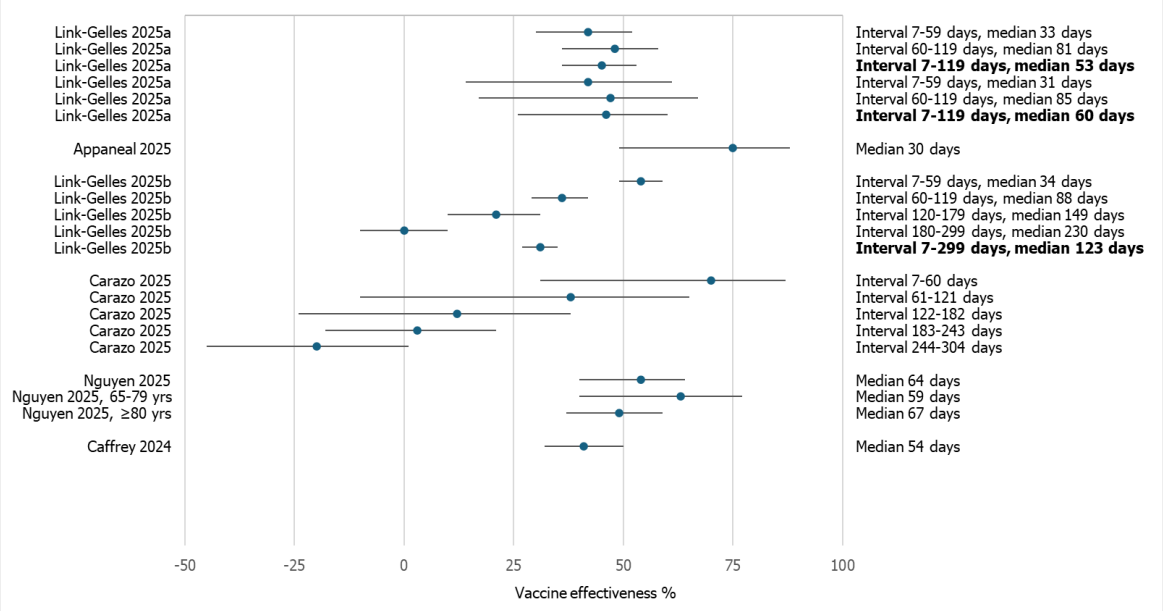
Across four case-control studies,[266, 269, 274, 275] overall estimates of VE against COVID-19-related hospitalisation for XBB.1.5 vaccines in older adults ranged from 30% (95% confidence interval (CI): 24% to 35%)[275] at up to 10 months post-vaccination to 54% (95% CI: 40% to 64%)[274] at a median 64 days post-vaccination. When restricted to the shortest reported follow-up period for each study, VE against COVID-19 related hospitalisation ranged from 41% (95% CI: 32% to 50%)[266] at a median 54 days post-vaccination to 70% (95% CI: 31% to 87%)[275] at 7 to 60 days post-vaccination. This latter study also stratified the results by circulating strain, with the reported VE of the XBB.1.5 vaccine among those aged 60 years and older being 54% (95% CI: 46% to 62%) during periods of XBB strain dominance and 23% (95% CI: 12% to 32%) and -1% (95% CI: -17% to 15%) during periods of JN.1 and KP.2 dominance, respectively.[275] A similar association was seen when results were aged-stratified for those aged 60 to 69 years, 70 to 79 years, and 80 years and older. The fifth case-control study reported the odds of hospitalisation or ED visits versus the odds of outpatient visits. The reported VE was 61% (95% CI: 48% to 71%) at a median 57 days post-vaccination.[268] In the same study, when stratified by the circulating SARS-CoV-2 strain, the VE for XBB.1.5 vaccines was higher for XBB.1.5 matched strains at 74% (95% CI: 58% to 84%) than for JN.1 strains at 48% (95% CI: 14% to 69%) at a median 57 days post-vaccination. A summary of vaccine effectiveness estimates against hospitalisation by period of specific SARS-CoV-2 strain dominance is provided in Figure 4.6.

Four of the six cohort studies that investigated XBB.1.5 vaccines, reported VE estimates against COVID-19-related hospitalisation for all adults aged 65 years and older.[267, 270, 272, 276] The reported VE estimates against hospitalisation ranged from 47% (95% CI: 28% to 61%)[270] at a median 3.9 months post-vaccination to 58%

(95% CI: 50% to 66%)[276] at 1 to 24 weeks post-vaccination. Two of the six cohort studies reported estimates of VE against COVID-19-related hospitalisation for age subgroups (namely, 65 to 74 years and 75 years and older in one study[271] and 65 to 79 years and 80 years and older in the other study[277]), the results of which are summarised in Table B.4.

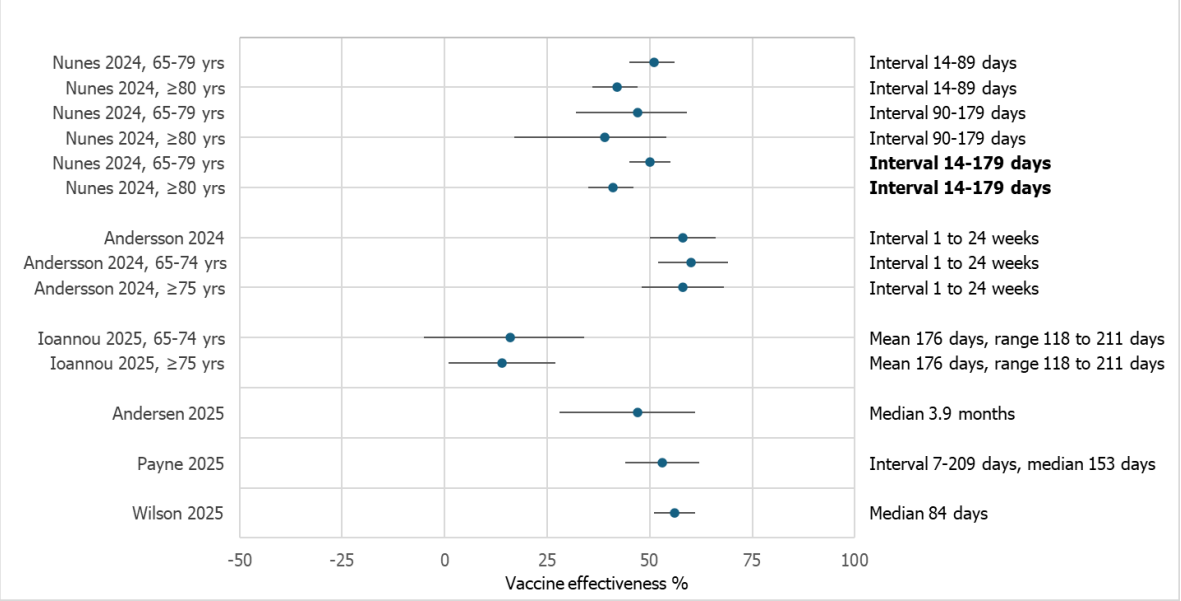
Two case-control studies reported VE estimates for more recent antigenically updated vaccine formulations; one study reported on mRNA KP.2 vaccines[263] and the other reported on mRNA KP.2 and or protein subunit JN.1 vaccines.[264] The VE against COVID-19-related hospitalisation ranged from 45% (95% CI: 36% to 53%)[264] at a median of 53 days post-vaccination to 75% (95% CI: 49% to 88%)[263] at a median of 30 days post-vaccination.

Figure 4.4 Vaccine effectiveness against hospitalisation among older adults from case-control studies included in the index review



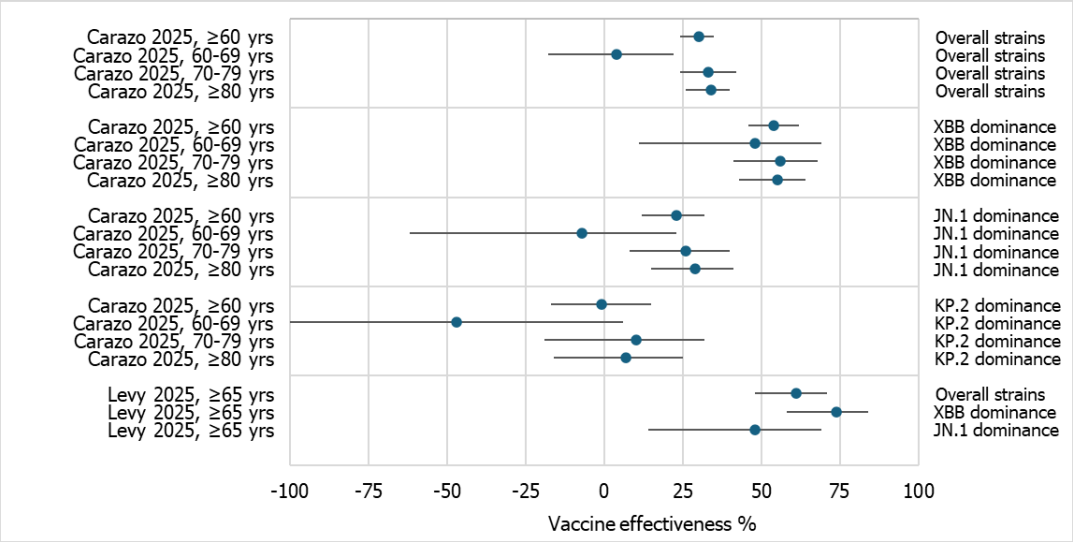
Notes: Link-Gelles 2025a included mRNA KP.2 or protein subunit JN.1 vaccines and Appaneal 2025 included mRNA KP.2 vaccines; both studies reported on adults aged 65 years and older. Link-Gelles 2025b included mixed XBB.1.5 vaccines among adults aged 65 years and older. The remaining three case-control studies included mRNA XBB.1.5 vaccines: Nguyen 2025 and Caffrey 2024 reported on adults aged 65 years and older; Carazo 2025 reported on adults aged 60 years and older. Nguyen 2025 included age-stratified results. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Figure 4.5 Vaccine effectiveness against hospitalisation among older adults from cohort studies included in the index review



Notes: The six cohort studies included XBB.1.5 vaccines: three (Ioannou 2025, Payne 2025 and Nunes 2024) included mixed XBB.1.5 vaccines and three (Andersen 2025, Andersson 2024, Wilson 2025) included mRNA XBB.1.5 vaccines. Each study reported on adults 65 years and older and three included age-stratified results. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Figure 4.6 Vaccine effectiveness against hospitalisation among older adults by period of SARS-CoV-2 strain dominance from case control studies included in the index review



Notes: The two case-control studies included mRNA XBB.1.5 vaccines. Carazo 2025 reported age-stratified results by period of SARS-CoV-2 strain dominance as overall strains, XBB dominance, JN.1 dominance and KP.2 dominance. Levy 2025 reported on adults aged 65 years and older by period of SARS-CoV-2 strain dominance as overall strains, XBB dominance and JN.1 dominance. For Carazo 2025 60-69 yrs during a period of KP.2 dominance, the 95% CI was too wide to display fully (-130 to 6).
Source: Scott et al.[57]

Intensive care unit admission

No studies from the index review reported on COVID-19-related intensive care unit (ICU) admissions.

One screening method ecological study from Netherlands (identified through the supplemental search) reported on COVID-19-related ICU admissions among adults aged 60 years and older.[283] Between October and December 2023, the VE of mRNA XBB.1.5 vaccination against ICU admissions was 73% (95% CI: 42% to 88%); see Table B.6.

Mortality and composite outcomes

Four cohort studies included in the index review reported on the effectiveness of XBB.1.5 vaccination against COVID-19-related mortality in older adults (Table B.7).[271, 272, 276, 277] One study included mRNA vaccines only[276] and three studies included mRNA and or protein subunit vaccines.[271, 272{Nunes, 2024 #392, 277] Two studies reported VE for all adults aged 65 years and older[272, 276] and three studies provided age-stratified results.[271, 276, 277] Studies ranged in size from 65,978 to 14,234,785 individuals, and follow-up duration ranged from an interval of 14 to 89 days to a

range of 118 to 211 days post-vaccination. Each of the four studies included mRNA XBB.1.5 vaccines, three of which also included protein subunit XBB.1.5 vaccines. In general, vaccine estimates varied between studies with no consistent trend in effectiveness. One study included incremental follow-up periods post-vaccination (0 to 3 months, 3 to 6 months) with the point estimates slightly lower at the longer follow-up intervals, but confidence intervals overlapped.[277] Three studies reported VE estimates disaggregated by age, but there was no consistent pattern; confidence intervals typically overlapped. A summary of the vaccine effectiveness estimates against mortality among older adults is provided in Figure 4.7.

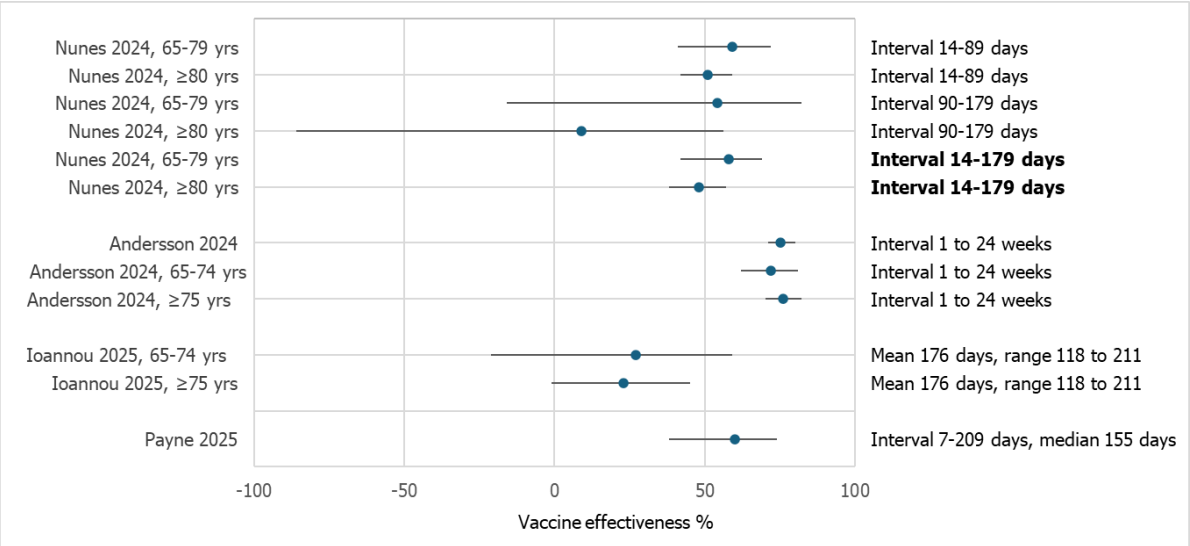
One cohort study of adults aged 65 years and older was conducted in those living with ESKD (without any additional immunocompromising conditions). The reported VE of mixed XBB.1.5 vaccines against COVID-19-related mortality was 60% (95% CI: 38% to 74%) at a median 155 days post-vaccination.[272] In the other cohort study, the reported VE of mRNA XBB.1.5 vaccines against COVID-19-related mortality in the general population aged 65 years and older was 75% (95% CI: 71% to 80%) at 1 to 24 weeks post-vaccination.[276]

For the age-stratified results among older adults, three cohort studies provided VE estimates for different age bands across the studies. In those aged 65 to 79 years, a study of mixed XBB.1.5 vaccines reported a VE of 58% (95% CI: 42% to 69%) against COVID-19-related mortality at 14 to 179 days post-vaccination.[277] In those aged 65 to 74 years, another cohort study of mixed XBB.1.5 vaccines reported a VE of 27% (95% CI: -21% to 59%) at a mean 176 days post-vaccination.[271] In two studies of those aged 75 years and older, the reported VE for XBB.1.5 vaccines ranged from 23% (95% CI: -1% to 45%)[271] at a mean 176 days post-vaccination (for mixed XBB.1.5 vaccines) to 76% (95% CI: 70% to 82%) at 1 to 24 weeks post-vaccination (for mRNA XBB.1.5 vaccines).[276] In those aged 80 years and older, one cohort study of mixed XBB.1.5 vaccines reported a VE of 48% (95% CI: 38% to 57%) at 14 to 179 days post-vaccination.[277]

Three studies (two cohort studies and one case-control study) reported on composite outcomes, which varied in definition from study to study. One cohort study of adults aged 65 years and older with ESKD defined critical illness as hospitalisation with ICU or critical care unit admission or mechanical ventilation or death.[272] In this study, the reported VE for mixed XBB.1.5 vaccines was 51% (95% CI: 34% to 64%) at a median 155 days post-vaccination. Another cohort study reported on severe hospitalisation or death occurring within 28 days of a positive COVID-19 test among adults aged 60 years and older over three timeframes (each lasting two months).[279] For mixed XBB.1.5 vaccines, the reported VE ranged from 36% (95% CI: 21% to 47%) between February and March 2024 to 60% (95% CI: 51% to 67%) between October and November 2023. One case-control study

reported on hospitalisation or death among adults aged 65 years and older by period of either XBB strain dominance or JN.1/KP.2 strain dominance.[278] For mRNA XBB.1.5 vaccines, the reported VE (at up to three months post-vaccination) was 68% (95% CI: 62% to 73%) during XBB strain dominance and 60% (95% CI: 52% to 67%) during JN.1/KP.2 strain dominance.

Figure 4.7 Vaccine effectiveness estimates against mortality among older adults from the index review



Notes: The four cohort studies included XBB.1.5 vaccines; one (Andersson 2024) included mRNA XBB.1.5 vaccines and three (Nunes 2024, Ioannou 2025 and Payne 2025) included mixed XBB.1.5 vaccines. The four studies reported on adults aged 65 years and older and three reported age-stratified results. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.

Source: Scott et al.[57]

Long-COVID

One cohort study included in the index review reported on overall outcomes among those aged 60 years and older with post-acute sequelae, from the date of infection until 31 to 365 days later.[282] The study compared outcomes in individuals who received bivalent booster vaccination with outcomes in individuals vaccinated with the original COVID-19 monovalent vaccines. The reported VE against any post-acute sequelae in those aged 60 years and older was 16% (95% CI: -9 to 34%). Post-acute sequalae included 34 long-term disorders and health conditions covering cardiovascular, neurological, psychiatric, endocrine, autoimmune, respiratory, renal and gastrointestinal outcomes.

No other studies were identified from the index review or supplemental search for long-COVID outcomes among older adults.

Residents of long-term care facilities

Symptomatic or medically attended infection

None of the primary studies included in the index review[57] or supplemental search reported on symptomatic or medically attended infection outcomes specifically in those living in LTCFs.

Hospitalisation

None of the primary studies included in the index review[57] or supplemental search reported on hospitalisation outcomes specifically in those living in LTCFs.

Intensive care unit admission

None of the primary studies included in the index review[57] or supplemental search reported on ICU related outcomes specifically in those living in LTCFs.

Mortality

None of the primary studies included in the index review[57] or supplemental search reported on mortality outcomes specifically in those living in LTCFs.

Long COVID

None of the primary studies included in the index review[57] or supplemental search reported on long COVID outcomes specifically in those living in LTCFs.

Immunocompromising conditions

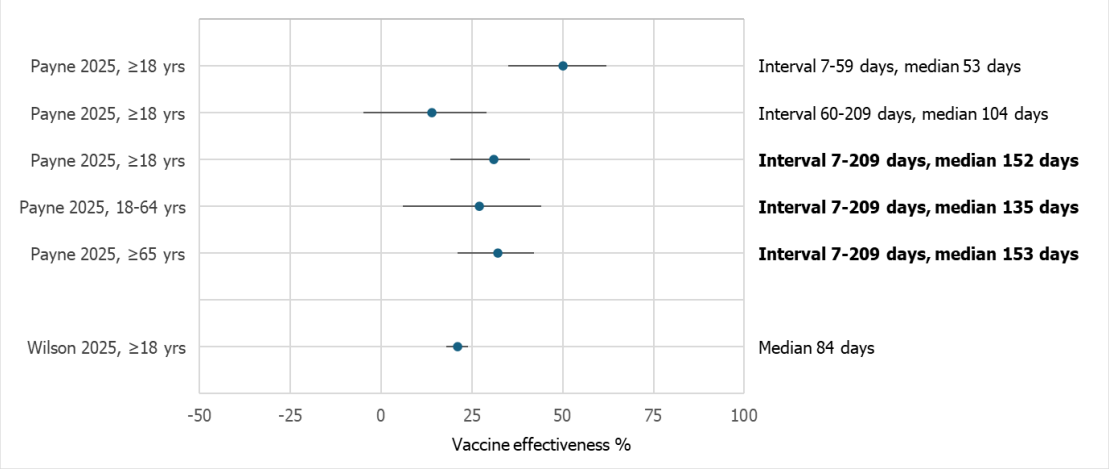
Symptomatic or medically attended infection

Three studies (two cohort studies and one case-control study) reported on symptomatic or medically attended infection among adults with immunocompromising conditions (Table B.9).[266, 267, 272] Studies ranged in size from 8,125 to 472,980 individuals, and follow-up duration ranged from a median of 52 days to 153 days post-vaccination. All three studies included mRNA XBB.1.5 vaccines, one of which also included XBB.1.5 protein subunit vaccines. Estimates of VE varied between studies. There was evidence of waning effectiveness over time in the one study that reported at incremental follow-up periods. One study presented data disaggregated by age sub-groups, with no evidence of a difference in VE. No disaggregated data were presented by vaccine type.

In the case-control study of those aged 18 years and older, mRNA XBB.1.5 vaccination had a reported VE against ED and UC visits of 34% (95% CI: 22% to

45%) at a median 52 days post-vaccination and against outpatient visits of 40% (95% CI: 19% to 55%) at a median 54 days post-vaccination.[266] The two cohort studies reported on medically attended infection.[267, 272] One of the cohort studies included those with ESKD with one or more additional immunocompromising conditions and reported age stratified results.[272] For adults aged 18 years and older, the reported VE for mixed XBB.1.5 vaccines was 31% (95% CI: 19% to 41%) at a median 152 days post-vaccination. For adults aged 18 to 64 years, the reported VE was 27% (95% CI: 6% to 44%) at a median 135 days post-vaccination, and for adults aged 65 years and older, the reported VE was 32% (95% CI: 21% to 42%) at a median 153 days post-vaccination. There was evidence of waning vaccine effectiveness over time in this study, declining from 50% (95% CI: 35% to 62%) at a median 53 days post-vaccination to 14% (95% CI: -5% to 29%) at a median 104 days post-vaccination. The other cohort study included those aged 18 years and older with immunocompromise, in which the reported VE of mRNA XBB.1.5 vaccines against medically attended infection was 21% (95% CI: 18% to 24%) at a median 84 days post-vaccination.[267] A summary of the vaccine effectiveness estimates against medically attended infection is provided in Figure 4.8.

Figure 4.8 Vaccine effectiveness estimates against medically attended infection among those with immunocompromising conditions from the index review



Notes: Wilson 2025 included mRNA XBB.1.5 vaccines and reported on adults aged 18 years and older with immunocompromising conditions. Payne 2025 included mixed XBB.1.5 vaccines and reported age-stratified results. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Hospitalisation

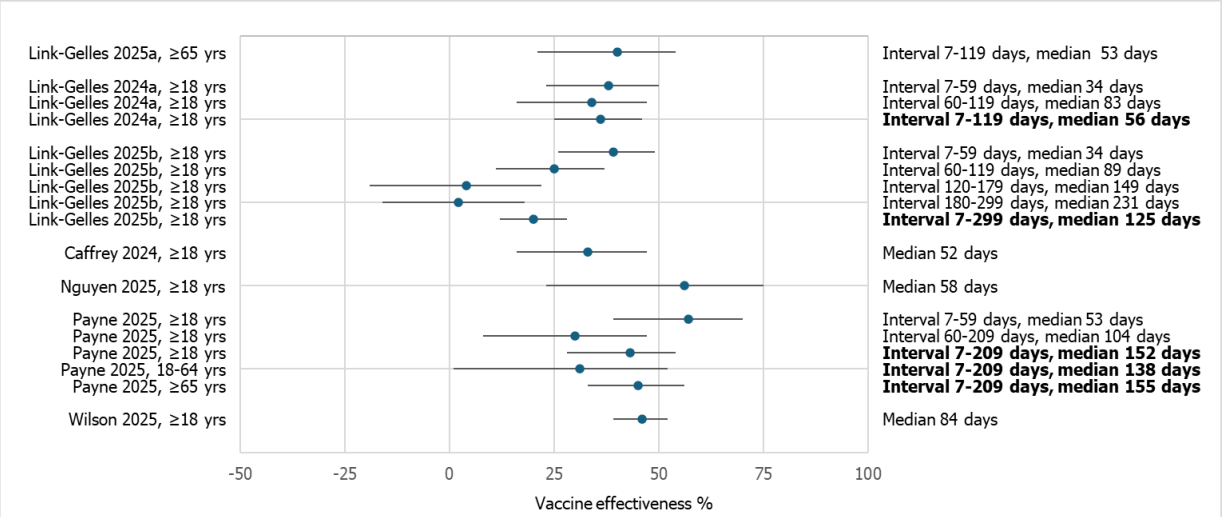
Seven studies from the index review reported on COVID-19-related hospitalisation among those with immunocompromising conditions, of which five were case-control studies[264, 266, 269, 274, 280] and two cohort studies.[267, 272] The definition of

immunocompromising conditions varied across the studies. Studies ranged in size from 278 to 472,980 individuals, and follow-up duration ranged from a median of 35 days to a median of 231 days post-vaccination. Six studies included XBB.1.5 vaccines (four of which included mRNA vaccines only and three included mRNA and protein subunit vaccines). In general, estimates of VE varied between studies. Two of three studies that provided incremental follow-up periods included intervals up to or beyond six months; in both studies, point estimates were lower at longer periods of follow-up suggesting waning effectiveness over time. One study reported VE estimates disaggregated by age; while a higher VE point estimate was reported in the older age group, the confidence intervals overlapped. No study provided disaggregated data by vaccine type. Details of the definitions used for immunocompromise differed between studies and are included in Table B.10. A summary of the vaccine effectiveness estimates against hospitalisation is provided in Figure 4.9.

One case-control study reported on COVID-19 related hospitalisation among adults aged 65 years and older with immunocompromising conditions who received mRNA KP.2 or protein subunit JN.1 vaccines from September 2024 through January 2025.[264] The reported VE was 40% (95% CI: 21% to 54%) at a median of 53 days post-vaccination.

Six studies (four case-control studies and two cohort studies) reported on XBB.1.5 vaccines among those aged 18 years and older with immunocompromising conditions. Across the four case-control studies,[266, 269, 274, 280] VE ranged from 20% (95% CI: 12% to 28%)[269] at a median of 125 days post-vaccination to 56% (95% CI: 23% to 75%)[274] at a median of 58 days post-vaccination. The reported VE from the two cohort studies ranged from 43% (95% CI: 28% to 54%)[272] at a median of 152 days post-vaccination to 46% (95% CI: 39% to 52%)[267] at a median of 84 days post-vaccination. One of the two cohort studies reported the VE of XBB.1.5 vaccines in those with ESKD and one or more additional immunocompromising condition, with the results stratified by age group.[272] Among those aged 18 to 64 years, VE was 31% (95% CI: 1% to 52%) at a median of 138 days post-vaccination, while for those aged 65 years and older VE was 45% (95% CI: 33% to 56%) at a median of 155 days post-vaccination.

Figure 4.9 Vaccine effectiveness estimates against hospitalisation among adults with immunocompromising conditions from the index review



Notes: Case-control studies – Link-Gelles 2025a included mRNA KP.2 and protein subunit JN.1 vaccines. The other four case-control studies included XBB.1.5 vaccines: two (Link-Gelles 2024a and Link-Gelles 2025b) included mixed XBB.1.5 vaccines; two (Caffrey 2024 and Nguyen 2025) included mRNA XBB.1.5 vaccines. Cohort studies – The two cohort studies included XBB.1.5 vaccines: Payne 2025 included mixed XBB.1.5 vaccines and reported age-stratified results; Wilson 2025 included mRNA XBB.1.5 vaccines. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Intensive care unit admission

None of the primary studies included in the index review or supplemental search reported on ICU related outcomes for those with immunocompromising conditions.

Mortality and composite outcomes

Two studies included in the index review reported on the vaccine effectiveness against mortality and or composite outcomes in those with immunocompromising conditions (see Table B.11). The two studies ranged in size from 23,163 to 34,076 individuals, and follow-up duration ranged from a median of 34 to 230 days in one study and 53 to 156 days in the other. Both studies included mRNA or protein subunit XBB.1.5 vaccines, but did not present disaggregated data by vaccine type. The VE differed between studies. In both studies, there was a decline in VE point estimates over time, suggesting possible waning effectiveness, but confidence intervals overlapped. One study reported VE estimates disaggregated by age; while a higher VE point estimate was reported in the older age group, the confidence intervals overlapped.

One cohort study from the index review reported on COVID-19-related mortality and critical illness (defined as hospitalisation with ICU or critical care unit admission, or mechanical ventilation requirement, or death) among those with ESKD and one or more additional immunocompromising condition.[272] This study reported on mixed XBB.1.5 vaccination and results were stratified by age group. The reported VE was 61% (95% CI: 36% to 77%) against COVID-19-related mortality and 52% (95% CI: 30% to 66%) against critical illness at a median of 153 days post-vaccination in those aged 18 years and older. In those aged 18 to 64 years, the reported VE was 60% (95% CI: -7% to 66%) against COVID-19-related mortality and 42% (95% CI: -9% to 70%) against critical illness at a median of 142 days post-vaccination. In those aged 65 years and older, the reported VE was 61% (95% CI: 40% to 75%) against COVID-19-related mortality and 54% (95% CI: 33% to 68%) against critical illness at a median of 156 days post-vaccination.

The other case-control study that reported on critical illness defined it as admission to ICU or in-hospital death.[269] In those aged 18 years and older with an immunocompromising condition, the reported VE was 40% (95% CI: 26% to 51%) at a median of 125 days post-vaccination.

Long COVID

None of the primary studies included in the index review or supplemental search reported on long COVID outcomes in those with immunocompromising conditions.

Underlying medical conditions

Symptomatic or medically attended infection

The index review included one case-control study and two cohort studies that reported on these outcomes in adults with underlying medical conditions and thus considered to be at higher risk of severe disease (Table B.12).[266, 267, 272] The intervention in each of the studies was mRNA XBB.1.5 vaccination (one study also included mRNA protein subunit vaccines), but the study populations differed with respect to the specific underlying medical conditions. The studies ranged in size from 13,048 to 1,532,356 individuals, and follow-up duration ranged from a median of 54 days to 150 days post-vaccination. One study provided evidence of a small decrease in VE over time up to six months post-vaccination. Effectiveness estimates were similar when disaggregated by age-group in one study and confidence intervals overlapped.

The case-control study reported on ED or UC visits and outpatient visits among individuals aged 18 years and older with obesity who received mRNA XBB.1.5 vaccination.[266] The reported VE was 44% (95% CI: 35% to 52%) at a median of

56 days post-vaccination for ED or UC visits and 34% (95% CI: 19% to 47%) at a median of 54 days post-vaccination for outpatient visits.

Two cohort studies reported on medically attended infection in those with underlying conditions.[267, 272] One cohort study reported aged-stratified results for mixed XBB.1.5 vaccines among adults with ESKD. The reported VE in adults aged 18 to 65 years was 40% (95% CI: 27% to 51%) at a median of 131 days post-vaccination and 43% (95% CI: 36% to 50%) at a median of 150 days post-vaccination when considering all adults aged 18 years and older. The other cohort study reported on mRNA XBB.1.5 vaccination among adults 18 years and older belonging to a high-risk cohort, defined as having underlying medical conditions associated with increased risk of severe COVID-19 outcomes as noted in Table B.12.[267] The reported VE was 23% (95% CI: 21% to 24%) at a median of 84 days post-vaccination.

Hospitalisation

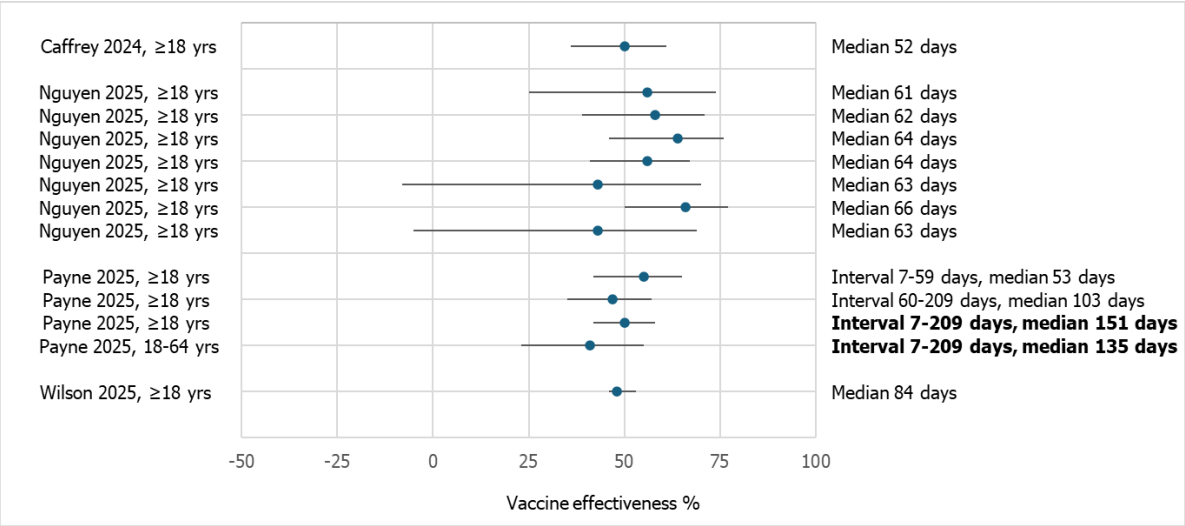
The index review included four studies (two cohort and two case-control studies) that reported on COVID-19 related hospitalisation among those with underlying medical conditions (Table B.13).[266, 267, 272, 274] A summary of the vaccine effectiveness estimates against hospitalisation is provided in Figure 4.10. Studies ranged in size from 92 to 1,532,356 individuals, and follow-up duration ranged from a median of 52 days to 151 days post-vaccination. Each of the studies included mRNA XBB.1.5 vaccines (one study also included protein subunit XBB.1.5 vaccines). One study reported VE estimates by incremental follow-up period; while point estimates decreased over time indicating waning immunity, confidence intervals overlapped. The same study provided VE estimates disaggregated by age groups; while VE point estimates were higher for the older cohort, confidence intervals overlapped.[272] No disaggregated data were presented by vaccine type.

The two case-control studies included mRNA XBB.1.5 vaccines.[266, 274] The reported VE in one study among adults with obesity was 50% (95% CI: 36% to 61%) at a median of 52 days post-vaccination. The other case-control study reported VE for those aged 18 years and older by type of chronic condition.[274] Across the seven types of chronic condition included, the VE ranged from 43% (95% CI: -8% to 70%) at a median of 63 days post-vaccination among those with chronic liver disease to 66% (95% CI: 50% to 77%) at a median of 66 days post-vaccination among those with renal disease.

One of the two cohort studies reported on a high-risk cohort (as defined in Table B.13) aged 18 years and older who received mRNA XBB.1.5 vaccination.[267] The reported VE was 48% (95% CI: 46% to 53%) at a median of 84 days post-vaccination. The other cohort study included adults with ESKD who received mixed

XBB.1.5 vaccines and reported age-stratified results.[272] When considering all adults aged 18 years and older the reported VE was 50% (95% CI: 42% to 58%) at a median of 151 days post-vaccination, while when limited to adults aged 18 to 64 years the reported VE was 41% (95% CI: 23% to 55%) at a median of 135 days post-vaccination.

Figure 4.10 Vaccine effectiveness against hospitalisation among those with underlying medical conditions from the index review



Notes: Case-control studies – The two case-control studies (Caffrey 2024 and Nguyen 2025) included mRNA XBB.1.5 vaccines and reported on adults aged 18 years and older with underlying medical conditions. Nguyen 2025 stratified results by medical conditions as follows: asthma; lung disease; cardiovascular disease; hypertension; chronic liver disease, renal disease, type two diabetes mellitus. Cohort studies – The two cohort studies included XBB.1.5 vaccines: Payne 2025 included mixed XBB.1.5 vaccines and Wilson 2025 included mRNA XBB.1.5 vaccines. Payne 2025 reported age-stratified results. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Intensive care unit admission

None of the primary studies included in the index review or the supplemental search reported on this outcome in those living with underlying medical conditions.

Mortality

One cohort study from the index review reported on COVID-19 related mortality and critical illness outcomes at multiple intervals among adults with ESKD who received mixed XBB.1.5 vaccines with results also disaggregated by age (Table B.15).[272] This study included 112,250 individuals and overall follow-up was a median of 151 days post-vaccination. When reported by incremental follow-up period, there was evidence of waning effectiveness over time for both outcomes from the difference in

point estimates, however, the confidence intervals overlapped. When disaggregated by age sub-groups there was evidence of a difference with a higher point estimate reported for the older cohort, although confidence intervals overlapped.

When considering all adults aged 18 years and older the reported VE for mortality was 59% (95% CI: 41% to 72%) at a median of 151 days post-vaccination, while for those aged 18 to 64 years, VE was 58% (95% CI: 1% to 82%) at a median of 135 days post-vaccination.

Within this cohort study, critical illness was defined as requiring hospitalisation with ICU or critical care unit admission or mechanical ventilation, or death (Table B.15).[272] For those aged 18 years and older the reported VE was 49% (95% CI: 32% to 61%) at a median of 151 days post-vaccination and for those aged 18 to 64 years the reported VE was 39% (95% CI: -3% to 64%) at a median of 135 days post-vaccination.

Long COVID

None of the primary studies included in the index review or supplemental search reported on long COVID outcomes in those with underlying medical conditions.

Pregnant individuals

Symptomatic or medically attended infection

None of the primary studies included in the index review or supplemental search reported on this outcome in pregnant individuals.

Hospitalisation

None of the primary studies included in the index review or supplemental search reported on this outcome in pregnant individuals.

Intensive care unit admission

None of the primary studies included in the index review or supplemental search reported on this outcome in pregnant individuals.

Mortality

None of the primary studies included in the index review or supplemental search reported on this outcome in pregnant individuals.

Long COVID

None of the primary studies included in the index review or supplemental search reported on long COVID outcomes in pregnant individuals.

Healthcare workers

Symptomatic or medically attended infection

One cohort study from the index review reported on moderate infection among healthcare workers who had received either XBB.1.5 or bivalent original/omicron BA.4/5 vaccines in October 2023 compared to those with a waned booster from the prior vaccination campaign.[281] Moderate infection was defined as COVID-19 related infection with clinically relevant symptoms such as influenza-like illness or acute respiratory illness lasting five days or more, or any sick leave (Table B.16). VE estimates (at six months follow-up) were reported for XBB.1.5 and or bivalent/original BA.4/5 vaccines, and for each of the two vaccines separately. The reported overall VE for XBB.1.5 and or bivalent/original BA.4/5 vaccines was 40% (95% CI: 20% to 55%). VE differed by antigen type. For XBB.1.5 vaccines alone, the reported VE was 47% (95% CI: 28% to 62%), and for bivalent original/omicron BA.4/5 vaccines the reported VE was 2% (95% CI: -36% to 30%).

One cohort study of hospital-based healthcare workers from seven European countries reported no evidence of protection against symptomatic or asymptomatic SARS-CoV-2 infection in those vaccinated with any COVID-19 vaccine (82% received XBB.1.5 adapted vaccines and 18% received non-XBB.1.5 adapted vaccines) compared to those who were unvaccinated (Table B.17).[284] While there was evidence of waning protection overtime, none of the reported estimates were statistically significant.

Hospitalisation

None of the primary studies included in the index review or supplemental search reported on this outcome in healthcare workers.

Intensive care unit admission

None of the primary studies included in the index review or supplemental search reported on this outcome in healthcare workers.

Mortality

None of the primary studies included in the index review or supplemental search reported on this outcome in healthcare workers.

Long COVID

None of the primary studies included in the index review or supplemental search reported on long COVID outcomes in healthcare workers.

General population aged 18 to 59 years

Symptomatic or medically attended infection

Five studies (three case-control and two cohort studies) from the index review reported on these outcomes among those in the general population aged 18 to 59 years old (Table B.18).[264, 266, 267, 269, 271] Studies ranged in size from 13,175 to 1,064,028 individuals, and follow-up duration ranged from a median of 34 days to a median of 230 days post-vaccination. Four studies included mRNA XBB.1.5 vaccines (two of which also included XBB.1.5 protein subunit vaccines). Estimates of VE varied between studies. In the two studies that reported VE estimates at incremental follow-up periods, there was evidence of waning effectiveness over time; one study provided evidence of waning effectiveness up to four months post-vaccination while the other provided evidence of waning effectiveness at more than six months post-vaccination. One study reported data disaggregated by age within those aged 18 to 64 years (18 to 49 years and 50 to 64 years), with no clear evidence of a difference in VE. The studies did not report disaggregated data by vaccine type.

Three case-control studies reported on ED or UC visits among adults aged 18 to 64 years.[264, 266, 269] One of the case-control studies included mRNA KP.2 or protein subunit JN.1 vaccines and the reported overall VE was 30% (95% CI: 20% to 39%) at 7 to 119 days post-vaccination.[264] The other two case-control studies included mRNA XBB.1.5 vaccines,(Caffrey, 2024 #379} or mixed XBB.1.5 vaccines.[269] The reported VE ranged from 22% (95% CI: 18% to 26%)[269] at a median 116 days post-vaccination to 48% (95% CI: 37% to 57%)[266] at a median 54 days post-vaccination.

One case-control study reported on outpatient visits among adults aged 18 to 64 years who received mRNA XBB.1.5 vaccines.[266] The reported VE was 34% (95% CI: 14% to 50%) at a median 51 days post-vaccination.

Two cohort studies reported on SARS-CoV-2 related infection among adults aged 18 to 64 years.[267, 271] One cohort study included mixed XBB.1.5 vaccines and reported the VE against SARS-CoV-2 infection, which primarily but not exclusively comprised medically attended SARS-CoV-2 infection.[271] The reported VE was 9% (95% CI: 2% to 15%) at a mean 176 days post-vaccination. The other cohort study included mRNA XBB.1.5 vaccines and reported on medically attended cases with age-stratified results at a median 84 days post-vaccination.[267] For adults aged 18 to 49 years, the

reported VE was 28% (95% CI: 25% to 30%) and for adults aged 50 to 64 years the reported VE was 25% (95% CI: 23% to 27%).

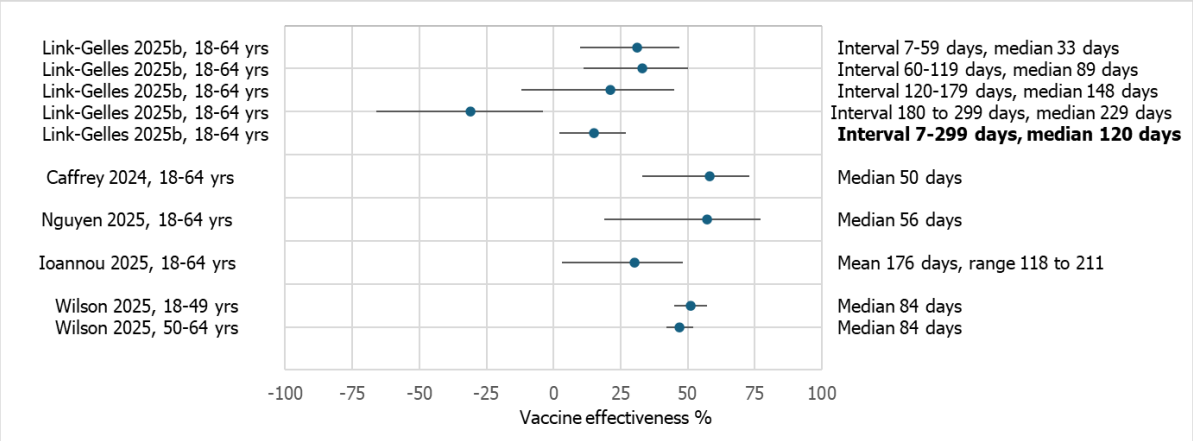
Hospitalisation

Five studies from the index review (three case-control and two cohort studies) reported on COVID-19 related hospitalisation among adults aged 18 to 64 years who received XBB.1.5 vaccines;[266, 267, 269, 271] see Table B.20. Studies ranged in size from 13,175 to 1,064,028 individuals, and follow-up duration ranged from a median of 33 days to a median of 229 days post-vaccination. Each study included mRNA XBB.1.5 vaccines (two of which also included protein subunit XBB.1.5 vaccines). Estimates of VE varied between studies. In general, effectiveness was highest at shorter follow-up periods post-vaccination. One study reported incremental follow-up periods, providing evidence of waning effectiveness over time. One study also reported data disaggregated by age for this cohort, with no clear evidence of a difference in VE. No study provided disaggregated data by vaccine type. A summary of the vaccine effectiveness estimates against hospitalisation is provided in Figure 4.11.

Two of the case-control studies included mRNA XBB.1.5 vaccines,[266, 274] and one included mixed XBB.1.5 vaccines.[269] The reported VE ranged from 15% (95% CI: 2% to 27%)[269] at a median 120 days post-vaccination to 58% (95% CI: 33% to 73%)[266] at a median 50 days post-vaccination.

One of the two cohort studies included mixed XBB.1.5 vaccines and reported an overall VE of 30% (95% CI: 3% to 48%) over a mean follow-up period of 176 days among adults aged 18 to 64 years.[271] The other cohort study included mRNA XBB.1.5 vaccines and reported age-stratified results over a median 84 days post-vaccination.[267] The reported VE was 51% (95% CI: 45% to 57%) for adults aged 18 to 49 years and 47% (95% CI: 42% to 52%) for adults aged 50 to 64 years.

Figure 4.11 Vaccine effectiveness estimates against hospitalisation among those in the general population aged 18 to 59 years from the index review



Notes: Case-control studies – The three case-control studies reported on adults aged 18 to 64 years and included XBB.1.5 vaccines: Two (Caffrey 2024 and Nguyen 2025) included mRNA XBB.1.5 vaccines and Link-Gelles 2025b included mixed XBB.1.5 vaccines. Cohort studies – The two cohort studies reported on adults aged 18 to 64 years and included XBB.1.5 vaccines. Ioannou 2025 included mixed XBB.1.5 vaccines. Wilson 2025 included mRNA XBB.1.5 vaccines and reported age-stratified results. Bold text denotes overall follow-up periods for studies with multiple follow-up times post-vaccination.
Source: Scott et al.[57]

Intensive care unit admission

None of the primary studies included in the index review[57] or supplemental search reported on this outcome for this sub-group.

Mortality

One cohort study included in the index review reported on COVID-19 related mortality among adults aged 18 to 64 years who received mixed XBB.1.5 vaccines.[271] The study included 157,266 individuals, as presented in Table B.22. The reported VE was 84% (95% CI: 21% to 100%) over a mean follow-up of 176 days.

Long COVID

One cohort study included in the index review reported COVID-19 related post-acute sequelae from the date of infection until 31 to 365 days later.[282] The study included adults aged 18 to 59 years who received a bivalent booster original/omicron BA.4-5 vaccine. The reported VE against any post-acute sequelae was 49% (95% CI: 38% to 59%). Post-acute sequalae included 34 long-term disorders and health conditions

covering cardiovascular, neurological, psychiatric, endocrine, autoimmune, respiratory, renal and gastrointestinal outcomes.

4.3.3 Safety of COVID-19 vaccines

The studies discussed in this section were identified from the index review and cover periods from 2020 to 2023 but predominantly cover from 2020 to 2022. As such, they mostly related to original vaccine compositions and not Omicron-adapted vaccines. Some of the vaccines listed below, such as the viral vector recombinant vaccine ChAdOx1, have had their marketing authorisation withdrawn in the EU.[82] In such instances these data are for populations who received mixed vaccine types. No additional safety findings were identified from the supplemental search. Findings in relation to the safety of COVID-19 vaccines are presented by subgroups of interest: older adults, residents of LTCFs, those with immunocompromising conditions, those with underlying medical conditions, pregnant women, healthcare workers, and the general population aged 18 to 59 years.

Older Adults

Tables 4A.23 to 4A.27 summarise the eight studies included in the index review that reported on various adverse events of special interest (AESI) related to COVID vaccination in older adults.

Guillain-Barré syndrome

A 2025 self-controlled case series from the US reported that there was no significant association between Guillain-Barré syndrome (GBS) and COVID vaccination either with mRNA-1273 (RI 0.87, 95% CI: 0.52 to 1.47) or BNT162b2 (RI 0.39; 95% CI: 0.08 to 1.80) among adults aged 65 years or older, as presented in Table B.23.[285]

Myocarditis/Pericarditis

Two studies reported on the risk of myocarditis/pericarditis, as presented in Table B.24. One case control study from France showed no significant association between myocarditis/pericarditis and COVID vaccination following the first and second dose of BNT162b2 (first dose odds ratio (OR) 1.4, 95% CI: 0.70% to 2.90%; second dose OR 0.84, 95% CI:040% to1.80%) or mRNA-1273 (first dose OR 1.0, 95% CI 0.20 to 5.3; second dose OR 2.0, 95% CI 0.46 to 8.70) among adults aged 50 years and older.[286] However, the study reported an increased risk of myocarditis after the third dose of BNT162b2 (OR 2, 95% CI 1.1% to 3.8%) and mRNA-1273 (OR 3.00, 95% CI 1.20 to 7.80). One cohort study from Sweden reported age-stratified results of vaccination and risk of myopericarditis one to six weeks after vaccination for those aged 66 to 75 years and 76 years and older.[287] Among those aged 66 to 75 years,

while there was consistency in the direction of effect, a statistically significant increased risk of myopericarditis was only observed after the second dose (hazard ratio (HR) 1.85, 95% CI: 1.35 to 2.57). Among those aged 76 years and older, there was an increased risk of myopericarditis observed after each of the vaccine doses (first, second and third), as presented in Table B.24.

Stroke

Four studies reported mixed findings for the association of vaccination and stroke-related outcomes among older adults, as presented in Table B.25.[287-290] One case-control study reported no association for any stroke-related outcomes among those aged 60 years and older in Qatar.[288] One self-controlled case series from the US found no association between ischaemic stroke 1 to 42 days after vaccination among those aged 65 years and older.[290] Two studies reported findings of an inverse association between vaccination and stroke-related outcomes among older adults.[287, 289] One cohort study from the UK reported a reduced risk of stroke resulting in hospitalisation after vaccination with one or two doses of BNT162b2 (HR 0.17, 95% CI: 0.11 to 0.27) compared with no vaccination among those aged 50 to 87 years.[289] One cohort study from Sweden reported a reduced risk of stroke one to six weeks after vaccination compared with no vaccination;[287] this reduced risk was demonstrated after first and third doses among those aged 66 to 75 years and after second and third doses for those aged 76 years and older.

Venous thromboembolism

Two studies reported on venous thromboembolism or thromboembolic events following vaccination among older adults, with mixed findings as presented in Table B.26.[289, 291] One self-control case series from South Korea reported no association among those aged 65 to 74 years (incidence rate ratio (IRR) 1.16, 95% CI: 0.53 to 1.42) or 75 years and older (IRR 0.88, 95% CI: 0.69 to 1.13) at 0 to 21 days post-vaccination.[291] One cohort study from the UK reported a reduced risk of venous thromboembolism resulting in hospitalisation after vaccination with one or two doses of BNT162b2 or ChAdOx1nCoV-19 vaccines (HR: 0.43, 95% CI 0.27 to 0.67), or when considering specifically just the BNT162b2 vaccines (HR 0.45, 95% CI: 0.27 to 0.76), compared with no vaccination among those aged 50 to 87 years.[289]

Composite outcomes

One cohort study from England reported reduced risks of composite venous and arterial safety outcomes among older adults who received mRNA vaccines compared with no vaccination, as presented in Table B.27.[292] Results were reported for those aged 60 to 79 years and 80 years and older with a first and second dose of mRNA

BNT162b2 vaccine, followed by a booster dose of either mRNA-1273 or BNT162b2, over a follow up period of up to 24 weeks. The reduced risk of each composite outcome was found for those aged 60 to 79 years and those aged 80 years and older, and persisted from one week after vaccination through to between 13 and 24 weeks after vaccination. The composite venous outcome included pulmonary embolism, intracranial venous thrombosis, portal vein thrombosis and lower limb deep vein thrombosis. The composite arterial outcome included acute myocardial infarction, ischaemic stroke, and other arterial embolism events.

Long-term care facilities

No studies were identified from the index review[57] or supplemental search that reported safety findings specifically on those living in LTCFs.

Immunocompromising conditions

Tables 4A.28 to 4A.34 summarise the findings from three studies included in the index review that reported on various AESI related to COVID-19 vaccination among individuals with immunocompromising conditions.

Anaphylaxis

One self-controlled case series from England examined the association between anaphylaxis and various vaccine types and doses when considered collectively and separately by vaccine type among immunocompromised individuals aged 12 years and older within 1 to 28 days following vaccination.[293] There was no association between anaphylaxis risk and vaccination for overall vaccination (that is, including BNT162b2, mNA-1273 or ChAdOx1 vaccines) or BNT162b2 mRNA vaccination only. However, the study reported a statistically significant higher risk of anaphylaxis following a third vaccine dose with mRNA-1273 (IRR 6.87, 95% CI 1.64 to 28.72); of note though, this finding was based on five events only and so should be interpreted with caution, as noted in Table B.28.

Guillain-Barré syndrome

Two self-controlled case series reported no significant association with GBS among immunocompromised individuals after vaccination, as presented in Table B.29.[285, 293] One study using data from the Global Vaccine Data Network from 14 study sites reported no association between COVID-19 mRNA vaccination and GBS during a risk period from 1 to 42 days after vaccination (relative incidence (RI) 0.78, 95% CI: 0.54 to 1.14).[285] The other study was from England and reported no association between vaccination with mRNA vaccines or adenoviral vector vaccines and GBS risk,

from 1 to 28 days after vaccination in individuals aged 12 years and older (IRR 2.22, 95% CI: 0.46 to 10.73).[293]

Myocarditis/pericarditis

One self-controlled case series from England reported on myocarditis and pericarditis risk following COVID-19 vaccination (up to three doses) among those aged 12 years and older with immunocompromise (Table B.30).[293] The study reported the risk both for any COVID-19 vaccine (mRNA vaccine [BNT162b2, mRNA-1273] or adenoviral vector vaccine [ChAdOx]) within 1 to 28 days after vaccination and separately the risk of pericarditis for the mRNA vaccine BNT162b2. No significant association was noted for either myocarditis (first or second dose) or pericarditis (first, second or third dose) following any COVID-19 vaccination. However, a reduced risk of pericarditis following the first dose of mRNA vaccine BNT162b2 (IRR 0.86, 95% CI 0.49 to 0.89), with no association after the second or third doses.

Stroke

One self-controlled case series from England reported on the risk of ischaemic stroke, haemorrhagic stroke and any stroke or transient ischaemic attack (TIA) among those aged 12 years and older with immunocompromise following different doses of any COVID-19 vaccine and then separately for each vaccine type, as presented in Table B.31.[293] For all outcomes and irrespective of the vaccine type or dose, there was no evidence of increased risk of stroke; the point estimates consistently suggested an inverse relationship (lower incidence with vaccination); however the association was not always statistically significant. For COVID-19 vaccination (any), there was a reduced risk of ischaemic stroke 1 to 28 days after the first, second and third dose compared with the periods outside of this window (>28 days before or after the vaccine dose). When considered by vaccine type, for BNT162b2 vaccination, this association remained after the first and third doses, with no association after the second dose. For mRNA-1273 vaccination, there was no information for the first or second doses and no association after the third dose. For haemorrhagic stroke, there was a reduced risk for overall vaccination after the first and second dose, while for BNT162b2 vaccination there was a reduced risk after the first dose. There was no association after other doses, and no information for mRNA-1273 vaccination only. For any stroke or TIA, COVID-19 vaccination (any) was associated with a reduced risk after the first, second and third dose. When considered specifically by vaccine type, data were available for the first three doses of BNT162b2 and for the third dose of mRNA-1273. All point estimates suggested an inverse association (that is, lower incidence) following vaccination; however the result was only statistically significant for the first and third doses of BNT162b2.

Immune thrombocytopenic purpuria

One self-controlled case series from England reported on risk of immune thrombocytopenic purpuria after COVID-19 vaccination among those aged 12 years and older with immunocompromise, as presented in Table B.32.[293] The study noted no significant association between COVID-19 vaccination and immune thrombocytopenic purpuria up to 28 days post vaccination, either when considered for any COVID-19 vaccination (mRNA vaccine [BNT162b2, mRNA-1273] or adenoviral vector vaccine [ChAdOx1]), or when considering specifically the BNT162b2.

Venous thromboembolism

One self-controlled case series from England reported on the risk of venous thromboembolism among those aged 12 years and older with immunocompromise, as presented in Table B.33.[293] When considering any COVID-19 vaccination (that is, with any dose of an mRNA or adenoviral vector vaccine), there was a reduced risk of venous thromboembolism 1 to 28 days after the first, second and third vaccination doses compared with outside of the risk period This association was also seen when considering specifically the BNT162b2 vaccine. For mRNA-1273 vaccination only, information was only available after the third dose, for which there was no association.

Immune-related adverse events

One cohort study from the US reported on the risk of immune-related adverse events following COVID-19 booster vaccination with an mRNA bivalent vaccine among patients with advanced non-small cell lung cancer receiving immune checkpoint inhibitor treatments, as presented in Table B.34.[294] No association was seen between vaccination and any grade of immune-related adverse events.

Underlying medical conditions

Sections 4.3.3.4.1 to 4.3.3.4.3 summarise the findings from four studies included in the index review that reported on various AESI related to COVID-19 vaccination among individuals with underlying medical conditions.

Guillain-Barré syndrome

One self-controlled case series using data from the Global Vaccine Data Network from 14 study sites reported on GBS risk after vaccination among adults with a co-morbidity.[285] No association (RI 0.85, 95% CI: 0.55 to 1.32) was observed between

COVID-19 mRNA vaccination and GBS during a risk period from 1 to 42 days after vaccination, as presented in Table B.35.

Stroke

Two studies reported on risk of stroke-related events after vaccination among those with underlying medical conditions, as presented in Table B.36.[288, 295] One cohort study from South Korea reported on stroke-related hospital admission experienced by patients with Moyamoya disease during 2021;[295] the study reported a decreased odds of stroke-related hospital admission (OR 0.17, 95% CI: 0.13 to 0.22) among vaccinated patients compared with those who were unvaccinated. One case-control study from Qatar reported on the odds of any stroke in those with one, two and three co-existing conditions following COVID-19 vaccination from December 2020 to April 2023.[288] While the point estimates suggested a lower odds of stroke in vaccinated compared with unvaccinated individuals for all three subgroups, the result was only statistically significant in those with three co-existing conditions (OR 0.64, 95% CI: 0.47 to 0.88).

Thromboembolic events

One self-controlled case series from South Korea reported on the risk of thromboembolic events among those aged 12 years and older with a diagnosis of atrial fibrillation or flutter, as presented in Table B.37.[291] When considering any COVID-19 vaccination (mRNA or viral vector vaccines), no increase in risk was observed during the pre-risk or risk periods compared with the control period (>22 days before or after vaccination). When considering by specific vaccine, an inverse relationship (that is a reduced risk of thromboembolic events) was observed with BNT162b2 vaccination (IRR 0.74, 95% CI: 0.56 to 0.97) during the risk period compared with the control period. No association was identified for mRNA-1273 vaccination.

Pregnant individuals

Sections 4.3.3.5.1 to 4.3.3.5.4 summarise the findings from 19 studies included in the index review that reported on various AESI related to COVID-19 vaccination (stillbirth or foetal loss; low birthweight or small for gestational age; venous thromboembolism or ICU admission; and congenital anomalies) of pregnant women.

Stillbirth or foetal loss

Five studies (four case-control studies and one cohort study) reported on the risk of stillbirth or foetal loss among pregnant women following COVID-19 vaccination.[296-300] No increased risk was observed following COVID-19 vaccination in any of the

studies when considered for any COVID-19 vaccine or by specific vaccine type, as presented in Table B.38.

Low birthweight, small for gestational age, preterm birth or low Apgar scores

Four studies (two case control studies and three cohort studies) evaluated the risk of low birth weight, preterm birth, small gestational weight or low Apgar scores among pregnant populations and preterm infants following COVID-19 vaccination.[298, 299, 301, 302] An additional case-control study from Israel reported on small for gestational age and low Apgar score, but did not present effect estimates.[300] This study is included in Table B.39 but not discussed in this section due to the absence of effect estimates. No study reported an increased risk of any of these outcomes, either when considered for COVID-19 vaccination (any) or by specific COVID-19 vaccine.

One case-control study from England reported on the odds of COVID-19 vaccination and low birthweight, premature birth and low Apgar scores among pregnant individuals aged 18 to 50 years between April 2021 and March 2022.[298] For any COVID-19 vaccination exposure, there was a lower odds of low birthweight (OR 0.86, 95% CI: 0.79 to 0.93) premature birth (OR 0.89, 95% CI: 0.85 to 0.92), and low Apgar score (OR 0.89, 95% CI: 0.80 to 0.98), as presented in Table B.39. For BNT162b2 vaccination specifically, there was a lower odds of low birthweight and premature birth, but no statistically significant association for low Apgar score. For mRNA-1273 vaccination there was a lower odds for each of the three outcomes.

One cohort study from England reported on risk of preterm birth and small for gestational age among vaccinated pregnant individuals aged 18 to 45 years compared with those who had no prior COVID-19 vaccination between May 2021 and October 2022, as presented in Table B.39.[299] For overall COVID-19 vaccination (that is, viral vector and mRNA vaccines) there was a reduced risk of preterm birth between 24 and less than 32 weeks gestational age (HR 0.74, 95% CI: 0.63 to 0.88). For BNT162b2 mRNA vaccination, there was a reduced risk of preterm birth between 24 and less than 32 weeks gestational age (HR 0.79, 95% CI: 0.65 to 0.97) and between 32 and 36 weeks gestational age (HR 0.93, 95% CI: 0.87 to 0.99). There was no association between COVID-19 vaccination and risk of small for gestational age.

One cohort study from South Korea reported on the odds of mRNA COVID-19 vaccination and preterm birth among pregnant individuals aged 20 to 49 years between February and December 2022, as presented in Table B.39.[301] There was a lower odds of preterm birth among those who received an mRNA COVID-19 vaccine during pregnancy compared with those who did not (OR 0.83, 95% CI: 0.75 to 0.91).

One cohort study from the US among pregnant US military service members reported on the odds of COVID-19 vaccination and preterm birth, small for gestational age and low birthweight between Jan and December 2021.[302] There was no association between any COVID-19 vaccination and odds of any outcome, as presented in Table B.39.

Venous thromboembolism or ICU admission during pregnancy

Three studies reported on venous thromboembolism, ICU admission and neonatal ICU (NICU) admission following COVID-19 vaccination as presented in Table B.40.[298, 299, 302]

One case-control study from England reported on the risk of venous thromboembolism and of ICU admission among pregnant individuals aged 18 to 50 years following at least one dose of COVID-19 vaccination during pregnancy between April 2021 and March 2022.[298] Results were reported both for any COVID-19 vaccine (including mRNA and viral vector vaccines) and then by specific vaccine type. No association was observed between COVID-19 vaccination (any) and venous thromboembolism (or when considered specifically for mRNA-1273 vaccination or viral vector vaccination). However, a reduced risk of venous thromboembolism was reported for those vaccinated with BNT162b2 vaccines compared with no vaccination (OR 0.33, 95% CI: 0.11 to 0.99). For risk of ICU admission, there was no association with BNT162b2 vaccination or viral vector vaccination. There was a reduced risk of ICU admission for overall COVID-19 vaccination (OR 0.85, 95% CI: 0.76 to 0.95) and for mRNA-1273 vaccination (OR 0.65, 95% CI: 0.52 to 0.81).

One cohort study from England reported on the risk of venous thromboembolism among pregnant individuals aged 18 to 49 years who received COVID-19 vaccination before pregnancy compared with those with no prior COVID-19 vaccination.[299] The risk was assessed both for any COVID-19 vaccine (mRNA or viral vector vaccines) and then by specific vaccine type. While the point estimates suggested an increased risk of venous thromboembolism following vaccination, the association was only statistically significant for viral vector vaccination (HR 1.54, 95% CI: 1.1 to 2.16).

One cohort study from the US reported on the risk of NICU admission within 28 days of birth among pregnant US military service members who received a COVID-19 vaccine during pregnancy compared with those who did not.[302] As presented in Table B.40, there was no association between any COVID-19 vaccination during pregnancy and NICU admission.

Congenital anomalies

Three studies (two cohort studies and one case-control study) reported on the risk of congenital anomalies following COVID-19 vaccination during pregnancy (see Table B.41).[300, 301, 303] One case-control study reported a similar incidence of major congenital anomalies among recipients of the mRNA BNT162b2 COVID-19 vaccine and unvaccinated participants (vaccinated n=4/78, unvaccinated n=3/78).[300] Similarly, no increased risk of congenital anomalies was observed following vaccination with an mRNA COVID-19 vaccine during pregnancy in either of two cohort studies.[301, 303].

Healthcare workers

No studies were identified from the index review[57] that reported safety findings specifically for healthcare workers.

General population aged 18 to 59 years

Five studies from the index review reported on relevant AESI outcomes among the general population aged 18 to 59 years.[285-288, 292] The AESI considered included Guillain-Barré syndrome, myocarditis, stroke, and a composite outcome (combined venous and arterial events). These are reported in sections 4.3.3.7.1 to 4.3.3.7.4 below.

Guillain-Barré syndrome

One self-controlled case series using data from the Global Vaccine Data Network from 14 study sites reported on the relative incidence of GBS among those aged 18 to 64 years who received COVID-19 mRNA vaccination.[285] There was no association between receipt of vaccine and GBS risk, as presented in Table B.42.

Myocarditis

Two studies (one cohort study and one case-control study) reported on the risk of myocarditis or myopericarditis and COVID-19 vaccination.[286, 287] One case-control study from France reported on the odds of vaccination with mRNA vaccines and risk of myocarditis among those aged 12 to 29 years and 30 to 49 years, from December 2020 to November 2022.[286] For BNT162b2 vaccines, there was an increased risk of myocarditis after first, second and third vaccine doses for both age groups, as presented in Table B.43. For mRNA-1273 vaccines, there was no association after the first dose among those aged 12 to 29 years, but an increased risk after the second dose, and an increased risk after each dose among those aged 30 to 49 years.

One cohort study from Sweden reported on the risk of myopericarditis after any COVID-19 vaccine dose (mRNA vaccines or viral vector vaccines) among those aged 18 to 25 years and 41 to 65 years, from December 2020 to December 2022.[287] There was no association reported between any COVID-19 vaccine dose and myopericarditis risk for either age group, as presented in Table B.43.

Stroke

Two studies (one cohort study and one case-control study) reported on the association between COVID-19 vaccination and the risk of stroke.[287, 288] One case-control study from Qatar reported on any stroke among those aged less than 40 years and 40 to 59 years of age from December 2020 to April 2023.[288] There was no association between COVID-19 vaccination and risk of stroke among those aged less than 40 years, as presented in Table B.44. However, there was a lower risk of stroke among vaccinated participants aged 40 to 59 years compared with unvaccinated individuals (OR 0.8, 95% CI: 0.66 to 0.96). One cohort study from Sweden reported on the association between any COVID-19 vaccine dose (with mRNA or viral vector vaccines) and stroke one to six weeks later among those aged 41 to 65 years, from December 2020 to December 2022.[287] While point estimates suggested a lower risk of stroke within one to six weeks following COVID-19 vaccination compared with no vaccination, the result was only statistically significant for the second and third doses (First dose: HR 0.89, 95% CI: 0.79 to 1.01; second dose: HR 0.81, 95% CI: 0.71 to 0.93; third dose: HR 0.63, 95% CI: 0.53 to 0.75.

Composite outcomes

One cohort study from England reported on the association between COVID-19 vaccination (with first and second dose of mRNA BNT162b2 vaccine and either a booster dose of BNT162b2 or mRNA-1273 vaccines) and risks of composite venous or arterial outcomes among those aged less than 40 years and 40 to 59 years, from December 2020 to January 2022.[304] The composite venous outcome included pulmonary embolism, intracranial venous thrombosis, portal vein thrombosis and lower limb deep vein thrombosis, as noted in Table B.45. The composite arterial outcome included acute myocardial infarction, ischaemic stroke, and other arterial embolism events.

Among those aged less than 40 years, there was no association between COVID-19 mRNA vaccination and composite venous outcomes. Among those aged 40 to 59 years, there was a decreased risk of composite venous outcomes for those who received two doses of BNT162b2 and either a booster dose of mRNA-1273 (for both weeks one to four and 5 to 24 post-vaccination) or BNT162b2 (for weeks two, three to four, 5 to 12, and 13 to 24 post-vaccination), as presented in Table B.45.

Among those aged less than 40 years, the association between COVID-19 vaccination and risk of composite arterial outcomes differed by mRNA vaccine booster, as presented in Table B.45. For those who received three doses of BNT162b2, there was no association with risk of composite arterial outcomes. For those who received two doses of BNT162b2 and a booster dose of mRNA-1273, there was a reduced risk of composite arterial outcomes at each time point post-vaccination. Among those aged 40 to 59 years, results were mixed. For those who received two doses of BNT162b2 and a booster dose of mRNA-1273, there was a reduced risk of composite arterial outcomes at one week post-vaccination, no association from weeks 2 to 12 post-vaccination, and an increased risk from weeks 13 to 24 post-vaccination. For those who received three doses of BNT162b2, there was a reduced risk of composite arterial outcomes at each time point post-vaccination.

4.3.4 Quality appraisal

As noted in section 4.2, one systematic review was identified for inclusion, referred to in section 4.3.1 as the index review, which evaluated the efficacy, effectiveness and safety of COVID-19 vaccines (licensed for use in the US). Two reviewers from the HIQA evaluation team independently appraised the quality of the index review using the AMSTAR 2 tool.[257] The AMSTAR 2 tool is not designed to provide an overall quality score; however, the authors of the tool have proposed that the confidence in the quality of seven critical domains, which can substantially affect the validity of a review and its conclusions, can inform overall confidence in the quality of seven critical domains, which can substantially affect the validity of a review and its conclusions, can inform overall confidence in the results of the review.[257] Critical weaknesses were identified with respect to critical domain Item 4, Item 7, and Item 15, which relate to the identification of relevant literature through the search strategy, justification for excluding studies, and impact of publication bias (Table B.46). No critical weaknesses were identified regarding the analysis or risk of bias assessments therefore limiting the weakness of the index review to the identification, and exclusion of, relevant literature. While it is important to acknowledge that these critical weaknesses may have resulted in missing relevant literature, this risk has been somewhat managed through supplementing the evidence from the index review with additional data from European, UK and US platforms, as described in section 4.2.

The index review authors undertook quality appraisal of the observational studies included in their review using the appropriate Newcastle Ottawa Scale (NOS)[305] (NOS for Cohort Studies,[305] NOS for Case-Control Studies,[305] or NOS for Cross-Sectional Studies-Simplified)[306]. Eighteen of the 20 studies from the index review reporting VE estimates included in this chapter were assessed by the index review

authors as being at low risk of bias. Two studies were considered at high risk of bias.[268, 275] Each of the 19 studies from the index review reporting on adverse events of special interest safety outcomes included in this chapter were assessed by the index review authors as being at low risk of bias. The authors noted that for cohort and case-control studies, studies were classified as high risk of bias if any of the individual domains were determined to be at high risk of bias. A breakdown of the individual domains was not provided by the authors of the index review.

4.3.5 Pharmacovigilance

As outlined in Chapter 2, there are four mRNA vaccines and two protein subunit vaccines authorised, or recommended for authorisation, by the EMA for the prevention of COVID-19, as of May 2026. Summaries of the safety profile and most frequent adverse reactions to authorised COVID-19 vaccines, extracted from the Summary of Product Characteristics (SmPCs), are presented in sections 4.3.5.1 through 4.3.5.5. These typically included injection site pain, fatigue, headache and myalgia, were mostly mild to moderate in severity and resolved within a few days following vaccination. An overview of the known adverse events for each vaccine is presented in section 4.3.5.6.

Comirnaty®

According to section 4.8 of the EMA SmPC for Comirnaty® vaccines, the safety of the latest antigenically updated Comirnaty® vaccines is inferred from prior Comirnaty® vaccines.[7] For XFG strain vaccines, the safety was inferred from safety data of the prior vaccines. For XBB.1.5, JN.1 and KP.2 strain vaccines the safety profile was reported as similar to the overall Comirnaty® safety profile. The most frequent adverse events were mild-to-moderate in severity for each vaccine and included injection site pain, fatigue, headache, and myalgia (Table B.47).

Section 4.8 of the SmPC additionally notes the increased risk of myocarditis after vaccination with the Comirnaty® vaccine, commenting that the increased risk is highest in younger males.[7] Specifically, the results of two European pharmacoepidemiological studies reporting on excess risk are highlighted. One study found there were 0.27 (95% CI: 0.26 to 0.28) extra cases of myocarditis in 12- to 29-year-old males per 10,000 compared with unexposed persons seven days after a second dose of the Comirnaty® vaccine. One study found there were 0.27 (95% CI: 0.26 to 0.28) extra cases of myocarditis in 12- to 29-year-old males per 10,000 compared with unexposed persons seven days after a second dose of the Comirnaty® vaccine. The second study found 0.56 (95% CI: 0.37 to 0.74) extra cases of myocarditis among 16- to 24-year-old males per 10,000 compared with unexposed persons 28 days after a second dose of the Comirnaty® vaccine.

Spikevax®

According to section 4.8 of the EMA SmPC for Spikevax® vaccines, the safety of the latest antigenically updated Spikevax® vaccines is provided for strains XBB.1.5 and earlier and the safety profile is considered similar to that of the Spikevax® original vaccine.(53) For the Spikevax® original vaccine, the most frequently reported adverse events among adults 18 years and older were pain at the injection site, fatigue, headache, and myalgia (Table B.48). These reactions were noted as mild to moderate in intensity and resolved within a few days after vaccination.

Section 4.8 of the SmPC notes the increased risk of myocarditis after vaccination with the Spikevax® original strain vaccine, commenting that the increased risk is highest in younger males.(53) Specifically, the results of two European pharmacoepidemiological studies reporting on excess risk are highlighted. One study found there were 1.32 (95% CI: 1.30 to 1.33) extra cases of myocarditis in 12- to 29-year-old males per 10,000 compared with unexposed persons seven days after a second dose of Spikevax® original vaccine. The second study found 1.88 (95% CI: 0.96 to 2.80) extra cases of myocarditis among 16- to 24-year-old males per 10,000 compared with unexposed persons 28 days after a second dose of Spikevax® original vaccine.

mCombriax®

According to section 2 of the EMA SmPC for the Quadrivalent Influenza and COVID-19 mRNA Combination Vaccine (mCombriax®), the vaccine composition includes SARS-CoV-2 Omicron XBB.1.5.(307) According to section 4.8 of the EMA SmPC, the most commonly reported adverse events included injection site pain, fatigue, myalgia, headache, arthralgia, chills, lymphadenopathy, nausea or vomiting, and pyrexia (Table B.49). These reactions had a median onset of two days post-vaccination and a median duration of three days.(307)

Nuvaxovid®

According to section 4.8 of the EMA SmPC for Nuvaxovid® vaccines, the safety profile for the most recent antigenically updated XFG, JN.1 and XBB.1.5 Omicron adapted vaccines is inferred from the original and BA.5 Omicron adapted vaccines.(56) The most frequent adverse events for these prior vaccine strains included injection site tenderness, injection site pain, fatigue, myalgia, and headache (Table B.50). These reactions were typically mild to moderate in severity with a median duration of two days or fewer for local events and one day or fewer for systemic events.

Bimervax®

According to section 4.8 of the EMA SmPC for Bimervax® vaccines, the safety profile for the most recent antigenically updated XFG.1.1, LP.8.1 and XBB.1.16 Omicron adapted vaccines is inferred from the original, heterodimer B.1.351 and B.1.1.7 and Omicron adapted XBB.1.16 vaccines.[55] The most frequent adverse events for these prior vaccine strains included injection site pain, headache, fatigue and myalgia (Table B.51). These were mostly mild to moderate in severity with a duration of one to three days.

Overall frequency of known adverse reactions

An overview of the frequency of known adverse reactions for each of the licensed vaccines is provided in Table B.52, summarising the data presented in the corresponding table from the undesirable effects section 4.8 of the respective SmPCs.

4.4 Discussion

This assessment of the effectiveness and safety of antigenically updated Omicron-adapted COVID-19 vaccines is based on evidence from a systematic review (referred to as the index review) that was funded by the Vaccine Integrity Project of the Center for Infectious Disease Research and Policy and published in October 2025.[57] Twenty of the 29 primary studies reporting on relevant COVID-19 VE outcomes and 19 of the 26 primary studies reporting on AESI were considered eligible for inclusion in this analysis. A supplemental search of database sources from Europe, the UK and the US identified 21 additional primary studies that were considered eligible for inclusion, two of which provided data relating to COVID-19 VE outcomes for which data were lacking or limited in the index review.[283, 284]

In general, Omicron-adapted vaccines were associated with a significant reduction in severe COVID-19 across several of the population groups considered relevant to this HTA, although there was a consistent trend of waning protection over time, particularly for studies that reported over long follow-up intervals. When considering the relative VE estimates reported throughout it is important to note that the reference population typically had some degree of prior protection from previous COVID-19 vaccination ranging from six months prior to the study period to their primary series of vaccinations with the original ancestral vaccines. Estimates of VE varied between studies and while there was evidence of waning effectiveness over time, protection against hospitalisation and mortality was still observed at five to six months post-vaccination, specifically in older people, those living with immunocompromise, those living with underlying medical conditions and those aged 18 to 59 years in the general population. While some estimates of VE may appear to be modest, it is important that these effects are viewed in the context of the burden of COVID-19 within the subgroup of interest. As outlined in Chapter 3, there is

evidence of a substantial and disproportionate burden associated with COVID-19 in the oldest adults. As such, a VE of 30% to 40% still represents a considerable reduction in COVID-19-related burden. Moreover, VE estimates for COVID-19, as reported in this chapter, are similar to those demonstrated for influenza.[57, 254, 308]

Estimates of effect were typically higher for outcomes related to severe disease (namely, hospitalisation and mortality) compared to medically attended infection and ED or UC visits. It is also worth noting that where VE estimates were disaggregated by age, there was no consistent pattern and confidence intervals typically overlapped; a finding that has also been observed previously.[309] While no evidence was identified specifically relating to those living in LTCFs, it is acknowledged that the evidence identified for older adults is applicable to people living within these settings given the demographics of these populations. Moreover, high levels of protection against severe COVID-19 were previously documented for this population during the early years of the pandemic. For example, a 2024 systematic review of COVID-19 outbreaks in aged care facilities (including nursing homes, LTCFs and skilled nursing facilities) identified 38 articles from 12 countries that reported on outbreaks occurring over a period of six months between January and July 2021.[310] The pooled VE among fully vaccinated residents was 73% (95% CI: 49% to 86%) against COVID-19 infection, 90% (95% CI: 68% to 97%) against COVID-19 hospitalisation and 83% (95% CI: 58% to 93%) against mortality, compared with unvaccinated residents.

The evidence included in this chapter largely relates to Omicron-adapted mRNA COVID-19 vaccines. While some studies included other vaccine types (for example, protein subunit COVID-19 vaccines), only small numbers of participants received these vaccine types. Moreover, studies did not typically report findings disaggregated by vaccine type. As such, it is not possible to determine a comparative effectiveness of one vaccine type versus another based on the evidence included in this chapter. There was evidence that the VE of XBB.1.5-adapted vaccines against hospitalisation was lower during periods of JN.1 and KP.2 subvariant dominance. Similar findings have also been reported in a previous systematic review of XBB.1.5-adapted or bivalent mRNA vaccines that included over 53 million participants across 21 studies.[309] The authors reported that during the period of JN.1 subvariant dominance, the reported VE declined from 54% to 28% against infection, 68% to 46% against hospitalisation, and 77% to 57% against death. This highlights the importance of strain-specific updates to COVID-19 vaccines, which is reflective of the approach that has long been adopted for influenza vaccinations.[311] Indeed, on 29 May 2026, the EMA's Emergency Task Force recommended updating COVID-19 vaccines to target the new SARS-CoV-2 variant XFG for the 2026/2027 vaccination campaign.[42]

While the evidence of effectiveness reported in this chapter is specific to Omicron-adapted COVID-19 vaccines, it builds on and is broadly consistent with previous systematic reviews of the effectiveness of COVID-19 vaccines in general (that is, not specifically Omicron-adapted vaccines). For example, in a systematic review of 56 million participants enrolled in 33 European studies, the overall VE of the complete primary series against infection with, and severe disease from, any SARS-CoV-2 variant was 71% and 87%, respectively.(312) The VE against infection was lower for Omicron than for pre-Omicron strains (26% versus 77%) highlighting the importance of strain-matching. Moreover, VE against infection was lower than against severe disease (63% versus 93%), suggesting that optimising vaccination uptake among those at increased risk of severe disease may be of greater importance than the indirect protection offered through population immunity and reduced transmission. Reported VE against infection (with any variant) decreased from 69% to 39% at six months post-vaccination, though booster vaccines were reported to have restored VE to 76%; this was maintained at 58% at three months post-vaccination. Vaccine effectiveness against severe outcomes caused by Omicron was over 50% at six months after completion of the primary series. Boosters restored the VE to 88% and this was maintained at 79% after three months.(312)

Moreover, recent interim results from the Canadian Sentinel Practitioner Surveillance Network for 2025/26 COVID-19 vaccination were published in May 2026 and reported a VE of 53% against medically attended outpatient visits among those aged 65 years and older at a median nine weeks post-vaccination.(313) Additionally, in a Danish cohort study of over 1.2 million people aged 65 years and older (published in December 2025), the VE for BNT162b2 JN.1 was 70% against hospitalisation and 76% against death, with little evidence of waning effectiveness observed at four months post-vaccination. The VE of mRNA-1273 JN.1 was 85% against hospitalisation and 96% against death, but the authors noted that those vaccinated with mRNA-1273 JN.1 were younger and healthier. This study also demonstrated that high levels of protection were provided by BNT162b2 JN.1 vaccination against hospitalisation and against death after infection with KP.2.1.1 (72% and 91%, respectively) and XEC (77% and 76%, respectively) strain variants over this four-month period.(314)

Only one study included in this chapter reported on the VE of Omicron-adapted vaccines against long COVID with a difference in protection by age group; there was no evidence of protection reported for those aged 60 years and older, whereas a VE of 49% was reported for those aged 18 to 59 years.(282) Previous systematic reviews have reported a protective effect. For example, a systematic review of 31 observational studies (search dates: 1 January 2022 to 1 March 2024) reported pooled VE estimates against long COVID following primary course and or booster

vaccination.[315] Long COVID was defined as any condition or symptom described by the included study as long COVID, provided it was reported at least four weeks after the acute SARS-CoV-2 infection. The reported VE values were 23%, 19% and 26% for participants who had received any vaccination, a primary course and or a booster vaccination, respectively, compared with unvaccinated participants. Among the vaccinated population, additional doses were associated with added protection against long COVID, demonstrating the additional clinical advantages of COVID-19 vaccinations beyond the prevention of acute infections and severe disease. However, the authors noted significant variation in the definition of long COVID across the included studies, and studies that used a broader definition of long COVID or self-assessment may overestimate or misdiagnose the presence of the condition.[315] In another systematic review, the pooled VE against post-COVID-19 condition (defined as the continuation or development of new symptoms assessed three months or more after SARS-CoV-2 infection) was 41%, and against long COVID (defined as the continuation or development of new symptoms four weeks after SARS-CoV-2 infection) was 34%.[197] This lack of consensus on the definition of long COVID has been discussed in Chapter 3, and it remains an ongoing issue.

While there were no studies identified (from the index review or supplemental search) on the effectiveness of Omicron-adapted COVID-19 vaccines among pregnant individuals, previous evidence of effectiveness supports COVID-19 vaccination during pregnancy to prevent severe disease and adverse maternal and child outcomes. Moreover, in general, vaccination during pregnancy was not associated with an increased risk of adverse pregnancy or perinatal outcomes.[316] Again, it is important to consider the evidence of effectiveness in the context of the observed burden of COVID-19 in a population group. As reported in Chapter 3, SARS-CoV-2 infection has previously been associated with an increased risk of complications in pregnant women, particularly evident during the Alpha and Delta phases of the pandemic.[119] However, this risk has decreased in the post-Omicron era. Irish data show that there were 23 pregnant and 12 postpartum women admitted to ICU in Ireland (from March 2020 to August 2021).[317] Of these admissions, 61% of pregnant and 50% of postpartum women required invasive ventilation, and three required extracorporeal membrane oxygenation.[317] In contrast, two pregnant women were admitted to the ICU with COVID-19 in 2022 (neither required mechanical ventilation),[318] and in 2023, no pregnant or postpartum women were admitted to ICU with COVID-19.[8] As such, NIAC has advised that this population group should avoid exposure to SARS-CoV-2 where possible and, following discussion with a healthcare professional, be vaccinated with a COVID-19 vaccine, particularly if they have other risk factors which put them at increased risk of severe disease.

The findings reported in this chapter are in line with the existing literature base as it pertains to the safety profile of COVID-19 vaccines, which is largely favourable. While the evidence on the safety of COVID-19 vaccines typically related to original vaccine compositions, not Omicron-adapted vaccines, health authorities internationally continue to rigorously monitor the safety of COVID-19 vaccines.[319-322] As with all medicines, COVID-19 vaccines have side effects, with the most commonly reported side effects being headache, fever, fatigue and pain at the injection site. These local and systemic effects are typically mild to moderate and self-limiting, resolving a few days after vaccination.[319] According to post-marketing safety surveillance of authorised COVID-19 vaccines, the frequency of myocarditis and pericarditis, where known, is very rare, occurring in fewer than 1 in 10,000 vaccinations, typically within 14 days of vaccination.[319] It is also worth noting that SARS-CoV-2 infection itself is a risk factor for myocarditis and pericarditis. Using national-level data from the English National Immunisation Database of COVID-19 vaccination, a study of acute cardiac outcomes after SARS-CoV-2 vaccination or infection estimated extra myocarditis events to be between 1 and 10 per million persons in the month following vaccination. This was substantially lower than the 40 extra myocarditis events per million persons observed following SARS-CoV-2 infection.[323] While there was no evidence of an association between COVID-19 vaccination and Guillain-Barré syndrome reported in this chapter, this has previously been reported as very rare side effect (less than 1 case in 10,000 people vaccinated) of the COVID-19 vaccines Jcovden® and Vaxzevria®, both of which have had their marketing authorisations withdrawn by the European Commission.[82, 83] It is also worth noting that studies included in this chapter either found no association between COVID-19 vaccination and stroke, or they observed a reduced risk of stroke in vaccinated compared with unvaccinated individuals.

There are several strengths and limitations to this analysis. A comprehensive search strategy was employed which identified systematic reviews published since the end of 2024 that included disaggregated VE data from 2023 onwards for various population sub-groups. While only one review was identified for inclusion, it reported VE estimates and safety data for five of the seven population groups of interest to this HTA. This index review identified VE evidence for a range of outcomes and for multiple Omicron-adapted vaccine strains (although evidence primarily related to XBB.1.5 vaccines). Data were extracted from the primary studies reported within the index review due to our requirement for data to be disaggregated by specific population groups. While the quality appraisal of the index review yielded an overall assessment of critically low quality, no critical weaknesses were identified regarding the analysis or risk of bias assessments. In addition, all but two of the primary studies were assessed by the review authors to be at low risk of bias. As such, the primary weakness of the index review related to the lack of grey literature searching

and adequate assessment of publication bias. To manage this risk, the evidence from the index review was supplemented with additional data from European, UK and US platforms, as described in section 4.2; the findings from these additional studies aligned with those reported in the index review. No evidence was identified from the index review or supplemental search regarding the VE of Omicron-adapted vaccines in those in LTCFs and pregnant individuals, while across all populations there was very limited evidence identified for the effectiveness of these vaccines against ICU and long COVID outcomes. In addition, it was not possible to compare differences in risk by individual medical condition as this was outside of the scope of the HTA. Only one European case-control study[274] reported results by type of chronic health condition (Table B.13). It is important to acknowledge that the risk group comprising those with underlying medical conditions encompasses a broad range of different conditions whose risk of COVID-19 disease may differ. No evidence from RCTs was identified for inclusion, meaning no data were included relating to the efficacy of Omicron-adapted COVID-19 vaccine. While safety data were limited to observational studies reporting on associations between original and bivalent COVID-19 vaccines and AESI, these data were supplemented by post-marketing surveillance data relating to the safety of authorised COVID-19 vaccines. Finally, given the timing of this HTA, this chapter does not include effectiveness data for newer COVID-19 technologies (such as, mCombriax® or mNexspike®).[51, 307]

5 Economic evaluation

Key points

- An economic model was developed to characterise the incidence of notified cases of COVID-19 in Ireland and estimate the cost effectiveness and budget impact of COVID-19 vaccination programmes for the general population of adults aged 60 years and above in Ireland. The budget impact of COVID-19 vaccination for specific population groups was also estimated.
- The economic evaluation for the general population aged 60 years and above assessed the following two vaccination strategies:
    - Strategy 1 (S1) – a vaccine offered twice each year for those aged 80 years and above
    - Strategy 2 (S2) – a vaccine offered twice each year for those aged 80 years and above (S1) and once each year for those aged 60 to 79 years.
- The five-year budget impact was estimated for a range of strategies as defined by the National Immunisation Advisory Committee recommendations for COVID-19 vaccination.
- Model parameters including but not limited to disease incidence, hospitalisation and mortality rates, costs, utility values and quality-adjusted life year losses were estimated from a variety of published sources and national datasets for Ireland.
- Based on evidence from Chapter 4, model parameter estimates for average annual vaccine effectiveness (notified cases) were:
    - 80 years and older: medically attended visits - 18%; ED visits - 29%; hospitalisations - 36%; deaths - 55% (assuming twice yearly vaccination)
    - 60 to 79 years: medically attended visits - 12%; ED visits - 22%; hospitalisations - 27%; deaths - 52% (assuming once yearly vaccination).
- Results from the epidemiological analysis using 2025 notified case data indicate that in a single year, vaccination is associated with a decrease in notified COVID-19 cases. Reductions associated with S1 (those aged 80 years and above), compared with no vaccination, ranged from 11% for notified cases of COVID-19 to 33% for notified deaths with COVID-19. Overall reductions for S2

(those aged 60 years and above), compared with no vaccination, ranged from 8% for notified cases of COVID-19 to 29% for notified deaths with COVID-19.

- From the payer perspective, at a vaccine cost of €75 per dose (ex VAT) and assuming 2025 incidence of notified COVID-19, the incremental cost effectiveness ratios (ICERs) for S1 compared with no vaccination was €56,500 per quality-adjusted life year (QALY) and the ICER for S2 compared with S1 was €202,000. Both ICERs exceeded a willingness-to-pay (WTP) threshold of €45,000 per QALY gained. In a scenario analysis assessing a strategy of vaccination from aged 75 years, the ICER was €80,000 per QALY when compared with S1.
- Based on the assumptions in the model, the vaccine cost would need to be less than €60 per dose for S1 to be cost effective at a WTP threshold of €45,000 per QALY. A scenario analysis, where incidence of notified COVID-19 was varied, demonstrated that using:
    - 2024 incidence data in the model, the ICER for S1 compared with no vaccination fell to €15,500 per QALY.
    - 2023 incidence data in the model, S1 was cost-saving (less costly and more effective) compared with no vaccination.
- The five-year incremental budget impact versus no vaccination was €111.5 million for S1 and €307.0 million for S2. The majority of costs incurred for both vaccination strategies over the five-year time horizon related to vaccine procurement (approximately 71% to 75%). Total cost offsets (largely relating to hospitalisation and long-term care post COVID-19) as a percentage of total costs incurred, were 28% and 15% for S1 and S2, respectively.
- The budget impact model for specific populations only considered the costs incurred over a five-year period. Due to a lack of relevant epidemiological data for Ireland, costs averted were not estimated. The five-year budget impact versus no vaccination for specific population groups was as follows:
    - €37.4 million for Strategy 3 - a vaccine offered twice each year for those aged 18 to 79 years living in a long-term care facility for older adults
    - €18.0 million for Strategy 4 - a vaccine offered twice each year for those aged six months and older with immunocompromise associated with a suboptimal response to vaccination

- €21.1 million for Strategy 5 – a vaccine offered once each year for those aged six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death
- €18.1 million for Strategy 6 - a vaccine offered once each year for health and care workers who choose to receive a vaccine
- €6.8 million for Strategy 7 - a vaccine offered once each year for pregnant adolescents and adults
- €63.8 million for Strategy 8 - a vaccine offered once each year for all others aged 18 to 59 years not included in other specific population groups.

- While this analysis demonstrates that vaccination against COVID-19 is associated with reductions in outcomes associated with COVID-19, the strategies assessed in the base-case economic analysis would be considered not cost effective at the modelled vaccine price at a WTP threshold of €45,000 per QALY. However, as demonstrated in the results of the sensitivity and threshold analyses, the outcome of this economic evaluation is highly sensitive to both the assumed price of the vaccine and the incidence of COVID-19 going forward. As such, both parameters require careful consideration in informing decision-making regarding future COVID-19 vaccination policy.

5.1 Introduction

An economic model of COVID-19 vaccination was developed as part of this HTA to support decision-making relating to potential changes to the provision of COVID-19 vaccination in Ireland. Those potential changes will affect the groups for whom COVID-19 vaccination is funded by the Health Service Executive (HSE) for the 2027/2028 vaccination campaign onwards. This chapter describes the cost-utility analysis (CUA) and budget impact analysis (BIA) conducted for two vaccination strategies under consideration for adults aged 60 years and above. Separately, the chapter describes the BIAs conducted for six vaccination strategies under consideration for specific population groups as recommended by the National Immunisation Advisory Committee (NIAC).[9]

5.2 Methods

The analyses described in this chapter were conducted in line with national HTA guidelines,[324, 325] reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement,[326] and undertaken in Microsoft Excel® 2016.

5.2.1 Study objective

The purpose of this economic analysis was to estimate the cost effectiveness and budget impact of COVID-19 vaccination programmes for the general population aged 60 years and older in Ireland and the budget impact of COVID-19 vaccination programmes for other specific population groups. The CUA estimates the costs and outcomes of a COVID-19 vaccination programme from 2027 onwards, comparing vaccination strategies with no vaccination and or alternative strategies, while the BIA provides a means of predicting the potential financial impact of a COVID-19 vaccination programme.

5.2.2 Intervention and target population

The economic model for a COVID-19 vaccination programme for the general population aged 60 years and above assessed the following two vaccination strategies:

- a vaccine offered twice each year for those aged 80 years and above
- a vaccine offered twice each year for those aged 80 years and above and once each year for those aged 60 to 79 years.

The budget impact model for the specific population groups assessed the following six vaccination strategies:

- a vaccine offered twice each year for those
  - aged 18-79 years living in long term care facilities (LTCFs) for older adults
  - aged six months and older with immunocompromise associated with a suboptimal response to vaccination

- a vaccine offered once each year for those:
  - aged six months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death
  - health and care workers who choose to receive a vaccine
  - pregnant adolescents and adults who, following discussion with a healthcare provider, choose to receive a vaccine
  - adults aged 18-59 years not included in the groups under the first four bullet points above who, following discussion with a healthcare provider, choose to receive a vaccine.

As the economic analysis is conducted to inform a COVID-19 vaccination programme from 2027 onwards, population projections (using the M2 method) based on Census 2022 for the general adult population were used in the model (Table 5.1).[327]

Table 5.1 Population estimates used in the model for the general adult population

Age group (years)	2027	2028	2029	2030	2031
60-64	312,500	317,900	322,500	328,900	337,300
65-69	271,100	279,200	287,600	295,100	300,600
70-74	228,300	231,600	236,700	242,700	250,200
75-79	184,700	190,000	193,700	198,200	202,700
60-79	996,600	1,018,700	1,040,500	1,064,900	1,090,800
≥80	231,800	243,700	256,100	268,600	280,700

For the specific population groups, 2027 population estimates were based on general population growth from the year of capture of the relevant data for those:

- with immunocompromise associated with a suboptimal response to vaccination
- with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death
- health and care workers
- others who choose to receive a vaccine.

It was assumed that from 2028 to 2031 inclusive, the population estimates for the groups above increase in line with general population projections. For those living in LTCFs for older adults, an annual growth rate of 3.5% was assumed.[146] The population estimates for pregnant people were based on projections published by the Central Statistics Office (CSO).[328] All estimates are provided in Table 5.2 below.

Table 5.2 Population estimates used in the model for specific population groups

Specific population groups	2027	2028	2029	2030	2031
Living in LTCFs for older adults	34,147	35,274	36,438	37,640	38,882
Immunocompromise associated with a suboptimal response to vaccination	67,080	67,670	68,254	68,820	69,378
Medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death	113,980	115,489	116,506	117,511	118,486
Health and care workers	253,311	256,666	258,926	261,158	263,325
Pregnant adolescents and adults	53,723	53,030	52,544	52,238	51,967
Others who choose to receive a vaccine	2,701,586	2,737,366	2,761,468	2,785,274	2,808,387

Key: LTCF – long-term care facilities.

5.2.3 Study design

A CUA was undertaken to estimate the incremental cost and health benefits associated with COVID-19 vaccination for adults aged 60 years and above, comparing vaccination to no vaccination and or alternative vaccination strategies. The analysis was undertaken within a decision-analytic framework that simulated the costs and patient outcomes associated with COVID-19 infection over a one-year time period. Health benefits were expressed in terms of quality-adjusted life-years (QALYs), which reflect the impact of the intervention on individual patients' quality and quantity of life. The BIA estimated the five-year incremental cost to the HSE of implementing a COVID-19 vaccination programme for the selected target populations.

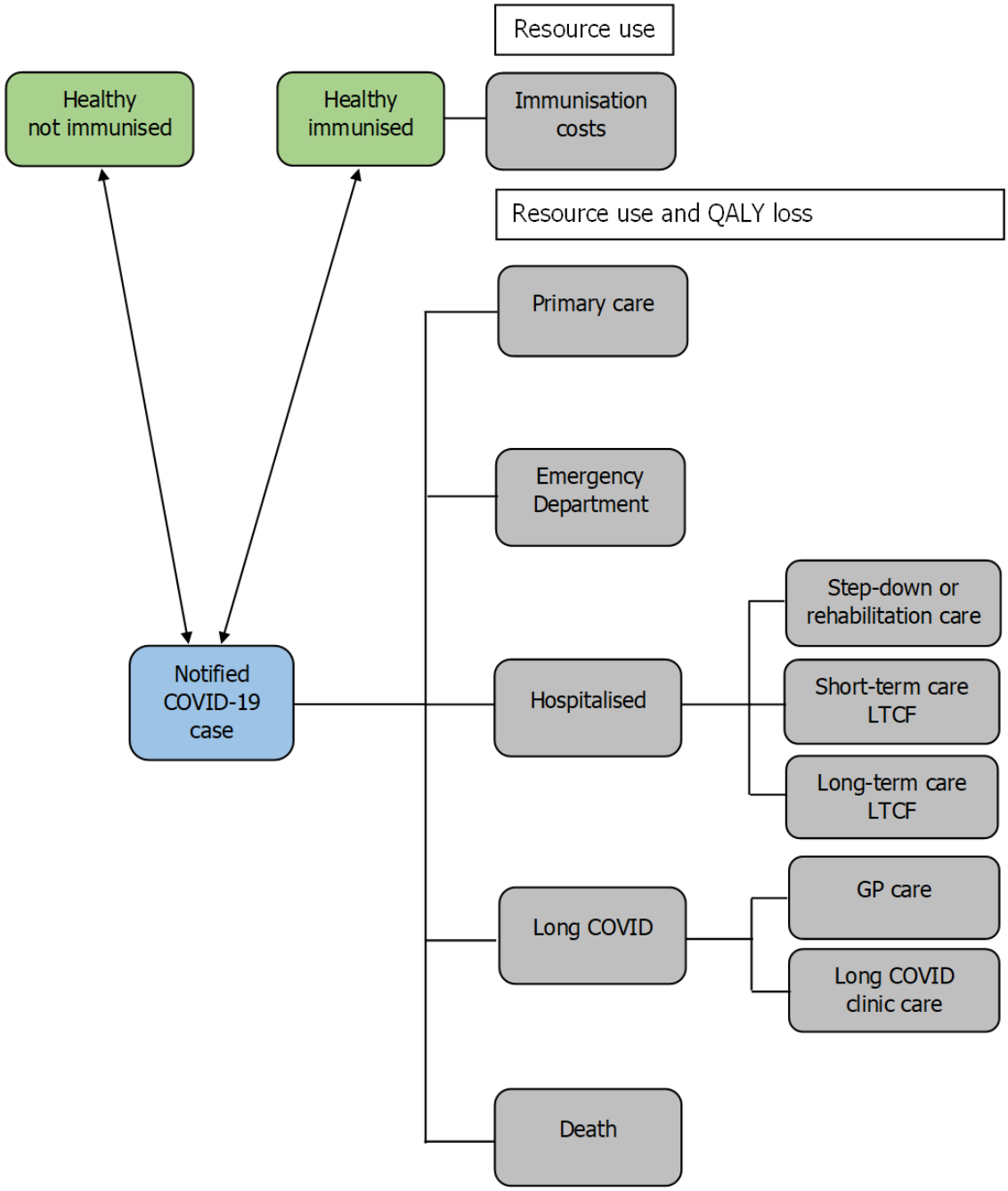
5.2.4 Model overview

For the economic evaluation, a probabilistic, age-structured model of COVID-19 was developed for Ireland. COVID-19 is a notifiable disease in Ireland and data on notified cases are published by the Health Protection Surveillance Centre (HPSC) and publicly available.[231] The model, developed in Microsoft Excel® 2016, presents the incidence of notified cases in the adult population aged 60 years and above in Ireland for:

- COVID-19
- emergency department (ED) attendance with COVID-19
- hospitalisation with COVID-19
- death with COVID-19.

Long COVID following acute infection was incorporated into the model. Additionally, post-acute admissions to a step-down or rehabilitation facility and to a LTCF for short- and long-term care were included in the model, where appropriate (Figure 5.1).

Figure 5.1 Model structure



Key: GP - general practitioner; LTCF - long-term care facility; QALY – quality-adjusted life year.

In the model, costs (in 2026 Irish euro) and QALYs were assigned to the health outcomes above, both with and in the absence of COVID-19 vaccination. In the CUA, this enabled the calculation of incremental costs and incremental QALYs associated with alternative COVID-19 vaccination strategies. Where the data allowed, the BIA included cost savings as a result of vaccination (for example, reductions in primary care; ED attendance; hospitalisation; step-down or rehabilitation care and short- and long-term care in a LTCF following COVID-19 hospitalisation; outpatient attendance

for long COVID). The net budget impact per annum and total budget impact over five years were estimated, defined as the difference in average annual costs between vaccination and no vaccination.

5.2.5 Perspective, time horizon and discounting

The CUA adopted the perspective of the Irish publicly funded health and social care system (that is, the payer), namely the HSE, incorporating direct medical costs to the HSE. Costs and outcomes were estimated over a one-year time horizon with the following exceptions:

- the QALY loss associated with COVID-19-related death and long COVID were estimated based on a lifetime time horizon
- the costs and QALY loss associated with long-term care in a LTCF following hospitalisation with COVID-19 were estimated based on the average length of stay (2.48 years) in a nursing home in Ireland.[147]

Costs and QALY losses accruing beyond one year were discounted at a rate of 4% as specified in national guidelines.[324] Discounting reflects a societal preference for benefits to be realised in the present and costs to be experienced in the future. In the BIA, the incremental costs associated with introducing a COVID-19 vaccination programme were estimated over a five-year time horizon. To reflect the actual cost to the HSE in each year reported, and ensure consistency with national guidelines,[325] no discounting was applied in the BIA.

5.2.6 Model input parameters

Incidence rates, probabilities, costs and QALY losses were estimated from a variety of published sources and national datasets for Ireland, including those published by the CSO, the HPSC, and the Healthcare Pricing Office (HPO) (for Hospital InPatient Enquiry (HIPE) data). These sources were also supplemented by input provided by experts where necessary. Additionally, the National Immunisation Office (NIO) provided input and advice relating to vaccination programme costs relevant for Ireland.

Model inputs were selected with consideration to the hierarchy of evidence, as well as generalisability to the Irish context. Inputs for the BIAs were consistent with those used in the CUA with the exception that VAT was added (where applicable). In line with national guidelines, only direct costs were included; indirect costs, such as productivity gains associated with reduced morbidity arising from vaccination, were excluded from the BIAs.[325] All economic model input parameters, including base-case, upper and lower bound values, are provided in Appendix C.1.

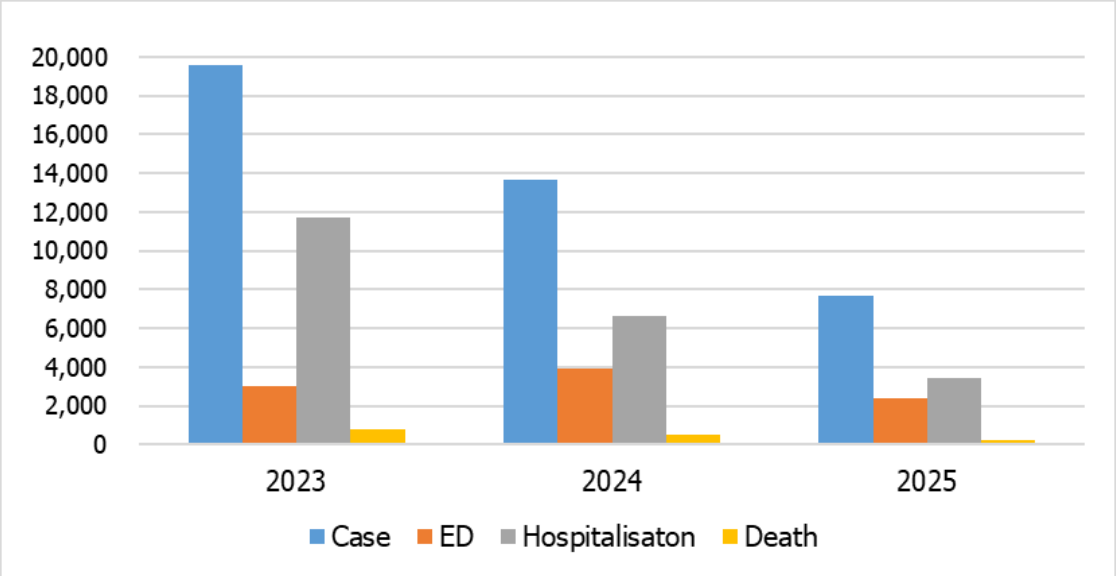
Health outcomes – notified COVID-19

The model was built using Irish demographic data and epidemiological data of notified COVID-19 cases, including ED attendance, hospitalisations and deaths, sourced from the HPSC. As testing for COVID-19 is not conducted on all suspected cases, the notified case data do not fully reflect the incidence of medically attended COVID-19 with vaccination. However, in the absence of consistent data reporting overall incidence of medically attended COVID-19 in Ireland, the notified case data were used in the model.

Incidence of notified cases of COVID-19 with and without vaccination

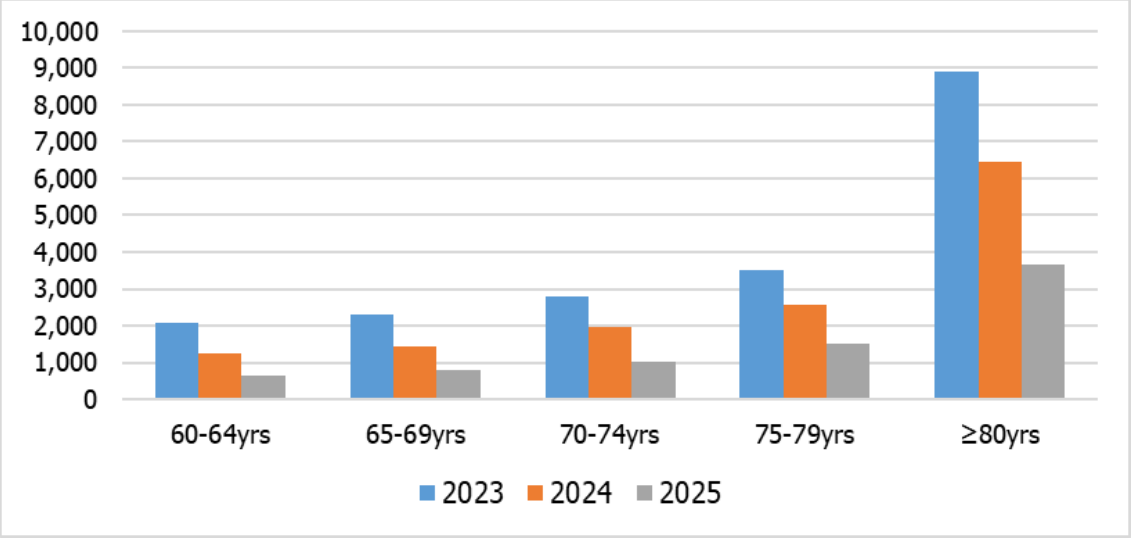
The notified case data for COVID-19 published by the HPSC incorporates the effect of the current COVID-19 vaccination programme in Ireland (Chapter 3). Data for the calendar years 2023, 2024 and 2025 show a clear downward trajectory in the number of notified COVID-19 cases, ED attendance, hospitalisations and deaths (Figure 5.3 - Figure 5.6), with that downward trajectory continuing into week 18 of 2026. To establish the probability of COVID-19 with vaccination (Table 5.3), the model was developed based on observed notified COVID-19 case data from the most recent full calendar year (2025).

Figure 5.2 Number of notified COVID-19 cases for those aged ≥60yrs in Ireland by outcome and year.



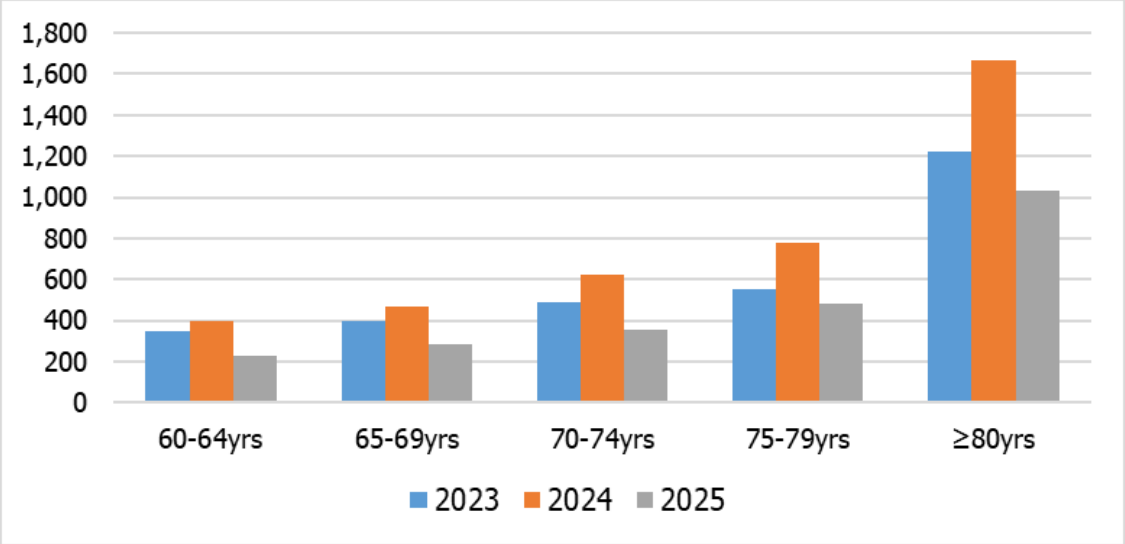
Key: ED – emergency department.
Source: Health Protection Surveillance Centre.

Figure 5.3 Total number of notified COVID-19 cases in Ireland by age group and year



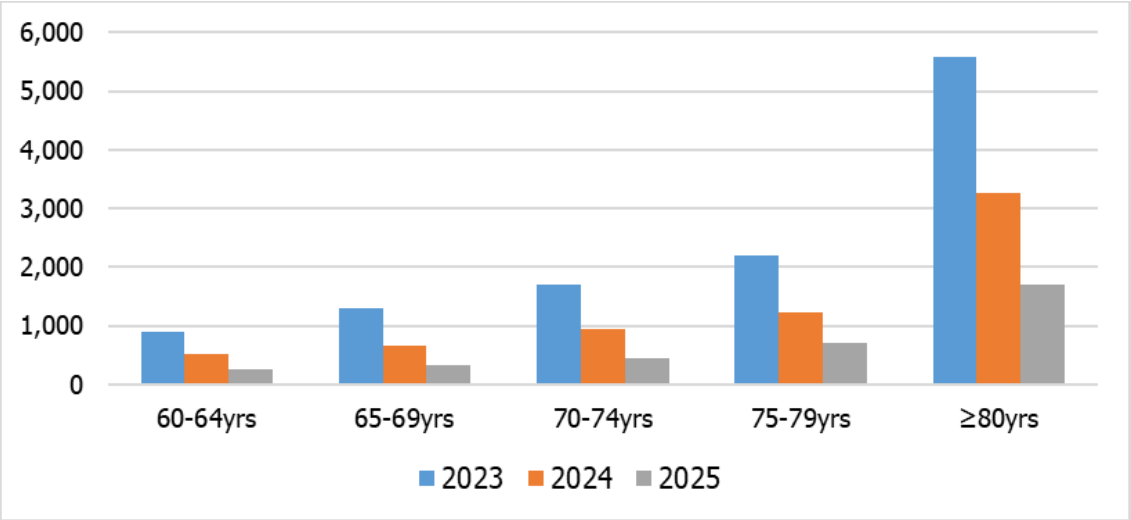
Source: Health Protection Surveillance Centre.

Figure 5.4 Total number of notified COVID-19 emergency department attendances in Ireland by age group and year



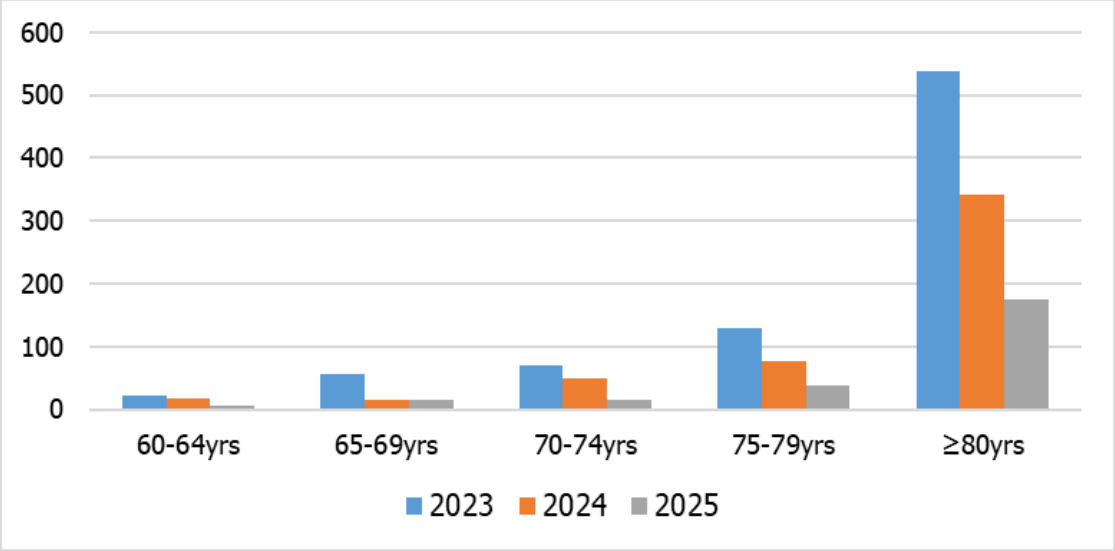
Source: Health Protection Surveillance Centre.

Figure 5.5 Total number of notified COVID-19 hospitalisations in Ireland by age group and year



Source: Health Protection Surveillance Centre.

Figure 5.6 Total number of notified COVID-19 deaths in Ireland by age group and year



Source: Health Protection Surveillance Centre.

The probability of COVID-19 in the absence of COVID-19 vaccination (the counterfactual), was estimated based on:

- the probability of COVID-19 with vaccination
- current COVID-19 vaccination coverage rates in Ireland,[329]
- estimated vaccine effectiveness rates.

The probabilities are listed in Table 5.3 below.

Table 5.3 Annual population probability of COVID-19 health outcomes

Age group (years)	Outcome	2025	Counterfactual
60-64	Notified Case	0.2051%	0.2136%
65-69		0.2932%	0.3054%
70-74		0.4564%	0.4754%
75-79		0.8154%	0.8492%
≥80		1.5854%	1.7856%
60-64	Notified ED Presentation	0.0723%	0.0780%
65-69		0.1040%	0.1122%
70-74		0.1564%	0.1687%
75-79		0.2620%	0.2826%
≥80		0.4465%	0.5438%
60-64	Notified Hospitalisation	0.0806%	0.0887%
65-69		0.1188%	0.1307%
70-74		0.1971%	0.2169%
75-79		0.3785%	0.4164%
≥80		0.7304%	0.9369%
60-64	Notified Death	0.0016%	0.0019%
65-69		0.0059%	0.0071%
70-74		0.0066%	0.0079%
75-79		0.0211%	0.0255%
≥80		0.0759%	0.1128%

Key: ED – emergency department.
Source: Estimated based on HPSC notified case data,[231] COVID-19 vaccination coverage rates[329] and estimated vaccine effectiveness.

Prevalence of long COVID following acute infection

As discussed in Chapter 3, the prevalence of long COVID following acute infection is highly uncertain. In the absence of centrally collated national data, data on the number of new patients attending long COVID clinics in Ireland in 2025 and 2026 were sourced from personal communication with HSE personnel. These data were used to estimate the probability (0.85% of notified COVID-19 cases) of long COVID following COVID-19 infection in the target population (60 years and above).

Probability of post-acute discharge to a step-down or rehabilitation facility following hospitalisation with COVID-19

The probability of discharge to a facility for step-down or rehabilitation care following hospitalisation with COVID-19 (Table 5.4) was estimated based on the proportion (by age group) of HIPE discharges in 2024 with a principal diagnosis of COVID-19 that were discharged to a non-acute hospital not in HIPE or to an external rehabilitation facility.

Probability of post-acute discharge to a long-term care facility following hospitalisation with COVID-19

The probability of discharge to a LTCF following hospitalisation with COVID-19 (Table 5.4) was estimated based on the proportion (by age group) of HIPE discharges in 2024 with a principal diagnosis of COVID-19, that were discharged to a nursing home, convalescent home or long stay accommodation where the discharge did not have the same admission source. This proportion was applied to the notified hospitalised COVID-19 data. Of note, cases that were admitted from and then discharged back to an LTCF do not result in newly incurred long-term care costs. As such, LTCF costs attributable to COVID-19 included in the economic model were based on hospital discharges that did not originate from a nursing home, convalescent home or long stay accommodation only. The proportion of discharges to short- or long-term care within a LTCF were estimated based on the available data relating to the proportion of publicly funded short- and long-term stay residents in LTCFs.[147]

Table 5.4 Probability of post-acute discharge to a step-down or rehabilitation facility and long-term care facility by age group following hospitalisation with COVID-19

Age group (years)	Probability of discharge to a step-down or rehabilitation facility (%)	Probability of discharge to a long-term care facility for short-term care (%)	Probability of discharge to a long-term care facility for long-term care (%)
60-64	0.0	0.3	1.4
65-69	0.7	0.7	3.7
70-74	0.4	0.6	3.4
75-79	0.3	0.7	3.9
≥80	1.0	1.5	8.0

Source: 2024 Discharge data from Hospital InPatient Enquiry (HIPE) System with a principal diagnosis of COVID-19.

Vaccine effectiveness against COVID-19

Chapter 4 presents the data relating to vaccine effectiveness against medically-attended COVID-19, ED attendance and hospitalisation for COVID-19, and death due to COVID-19 over varying follow-up time periods. Based on the evidence included in Chapter 4, it was not possible to determine if effectiveness against COVID-19 differs by vaccine type. As such, vaccine equivalence was assumed for the purpose of modelling. As there is uncertainty regarding the seasonality of COVID-19,[330, 331] the timing of vaccine administration was not considered important when interpreting the available study data. A meta-regression analysis was conducted on the data reported in Chapter 4, using the *metafor* package in R, to understand how vaccine effectiveness changes over time. Using data from multiple follow-up periods (within and across studies), vaccine effectiveness by outcome was estimated as follows:

- aged 60 to 79 years: average vaccine effectiveness of one vaccine dose over a 12-month period (Table 5.5 and Appendix C.2)
- aged 80 years and above: the combination of the average vaccine effectiveness to 12 months for those receiving one vaccine dose, coupled with the average vaccine effectiveness to six months for those receiving two vaccine doses (Table 5.5 and Appendix C.2).

Table 5.5 Estimated average 12-month vaccine effectiveness against COVID-19 by outcome and age group

COVID-19 outcome	Age group (years)	Number of doses	Estimate of average 12-month vaccine effectiveness (%) (95% CI)
Medically-attended	60-79	1	0.1202 (0.0778 – 0.1568)
ED attendance			0.2193 (0.1302 – 0.2969)
Hospitalisation			0.2745 (0.2226 – 0.3221)
Death			0.5193 (0.2940 – 0.6716)
Medically-attended	≥80	2	0.1836 (0.1214 – 0.2423)
ED attendance			0.2943 (0.2097 – 0.3702)
Hospitalisation			0.3625 (0.3148 – 0.4070)
Death			0.5530 (0.3773 – 0.6792)

Key: ED – emergency department; VE - vaccine effectiveness.
Source: Estimated by performing a meta-regression on data from Chapter 4 examining vaccine effectiveness by outcome over time. The meta-regression was performed using the *metafor* package in R.

Safety of vaccines for protection against COVID-19

With respect to adverse events, the risk of a Grade 3 solicited adverse reaction among vaccine recipients and the associated impact on quality of life was incorporated into the model. The probability of a Grade 3 solicited severe adverse event (2.6%) was sourced from a recently published economic evaluation.[332]

While two single studies from Chapter 4 reported an increased risk of myocarditis and myopericarditis following vaccination, post-marketing safety surveillance of authorised COVID-19 vaccines reported the frequency of myocarditis or pericarditis as very rare. Given the rarity of adverse events of special interest and the uncertainty relating to the associated cost and QALY impact on adults who receive the COVID-19 vaccine, this has not been incorporated into the model.

Quality of life estimates

In the model, health benefits are expressed in terms of QALYs gained. QALYs reflect the impact of an intervention on patients' quality and length of life, estimated using self-reported utilities or health-related quality of life. No single high-quality study was identified that reported health state utility values (HSUVs), measured using the EQ-5D, for medically-attended COVID-19, ED attendance and hospitalisation outcomes included in the model. However, a series of economic evaluations of COVID-19 vaccination published between 2021 and 2025 were identified which reported QALY losses for these outcomes.[332-336] As the QALY losses varied considerably between studies, the estimates from one study, representing the mid-point estimate within the range covered by estimates across all studies, were used as the base-case parameter values in the model.[333] The upper and lower bound values (Appendix C.1) applied to each parameter capture the estimates from the

remaining four studies. Using published life tables for Ireland,[337] age-specific QALY loss due to COVID-19-related mortality was estimated over the life course.

A UK study measuring the impact of long COVID on health-related quality of life (HRQoL) reported a mean HSUV of 0.49 for those who self-reported long COVID over a period of three months.[338] As there are a lack of long-term data relating to the duration of HRQoL loss due to long COVID, it was assumed that the HSUV applies over the life course.

Based on a study conducted in Ireland,[339] an average HSUV of 0.5165 over a six-month duration was estimated for those hospitalised with COVID-19 and discharged to a non-acute hospital not in HIPE or rehabilitation facility. This HSUV was used to estimate the associated QALY loss (Table 5.7). The same approach was used for discharges to a LTCF for short-term care. For discharges to a LTCF for long-term care, baseline utility as reported for the general population was adjusted downwards by 0.091.[340] QALY losses were then estimated based on the HSUV of 0.5165 estimated above and the average length of stay in a LTCF in Ireland (2.48 years).[147]

It was assumed that vaccine recipients who experience Grade 3 solicited adverse reactions following COVID-19 vaccination experience the equivalent of two days QALY loss for a notified case of COVID-19 (0.001286).

Table 5.6 Estimated average quality-adjusted life year losses for COVID-19 outcomes

Age group (years)	GP visit (symptomatic infection)	Hospitalisation (including ICU)*	ED attendance†
60-64	0.0045	0.0176	0.0110
65-69	0.0045	0.0176	0.0111
70-74	0.0045	0.0175	0.0110
75-79	0.0045	0.0175	0.0110
≥80	0.0045	0.0175	0.0110

Key: ED – Emergency Department; GP – General Practitioner; ICU - intensive care unit.
*QALY losses for hospitalisation were estimated as a weighted average loss (using reported QALY losses for hospitalised cases with and without an ICU stay reported in Miranda et al. 2025) accounting for the proportion of hospitalised cases within each age group that were admitted to the ICU in Ireland.
†The QALY loss for ED attendance by age was assumed to be the mid-point between the QALY loss for a GP visit and hospitalisation.
Source: Miranda et al. 2025.[332-336]

Table 5.7 Baseline health state utility values and estimated quality-adjusted life year loss for post-acute rehabilitation care for COVID-19

Age group (years)	Baseline HSUVs*	QALY loss for post-acute step-down or rehabilitation care and short-term care in a LTCF†
60-64	0.90730	0.1907
65-69	0.87900	0.1808
70-74	0.87900	0.1808
75-79	0.84100	0.1618
≥80	0.84100	0.1618

Key: HSUV – health state utility value; LTCF – long-term care facility; QALY – quality-adjusted life year.
***Source:** Hobbins et al. 2018;[341] †McCarthy et al. 2024.[339]

Vaccination programme inputs

Vaccination coverage rates for the COVID-19 vaccination strategies modelled were informed by uptake rates for the HSE's COVID-19 vaccine programme 2025/2026 autumn/winter campaign in Ireland.[329] Coverage rates used in the model are summarised in Table 5.8 below. Of note, while all those aged 80 years and above in the general adult population are eligible for twice-yearly vaccination, not everyone chooses to receive two doses. Therefore, currently there is a mix of people receiving one or two COVID-19 vaccine doses in a 12-month period. For the purpose of the model, we assumed that all those aged 80 years and above in the general adult population who avail of the spring vaccine have also availed of the autumn vaccine. As such, coverage for those aged 80 years and above in the general adult population who receive two doses in a one-year period was estimated using the spring

programme coverage rate. Coverage for those availing of only one dose in a 12-month period was estimated based on the difference in coverage rates between the autumn and spring programmes.

With respect to costs, the vaccination strategies under consideration in this economic analysis include:

- product procurement costs
- administration costs (administration fee)
- HSE National Cold Chain Service including 'pick and pack' costs
- the cost of a public health information campaign (year one only)
- the cost of development of a training module (year one only)
- an ongoing programme management cost to maintain IT and data systems for recording vaccination
- the ongoing cost of a national programme manager to oversee implementation and operation of the programme.

Table 5.8 Coverage rates for COVID-19 vaccination strategies included in the model

Vaccination strategy	Assumed Coverage (%)	
	Autumn	Spring
S1 – adults aged 80 years and above	60.8	32.3*
S2 – adults aged 60 to 79 years	33.2	
S3 – adults aged 18-79 years living in long term care facilities for older adults	74.2	76.4*
S4 - aged 6 months and older with immunocompromise associated with a suboptimal response to vaccination	18.2	14.6*
S5 - aged 6 months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death	23.6†	N/A
S6 - health and care workers who choose to receive a vaccine	8.7	N/A
S7 - pregnant adolescents and adults who, following discussion with a healthcare provider, choose to receive a vaccine	6.5**	N/A
S8 - adults aged 18-59 years not included in the groups above who, following discussion with a healthcare provider, choose to receive a vaccine	3.6**	N/A

Key: N/A - not applicable; S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5; S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8.

*Sourced from 2024/2025 COVID-19 Spring Booster Programme uptake.(342)

**Sourced from 2024/2025 COVID-19 Autumn Programme uptake.(343)

†In the absence of Irish data, the uptake rate was assumed based on a relevant uptake rate from England.(213)

The vaccination product, administration and pick and pack costs are variable and are influenced by the size of the eligible population for each strategy and uptake. The public health information campaign and the development of a training module are once-off implementation costs, which would likely apply similarly with the introduction of any new programme(s) or substantial change to an existing programme. These costs would apply irrespective of the target populations considered and do not vary with vaccination uptake.

Included costs were informed by:

- publicly available published prices for COVID-19 vaccines from a number of sources in Europe(344-347)
- current payments to primary care contractors for the administration of vaccines
- discussions with the NIO
- HSE Consolidated Salary Scales.(348)

Table 5.9 Average vaccination programme costs – base-case analysis

Cost item	Unit Cost (ex VAT)	Units
COVID-19 vaccine	€75.00	Variable
Vaccine administration - adult vaccine	€25.00	
Pick and pack (per single dose pack)	€1.39	
Storage and distribution (per annum)	€600,000	1
Programme manager (Grade VIII clerical) (per annum)	€140,341	1 x WTE
Programme management (IT system maintenance)*	€100,000	1
Once-off vaccination programme implementation costs		
Public health information campaign (adult programme)	€500,000	1
Development of training module	€50,000	1

Key: VAT - value-added tax; WTE - whole-time equivalent.
*As a COVID-19 vaccination programme is already in place, maintenance of the IT system for recording and monitoring was assumed to be 10% of the cost of a new IT system.

Cost inputs

In accordance with national HTA guidelines, all costs are presented in 2026 Euro (€).[324, 325] All costs were derived from Irish sources; those from years prior to 2026 were adjusted using the Consumer Price Index for health and relevant sub-indices.[349] In the CUA, the costs associated with notified COVID-19 from the payer perspective included those costs relating to: general practitioner (GP) visits for those with a GP visit or medical card prescription medication; ED attendance; hospitalisation; post-acute step-down or rehabilitation care; post-acute short- and long-term care in a LTCF; and long COVID clinics.

Primary care

It was assumed that all cases of notified COVID-19 attend their GP. The proportion of people with a GP visit and or medical card was sourced from the HSE Primary Care Reimbursement Service (PCRS) eligibility data as of February 2026 Table 5.10).[350] In the absence of Irish-specific data, the frequency of GP visits related to notified cases of COVID-19 were sourced from expert opinion in Ireland (Table 5.11). The frequency of GP visits related to long COVID were sourced from the international literature and assumed to be five additional visits per annum and were limited to one year.[351, 352] The average cost of a GP consultation for a public patient (€56) was sourced from a study that estimated unit costs for non-acute medical care in Ireland and inflated to 2026 prices.[349, 353]

HSE prescribing guidelines and recommended treatment courses for COVID-19 were used to identify treatment items for COVID-19.[354] The only prescription item that

was costed for the treatment of COVID-19 was the anti-viral medicine Paxlovid®. Data obtained from the PCRS enabled estimates of the proportion of notified COVID-19 cases that were prescribed Paxlovid® in 2025 (Table 5.11). The full cost of prescription items is borne by the HSE for holders of a medical card, except for a co-payment of €1.50 for those aged less than 70 years and €1 for those aged 70 years and older. Given the high cost of Paxlovid®, it was assumed that non-medical card holders would access Paxlovid® under the Drugs Payment Scheme (DPS). While the DPS has a monthly co-payment of €80, this is applied at the level of the family and applies to all approved prescribed medications. Given that HSE clinical guidance limits use of Paxlovid® to selected seriously immunocompromised COVID-19 patients, it was assumed that these individuals would have comorbidities for which they currently receive other prescription medications and as such that the full cost of a prescription for Paxlovid® would be borne by the HSE. Cost data for Paxlovid® were sourced from the PCRS (https://www.sspcrs.ie/druglist/pub) and an average cost of €871 (ex VAT) was estimated using relevant published guidelines.[355]

Table 5.10 Estimated proportion of the population assessed as eligible for a GP visit card or a medical card

Age group (years)	Proportion of population eligible for GP visit card (%)	Proportion of population eligible for medical card (%)
60-64	4.0	29.0
65-69	4.1	36.7
70-74*	40.8	52.7
75-79	26.1†	73.9
≥80	26.1†	73.9

*All individuals in this age group are eligible to apply for a GP visit card. As such, the rows should sum to 100%. Where they do not sum to 100%, the discrepancy may be due to the fact that those who are entitled to apply for a GP visit card may not have done so as yet, or they may not have been able to register with a GP who holds a General Medical Service (GMS) Scheme contract.
†This figure was adjusted from 30.9% to ensure that the total proportion of the population eligible for a GP visit card or medical card in these age groups did not exceed 100%.
Source: Health Service Executive[350]

Table 5.11 Average number of GP visits per notified COVID-19 case, and probability of prescription for Paxlovid®

Age group (years)	Mean number of GP visits per notified case of COVID-19†	Percentage of notified COVID-19 cases issued a prescription for Paxlovid®‡
60-64	2.1	18
65-69	2.0	16
70-74	2.0	15
75-79	4.0	13

Age group (years)	Mean number of GP visits per notified case of COVID-19[†]	Percentage of notified COVID-19 cases issued a prescription for Paxlovid®[‡]
≥80	4.0	9

Sources:
[†]Assumed the same as that used for a notified case of respiratory syncytial virus (RSV) in a recently published HTA of RSV Immunisation in Ireland.[356]
[‡] Informed by claims data supplied by the HSE's Primary Care Reimbursement Service (PCRS)

Emergency department attendance and long COVID clinic visits

Average costs of €520 and €242 were applied for ED attendance and an outpatient appointment, respectively. These were estimated based on cost data provided by the HSE HPO. Based on personal communication with a specialist from one of the HSE's National long COVID services, it was assumed that those with long COVID attend a long COVID clinic twice per annum. The cost of a consultation at a long COVID clinic was assumed to be the same as that for an outpatient appointment.

Hospitalisation

The average cost of COVID-19-related hospitalisation was estimated based on the diagnosis related groups (DRGs) for hospitalisations with a principal diagnosis of COVID-19 in 2024 (most recent year that data are available) from the HIPE system (Table 5.12).

Table 5.12 Diagnosis-related groups, inpatient inlier prices and number of notified hospitalised cases with a principal diagnosis of COVID-19

DRG	Inpatient inlier price from 2026 Activity-Based Funding Admitted Patient Price List	Number of notified hospitalised cases of COVID-19 in those aged ≥60yrs
B82C	€6,597	1
T01A	€98,065	1
T01B	€43,327	1
T01C	€19,223	3
T63A	€10,693	846
T63B	€4,449	991

Key: DRG – Diagnosis-Related Group.
Source: Hospital In-Patient Enquiry (HIPE) system and Healthcare Pricing Office Activity Based Funding Admitted Patient Price List 2026.

For each age group, a weighted average hospitalisation cost was estimated based on the relevant DRGs for that age group and the Activity Based Funding Admitted Patient Price List for 2026.

For each age group, a weighted average hospitalisation cost was estimated based on the relevant DRGs for that age group and the Activity Based Funding Admitted Patient Price List for 2026.[357] The hospitalisation costs provided in **Error! Not a valid bookmark self-reference.** are estimated average costs; individual cases could incur higher or lower costs depending on the underlying diagnosis, intensity of treatment and length of stay.

Table 5.13 Estimated average cost of a notified hospitalised case with COVID-19

Age group (years)	Estimated average cost of a notified hospitalised case with COVID-19 (€)
60-64	6,638
65-69	6,955
70-74	7,586
75-79	7,532
≥80	7,518

Source: Estimated based on data from the Hospital Inpatient Enquiry (HIPE) System and Diagnosis Related Groups (DRGs) listed in Table 5.12.

Post-acute care in a step-down or rehabilitation facility

A weekly cost of €2,010 was assumed for step-down care in a non-acute hospital or rehabilitation centre following discharge from an acute hospital.[358] Based on expert opinion, an average length of stay of six weeks was assumed.[137]

Post-acute short- and long-term care in a long-term care facility

The national average weekly cost of short-term care in a LTCF was estimated to be €1,658 and it was assumed that 100% of this cost is publicly funded.[359] The estimate was calculated based on average financial turnover per bed for all operational incomes and fair deal rates and the distribution of residents in LTCFs by funding classification.[359] The national average weekly cost of long-term care in a LTCF was estimated to be €1,213 and it was assumed that 69% of this cost is publicly funded.[359] Based on expert opinion, the average length of stay for short-term care in a LTCF was assumed to be six weeks).[137] For those discharged to a LTCF for long-term care, the average length of stay was assumed to be 2.48 years.[147]

5.2.7 Model outputs

In the CUA, incremental costs and QALYs were estimated and then used to calculate a cost-effectiveness ratio — the incremental cost per QALY gained. In the first instance, vaccination strategies were compared with no vaccination to estimate an average cost-effectiveness ratio (ACER). The strategies were then ordered by increasing cost and compared with the previous least costly alternative to estimate an incremental cost-effectiveness ratio (ICER). In accordance with national HTA guidelines, the ICERs were reported relative to willingness-to-pay (WTP) thresholds of €20,000 and €45,000 per QALY gained.[324] For the BIA, incremental costs associated with, and costs averted as result of the introduction of an vaccination

programme, were estimated and used to calculate the budget impact over five years.

5.2.8 Assessment and quantification of uncertainty

Probabilistic and deterministic sensitivity analyses (PSA and DSA, respectively) were conducted to test the robustness of the economic model outputs.

Sensitivity analysis for cost-utility analysis and budget impact analysis

Parameter uncertainty was assessed using a Monte Carlo simulation with 10,000 iterations. Each model parameter that was not fixed was defined by a statistical distribution to represent uncertainty in the mean parameter value. For each parameter, an appropriate statistical distribution was selected (for example, a beta distribution for a probability). Parameter values were then drawn as random variates from their specified distributions and the total costs and benefits were recalculated. The total costs and QALYs for each simulation were recorded and used to quantify the proportion of simulations that were considered cost effective with respect to an illustrative WTP threshold (that is, €45,000 per QALY). The output was presented on a cost-effectiveness plane. While there is no specific guidance available on the optimal number of simulations necessary to reach convergence,[360] model convergence was assessed after 10,000 simulations.

One-way sensitivity analysis (OWSA) for each vaccination strategy was conducted by fixing each parameter in turn at its upper and lower bounds, while all other parameters were held at their mean. The impact of extreme variation in single-input parameters on the model outputs was presented on tornado plots. This provides a visual representation of the sensitivity of the model to the uncertainty associated with individual parameters.

Scenario analysis for cost-utility analysis

Given the uncertainty relating to the trajectory of the incidence of COVID-19 into the future, a number of scenario analyses were conducted. Both the 2023 and 2024 incidence data were used to examine the impact of higher incidence of COVID-19 on the cost effectiveness of the two vaccination strategies assessed in the base-case analysis.

The probability of a notified hospitalised case of COVID-19 being discharged to a LTCF was estimated based on the proportion (by age group) of HIPE discharges in 2024 with a principal diagnosis of COVID-19 that were discharged to some form of post-acute care (such as, a nursing home, convalescent home or long stay accommodation) and where the discharge did not have the same admission source. There is uncertainty regarding this estimate due to the difference in the absolute

number of hospitalised discharges with a principal diagnosis of COVID-19 from HIPE and the absolute number of notified hospitalised cases of COVID-19 as reported by the HPSC. As such, a scenario analysis was conducted where the probability was estimated based on the absolute number of discharges with a principal diagnosis of COVID-19 from HIPE and the absolute number of notified hospitalised cases of COVID-19.

The two strategies assessed in the base-case analysis considered vaccination for those aged 80 years and above (S1) and those 60 years and above (S2). An additional strategy, vaccination for those aged 75 years and above, was assessed in a scenario analysis.

Threshold analysis for cost-utility analysis

A threshold analysis estimates the conditions above or below which the model output may become cost effective, by substituting the point estimate for a wide sequence of values and recording the variation in model outputs. Given the uncertainty around the price the HSE would have to pay for the vaccine, a threshold analysis was used to explore the impact on cost effectiveness of different prices for the product.

5.2.9 Model validation and calibration

Internal validation of model was conducted in accordance with HIQA's internal Quality Assurance Framework. All model inputs, calculations, and model outputs were reviewed by a second economic modeller.

5.3 Results

5.3.1 Epidemiological analysis for COVID-19 vaccination strategies

Based on 2025 notified cases data, estimated intervention effectiveness (Table 5.5) and current COVID-19 vaccination coverage rates (Table 5.8), the annual model output for the number of notified COVID-19 cases by age, outcome and strategy, is reported below (Table 5.14). Vaccination is associated with a decrease in notified COVID-19 cases. Reductions associated with S1, compared with no vaccination, ranged from 11% for notified cases of COVID-19 to 33% for deaths among notified cases with COVID-19 for those aged 80 years and above. Overall reductions for S2, compared with no vaccination, ranged from 8% for notified cases of COVID-19 to 29% for notified deaths with COVID-19 for the total population aged 60 years and above.

Table 5.14 Annual number of notified COVID-19 cases (% reduction compared with no vaccination) by vaccination strategy outcome and age group

Strategy		60-79yrs	≥80yrs	Total
Cases	No vaccination	4,150	4,139	8,289
	S1: 2-dose ≥80yr olds	4,150 (0%)	3,677 (-11%)	7,827 (-6%)
	S2: 2-dose ≥80yr olds and 1-dose 60-79yr olds	3,984 (-4%)	3,677 (-11%)	7,661 (-8%)
ED visits	No vaccination	1,455	1,261	2,716
	S1: 2-dose ≥80yr olds	1,455 (0%)	1,035 (-18%)	2,490 (-8%)
	S2: 2-dose ≥80yr olds and 1-dose 60-79yr olds	1,349 (-7%)	1,035 (-18%)	2,384 (-12%)
Hospitalisations	No vaccination	1,896	2,172	4,067
	S1: 2-dose ≥80yr olds	1,896 (0%)	1,693 (-22%)	3,589 (-12%)
	S2: 2-dose ≥80yr olds and 1-dose 60-79yr olds	1,723 (-9%)	1,693 (-22%)	3,416 (-16%)
Deaths	No vaccination	91	261	352
	S1: 2-dose ≥80yr olds	91 (0%)	176 (-33%)	267 (-24%)
	S2: 2-dose ≥80yr olds and 1-dose 60-79yr olds	75 (-17%)	176 (-33%)	251 (-29%)

Key: S1 - Strategy 1; S2 - Strategy 2; S3 - Strategy 3; S4 - Strategy 4; S5 - Strategy 5; S6 - Strategy 6; S7 - Strategy 7; S8 - Strategy 8.

5.3.2 Cost-utility analysis for COVID-19 vaccination strategies

Base-case analysis

The reported ICER reflects the mean ICER obtained by PSA with 10,000 simulations. Convergence testing indicated that the number of simulations was sufficient to provide a stable result. For the vaccination strategies under consideration, a stable estimate of the ICER was achieved after approximately 500 simulations (Appendix C.3).

Overall, from the payer perspective and over a 12-month time horizon, both vaccination strategies were both more costly and more effective (generating incremental QALY gains) than no vaccination. Strategy 1 generated the smallest incremental costs compared with no vaccination; it also generated the largest incremental QALY gains. The ACERs, which compare each of the two strategies with no vaccination, are detailed in Table 5.15. From the payer perspective, over a 12-month time horizon S1 had the lowest ACER at €56,519 per QALY gained.

Table 5.15 Average cost-effectiveness ratios for vaccination strategies against notified COVID-19

Intervention	Total cost €, millions	Total QALYs	Incremental costs €, millions	Incremental QALYs	ACERs (€/QALY)†
No vaccination	61.1	1,070,632	-	-	-
S1: 2-dose ≥80yr olds	77.8	1,070,928	16.7	296	56,519
S2: 2-dose ≥80yr olds and 1-dose 60 to 79yr olds	109.3	1,071,084	48.2	455	106,098

Key: ACER - average cost-effectiveness ratio; QALYs - quality-adjusted life years.
†ACER compares each vaccination strategy with no vaccination.

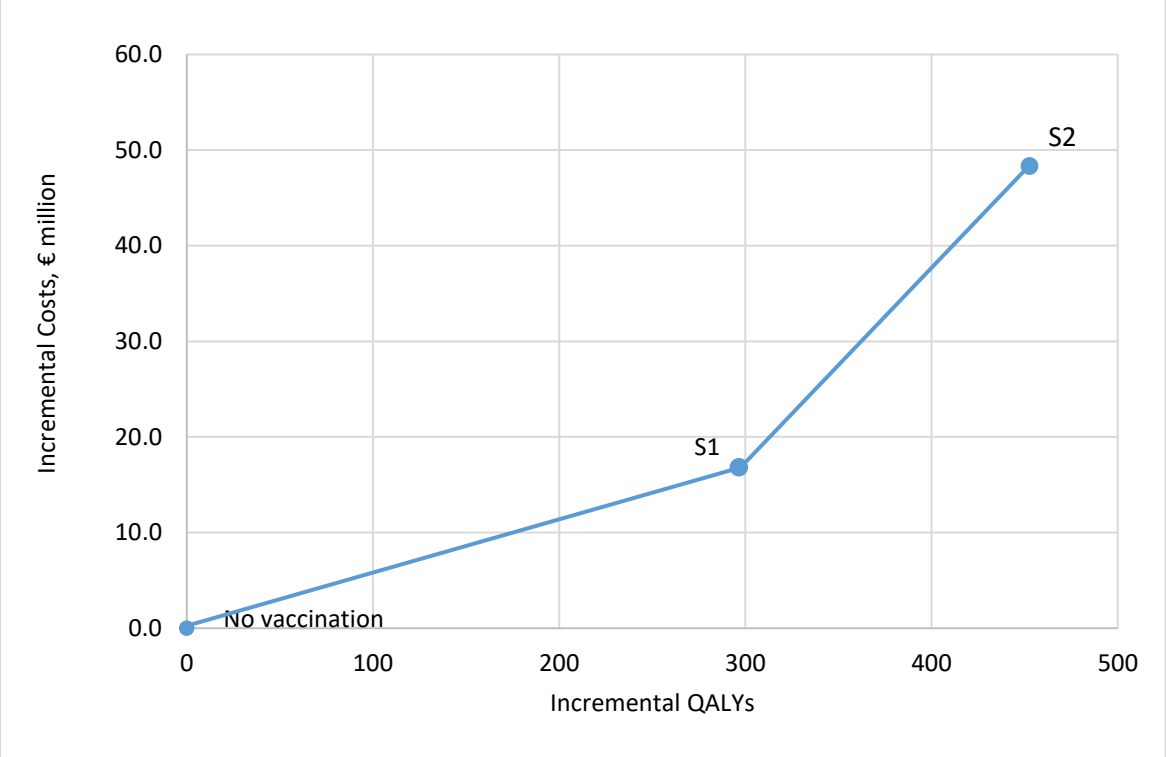
Given that there are two vaccination strategies under consideration and the goal is to maximise health gain, it is necessary to conduct an incremental analysis comparing all mutually exclusive strategies directly. As policy decisions are subject to a budget constraint, ICERs were estimated by ordering the vaccination strategies by increasing cost and comparing each strategy with the preceding least costly strategy. In the incremental analysis, the ICER for S2 compared with S1 is €202,120 (Table 5.16). The results were plotted on the cost-effectiveness plane (Figure 5.7), which clearly illustrates the relative positions of each of the vaccination strategies under consideration on the cost-effectiveness frontier. Based on the results of the incremental analysis, neither of the two vaccination strategies would be deemed cost effective at a WTP threshold of €45,000 per QALY.

Table 5.16 Incremental cost-effectiveness ratios for vaccination strategies against notified COVID-19

Intervention*	Total cost €, million	Total QALYs	Incremental costs €, million (95% CI)	Incremental QALYs (95% CI)	ICER† (€/QALY)
No vaccination	61.1	1,070,632	-	-	-
S1: 2-dose ≥80yr olds	77.8	1,070,928	16.7 (12.4 – 21.3)	296 (160 – 436)	56,519
S2: 2-dose ≥80yr olds and 1-dose 60 to 79yr olds	109.3	1,071,084	31.5 (25.8 – 37.9)	156 (85 – 223)	202,120

Key: ICER – incremental cost-effectiveness ratio; QALYs – quality-adjusted life-years; S1 - Strategy 1; S2 - Strategy 2.
*Ordered from least costly to most costly vaccination strategy.
†ICER compares each vaccination strategy with the previous least costly strategy.

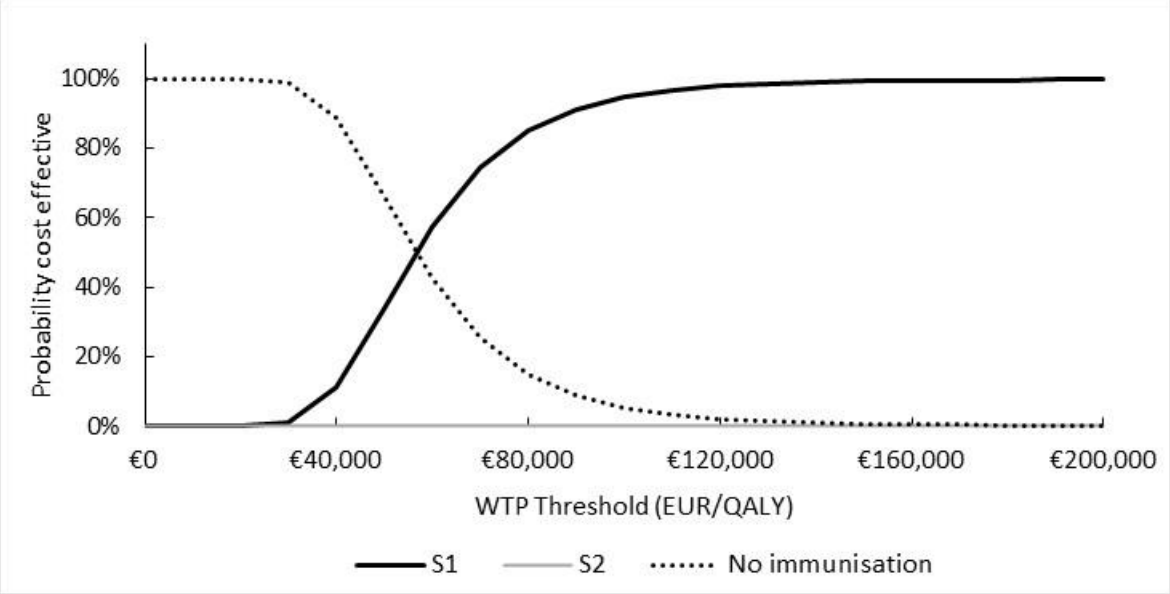
Figure 5.7 Cost-effectiveness frontier for COVID-19 vaccination strategies



Key: QALY – quality-adjusted life year; S1 – Strategy 1: 2-dose 80 years and above; S2 - Strategy 2: 2-dose 80 years and above and 1-dose 60 to 79 yrs old.

The cost-effectiveness acceptability curve summarises the uncertainty in the results of the economic evaluation. It plots the proportion of times that each of the alternative strategies under consideration has the greatest net monetary benefit (that is, the intervention's value in monetary terms) across a range of WTP thresholds. At a WTP threshold of €45,000 per QALY, S1 has a 22% probability of being cost effective. At a WTP threshold of €57,000 per QALY, S1 has a 51% probability of being cost effective, rising to 95% at €100,000 per QALY (Figure 5.8).

Figure 5.8 Cost-effectiveness acceptability curves for COVID-19 vaccination strategies

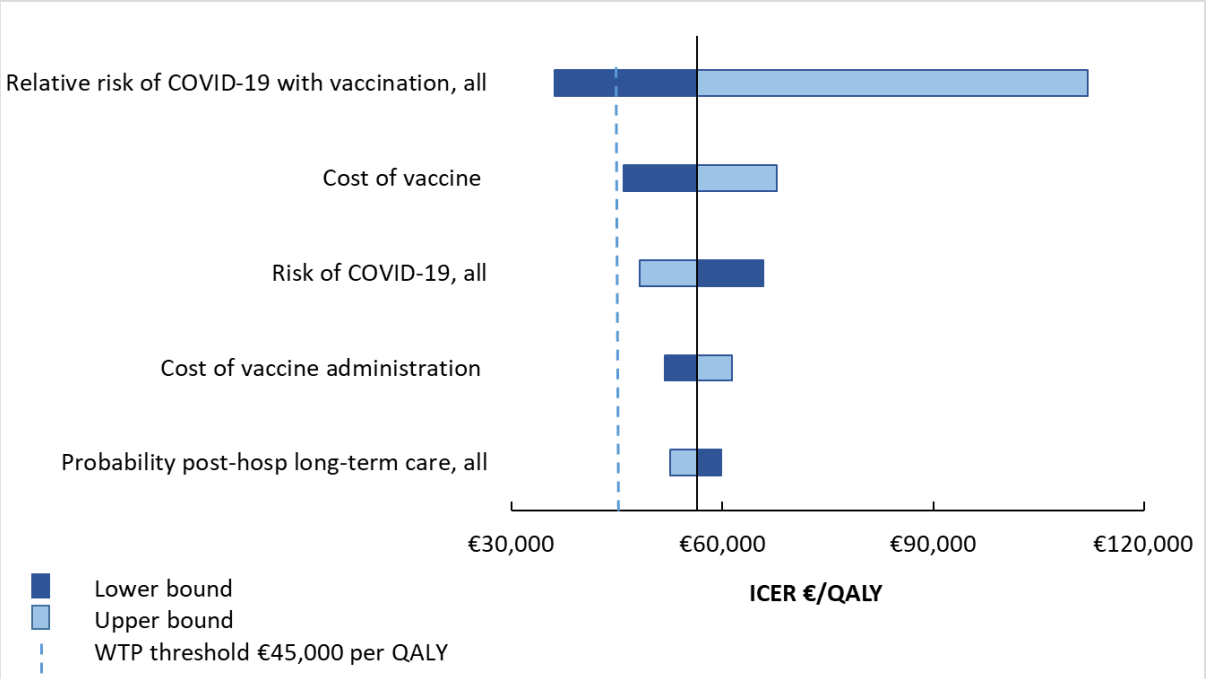


Key: QALY – quality-adjusted life year; S1 – Strategy 1: 2-dose 80 years and above; S2 - Strategy 2: 1-dose 60 to 79yrs old and 2-dose 80yrs old and above; WTP – willingness-to-pay.
Notes: The probability of S2 being cost effective does not exceed 0% at WTP thresholds between €0 and €200,000 per QALY.

Univariate sensitivity analysis

When conducting OWSA, all input parameters are varied individually and ranked in order of increasing influence on the uncertainty in the ICER. To demonstrate the impact of parameter uncertainty, a deterministic OWSA was conducted from the payer perspective comparing the intervention with the lowest ICER, with no vaccination. Although all parameters were varied in the analysis, only those that resulted in a ≥10% fluctuation from the mean ICER are presented. The OWSA conducted on the relative risk of COVID-19 with vaccination resulted in the greatest fluctuation from the mean ICER. The ICERs ranged from €36,000 per QALY when values for all parameters for the relative risk of COVID-19 with vaccination were simultaneously set to their lower bounds, to €112,000 per QALY when the same parameter values were simultaneously set to their upper bounds. When the cost of the COVID-19 vaccine was set to the lower bound of €61, the ICER for S1 versus no vaccination is €45,925 per QALY (Figure 5.9).

Figure 5.9 Tornado plot of univariate sensitivity analysis for ICER for Strategy 1 (2-dose for those aged ≥80 years) versus no vaccination



Key: ICER - incremental cost-effectiveness ratio; QALY – quality-adjusted life year; S1 – Strategy 1: 2-dose 80 years and above; WTP – willingness-to-pay.

Scenario analysis for incidence of notified COVID-19 cases

As stated in Section 5.2.6, there is considerable uncertainty regarding the trajectory of incidence of COVID-19 into the future. As such, two scenario analyses were conducted where both the 2023 and 2024 notified COVID-19 case data were used in the model. The model results when using 2023 notified COVID-19 case data are provided in Table 5.17. S1 is dominant as the cost is lower and effect greater than both no vaccination and S2. S1 would therefore be considered a cost-saving strategy. The ICER for S2 compared with S1 is €45,384 per QALY.

Table 5.17 Incremental cost-effectiveness ratios for vaccination strategies against notified COVID-19 using 2023 notified case data

Intervention*	Total cost €, million	Total QALYs	Incremental costs €, million	Incremental QALYs	ICER† (€/QALY)
No vaccination	202.9	1,065,690	-	-	-
S1: 2-dose ≥80yr olds	201.1	1,066,633	-1.8	943	Dominant‡
S2: 2-dose ≥80yr olds and 1-dose 60 to 79yr olds	227.5	1,067,216	26.4	583	45,384

Key: ICER – incremental cost-effectiveness ratio; QALYs – quality-adjusted life-years; S1 - Strategy 1; S2 - Strategy 2.
*Ordered from least costly to most costly vaccination strategy.
†ICER compares each vaccination strategy with the previous least costly strategy.
‡This strategy is classified as dominant as the cost is lower and the effect is greater than the previous least costly strategy.

The model results when using 2024 notified COVID-19 case data are provided in Table 5.18. The ICER for S1 compared with no vaccination is €15,323 per QALY and therefore the strategy would be considered cost effective at a WTP threshold of €20,000 and €45,000 per QALY.

Table 5.18 Incremental cost-effectiveness ratios for vaccination strategies against notified COVID-19 using 2024 notified case data

Intervention*	Total cost €, million	Total QALYs	Incremental costs €, million	Incremental QALYs	ICER† (€/QALY)
No vaccination	118.8	1,068,471	-	-	-
S1: 2-dose ≥80yr olds	127.9	1,069,062	9.1	591	15,323
S2: 2-dose ≥80yr olds and 1-dose 60 to 79yr olds	157.4	1,069,397	29.5	335	88,223

Key: ICER – incremental cost-effectiveness ratio; QALYs – quality-adjusted life-years; S1 - Strategy 1; S2 - Strategy 2.
*Ordered from least costly to most costly vaccination strategy.
†ICER compares each vaccination strategy with the previous least costly strategy.

Scenario analysis for probability of discharge to a long-term care facility following hospitalisation with COVID-19

As discussed in section 5.2.8, a scenario analysis was conducted where the probability of discharge to a LTCF following hospitalisation with COVID-19 was estimated based on the absolute number of discharges with a principal diagnosis of COVID-19 from HIPE and the absolute number of notified hospitalised cases from

the HPSC. The probabilities used in the base-case and scenario analysis are provided in Table 5.19. Of note, the probabilities used in the scenario analysis are lower than the lower bound values used in the one-way sensitivity analysis above. When the lower probabilities are used in the model, the deterministic ICER for S1 compared with no vaccination increases to €64,420 per QALY. This compares with an ICER of €56,519 per QALY in the base-case analysis.

Table 5.19 Probability of discharge to a long-term care facility by age group for base-case and scenario analysis

Age group (years)	Base-case		Scenario analysis	
	Probability of discharge to LTCF for short-term care	Probability of discharge to LTCF for long-term care	Probability of discharge to LTCF for short-term care	Probability of discharge to LTCF for long-term care
60-64	0.3%	1.4%	0.2%	0.9%
65-69	0.7%	3.7%	0.3%	1.6%
70-74	0.6%	3.4%	0.3%	1.8%
75-79	0.7%	3.9%	0.4%	1.9%
≥80	1.5%	8.0%	0.8%	4.6%

Key: LTCF – long-term care facility.

Scenario analysis for a strategy vaccinating those aged 75 years and above

A scenario analysis was conducted where a third strategy, Strategy 1a (S1a), was added to the possible vaccination strategies. S1a included vaccination for those aged 75 years and above, with two doses offered to those aged 80 years and above and one dose offered to those aged 75 to 79 years. The results of the probabilistic incremental analysis are presented in Table 5.20 where the ICER for S1a, compared with S1, is €79,731. S1a would therefore be considered not cost effective at a WTP threshold of €45,000 per QALY.

Table 5.20 Incremental cost-effectiveness ratios including a strategy offering vaccination against notified COVID-19 to those aged 75 years and above

Intervention*	Total cost €, million	Total QALYs	Incremental costs €, million	Incremental QALYs	ICER† (€/QALY)
No vaccination	61.1	1,070,632	-	-	-
S1: 2-dose ≥80yr olds	77.8	1,070,928	16.7	296	56,519
S1a: 2-dose ≥80yr olds and 1-dose 75 to 79yr olds	83.1	1,070,995	5.3	67	79,731
S2: 2-dose ≥80yr olds and 1-dose 60 to 79yr olds	109.3	1,071,084	26.2	89	293,891

Key: ICER – incremental cost-effectiveness ratio; QALYs – quality-adjusted life-years; S1 - Strategy 1; S2 - Strategy 2; S1a - Strategy 1a.
*Ordered from least costly to most costly vaccination strategy.
†ICER compares each vaccination strategy with the previous least costly strategy.

Threshold analysis for the cost of the vaccine

Given the uncertainty around the cost of the vaccine, a deterministic threshold analysis was conducted to assess the impact of a lower vaccine price (beyond the reduction used in the OWSA) on the cost effectiveness of COVID-19 vaccination. All other parameters were held at their mean value during the analysis. The price of the vaccine was varied in €25 increments at levels ranging from €25 to €125 (wholesale price ex VAT). The incremental analysis was repeated with the ICER results reported in Table 5.21. At a vaccine price of €25 (wholesale price ex VAT), the ICER for S1 versus no vaccination was €19,756 per QALY, rising to €45,192 per QALY at a vaccine price of €60.

Table 5.21 Incremental cost-effectiveness ratio for Strategy 1 versus no vaccination at varying vaccine prices

Vaccine price (wholesale ex VAT)	ICER (€/QALY) S1 v No Vaccination	ICER (€/QALY) S2 v S1
€25	19,756	94,734
€50	37,925	147,215
€60	45,192	168,207
€75	56,093	199,695
€100	74,262	252,175
€125	92,431	304,656

Key: ICER – incremental cost-effectiveness ratio; QALY – quality-adjusted life year; S1 – Strategy 1: 2-dose 80 years and above; VAT – value-added tax.

5.3.3 Budget impact analysis for COVID-19 vaccination strategies

The BIA for each of the vaccination strategies is presented relative to no vaccination. The budget impact is conducted from the payer perspective and is limited to the vaccination programme costs (Table 5.9) and, where available, the costs averted as a result of a decrease in incidence of notified COVID-19 associated with the provision of a vaccination programme. In line with national guidelines, VAT is included in the BIA.[325] VAT on non-oral drugs (such as injectables) is standard rated (23% as of October 2025),[361] while services delivered by a recognised medical professional for the purpose of protecting health (for example, vaccine administration) are VAT exempt.[362] Potential organisational issues associated with a COVID-19 vaccination programme are described in Chapter 6.

Base-case analysis for adults aged 60 years and older in the general population

The five-year incremental budget impact versus no vaccination was €111.5 million for S1 and €307.0 million for S2 (Table 5.22).

Table 5.22 Results of base-case analysis for five-year incremental budget impact for COVID-19 vaccination strategies versus no vaccination

Strategy	Number Eligible (year 1)	Number of people vaccinated (year 1)†	Total costs incurred €, million (95% CI)	Total costs averted €, million (95% CI)	5-year incremental budget impact €, million*
S1: 2-dose ≥80yr olds	231,800	140,934	155.7 (129.6 -184.6)	44.2 (31.9 – 59.4)	111.5
S2: 2-dose ≥80yr olds and 1-dose 60 to 79yr olds	1,228,400	471,806	361.5 (303.7 -425.4)	54.5 (39.8 - 72.7)	307.0

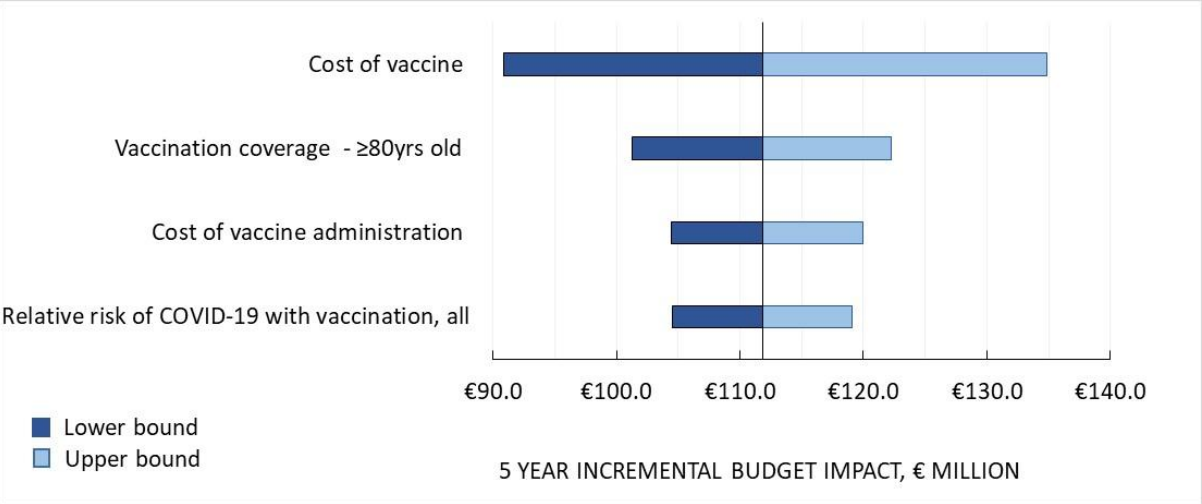
Key: CI – confidence interval; S1 – Strategy 1; S2 – Strategy 2.
*Compared with no vaccination.
†Based on coverage rates in those aged 80 years and above, it is assumed that 32% (45,099) of the vaccinated population receive two doses and the remainder one dose.

The majority of costs incurred for both vaccination strategies over the five-year time horizon related to vaccine procurement (approximately 71% to 75%). The second largest cost item was administration of the vaccine (25% to 23%). For S1, total cost offsets were 28% of total costs incurred, with hospitalisation (45%) and long-term care (52%) being the largest contributors to cost offsets. For S2, total cost offsets were 15% of total costs incurred, with hospitalisation (49%) and long-term care (48%) again contributing most to cost offsets.

Univariate sensitivity analysis for adults aged 60 years and above

To demonstrate the impact of parameter uncertainty, a deterministic OWSA was conducted from the payer perspective comparing the intervention with the lowest ICER from the base-case cost-utility analysis above, which was S1, with no vaccination. Although all parameters were varied in the analysis, only those that resulted in a ≥10% fluctuation from the mean incremental budget impact are presented (Figure 5.10). The OWSA conducted on the cost of the vaccine resulted in the greatest fluctuation from the mean incremental budget impact (ranging from €90.8 million to €134.8 million).

Figure 5.10 Tornado plot of deterministic univariate sensitivity analysis for BIA for Strategy 1 (2-dose for those aged 80 years and above) versus no vaccination



Base-case analysis for specific populations

The BIA for specific populations only considered the costs incurred over a five-year period. Due to a lack of relevant epidemiological data for Ireland, costs averted were not estimated. The five-year budget impact versus no vaccination ranged from €6.8 million for S7 (pregnant adolescents and adults) to €63.8 million for S8 (all others aged 18 to 59 years), with the results detailed in Table 5.23.

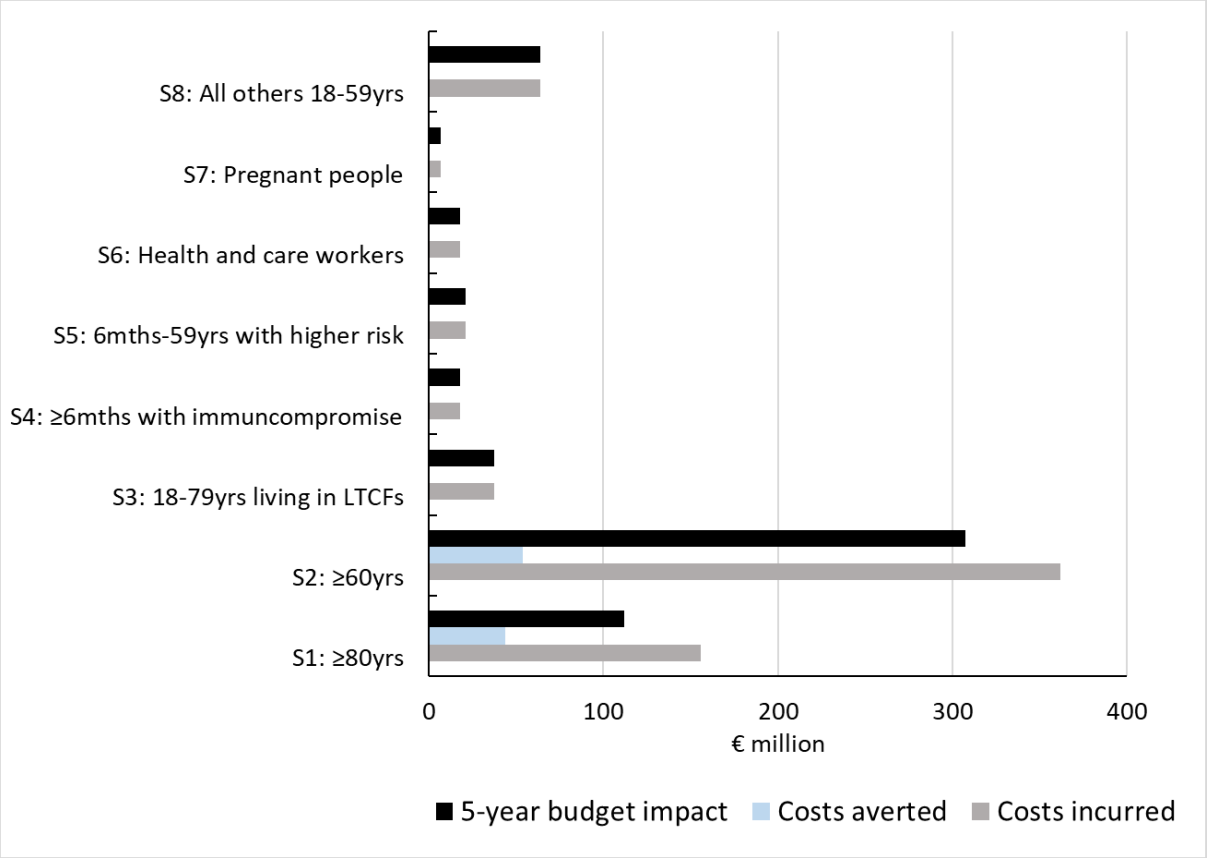
Table 5.23 Results of base-case analysis of five-year budget impact for COVID-19 vaccination for specific populations versus no vaccination

Vaccination strategy	Number eligible (year 1 - 2027)	Number vaccinated (year 1 - 2027)*	5-year budget impact €, million
S3 - adults aged 18-79 years living in long-term care facilities for older adults	34,147	25,713	37.4
S4 - aged 6 months and older with immunocompromise associated with a suboptimal response to vaccination	67,080	11,001	18.1
S5 - aged 6 months to 59 years with medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death	113,980	26,899	21.1
S6 - health and care workers who choose to receive a vaccine	253,311	21,750	18.1
S7 - pregnant adolescents and adults who, following discussion with a healthcare provider, choose to receive a vaccine	53,723	3,514	6.8
S8 - adults aged 18-59 years not included in the groups above who, following discussion with a healthcare provider, choose to receive a vaccine	2,701,586	97,257	63.8

Key: S1 – Strategy 1; S2 – Strategy 2; S3 – Strategy 3; S4 – Strategy 4; S5 – Strategy 5; S6 – Strategy 6; S7 – Strategy 7; S8 – Strategy 8.
*Estimated based on vaccination coverage rates in Table 5.8.

A summary of the five-year budget impact for all eight strategies considered in this assessment is provided in Figure 5.11. The estimates are based on the relevant population size as outlined in Table 5.2. In the event that multiple strategies were to be adopted, there may be overlap in terms of the included population. As such, the budget impact estimates provided in this analysis are conservative.

Figure 5.11 Summary of 5-year budget impact for COVID-19 vaccination strategies



Key: LTCF – long-term care facility.
Note: For Strategies 3, 4, 5, 6, 7 and 8, the data did not allow for the inclusion of costs averted.

5.4 Discussion

To support decision-making relating to changes to the provision of COVID-19 vaccination in Ireland for the 2027/2028 vaccination campaign onwards, this economic model was developed to characterise the incidence of medically attended COVID-19 cases in Ireland both with and in the absence of COVID-19 vaccination. The model was used to estimate the cost effectiveness and incremental budget impact of a COVID-19 vaccination programme in Ireland for adults in the general population aged 60 years and above and separately, to estimate the budget impact of COVID-19 vaccination for specific population groups. The analysis of cost effectiveness was conducted from the payer (HSE) perspective over one year, while the BIAs estimated the incremental cost to the HSE also over a five-year period.

5.4.1 Main findings

Results from the epidemiological analysis, using 2025 notified COVID-19 case data, indicate that in a single year, vaccination for those aged 60 years and older is associated with a decrease in notified COVID-19 cases.

In terms of cost effectiveness, in the base-case analysis neither of the two vaccination strategies was estimated to be cost effective from the payer perspective relative to no vaccination or the previous least costly strategy, at a WTP threshold of €45,000 per QALY. The probabilistic ICER for S1 (two-dose for those aged 80 years and above) compared with no vaccination was €56,519 per QALY, rising to €202,120 per QALY for S2 (two-dose for those aged 80 years and above and one-dose for those aged 60 to 79 years) compared with S1. A deterministic sensitivity analysis demonstrated that at a vaccine price of €60 (ex VAT), a 20% reduction from the base-case price of €75, the ICER for S1 compared with no vaccination fell to €45,192 per QALY. Given the uncertainty relating to the incidence of COVID-19 in a single year, a deterministic sensitivity analysis was conducted using both 2023 and 2024 notified case data. When 2024 case data were modelled, the ICER for S1 compared with no vaccination was €15,323, rising to €88,223 per QALY for S2 compared with S1. In the case of 2023 case data, S1 was cost-saving compared with no vaccination and the ICER for S2 compared with S1 was €45,384 per QALY.

In the base-case analysis, and assuming a price of €75 (ex VAT) for the vaccine, the five-year probabilistic incremental budget impact was €112.0 million and €307.6 million for S1 and S2, respectively. For S1, total cost offsets were 28% of total costs incurred, with hospitalisation (45%) and long-term care (52%) being the largest contributors to cost offsets. For S2, total cost offsets were 15% of total costs incurred, with hospitalisation (49%) and long-term care (48%) being the largest contributors to cost offsets.

For the specific population groups the five-year budget impact versus no vaccination ranged from €6.8 million for S7 (pregnant adolescents and adults) to €63.8 million for S8 (all other aged 18 to 59 years).

5.4.2 Limitations

As with any economic modelling exercise, the certainty of the results is limited by the choice of model, the underlying assumptions, the availability of data to populate the model, and the chosen parameter values.

The incidence of COVID-19 in Ireland is highly uncertain. While COVID-19 is a notifiable disease in Ireland, the notified case data are likely an underestimate of the total burden, and particularly the burden in primary care, as not all COVID-19 cases are laboratory confirmed and some discharges may not be coded (Chapter 3). Additionally, by limiting the model to notified cases of COVID-19 only, the full disutility of COVID-19 is not captured in the analysis. However, notified cases should represent the majority of cases that require medical care and thereby most of the impact of COVID-19 on healthcare resources and quality of life.

This study employed a static rather than a dynamic model which does not account for indirect effects of vaccination, including herd immunity, and therefore potentially underestimates the benefits of a COVID-19 vaccination programme. A dynamic transmission model requires calibration, that is, identifying model parameter values that align model outputs with empirical data. In the absence of observed data, calibration can result in erroneous parameter values leading to uncertainty around the validity of the model results. Given the incomplete data on population-level incidence of COVID-19 in Ireland (beyond the notified case data as described above), using a dynamic transmission model that is calibrated to estimated population level incidence of COVID-19 would potentially undermine the validity of the results of the economic evaluation. As such, the static model, using notified COVID-19 case data, is the most appropriate model choice in this instance.

In the absence of population level COVID-19 incidence data for Ireland, the base-case epidemiological model represents notified COVID-19 cases for the most recent full calendar year (2025). In reality, the incidence of COVID-19 and subsequent incidence of notified COVID-19 cases in any given year can fluctuate greatly and has been observed to have decreased markedly since the WHO declared an end to COVID-19 as a public health emergency in May 2023. As such, modelling incidence based on 2025 data may not reflect future incidence and therefore the cost-effectiveness of COVID-19 vaccination. Scenario analyses were therefore conducted using higher rates of notified COVID-19 cases from both 2023 and 2024 to understand the impact of an increase in incidence on the cost effectiveness of vaccination.

A number of parameter assumptions and values used in the economic model also present limitations. The cost of vaccines to the HSE are part of confidential pricing agreements with the vaccine manufacturers. Typically, these negotiations commence at the beginning of the procurement process following a decision regarding the eligible cohort for whom the vaccine will be funded. For the purpose of this HTA, and in the absence of indicated vaccine prices for Ireland, a unit cost of €75 (ex VAT) was assumed based on publicly available prices in a number of other European countries. The sensitivity and scenario analyses conducted for both the CUA and BIA highlight the considerable impact that the uncertainty associated with the cost of the vaccine had on the results of the economic analysis. In the event that negotiations on the vaccine price are undertaken as part of a competitive tender, careful examination of the analyses presented would be required to identify the potential impact on the cost effectiveness and affordability of vaccination. Additionally, where multiple products for protection against COVID-19 are available, the potential to negotiate price reductions, as part of a competitive tender, may be possible. The vaccination programme costs, including vaccine price, pick and pack, and cold storage and distribution, presented in Table 5.9, were informed by discussions with the NIO. As these costs may differ between different vaccine forms (such as multidose vials, single dose vials, single dose pre-filled syringes, and those requiring reconstitution and or thawing), the vaccination programme costs used in the model represent estimated average costs. Coverage rates used in the model for all vaccination strategies are based on the most recent available data for the target population groups. An increase in coverage rates for a population group, due to initiatives such as a targeted awareness campaign regarding the availability of a COVID-19 vaccine, may result in greater cost offsets due to a reduction in cases, but overall will result in an increase in the budget impact. With regard to the once-off vaccination programme implementation costs (information campaign and training module) included in the model, these costs may be an overestimate as there is a COVID-19 vaccination programme currently in place. However, given that the potential changes to the vaccination programme are uncertain at this point it was assumed that the equivalent once-off implementation costs of a new programme would apply. Additionally, annual programme costs relating to cold chain, IT system maintenance and programme management have been applied separately to each modelled vaccination strategy. If multiple strategies were to be implemented, a single cost for each of the annual programme costs would likely apply and the five-year budget impact presented may be an over-estimate.

There is considerable uncertainty relating to resource use and the resulting costs in primary care due to COVID-19. An assumption was made that all notified cases of COVID-19 would attend their GP. However, it is acknowledged that this may be an overestimate as some hospitalised cases may have presented directly to the ED

without first attending the GP. In the absence of Irish data, it was assumed that the frequency of GP visits for COVID-19 was the same as that for respiratory syncytial virus (RSV), as presented in a recently published HTA. It remains unclear as to whether this is an over- or under-estimate. Prescription data for the treatment of COVID-19 were limited to the anti-viral medicine Paxlovid® which may be used to treat early COVID-19 infection in selected seriously immunocompromised patients who are at increased risk of progressing to severe disease. Given its high cost relative to other prescription medications, the majority of prescription costs relating to COVID-19 are likely captured in this estimate. Additionally, in adopting a conservative approach, it was assumed that the HSE would cover the full cost of Paxlovid®, notwithstanding that some patients without a medical card may have been required to cover a portion of the cost if they had not already reached the €80 monthly limit under the DPS. Based on the sensitivity analysis conducted, changes in these parameter values would not materially alter the results of the economic analysis.

Parameter values relating to the probability of discharge to a step-down or rehabilitation facility for short-term care or to a LTCF for short- and long-term care are highly uncertain and may impact the results of the economic analysis. This uncertainty relates to the fact that the base-case parameter values were estimated based on HIPE discharge data and applied to the notified hospitalised data from the HPSC. As such, the base-case parameter values may be an overestimate of the proportion of patients with COVID-19 who require post-acute care. To address this limitation, sensitivity analyses were conducted to understand the impact of lower (than those used in the one-way sensitivity analysis) values for these parameters, on the results of the economic analysis. This analysis demonstrated that at the lower values, the ICER for S1 compared with no vaccination increased from €56,519 per QALY in the base-case scenario to €64,420 per QALY.

The probability of long COVID following COVID-19 infection for the target population was estimated based on data on the number of new patients attending long COVID clinics in Ireland in 2025 and 2026. It is recognised that these data may represent an underestimate, as not all patients with COVID-19 may attend a long COVID clinic. However, the estimate is broadly in line with recent data from the UK Office of National Statistics estimated that the prevalence of long COVID symptoms 12 weeks or more after acute COVID-19 infection in a large sample of adults and children was 1.8%. In terms of resource use for long COVID, it was assumed that those with long COVID attend their GP an additional five times in the first year with long COVID. This estimate was based on international data and while the use of such data present a limitation, the sensitivity analysis suggests that changes to this parameter value would not alter the overall results of the economic evaluation.

Health state utility values and or QALY losses associated with COVID-19 are highly uncertain due to a lack of published studies as well as data that are inconsistent and poorly reported. QALY losses for medically-attended COVID-19, ED attendance and hospitalisation with COVID-19 were sourced from recently published economic evaluations of COVID-19 vaccination. Three of the five studies were independent evaluations to inform national vaccination policy decisions, and it was ensured that the upper and lower bound values used in the probabilistic analysis captured the range of values used across the multiple studies. With respect to long COVID, there are a lack of data as to the duration of QALY loss. As such, it was assumed that QALY loss is sustained over the life course. This may represent an overestimate of the duration of QALY loss. Given the assumed low incidence of long COVID-19 in the target population, this assumption does not materially bias the results of the economic evaluation. Overall, while using international data presents a limitation and the uncertainty around all parameter values impacts the certainty of the results, a probabilistic model was used and extensive sensitivity analyses were conducted which confirmed the overall results of the economic evaluation.

5.4.3 Conclusion

While this analysis demonstrates that vaccination against COVID-19 is associated with improvements in outcomes associated with COVID-19, the strategies assessed in the base-case economic analysis would be considered not cost effective at the modelled vaccine price at a WTP threshold of €45,000 per QALY. However, as demonstrated in the results of the sensitivity and threshold analyses, the outcome of this economic evaluation is highly sensitive to both the assumed price of the vaccine and incidence of COVID-19 going forward. As such, both parameters require careful consideration in informing decision-making regarding future COVID-19 vaccination policy.

6 Discussion

Key points

- This chapter aims to provide an overall discussion and interpretation of the findings of this assessment. It also considers general organisational issues relating to the COVID-19 vaccination programme, in addition to ethical, patient and social considerations specific to any potential decision to restrict the groups for whom COVID-19 vaccination is funded.
- The HSE COVID-19 vaccination programme provides access to COVID-19 vaccination, in line with the National Immunisation Advisory Committee recommendations and the Department of Health policy, which is free at the point of care. In line with these recommendations, the programme:
    - preferentially provides an antigenically updated mRNA vaccine (Comirnaty®), with access provided through usual primary care vaccination sites (GP practices and pharmacies) and by HSE mobile vaccination teams.
    - provides access to the antigenically updated protein subunit vaccine Nuvaxovid® to the small number of individuals for whom an mRNA COVID-19 vaccine is clinically unsuitable. Nuvaxovid® is not routinely available through GP clinics and pharmacies, and instead is accessible through HSE vaccine clinics by appointment. These additional steps can represent a logistical barrier for some patients.
- Twice yearly vaccination campaigns have been run by the HSE in recent years, whereby the autumn/winter programme aligns with the seasonal influenza vaccination campaign. This aims to improve uptake rates and provide efficiencies for patients and providers where individuals are eligible to receive both vaccines. A second campaign is run approximately six months later in the spring for those for whom twice yearly vaccination is recommended with the aim of providing year-round protection. Access outside the seasonal campaigns is available, where clinically indicated.
- General organisational issues relating to the COVID-19 vaccination programme include:
    - Challenges associated with an existing model based on use of a multidose vial formulation, packaged in boxes of 10, that are delivered from the manufacturer frozen and which must be thawed and relabelled with a new, shorter "use by" date before transportation to primary

vaccination sites. This results in additional operational complexity, greater potential for dosing errors, and greater wastage compared with other vaccines provided through the HSE National Cold Chain Service (NCCS).

  - Efficiencies may be realised by moving to a refrigerated (never frozen), single dose, pre-filled syringe product when procurement contracts are retendered. This would be consistent with how most other vaccines are supplied, would reduce wastage, and provide efficiencies for NCCS staff in terms of vaccine storage and management, and healthcare staff in terms of vaccine administration.

  - Although a programme comprising a range of vaccine products may increase choice and potentially improve resilience, these benefits would need to be considered in the context of the cost difference (if any) between products and the additional logistical burden associated with making a range of products available.

  - Given the lack of seasonality with COVID-19 and evidence of waning vaccine effectiveness over time, more frequent campaigns may be required to promote uptake when national and international data suggest periods of higher circulation. Consideration could also be given to expanding access outside defined seasonal campaigns to anyone whose vaccination status is not considered to be current (within the preceding 180 or 365 days, as appropriate).

- Potential ethical, patient and social issues associated with a decision to restrict access to funded COVID-19 vaccination to those at the highest risk of severe disease and or on the basis of cost effectiveness include a potential:

  - increase in the incidence of notified cases, notified hospital admissions and mortality among non-eligible individuals. This is particularly the case if eligibility is based solely on age-based criteria, rather than also considering other groups known to be at increased risk of severe disease (such as those residing in long term care facilities for older adults or those living with immunocompromise), and those at increased risk of exposure (such as, health and care workers).

  - increased level of long-term disability among non-eligible groups who may go on to experience long COVID (if such illness could have been prevented by vaccination) and an associated reduced participation in the

labour market, or potential worsening of symptoms for those already living with long COVID.

    - reduction in the workload for healthcare staff due to a reduction in the number of individuals requiring vaccination. This efficiency is particularly relevant when considering subgroups for whom the current benefits of vaccination are limited given the decline in severity of COVID-19.

- In acknowledging the overall decline in the burden associated with COVID-19, a decision to change the groups eligible for COVID-19 vaccination should still be considered in the context of the overall resilience of a healthcare system that exhibits high bed occupancy rates. While COVID-19 lacks seasonality, the potential for vaccination to support reductions in winter overcrowding could strengthen resilience in the health service.
- Restricting access to funded COVID-19 vaccination could be perceived as curtailment of an individual's autonomy in those for whom it is no longer available. However, decisions about healthcare distribution should ensure that resources are allocated or reallocated fairly and that the opportunity costs (the value of the next best alternative forgone) of investments are considered. Funding interventions that are not cost effective could create issues of justice and equity with respect to a fair distribution of benefits and burdens. This is particularly important in the context of a finite healthcare budget and increasing demands for services provided.
    - While ordinarily, there may be potential to pay for a vaccine privately if access is not funded as part of a national programme, COVID-19 vaccines are not currently (as of August 2026) available for private purchase in Ireland. For authorised vaccines, such availability is at the discretion of the individual manufacturer.
- The assessment of cost effectiveness in this HTA was limited to age-based cohorts (that is, vaccination of older adults). Due to a lack of Irish epidemiological data, it was not feasible to evaluate the cost effectiveness of vaccinating other individuals at high risk of severe disease (such as those residing in long term care facilities for older adults and those living with immunocompromise) and those at increased risk of exposure (such as, health and care workers). However, this does not preclude a decision on whether to continue to provide COVID-19 vaccination for such individuals, given that policy decisions are informed by multiple domains and not just cost effectiveness.
    - As with any modelling exercise, the applicability of the findings is dependent on the underlying assumptions that underpin the model

structure and the chosen parameter values. Evidence included in this HTA relating to the burden of disease and effectiveness and safety of COVID-19 vaccination were collected at a specific point in time and the conclusions could change over time as the evidence base evolves.

  - This is particularly important given that the sensitivity and scenario analyses conducted as part of this assessment demonstrated that the economic evaluation is highly sensitive to both the assumed price of the vaccine and the incidence of COVID-19 going forward.

- Given the continuing uncertainty regarding future disease patterns, variant emergence and long-term health impacts, it will be important to continue the use of national and international surveillance data as well as NIAC recommendations to inform national COVID-19 vaccination policy.
- Any change to the national COVID-19 vaccination programme needs to be appropriately communicated to the public and healthcare providers. This would include:
  - timely information for those no longer eligible to funded vaccination who may have concerns about their risk of infection and severe disease
  - targeted outreach in relation to the population groups who remain eligible to optimise uptake and avoid wastage. This information should support an understanding of their ongoing risk of severe disease due to COVID-19 and the potential for this to be mitigated by remaining up-to-date with their vaccine recommendations.

A HTA is intended to support evidence-based decision-making as to the most efficient use of resources in the healthcare system. The aim of this HTA was to support the work of the Department of Health and provide advice to the Minister for Health and HSE to inform COVID-19 vaccination policy in Ireland. Specifically, and in the context of the updated COVID-19 vaccination recommendations published by the National Immunisation Advisory Committee (NIAC) the aim of this HTA was to provide advice in relation to the groups for whom COVID-19 vaccination is funded by the HSE for the 2027-2028 vaccination campaign onwards. A protocol for the HTA was published and an Expert Advisory Group comprising a broad range of key stakeholders established to support the assessment.

COVID-19, which is caused by SARS-CoV-2, is an infectious disease. Symptom severity of acute COVID-19 can range from asymptomatic to life threatening. Older adults, people with underlying health conditions and those living with immunocompromise are at higher risk of severe illness compared to the general

population. The HSE's COVID-19 vaccination programme, which first started at the end of 2020, provides access to COVID-19 vaccination, which is free at the point of care. Over time, there have been changes with respect to the groups for whom vaccination is recommended, the vaccine that is offered and the specific dosing intervals. The preferentially recommended vaccine is an antigenically updated mRNA vaccine which is available year-round; however, currently campaigns are run twice yearly, in the autumn/winter and again in the spring to promote and support uptake in those for whom vaccination is recommended.

6.1 Interpretation of the findings of this HTA

A HTA is founded on the synthesis of available evidence to address a specific policy question. The interpretation of that evidence is heavily influenced by the quality and quantity of information available, and the extent to which it is directly relevant and applicable to the policy question.

6.1.1 Description of technology

Since 2022, antigenically updated vaccines have been developed (and are regularly updated) based on advice by the World Health Organization (WHO) regarding appropriate COVID-19 vaccine antigen composition.[39] Antigenically updated COVID-19 vaccines currently authorised by the European Medicines Agency (EMA) include mRNA vaccines and protein subunit vaccines, with LP.8.1 variant-adapted vaccines preferentially recommended for the 2025/2026 vaccination campaign in Ireland.[44] Currently authorised COVID-19 vaccines are available in various forms which include multidose vials, single dose vials and single dose pre-filled syringes. Depending on the form, COVID-19 vaccines are either supplied by the manufacturer frozen to be thawed before use, or they are supplied ready to use at refrigerated temperatures. With ongoing developments in vaccine technology, it is likely that mRNA vaccine product lines will be simplified in time, with an ultimate goal of ready-to-use, refrigeration only, single dose forms that do not require reconstitution — an approach that would be consistent with how most other vaccines are supplied.

As the SARS-CoV-2 pandemic evolves to an endemic phase, there is an increased level of immunity due to past infections and or vaccinations among the Irish population. This, along with evolution of the virus, has resulted in a decline in rates of COVID-19 related morbidity and mortality.[92] As such, National Immunisation Technical Advisory Groups (NITAGs), including NIAC, have updated their recommendations over time. Most recently, this has included updated recommendations in relation to healthy pregnant women and for health and care workers without additional risk factors for severe disease.[8] Specifically, NIAC no longer recommend COVID-19 vaccination for all individuals in these groups, but access should still be made available should they choose to get a COVID-19 vaccine

following discussion with a healthcare professional. To date, availability of COVID-19 vaccines in Ireland has typically been dependent on whether a particular vaccine product has been preferentially recommended by the National Immunisation Advisory Committee (NIAC), and on opting into a joint procurement framework contract negotiated between the manufacturer and the European Commission's Health Emergency Preparedness and Response Authority.[36] With the impending end of this agreement, and as existing vaccine stock expire, there will be requirement for Ireland as well as other European countries to retender for their vaccine supplies. This provides an opportunity to consider a wide range of issues, including cost effectiveness. These are important domains in vaccine policy decisions in many countries, including Ireland. Depending on the remit of the NITAG, this evidence may be considered as part of the NITAG recommendation (such as in the UK and Germany) or subsequent to the NITAG recommendation, such as in Ireland when the policy decision may additionally be informed by a HTA.

6.1.2 Epidemiology and burden of disease

COVID-19 incidence data and hospital utilisation data were sourced from the Health Protection Surveillance Centre (HPSC) and Hospital In-Patient Enquiry (HIPE) system, respectively. Incidence data reflect medically attended notified cases, and as such, to be identified as a case, an individual must present to a healthcare setting, be tested and in the event of confirmed case, the data notified to the HPSC. Notified case rates have declined by 61% since 2023, with decreases seen in all age groups. Although the reported incidence of COVID-19 varies by age group (and consistently increases with increasing age), some of this variation may be due to differences in testing practices, which may be influenced by the age and or clinical presentation of the patient. Testing in primary care is likely limited to that required as part of sentinel surveillance and testing of subgroups at high risk of severe outcomes whereby knowledge of the specific pathogen would support clinical decision making, including for example, the need for antiviral therapy.[27] As such, the true burden of COVID-19 in primary care is likely higher than that reported. However, this risk-based approach to testing is in line with HSE guidance for testing for acute respiratory tract infections, which outlines that testing is not required in asymptomatic individuals (no clinical features of acute respiratory tract infection) or indeed in most people with clinical features, as the condition is generally self-limiting.[363] Moreover, identification of the specific viral agent is typically unnecessary for self-care and reducing transmission risks. Focusing on notified cases, hospitalisations and mortality prioritises the cases that have a definite need for medical care.

HPSC data for the years 2023 to 2025 indicate that the burden of COVID-19 in the total population has declined over time, with almost a 70% reduction in

hospitalisation and mortality rates over this time period. Although a reduction in burden was seen in all age groups, COVID-19 continues to have a disproportionate impact on the oldest adults. For example, despite representing less than 4% of the total population, those aged 80 years and older accounted for 27% of notified cases, 22% of notified ED visits, 36% of notified hospital admissions, 17% of notified intensive care unit (ICU) admissions and 64% of notified deaths over this three-year period.

HIPE data for 2023 and 2024 also highlight the substantial burden associated with COVID-19 on the secondary healthcare system. However, as highlighted in Chapter 3, data for these years are not directly comparable due to changes in how discharges are coded. This said, these data indicate that burden generally increased with age, with a disproportionate burden among the oldest adults. For example, in considering those with a principal diagnosis of COVID-19 in 2024, those aged 80 years and older accounted for 34% of discharges, 51% of the total bed days and had the longest average length of stay (10 days).

Data in this HTA in relation to the presence of comorbidities in those experiencing severe disease due to COVID-19 were limited to those admitted to ICU and for SARI cases. In each of the three years from 2023 to 2025, over 90% of COVID-19 notified ICU admissions were in those with one or more underlying medical conditions, while a similar trend is noted in SARI reports. Older adults are heterogeneous in terms of their health and healthcare requirements. Multimorbidity (the presence of two or more long-term conditions) is common among older adults. In a systematic review of the prevalence of multimorbidity and polypharmacy among adults (aged 18 years and older) and older adults (aged 65 years and older) in clinical and community settings, the prevalence of multimorbidity (when a cut-point of two or more conditions was used) ranged from 11% to 91% across 37 studies with samples of older adults in community (population-based) settings. When considering adults living in the community, the prevalence of multimorbidity (using the same definition) ranged from 28% to 61% across six studies.[364] Data from The Irish Longitudinal Study on Ageing (TILDA), reported that the population-weighted prevalence of multimorbidity in a representative sample of over 6,000 adults aged 50 years or older was 73%.[365] In a separate analysis of data from the Intellectual Disability Supplement to TILDA (IDS-TILDA), 84% of this population sample are living with two or more long term conditions.[366] Multimorbidity places individuals at higher risk for several conditions including increased vulnerability to COVID-19.[367, 368] Therefore, while the highest overall burden associated with COVID-19 has consistently been seen in those aged 80 years and older, it is possible that individuals in younger age groups have a risk of severe disease at least as high as that of the oldest old. This is particularly true of those living with immunocompromise as documented in the international literature, however national-

level data on the burden of COVID-19 in this population in Ireland are lacking.[115] Prioritisation of the future expansion of the SARI surveillance programme to additional hospital sites will improve epidemiological analyses of risk factors for severe disease and will also improve the sample size for monitoring vaccine effectiveness.

It has been well documented that, particularly early in the pandemic, those living in long-term care facilities were especially vulnerable to COVID-19 outbreaks and poorer outcomes.[110, 369] This vulnerability has been linked to demographics such as being of older age, health status (for example, living with increased frailty and multiple long-term conditions)[364, 368] and facility-specific characteristics (such as, cohorting of residents and movement of health and social care professionals and visitors).[370, 371] Based on the HPSC data used in this HTA, it was not possible to identify the proportion of notified COVID-19-related morbidity and mortality that occurred in those ordinarily resident in long-term care facilities. However, HIPE data showed that, across both years (2023 and 2024) and all discharge types (that is, discharges with either a principal or additional diagnosis of COVID-10), 6% were admitted from some form of LTCF such as, a nursing home, convalescent home or other long stay accommodation.

It is also worth noting that the observed COVID-19-related morbidity and mortality are in the context of an existing COVID-19 vaccination programme which offers funded COVID-19 vaccination to certain at-risk groups. Moreover, they are in the context of a highly effective vaccination campaign in the early stages of the pandemic, with over 90% uptake of a primary vaccination course in those aged 18 years and older and 97% uptake in those aged 60 years and older. As highlighted in Chapter 3, COVID-19 vaccination uptake data among older adults varies by age group, whereby uptake is almost twice as high in those aged 80 years and older compared with those aged 60 to 79 years. For those in whom vaccination is recommended twice yearly, uptake is substantially lower in the spring compared with the autumn/winter campaigns (for example, 32% vs 62% in the spring 2025 and 2024/2025 autumn/winter campaigns, respectively for those aged 80 years and older). Additionally, when considering just the period since September 2023, there has been a general trend of decreasing uptake in successive vaccination campaigns. This said, higher COVID-19 vaccination uptake rates were reported among Fair Deal residents of LTCFs, where vaccination campaigns are supported by HSE mobile vaccination teams. Uptake was 77%[149] and 76%[150] during the autumn/winter 2024/2025 and spring 2025 campaigns, respectively. This was the only group to meet or exceed the 75% target rate outlined in the National Immunisation Office (NIO) Strategic Plan 2024-2027, with substantially lower uptake documented in successive vaccination campaigns for other risk groups (for example, 18% and 45% in the 2025/2026 and 2024/2025 autumn/winter campaigns, respectively for

immunocompromised individuals).[238] Importantly however, HPSC data highlight that for older persons for whom vaccination status is known, over 85% of notified COVID-19 hospital and ICU admissions in 2025 were in those who had not been vaccinated as recommended within the previous 180 days. Similarly, for those aged 60 to 79 years, over 65% of notified COVID-19 hospital and ICU admissions were in those who had not been vaccinated as recommended within the previous 365 days. This highlights the important potential for vaccination to reduce the burden of severe disease in these cohorts.

The majority of the data identified in the context of this HTA relate to morbidity and mortality associated with acute COVID-19. There is a general lack of national level data, in Ireland and internationally, in relation to the prevalence and burden associated with long COVID (also known as post-COVID-19 condition).[372] Long COVID can have a substantial impact on an individual's quality of life, their ability to work and daily functioning. In turn, this places considerable burden on healthcare systems and economies internationally.[129] Reasons for the lack of data include the lack of consensus on a definition for this condition. While generally defined as symptoms persisting for three months or more after the acute phase of the illness, there are several formal definitions of long COVID used internationally,[129] making it difficult to identify, investigate and compare affected population groups, which in turn presents a challenge to the clinical management of these patients. Additionally, the condition can affect multiple organ systems involving several underlying pathophysiological processes and multiple potential molecular and cellular mechanisms. As such, there is no single biomarker to inform diagnosis and monitoring. Instead, the condition usually presents with clusters of, often overlapping, symptoms which can change over time (likely because of emerging variants and vaccination).[372] Proposed interventions for the management of long COVID are varied (for example, pharmaceutical interventions, physical activity and rehabilitation) with mixed evidence of effectiveness. While clinical guidance exists for the management of patients with long COVID,[193, 373] evidence-based, effective and definitive treatments are still lacking.[374, 375] Following publication of the HSE interim model of care for a national long COVID service, several COVID clinics were established to provide post-acute and long COVID care across Ireland.[163] The model of care suggests that all patients admitted to hospital with COVID-19 should be reviewed post discharge, with early review (four to six weeks post discharge) recommended for those with severe disease or who required ICU admission. Patients may also be referred from primary care. At these clinics, patients undergo a comprehensive assessment and a specific care plan is developed for the patient. In some cases, the patient may be discharged following this assessment, whereas those requiring ongoing specialist service support usually attend the clinic every six months.[137] While there are no centrally collated data for these clinics, four of the

six clinics established across Ireland provided data to inform this HTA. Across these clinics, on average, almost three quarters of those accessing the service were female (based on data from three clinics) and the median age was 47 years (based on data from one clinic), and in another clinic over 50% of patients were aged 40 to 60 years. Data from one clinic showed that, from 2023 to 2025, on average, 83% of those attending these clinics each year were returning patients. While international data suggest that the incidence of long COVID may be lower than earlier in the pandemic, it is recognised that even reduced incidence could still translate into a substantial number of overall cases, if high levels of SARS-CoV-2 transmission persist.

Overall, COVID-19 continues to be associated with severe disease, particularly in those with multiple risk factors, including advanced age. It is challenging to interpret changes in the burden of COVID-19 over time in Ireland given changes in testing practices, how data are coded and changes in vaccination uptake. This said, decreases in morbidity and mortality are in line with international trends and are likely driven by increasing population level-immunity, improved case management and the fact that current circulating variants cause similar or lower levels of disease severity compared with previous variants of concern. In its most recent risk assessment of COVID-19 in February 2026, the WHO assessed the overall risk of event spreading to be high and the potential for risk to human health to be moderate. However, the WHO acknowledges the future possibility that a variant associated with high clinical severity could emerge and once again overwhelm healthcare systems. This highlights the need for continued surveillance and the need for systems and measures to identify and protect those at highest risk of severe disease.[30]

6.1.3 Clinical effectiveness and safety

The assessment of the effectiveness and safety of antigenically updated Omicron-adapted COVID-19 vaccines was based on evidence from a systematic review (referred to as the index review) published in October 2025. Overall, data from the primary studies included 20 observational studies reporting on relevant COVID-19 vaccine effectiveness (VE) outcomes and 19 observational studies reporting on adverse events of special interest (AESIs). Two observational studies, identified through a supplemental search of EU, UK and US databases, reported on COVID-19 VE outcomes for which data were lacking or limited in the index review. The VE evidence predominantly related to mRNA XBB.1.5 vaccines covering periods from late 2023 through 2024. While some studies included protein subunit vaccines, typically only small numbers of participants received these vaccine types. Studies typically did not provide disaggregated data by vaccine type, so it was not possible to assess their relative effectiveness.

In general, Omicron-adapted vaccines were associated with a significant reduction in severe COVID-19 across several of the population groups considered relevant to this HTA, although there was evidence of waning effectiveness over time, particularly in studies that reported interval data over longer term follow-up periods. Estimates of effect varied between studies but were typically higher for outcomes related to severe disease compared to medically attended or symptomatic infections and emergency department or UC visits. While there was evidence of waning effectiveness over time, protection against hospitalisation and mortality was still observed at five to six months post-vaccination, specifically in older adults, those living with immunocompromise, those living with underlying medical conditions, and those aged 18 to 59 years in the general population. No consistent pattern was observed where VE estimates were disaggregated by age and confidence intervals typically overlapped, which has been reported previously.[309] In addition, there was evidence that the effectiveness of XBB.1.5-adapted vaccines against hospitalisation was lower during periods of JN.1 or KP.2 subvariant dominance; similar findings have also been reported previously.[309] While the index review and supplemental studies did not include evidence relating specifically to those living in long-term care facilities or those who are pregnant, previous evidence has demonstrated that COVID-19 vaccination is both safe and effective in these groups.[119, 310, 316] Older adults residing in LTCFs may have increased susceptibility to infection and severe disease outcomes due to a combination of risk factors such as advanced age (with associated immunosenescence), frailty, multimorbidity and close living quarters that can contribute to the spread of infection.[248]

While some estimates of VE may appear to be modest, it is important to view these effects in the context of the considerable burden associated with COVID-19, particularly among older adults, as described in Chapter 3. These findings build on and are broadly consistent with previous reviews of the effectiveness of COVID-19 vaccines (including pre-Omicron strains).[312] Furthermore, the effectiveness estimates for COVID-19 vaccines, as reported in this chapter, are similar to those demonstrated for influenza vaccines.[57, 308] Given evidence of waning protection over time, challenges remain in predicting the optimal timing of vaccination to ensure year round protection given that COVID-19 continues to lack seasonality.

One study reported on the effectiveness of Omicron-adapted vaccines against long COVID with a difference in protection by age group; there was no evidence of protection reported for those aged 60 years and older, but a VE of 49% was reported for those aged 18 to 59 years. Previous reviews have reported evidence of a protective effect of vaccination against long COVID,[197, 315] noting challenges due to the significant variation in the definition of long COVID across studies, with the acknowledgement that broader definitions or self-assessments may overestimate or misdiagnose the presence of the condition.[315]

As with many immunisations, COVID-19 vaccines have local and systemic side effects that are typically mild-to-moderate and self-limiting, resolving a few days after vaccination.[319] Post-marketing safety surveillance of authorised COVID-19 vaccines has found the frequency of AESI such as myocarditis and pericarditis to be very rare, occurring in fewer than 1 in 10,000 vaccinations, and it should be noted that SARS-CoV-2 infection is itself a risk factor for myocarditis and pericarditis. Overall, in considering the findings of this assessment and existing evidence from the wider literature, the safety profile of COVID-19 vaccines is largely favourable. While the safety findings from this assessment typically related to original vaccine compositions, health authorities internationally continue to rigorously monitor the safety of COVID-19 vaccines, and for the currently authorised COVID-19 vaccines the EMA has consistently found that the safety profile of antigenically updated strains is considered similar to that of the ancestral strain COVID-19 vaccines.[7, 53, 55, 56]

6.1.4 Economic evaluation

As described in Chapter 5, an economic model for a COVID-19 vaccination programme for the general population aged 60 years and above assessed the cost effectiveness and budget impact of the following two vaccination strategies:

- Strategy 1 (S1) – a vaccine offered twice each year for those aged 80 years and above
- Strategy 2 (S2) – a vaccine offered twice each year for those aged 80 years and above (as per S1) plus once each year for those aged 60 to 79 years.

As highlighted, due to insufficient Irish epidemiological data, it was not feasible to undertake cost effectiveness analysis for the other groups for whom NIAC has recommended vaccination (that is, those living in long-term care facilities, those with immunocompromise associated with a suboptimal response to vaccination, or those with medical conditions associated with a higher risk of severe disease) or for those groups for whom NIAC has recommended that access to a COVID-19 vaccine should be made available. Additionally, the budget impact model for these specific populations could only consider the costs incurred over a five-year period; costs averted were not estimated due to a lack of relevant data for Ireland.

Results from the epidemiological analysis, using 2025 notified COVID-19 case data, indicate that in a single year, vaccination is associated with a decrease in notified COVID-19 cases. S1 (twice yearly vaccination of those aged 80 years and older) demonstrated the largest reduction in notified case numbers across all COVID-19 outcomes compared with no vaccination. Reductions ranged from 11% for notified cases of COVID-19 to 33% for notified deaths with COVID-19. The reductions for S2 (twice yearly vaccination of those aged 80 years and older and once yearly vaccination of those aged 60 to 79 years), compared with no vaccination, ranged

from 8% for notified cases of COVID-19 to 29% for notified deaths with COVID-19. It is important to note that the reductions reflect both vaccine effectiveness and vaccine uptake, with the latter informed by the uptake rates reported by the HPSC. As highlighted in Section 6.1.2 above, with the exception of uptake for those living in LTCFs for older adults, uptake in all other subgroups has been substantially lower than the 75% target uptake rate identified by the NIO, with particularly low uptake rates in the spring campaigns.

From the payer perspective, at a vaccine cost of €75 per dose (excluding VAT) and assuming 2025 incidence of notified COVID-19, the incremental cost-effectiveness ratio (ICER) for S1 compared with no vaccination was €56,500 per quality-adjusted life year (QALY) and the ICER for S2 compared with S1 was €202,000 per QALY. Both ICERs exceeded a willingness-to-pay (WTP) threshold of €45,000 per QALY gained. In a scenario analysis assessing a strategy of vaccination from aged 75 years, the ICER was €80,000 per QALY when compared with S1. Based on the assumptions in the model, the vaccine cost would need to be less than €60 (ex VAT) per dose for S1 to be cost effective compared with no vaccination at a WTP of €45,000 per QALY. In a scenario analysis, where incidence of notified COVID-19 was varied, the ICER for S1 compared with no vaccination fell to €15,000 per QALY (using 2024 incidence data) and when using 2023 incidence data, S1 was cost saving (less costly and more effective) compared with no vaccination.

The five-year incremental budget impact versus no vaccination was €111.5 million for S1 and €307.0 million for S2. The majority of costs incurred for both vaccination strategies over the five-year time horizon related to vaccine procurement (approximately 71% to 75%). Total cost offsets (largely relating to hospitalisation and long-term care post COVID-19) as a percentage of total costs incurred, were 28% and 15% for S1 and S2, respectively.

The five-year budget impact versus no vaccination for other populations for whom NIAC has recommended vaccination or for whom access to vaccination is recommended ranged from €6.8 million for S7 (a vaccine offered once each year for pregnant adolescents and adults) to €63.8 million for S8 (a vaccine offered once each year for all others aged 18 to 59 years not included in other specific population groups).

As noted in Chapter 5, the economic evaluation is limited by the underlying assumptions, availability of data and chosen parameter values. Two key parameters influencing the cost effectiveness of a COVID-19 vaccination programme are the cost of the vaccine and incidence of the disease. Incidence data (that is, notified case data in this instance) may be influenced by testing practices. Should testing practices change, for example in response to reports of a newly circulating severe

variant, the reported incidence of COVID-19 may increase and or there may be differences in the proportion of notified cases that experience severe disease. These factors would impact the cost effectiveness of COVID-19 vaccination, as in general, as the burden of disease increases, cost effectiveness improves (lower ICERs).

While this analysis demonstrates that vaccination against COVID-19 is associated with reductions in outcomes associated with COVID-19, the strategies assessed in the base-case economic analysis would be considered not cost effective at a WTP threshold of €45,000 per QALY. However, the vaccine price and incidence of COVID-19 are highly uncertain parameters. A 20% reduction in the modelled price of the vaccine (from a base-case price of €75 to €60 ex VAT) would be required for S1 to be considered cost effective compared with no vaccination at a WTP threshold of €45,000 per QALY. If incidence of notified cases of COVID-19 was to return to 2024 levels, S1 would be cost effective, while if it returned to 2023 levels, S1 would be cost saving.

6.1.5 Organisational considerations

The organisational considerations that are relevant to this HTA are discussed below in the context of general considerations for the programme and in the context of a decision being made to restrict the cohorts for which COVID-19 vaccination is funded (compared to that funded during the 2025/2026 COVID-19 vaccination campaign).

Resources

Vaccine storage and handling

COVID-19 vaccines currently in use

COVID-19 vaccines must be transported, stored and maintained within appropriate temperatures and protection from light from the time of manufacture to administration.[9] The HSE's National Cold Chain Service (NCCS) is responsible for the storage and delivery of vaccines included in the Immunisation Schedule and funded by the Department of Health. These vaccines are delivered directly to general practitioner (GP) surgeries, local HSE offices and community pharmacies following online orders from them, with validated temperature records up to the point of delivery. The NIO is responsible for managing vaccine procurement and distribution, developing training and communication materials for health professionals and the general public.[376]

Comirnaty® LP.8.1 (that is, the mRNA COVID-19 vaccine currently used for all eligible age groups in Ireland) is delivered from the manufacturer to the NCCS at a temperature between -90 to -60°C and this storage temperature is maintained upon receipt.[377] This necessitates the use of specialised, ultra-low temperature freezers

and storage in centralised locations as most primary care sites and or clinics only have pharmaceutical fridges for cold medication storage. The receipt of frozen vaccines adds organisational complexity as it necessitates strict protocols around inventory management such as thawing frozen vials and relabelling them with a new "use by" date prior to transportation to administration sites at refrigerated temperatures. For example, thawed Comirnaty® vials have a shelf life of up to 10 weeks at 2 to 8°C (and up to 12 hours at 8 to 30°C). This shorter shelf life necessitates more frequent deliveries of a smaller number of vaccines to each administration site to ensure they are used before expiry. Additionally, the new "use by" date must be manually recorded in the patient's record post-vaccination as the batch number of the vaccine will automatically link to the original expiry date of the frozen product.

Particular organisational issues arise when considering multidose vial presentations. This presentation format facilitated mass vaccination during the initial stages of the pandemic and continues to provide efficiencies when vaccination is offered in dedicated vaccination centres or in congregated settings such as LTCFs where large numbers of individuals may be vaccinated on a given day. However, there is greater potential for wastage when considering other settings such as GP practices and community pharmacies. For example, a Comirnaty® multidose vial contains six doses and it is packaged in a box of ten multidose vials.[7] As such, the smallest number of doses that can be delivered to a primary care vaccination site is 60 doses. If initially frozen, all 60 doses will need to be used within 10 weeks. Moreover, after first puncture each vial must be used within 12 hours (when stored at 8 to 30 °C).[7] This may lead to wastage if fewer than six patients are scheduled to attend and or present for vaccination within this 12-hour window. The NIO have advised the HIQA Evaluation Team that this type of wastage has been more pronounced during spring vaccination campaigns when compared to autumn/winter campaigns given that twice yearly vaccination is only recommended for certain subgroups and given lower uptake during the spring campaigns. Providers are advised to cluster appointments to minimise this wastage, but it is acknowledged that this may be more difficult in rural areas or when demand is low. If the cohort for which COVID-19 vaccination is funded is restricted, for example, to only include those aged 80 years and older, cohorting of patients for vaccination would be even more critical to minimise vaccine wastage, especially if multidose products continue to be used. Even with cohorting, wastage could still occur if a minimum number of doses must be dispatched when considering specifically products (single or multidose) that were supplied frozen and which have a much shorter shelf-life once thawed. Aside from potential wastage, other drawbacks associated with multidose vials include the procurement of extra consumables such as syringes and needles,[377] risk of contamination if incorrect

aseptic technique is used when withdrawing doses,[378, 379] and risk of extracting and administering an incorrect dose.[380]

Implications of changing to alternative COVID-19 vaccine formulations

Both mRNA (mNexspike®, Comirnaty® and Spikevax®) and protein subunit (Nuvaxovid® and Bimervax®) COVID-19 vaccines are authorised as single dose pre-filled syringes, which are packaged in a single unit pack size.[7, 51, 53, 56] These single dose formulations (packaged in a single unit pack size) not only reduce the wastage associated with multidose vials, but also require fewer consumables. Additionally, as there are fewer steps in the preparation and administration of such formulations, this would reduce the potential for dosing errors and may reduce vaccination clinic workloads. Comirnaty® is also authorised as a harmonised paediatric formulation for all individuals aged 6 months to 11 years in a single dose vial (supplied frozen). Communication from the manufacturer indicated that this presentation is expected to become available from September 2026 onwards. It will require extra preparation steps and consumables when compared to a pre-filled syringe.

As outlined above, the mRNA COVID-19 vaccine that is currently available for use in Ireland is procured frozen, requiring a host of storage and handling considerations. Use of refrigerated-only formulations would streamline storage, distribution and handling as these formulations would not need to be thawed and relabelled prior to distribution to vaccination sites. Currently, Comirnaty® is the only authorised mRNA vaccine with refrigerated-only formulations, though it is noted that the shelf life is lower (12 months versus 18 months) compared to that of frozen Comirnaty® vials when they are stored at ultra-low temperatures.[7] Communication from the manufacturer during the public consultation indicated that supply of Comirnaty® 30mcg/0.3mL will transition to a refrigerated single-dose glass pre-filled syringe presentation from 2027 onwards. While antigenically adapted mRNA COVID-19 vaccines are preferentially provided through the HSE COVID-19 vaccination programme, in line with NIAC recommendations, it is noted that the authorised protein subunit COVID-19 vaccines (Nuvaxovid® and Bimervax®) (are also available as refrigerate only products (pre-filled syringes and single dose vials).

As highlighted in Chapter 6, there is substantial uncertainty in relation to the cost of COVID-19 vaccines as current availability in Ireland is limited to those vaccines recommended by NIAC and procured by the NIO. It is therefore unclear if there would likely be differences in the price per dose for vaccines procured as single dose versus multidose formulations and or for those supplied by the manufacturer frozen versus those supplied as refrigeration only. In comparing submitted prices as part of any competitive tender, it would be important to factor in potential differences in

storage and handling costs, wastage and staff time between the differing vaccine formats.

Use of a combination vaccine such as mCombriax® (indicated for protection against influenza and COVID-19 in adults aged 50 years and older)[49] would provide protection against two respiratory viruses via one injection, reducing the time required for administration, which may facilitate an increase in vaccination uptake.[381] It may also reduce administration errors associated with the administration of multiple vaccines. While the combined vaccine could be used during the influenza season (that is, the autumn/winter campaign), a separate COVID-19 only vaccine would still be required for the spring campaign in those for whom twice yearly COVID-19 vaccination is recommended. Therefore, providers may still have to procure multiple different vaccine types to cover all age groups and to allow for separate administration in those not eligible to receive both influenza and COVID-19 vaccinations, or in those with a preference not to receive their influenza and COVID-19 vaccine on the same day. Robust measures would continue to be required to mitigate against potential administration errors.

As highlighted in Section 6.1.3 above and in Chapter 4, the majority of the included evidence in this HTA relates to Omicron-adapted mRNA COVID-19 vaccines. It was not possible to determine if effectiveness differs by vaccine type.

Vaccine availability

While global COVID-19 vaccine production capacity expanded rapidly during the emergency phase of the pandemic, as with all vaccines, there is the potential for COVID-19 vaccine shortages, should international demand exceed available manufacturing capacity in the context of, for example, new or emerging public health threats. As such, there is an ongoing requirement to have clear criteria to identify those within the funded cohort for whom vaccination should be prioritised should vaccine shortages arise. If Ireland participates in a new joint procurement framework contract for COVID-19 vaccines, there may be operational efficiencies if it is with a company that has multiple authorised COVID-19 vaccine formulations available (that is, those indicated for use in those aged less than 12 years and in those aged 12 years and older).

While limiting a funded programme to one vaccine product can provide cost and operational efficiencies, it has been argued that a programme comprising varied vaccine products (for example, based on different vaccine platforms such as mRNA and protein-based vaccines) would be more resilient and would provide an alternative for individuals for whom a particular vaccine product is considered clinically unsuitable.[79] NIAC currently has a preferential recommendation for antigenically updated mRNA COVID-19 vaccines because of their extensive safety

data and effectiveness against COVID-19; a protein subunit COVID-19 vaccine can be used as an alterative in those for whom an mRNA COVID-19 vaccine is unsuitable, with Nuvaxovid® (antigenically updated) the preferred alternative.[8] To date, the HSE COVID-19 vaccination programme has procured a small number of Nuvaxovid® doses; however, it is not routinely available through GP clinics and pharmacies, and instead is accessible through HSE vaccine clinics by appointment.[382] These additional steps can represent a logistical barrier for some patients. Although a programme comprising a range of vaccine products may increase choice and potentially improve resilience, these benefits would need to be considered in the context of the cost difference (if any) between products and the additional logistical burden associated with making a range of products available.

Vaccine procurement arrangements aim to closely match the purchased amount with the projected uptake for the target population, so to minimise waste. If Ireland enters a new joint procurement agreement for COVID-19 vaccines, it may be important to have flexibility within the contract to scale up the quantity procured should a new variant of concern emerge, particularly if there is a decision to restrict the groups for whom vaccination is available in the first instance.

Staff related resources

As outlined in Table 3.14 (Chapter 3), during recent vaccination campaigns, most COVID-19 vaccines were administered by GPs (on average 55%), followed by community pharmacists and HSE vaccination teams (on average 30% and 15%, respectively). If funding of COVID-19 vaccines is restricted, for example to those aged 80 years and older, there may be opportunities to reduce the workload across all administration settings, the NIO and the HSE's NCCS. The procurement of refrigerated-only, single dose preparations may further reduce the workload for NIO and NCCS staff (with respect to storage and distribution of the vaccines) and healthcare staff (with respect to the preparation and administration of the vaccines), as outlined in above. As described in Chapter 3, identification of those at increased risk of severe COVID-19 based on the presence of underlying medical conditions and or immunocompromise is challenging due to incomplete data. Restricting access to a free COVID-19 vaccine based on age alleviates some of the burden placed on healthcare staff regarding identification of those eligible for vaccination. However, staff may also be required to spend considerable time with patients (who were previously eligible for vaccination) alleviating their concerns regarding their ineligibility for vaccination during the upcoming campaign.

As outlined above, the results from the epidemiological analysis using 2025 notified case data indicate that in a single year, vaccination is associated with a decrease (11% for S1 and 8% for S2) in notified COVID-19 cases. If funded COVID-19

vaccination is only offered to those aged 80 years and older, this may result in an increased incidence of symptomatic or medically attended COVID-19 amongst ineligible population groups. This may impact family members and or carers, and may also increase the burden within primary and secondary healthcare, reducing their capacity to provide care in other areas. It may also result in an increased burden of incidence of symptomatic or medically attended COVID-19 amongst healthcare workers themselves, further augmenting the burden observed in the health service if staff are unable to work due to illness. Moreover, vaccination appointments often present an opportunistic point of contact for healthcare providers to check in on a patient's health status more generally. Reducing the eligible cohort would reduce the potential for this opportunistic interaction.

Overall, a large evidence base demonstrates that COVID-19 vaccines have a favourable safety profile. The most commonly reported adverse events following COVID-19 vaccination are injection site pain, fatigue, headache and myalgia. These local and systemic reactions are generally mild to moderate in severity, self-limiting and transient in their presentation, resolving typically within one to three days. While it is not anticipated that these adverse events will result in additional primary care visits, it cannot be ruled out that some patients may present to the GP or pharmacy for assessment. It should also be borne in mind that where the COVID-19 vaccine is administered alongside other vaccines, it may be challenging to determine with which vaccine the adverse events are associated.

Information and awareness

All information materials for the general public are developed and distributed by the NIO who also manage the national immunisation website. An information campaign for the public is an important component of any change to the national immunisation schedule, to educate individuals regarding the changes that are being made, allay any concerns regarding the safety or effectiveness of the vaccine and enable informed consent. In the context of changes to the HSE COVID-19 Vaccination Programme, this should include information about the evolving epidemiological situation (that is, observed virus mutation and increased levels of immunity in the population due to past infection and or vaccination), as well as the observed reduced severity of COVID-19 across many population groups. It would also be pertinent to include information on the continued risk of severe disease (namely, hospital admission, ICU admission and death) observed in those at highest risk (most notably those of advanced age) and the benefits associated with vaccination. This information should be made available in a manner that is accessible to both eligible and ineligible population groups.

To support such a public awareness communication campaign, consideration would also need to be given to an educational programme for GPs, pharmacists and frontline nursing staff given their important role both in vaccine administration and as a trusted information source for vaccines given as part of the immunisation programme. Healthcare workers may need to dedicate additional time to explaining the rationale behind any change in the funding of and access to COVID-19 vaccinations to patients who may be concerned or confused about the changes. In the UK, following changes to funded COVID-19 vaccinations in 2025, community pharmacy teams spent considerable time explaining the changes to COVID-19 vaccination eligibility.[383] Many patients (who were eligible during the previous winter) had booked their vaccination appointment through the national booking system, but were not actually eligible for funded vaccination that year. In January 2026, a National Pharmacy Association survey of 450 pharmacies in England found that at least 50% of COVID-19 vaccination appointments during winter 2025/2026 were made by ineligible patients.[384] This highlights the need for a targeted public awareness campaign regarding any changes to the population groups eligible for COVID-19 vaccination. Should there be an option to access COVID-19 vaccines privately, it may be helpful for this information to be made available, should those no longer eligible for the funded programme wish to avail of this option. Targeted outreach would also be necessary for population groups who remain eligible to optimise uptake and protection and avoid wastage.

Anticipated vaccine uptake

Ireland has developed an integrated approach to COVID-19 surveillance that is consistent with advice from the WHO.[385] Vaccine uptake reporting for COVID-19 has been expanded in recent years to align with updated NIAC recommendations and key performance indicators.[386] Any changes to COVID-19 vaccination policy would necessitate updates to existing COVID-19 surveillance systems (of both incidence and vaccine uptake) to enable programme monitoring and evaluation.

As highlighted above and in Chapter 3, COVID-19 vaccination uptake data among older adults varies by age group, whereby uptake is almost twice as high in those aged 80 years and older compared with those aged 60 to 79 years, with a substantially lower uptake reported in the spring compared with the autumn/winter campaigns. Additionally, there has been a general trend of decreasing uptake in successive vaccination campaigns since September 2023. This trend of declining uptake may indicate a growing complacency or lack of awareness of the ongoing burden associated with COVID-19 in specific subgroups of the population. This downward trend has been observed for other vaccine-preventable diseases (such as, influenza), where existing challenges were exacerbated by the COVID-19 pandemic and misinformation surrounding vaccine safety profiles.[386, 387] As noted in Section

6.1.2 above, despite NIAC recommendations and access to the HSE COVID-19 vaccination programme, a high proportion of notified COVID-19-related hospital admissions among older adults are in those who are considered unvaccinated at the time of their infection. These data highlight the ongoing burden associated with COVID-19 in these age groups and underscore the importance of communicating the potential to mitigate this risk by availing of vaccination at the recommended intervals.

Key objectives of the National Health Protection Strategy for Immunisation are to monitor vaccine uptake, work with providers to boost collective vaccine uptake and target low-uptake groups with tailored programmes.[238] One of the key determinants of vaccination uptake is one's awareness of their eligibility for vaccination,[388] underscoring the importance of communicating any changes to COVID-19 vaccination policy to the public. While the risk of severe disease may vary within an age group, there is evidence that universal age-based recommendations achieve consistently higher vaccination coverage than more selective programmes based on identifying people in a clinical at-risk group. Moreover, age-based recommendations have advantages both in terms of delivery and ease of communication to the public.

If the funded programme is restricted to specific subgroups (for example, those aged 80 years and older) on the basis of cost effectiveness, it would still be important to consider the order in which other groups should be prioritised for vaccination, in the event that uptake in the target group is lower than anticipated, so to minimise any vaccine wastage. It would also be important to consider how such changes might be effectively communicated to these groups.

Timing of vaccination campaigns

As highlighted in Chapter 3, to date COVID-19 has lacked seasonality, with evidence of multiple peaks in activity throughout the year. Some of these peaks coincide with the influenza and RSV seasons (autumn/winter), further increasing pressure on healthcare providers. In recent years, twice yearly COVID-19 vaccination campaigns were run by the HSE with respect to the funded vaccination programme. Aligning the autumn/winter programme with the seasonal influenza vaccination campaign, aimed to improve uptake rates and provide efficiencies for patients and providers where individuals were eligible to receive both vaccines. A second campaign is run approximately six months later in the spring for those for whom twice yearly vaccination is recommended. However, it is noted that COVID-19 vaccines have also been available outside of defined seasonal campaigns where clinically indicated, including but not limited to pregnancy or anyone commencing a new period of immunosuppression or anyone who is previously unvaccinated and for whom a

COVID-19 vaccine is recommended as per the NIAC guidelines. While the aim is to provide year-round protection for those at high risk of severe disease, it is acknowledged that protection may be inadequate at times given evidence of waning protection, particularly as the time since vaccination increases and with the potential for peaks in circulation at any time of the year. This highlights the need for ongoing surveillance, and the potential requirement for more frequent information campaigns to promote vaccination uptake in eligible cohorts when national and international data suggest periods of higher circulation. Moreover, it highlights the continued importance of making COVID-19 vaccines available outside of defined seasonal campaigns, and potentially expanding this access to anyone whose vaccination status is not considered to be current (within preceding 180 or 365 days, as appropriate).

6.1.6 Ethical, patient and social considerations

Benefits and harms

The purpose of vaccination is to prevent or reduce the spread and severity of infectious disease. For many immunisation programmes, all or almost all of the target population are offered vaccination in the knowledge that perhaps only a small proportion will benefit. The benefit-harm balance must be considered at both the individual and population level. The decision to be vaccinated is made by individuals, typically from the perspective of what the perceived benefit-harm balance is for them personally. The decision-maker, on the other hand, must consider the benefit-harm balance at the population level. In this section, the benefit-harm balance is considered from an ethical perspective.

Benefits and harms at the individual level

The personal benefit to individuals at high risk of severe disease is the protective effect the vaccine offers, although this declines over time. Vaccination of these individuals also means they will be less likely to infect others and therefore it confers a benefit to those who may not be vaccinated. However, the benefit of vaccination to individuals at lower risk of severe disease raises the issue of whether it is ethical to vaccinate them in order to benefit others. Although the potential negative side effects of vaccination are relatively small, this issue is still of moral significance. The ethical principle of respect for persons means that people should not be used solely as a means to an end and that even small burdens and inconveniences should be avoided or minimised wherever possible. A policy based on respect for persons also contributes to public trust and willingness to participate in public health programmes generally, which is clearly in the public interest.

Mild local and systemic reactions to COVID-19 vaccinations are relatively common, but as noted are generally self-limiting and transient in their presentation. Post-marketing surveillance is important to understand the benefits and risks of COVID-19 vaccines. As outlined in Chapter 4 and in section 6.1.3, to date, pharmacovigilance reports for antigenically updated COVID-19 vaccines have not revealed any new safety concerns compared with those based on ancestral strains. When considering specific AESIs, such as Guillain-Barré syndrome and stroke, there was evidence of either no association or an inverse association (that is, reduced risk) between COVID-19 vaccination and these events. There is evidence of an increased risk of myocarditis and pericarditis following COVID-19 vaccination; however, these events are noted to be rare with an occurrence of fewer than 1 in 10,000 vaccinations (and occurring more commonly after a second dose and in younger males). While the evidence supports the safety of COVID-19 vaccines, potential harms need to be considered in terms of the individual's risk of severe disease and as such their potential to benefit from vaccine-related protection against SARS-CoV-2 infection and severe COVID-19.

Restricting the groups for whom COVID-19 vaccination is funded may deny patients the opportunity to make a decision for themselves based on their judgement of their individual potential for benefits and harms.[389] Moreover, it may result in an increased incidence of symptomatic or medically attended COVID-19 in ineligible population groups. Additionally, those previously eligible may have concerns about their perceived risk of infection and resultant illness (both acute COVID-19 illness and post-acute COVID-19 condition, that is, long COVID).

Benefits and harms at the population level

Community immunity occurs when circulation of a pathogen is significantly curtailed within a community because most of the people it encounters are immune.[390] This immunity may result from prior infection and or vaccination. The more people within a community are vaccinated, the more those who are not vaccinated are indirectly protected because the high immunisation rate reduces the likelihood of virus transmission. Therefore, the benefit provided by community immunity is the extra-protection provided towards non-immune people who are at high risk of severe disease. The infectiousness of the pathogen and the effectiveness of the vaccine determines the threshold for community immunity for any disease.[390, 391]

An understanding of how COVID-19 vaccination affects transmission of the virus at a population level should be taken into account when considering any funding policy changes. If COVID-19 vaccination reduced onward transmission of the virus, a population-level benefit of COVID-19 vaccination would be realised and restricting access to the vaccine would preclude this. However, in the context of emerging new

COVID-19 variants, there is a lack of evidence that COVID-19 vaccination significantly reduces the risk of transmitting SARS-CoV-2 to others.[392] As reported in Chapter 4, while transmission is reportedly lower when primary cases are vaccinated within 7 to 12 months, and more than 12 months, of infection, these findings were not statistically significant, suggesting that protection wanes over time (a finding that has been widely reported in the international literature).[57] Though, in a recent cohort study of 362 participants who tested positive for COVID-19 (and 760 of their household contacts), individuals vaccinated against COVID-19 within six months of illness onset were significantly less likely to transmit SARS-CoV-2 to their household contacts compared with those who were unvaccinated (VE 43% (95% confidence interval (CI): 7% to 65%)).[393]

Restricting the groups for which COVID-19 vaccination is funded (based solely on age) may result in an increase in severe acute COVID-19 illness, particularly in populations known to be at increased risk of severe disease (such as, those living in LTCFs and those living with immunocompromise) and those at increased risk of exposure (such as, health and care workers). International data highlight that these individuals are at increased risk of infection and that COVID-19 vaccination is both safe and effective in this population group. However, as Irish incidence data are lacking for these groups, this precluded evaluation of the cost effectiveness of COVID-19 vaccination in these groups. As policy decisions are informed by multiple domains and not just cost effectiveness, this does not preclude a decision to continue to provide COVID-19 vaccination for other subgroups at high risk of severe disease. Moreover, projections of national demand and bed capacity requirements for public acute hospitals in Ireland show that the number of inpatient beds in public acute hospitals in Ireland will need to increase by at least 40% by 2040.[394] While data included in this HTA show a decline in the overall burden of COVID-19 over time, there is still a disproportionate burden in older adults, particularly those aged 75 years and older (specifically, notified COVID-19-related hospitalisations and deaths). A decision to change the groups eligible for COVID-19 vaccination should still be considered in the context of the overall resilience of a healthcare system that exhibits high bed occupancy rates. While COVID-19 lacks seasonality, the potential for vaccination to support reductions in winter overcrowding could strengthen resilience in the health service considering the existing strain on services arising from a demand-capacity gap.

Reduced eligibility for funded COVID-19 vaccines may lead to an increased level of long-term disability among non-eligible groups who go on to experience long COVID following acute COVID-19 illness (if such illness could have been prevented by vaccination), which may further augment societal harms due to reduced participation in the labour market.[224]

Justice and equity

If funded COVID-19 vaccination is no longer provided to those previously eligible, this could be perceived as curtailment of an individual's autonomy. While ordinarily, there may be potential to pay for a vaccine privately if access is not funded as part of a national programme, COVID-19 vaccines are not currently (as of August 2026) available for private purchase in Ireland. For authorised vaccines, such availability is at the discretion of the individual manufacturer. Therefore, should this situation prevail, those who believe that they would benefit from COVID-19 vaccination (but who are no longer eligible) will not be able to make their own decision regarding receipt of it.

Restricting access may be regarded by some members of the public as a step taken for economic reasons rather than arising from a consideration of the risks and benefits of only vaccinating those at highest risk. Therefore, if proceeding with a restricted cohort, it is important to communicate this message clearly so as to reassure the public about the rationale and international scientific basis for this decision in order to maintain public trust in the vaccination programme. Restricting the groups for which COVID-19 vaccination is funded (based solely on age) may also overlook the increased risk of severe disease known to be present for other population groups, such as those living with underlying medical conditions and those living with immunocompromise.[115-118] Due to insufficient Irish epidemiological data, it was not feasible to undertake a cost-utility analysis for other subgroups groups prioritised for vaccination in the NIAC recommendations. As highlighted above, the lack of data and economic analyses should not preclude a policy decision that continues to provide COVID-19 vaccination for these population groups.

The targeting of specific population groups for vaccination may be seen as potentially discriminatory. Discrimination is regarding or treating others differently on the basis of a particular characteristic such as age, gender or ethnicity. There is however a difference between positive and negative discrimination – positive discrimination is giving more favourable treatment to those who have a particular characteristic, while negative discrimination is giving less favourable treatment. Not all discrimination is morally or ethically wrong. In the context of health policy, selection of particular groups for public health interventions is justified on the basis of risk assessment and effective curtailment of the spread of disease. Prioritisation of the use of resources, such as a vaccine, can also be justified on the same basis by targeting those most likely to benefit. Moving to vaccination of a restricted cohort is therefore justified as a specific protective measure for high-risk groups and avoidance of the burden of vaccination for those for whom it carries less benefit.

Additionally, while continued funding of a COVID-19 vaccination programme for a larger cohort improves equity of access, policy makers have a duty to ensure equitable allocation of resources. Decisions about healthcare distribution should ensure that resources are allocated or reallocated fairly and that the opportunity costs (the value of the next best alternative forgone) of investments are considered. Reconsideration of the groups for whom COVID-19 vaccination is funded is therefore appropriate at this time given the evidence of a decline in the burden of disease, and the potential for some of the current funding to be diverted to other programmes or interventions that could deliver a larger population health gain. Funding interventions that are not cost effective could create issues of justice and equity with respect to a fair distribution of benefits and burdens. This is particularly important in the context of a finite healthcare budget and increasing demands for services provided.

Ethical consequences of HTA

Choice of outcomes

The effectiveness of COVID-19 vaccination was considered in terms of the potential for reductions in notified COVID-19 cases and deaths. From an economic modelling perspective, the impact of alternative vaccination strategies for the current HSE COVID-19 vaccination programme was summarised by translating disease states into changes in quality of life. By summarising illness into a set of discrete health states, there is a risk that an economic model oversimplifies the experience of ill-health. The use of QALYs to capture health benefits does, however, enable the calculation of an ICER that is directly comparable with those estimated in other evaluations and against a reference willingness-to-pay threshold.

Timing of assessment and evidence availability

The evidence identified in Chapter 3 on the burden of disease and Chapter 4 on the effectiveness and safety of COVID-19 vaccination were collected at a specific point in time — the conclusions could change over time as the evidence base increases (for example, if more complete data become available for the populations where a lack of data were identified) and or there is a change in the transmissibility or clinical severity of the circulating variant(s). The effectiveness evidence considered was gathered from an index systematic review (literature published from June 2024 to 31 July 2025) and 21 additional studies that were not included in the index review but that provided data relevant to this HTA. As vaccine technologies and the epidemiological situation continues to evolve, it is likely that evidence on the effectiveness and safety of COVID-19 vaccination will also change. As such, given the continuing uncertainty regarding future disease patterns, variant emergence and long-term health impacts, it will be important to continue the use of national and

international surveillance data as well as NIAC recommendations to inform national COVID-19 vaccination policy.

Data sources and economic assumptions

As with any modelling exercise, both epidemiological and economic, the applicability of the findings is dependent on the underlying assumptions that underpin the model structure and the chosen parameter values (see Chapter 5 and Section 6.1.4). From an ethical perspective, the concern would be that the model structure or the limitations of the available data may result in conclusions that may unfairly disadvantage a particular population group. In this assessment, for example, as highlighted in Section 6.1.4 above, due to insufficient Irish epidemiological data, it was not feasible to undertake a cost-utility analysis for other subgroups for whom NIAC has recommended vaccination, that is, those living in LTCFs, those with immunocompromise associated with a suboptimal response to vaccination, or those with medical conditions associated with a higher risk of severe disease.

In the absence of population level COVID-19 incidence data by age for Ireland, the base-case epidemiological model represents notified COVID-19 cases only and therefore excludes suspected cases of COVID-19 that were not laboratory-confirmed. By limiting the model to notified cases of COVID-19, the full disutility and societal cost of COVID-19 are not captured in the analysis. However, notified cases should represent the majority of cases that require medical care and thereby the impact on both healthcare resources and quality of life associated with COVID-19. In this analysis, parameter uncertainty was explored through sensitivity and scenario analyses which demonstrated that the economic evaluation is highly sensitive to both the assumed price of the vaccine and incidence of COVID-19 going forward.

6.2 Conclusion

The findings of this HTA show that COVID-19 continues to disproportionately affect those of older age, both in terms of morbidity and mortality which results in a substantial burden on healthcare services. This burden is in the context of an existing COVID-19 vaccination programme which offers funded COVID-19 vaccination to certain at-risk groups, albeit acknowledging that current uptake rates are suboptimal. Serious adverse events are rare and while mild local and systemic reactions to COVID-19 vaccinations are relatively common, they are generally self-limiting and transient in their presentation. Overall, the evidence supports the safety and effectiveness of COVID-19 vaccines and any potential harms should be considered in the context of an individual's risk of severe disease and the protection offered against the same.

While the economic evaluation suggests that vaccination against COVID-19 is associated with reductions in outcomes associated with COVID-19, the strategies assessed in the base-case economic analysis would be considered not cost effective at a WTP threshold of €45,000 per QALY. However, the results of the economic evaluation are highly sensitive to the unit cost of the vaccine and incidence of COVID-19 going forward, both of which are key considerations in any decision-making and in procurement negotiations with vaccine manufacturers.

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Appendices

A. Appendix A Description of Technology

Table A.1 Posology, pharmaceutical form, container, shelf life and storage information relating to the antigenically updated mRNA vaccines authorised or recommended for authorisation in the EU

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
Posology	**≥50 years:** One dose of 0.32ml*. (If previously vaccinated with a COVID-19 vaccine, administer at least 3 months after the most recent dose)	**≥12 years:** One dose of 10 mcg/0.2ml. (If previously vaccinated with a COVID-19 vaccine, administer at least 3 months after the most recent dose)	**≥12 years:** ▪ With or without prior vaccination: One dose of 50mcg/0.5ml ▪ Immunocompromised with or without prior vaccination: One dose of 50mcg/0.5ml (additional doses in those who are severely immunocompromised may be given at the discretion of the healthcare provider) **5-11 years**: ▪ With or without prior vaccination: One dose of 25 mcg/0.25ml ▪ Immunocompromised with or without prior vaccination: One dose of 25 mcg/0.25ml (additional doses in those who are severely	**≥12 years:** A single dose of 30mcg/0.3mL (regardless of prior COVID-19 vaccination status) **5-11 years:** A single dose of 10mcg/0.3mL (regardless of prior COVID-19 vaccination status) **6 months - 4 years:** ▪ Without prior vaccination: A primary course of 2 doses of 10mcg/0.3ml ▪ With a completed primary course: A single dose of 10mcg/0.3ml

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
			immunocompromised may be given at the discretion of the healthcare provider) **6 months - 4 years**: ▪ Without prior vaccination and no known history of SARS-CoV-2 infection: Two doses of 25 mcg/0.25ml ▪ With prior vaccination or known history of SARS-CoV-2 infection: One dose of 25 mcg/0.25ml ▪ Immunocompromised and without prior vaccination: Two doses of 25 mcg/0.25ml (a third dose in severely immunocompromised may be given) ▪ Immunocompromised and with prior vaccination: One dose of 25 mcg/0.25ml (additional dose(s) in those who are severely immunocompromised may be given at the discretion of the healthcare provider).	

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
Pharmaceutical form & container	Dispersion for injection: A single dose pre-filled cyclic olefin copolymer syringe 0.32ml* (supplied frozen or thawed).	Dispersion for injection: A single dose pre-filled cyclic olefin copolymer syringe 10mcg/0.2ml (supplied frozen).	Dispersion for injection: ▪ Multidose vial (0.1mg/ml) with a blue cap containing either 5 doses of 50mcg/0.5ml each or 10 doses of 25mcg/0.25ml§ each (supplied frozen). ▪ Single dose 25mcg/0.25ml pre-filled cyclic olefin copolymer syringe (supplied frozen).§ ▪ Single dose 50mcg/0.5ml pre-filled cyclic olefin copolymer syringe (supplied frozen). The 0.5ml pre-filled syringe cannot be used to deliver a partial volume of 0.25ml.§	Dispersion for injection: ▪ A multidose vial with a grey cap containing 6 doses of 30mcg/0.3ml which does not require dilution (supplied frozen or as refrigerated only vials). ▪ A single dose 30mcg/0.3ml pre-filled glass syringe (refrigerated only). ▪ A multidose vial with a blue cap containing 6 doses of 10mcg/0.3ml which does not require dilution (supplied frozen). ▪ A single dose (10mcg/0.3ml) vial with a blue cap (supplied frozen).
Shelf life & storage	Pre-filled syringes ▪ Shelf life is 1 year at -40 °C to -15 °C. ▪ Within the shelf life of 1 year, the vaccine is stable for 30 days when stored at 2 °C to 8 °C and protected from light, after which the vaccine should be used	Pre-filled syringes: ▪ Shelf life is 1 year at -40ºC to -15ºC. ▪ Within the shelf life of 1 year, the vaccine is stable for 30 days when stored at 2°C to 8°C and protected from light, after which the vaccine should be used	Unopened frozen/ thawed multidose vials and pre-filled syringes: ▪ Shelf life (if stored at -50ºC to -15ºC) is 9 months. ▪ Within the period of 9 months, after removal from the freezer, the unopened vaccine vial/ pre-filled syringe may be stored	Unopened frozen single dose and multidose vials: ▪ The vaccine will be received frozen at −90°C to −60°C. ▪ Frozen vaccine can be stored either at −90°C to −60°C or 2°C to 8°C upon receipt. ▪ Shelf life is 18 months when stored at −90°C to −60°C.

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
	immediately or discarded. ▪ Once thawed, the vaccine should not be refrozen. ▪ Upon moving the vaccine to 2 °C to 8 °C storage, the outer carton should be marked with the new expiry date at 2 °C to 8 °C. ▪ Pre-filled syringes may be stored at 8 °C to 25 °C for up to 24 hours after removal from refrigerated conditions. During this time, pre-filled syringes may be handled in ambient light conditions. ▪ Do not refrigerate after being stored at 8 °C to 25 °C. Discard the syringe if not used within this time. **Special precautions for storage**	immediately or discarded. ▪ Once thawed, the vaccine should not be refrozen. ▪ Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new expiry date at 2°C to 8°C. ▪ Pre-filled syringes may be stored at 8°C to 25°C for up to 24 hours after removal from refrigerated conditions. During this time, pre-filled syringes may be handled in ambient light conditions. ▪ Do not refrigerate after being stored at 8°C to 25°C. Discard the syringe if not used within this time **Special precautions for storage**	refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. ▪ Chemical and physical stability has also been demonstrated for unopened vaccine vials/ pre-filled syringes when stored for 12 months at -50°C to -15°C provided that once thawed and stored at 2°C to 8°C, protected from light, the unopened vial will be used up within a maximum of 14 days (instead of 30 days, when stored at -50ºC to -15ºC for 9 months), but not exceeding a total storage time of 12 months. ▪ Upon moving the vaccine to 2°C to 8°C storage, the outer carton should be marked with the new discard date at 2°C to 8°C. ▪ If the vaccine is received at 2°C to 8°C, it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been	▪ Within the 18-month shelf life, the thawed (previously frozen) vials may be stored at 2°C to 8°C for up to 10 weeks. <u>Thawing procedure</u> Single dose vials: ▪ When stored frozen at −90°C to −60°C, 10-vial packs of single dose vials of the vaccine can be thawed at 2°C to 8°C for 2 hours or individual vials can be thawed at room temperature (up to 30°C) for 30 minutes. Multidose vials: ▪ When stored frozen at −90°C to −60°C, 10-vial packs of multidose vials of the vaccine can be thawed at 2°C to 8°C for 6 hours or individual vials can be thawed at room temperature (up to 30°C) for 30 minutes. <u>Thawed (previously frozen) vials</u> ▪ 10 weeks storage and transportation at 2°C to 8°C within the 18-month shelf life.

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
	▪ Store in a freezer at -40 °C to -15 °C. ▪ Once thawed, store in a refrigerator (2 °C to 8 °C) and do not refreeze. ▪ Keep the pre-filled syringe in the outer carton in order to protect from light. ▪ After thawing, pre-filled syringes may be stored refrigerated between 2 °C to 8 °C for up to 30 days prior to use.	▪ Store in a freezer at -40ºC to -15ºC. ▪ Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze. ▪ Keep the pre-filled syringes in the outer carton to protect from light. ▪ After thawing, pre-filled syringes may be stored refrigerated between 2°C to 8°C for up to 30 days prior to use.	marked with the new discard date at 2°C to 8°C. ▪ Within this period, up to 36 hours may be used for transportation of the multidose vial at 2°C to 8°C. ▪ Pre-filled syringe transport duration is limited by the shipper qualification duration. ▪ Once thawed, the vaccine should not be refrozen. ▪ The unopened vaccine/pre-filled syringe may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions. <u>Punctured multidose vials</u> ▪ Chemical and physical in-use stability has been demonstrated for 19 hours at 2°C to 25ºC after initial puncture (within the allowed use period of 30 days or 14 days at 2°C to 8ºC, respectively and including 24 hours at 8°C to 25ºC).	▪ Upon moving the vaccine to 2°C to 8°C storage, the updated expiry date must be written on the outer carton and the vaccine should be used or discarded by the updated expiry date. ▪ The original expiry date should be crossed out. ▪ If the vaccine is received at 2°C to 8°C it should be stored at 2°C to 8°C. The expiry date on the outer carton should have been updated to reflect the refrigerated expiry date and the original expiry date should have been crossed out. ▪ Prior to use, the unopened vials can be stored for up to 12 hours at temperatures between 8°C and 30°C. ▪ Thawed vials can be handled in room light conditions. ▪ Once thawed, the vaccine should not be re-frozen. <u>Handling of temperature excursions for previously frozen vials during refrigerated storage</u>

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
			▪ From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user. **Special precautions for storage** Multidose vials/ pre-filled syringe ▪ Store in a freezer at -50ºC to -15ºC. ▪ Once thawed, store in a refrigerator (2°C to 8°C) and do not refreeze. ▪ Keep the vial/ pre-filled syringe in the outer carton to protect from light. Transportation of thawed multidose vials in liquid state at 2°C to 8°C ▪ If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid	▪ Stability data indicate that the unopened vial is stable for up to 10 weeks when stored at temperatures from -2°C to 2°C, within the 10-week storage period between 2°C and 8°C. ▪ Stability data indicate the vial can be stored for up to 24 hours at temperatures of 8°C to 30°C, including up to 12 hours following first puncture. ▪ This information is intended to guide healthcare professionals only in case of temporary temperature excursion. Unopened refrigerated only multidose vials: ▪ The vaccine will be received and stored at 2°C to 8°C (refrigerated only). ▪ Shelf life is 12 months at 2°C to 8°C. Opened vials ▪ Chemical and physical in-use stability has been demonstrated for 12 hours at 2ºC to 30ºC, which includes

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
			state for up to 36 hours at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). ▪ Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use. <u>Transportation of thawed pre-filled syringes in liquid state at 2°C to 8°C</u> ▪ If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed pre-filled syringes in liquid state at 2°C to 8°C (within the 30 days or 14 days shelf life, respectively, at 2°C to 8°C). ▪ Once thawed and transported in liquid state at 2°C to 8°C, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use.	up to 6 hours transportation time. ▪ From a microbiological point of view, unless the method of opening precludes the risks of microbial contamination, the product should be used immediately. ▪ If not used immediately, in-use storage times and conditions are the responsibility of the user. <u>Glass pre-filled syringes</u> ▪ The vaccine will be received and stored at 2°C to 8°C. ▪ Shelf life is 12 months at 2°C to 8°C. ▪ Prior to use, pre-filled syringes can be stored for up to 12 hours at temperatures of 8°C to 30°C and can be handled in room light conditions. **<u>Special precautions for storage</u>** <u>Frozen vials</u> ▪ Frozen vials have printed expiry at −90°C to −60°C.

	mCOMBRIAX®*[49, 50]	mNexspike®[51]	Spikevax®[53]	Comirnaty®[7]
			▪ Pre-filled syringe transport duration is limited by the shipper qualification duration.	▪ Store single dose frozen vials and multidose frozen vials in a freezer at −90°C to −60°C. <u>Refrigerated only vials and glass pre-filled syringes</u> ▪ Refrigerated only vials have printed expiry at 2°C to 8°C ▪ Store refrigerated only vials and glass pre-filled syringes at 2°C to 8°C. ▪ Do not freeze. <u>Vials and pre-filled syringes</u> ▪ Store the vaccine in the original package in order to protect from light. ▪ During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

*Each 0.32ml dose contains 8.3mcg A/Wisconsin/67/2022 (A/H1N1)pdm09, 8.3mcg A/Darwin/6/2021 (A/H3N2), 8.3mcg B/Austria/1359417/2021 (B/Victoria lineage) and 6.7mcg SARS-CoV-2 Omicron XBB.1.5.[50]

§Doses of 0.25ml are used in children less than 12 years of age.[85]

Table A.2 Posology, pharmaceutical form, container, shelf life and storage information relating to the protein subunit vaccines authorised in the EU

	Nuvaxovid®[56]	Bimervax®[55]
Posology	**≥12 years:** A single dose of 0.5ml regardless of prior COVID-19 vaccination status.	**≥12 years:** A single dose of 0.5ml* regardless of prior COVID-19 vaccination status.
Pharmaceutical form & container	Dispersion for injection ▪ Single dose pre-filled syringe of 5mcg/0.5ml (refrigerated only) ▪ Single dose vial of 5mcg/0.5ml (refrigerated only)	Emulsion for injection ▪ Single dose pre-filled syringe of 40mcg/0.5ml (refrigerated only) ▪ Single dose vial of 40mcg/0.5ml (refrigerated only)
Shelf life & storage	Unopened vial: ▪ Shelf life is 9 months at 2°C to 8°C, protected from light. ▪ Unopened Nuvaxovid® JN.1 vaccine has been shown to be stable up to 12 hours at 25°C. ▪ Storage at 25°C is not the recommended storage or shipping condition but may guide decisions for use in case of temporary temperature excursions during the 9-month storage at 2°C to 8°C. Punctured vial ▪ From a microbiological point of view, after opening the vaccine should be used immediately. ▪ The single dose vial should be discarded after one dose withdrawal and administration Pre-filled syringe ▪ Shelf life is 9 months at 2°C to 8°C, protected from light. ▪ The pre-filled syringe should be discarded after administration. **Special precautions for storage**	Shelf life is 1 year at 2ºC to 8ºC. **Special precautions for storage** ▪ Store in a refrigerator (2°C to 8°C). ▪ Do not freeze. ▪ Keep the vials and pre-filled syringes in the outer carton in order to protect from light.

	Single dose vial ▪ Store in a refrigerator (2°C to 8°C). ▪ Do not freeze. ▪ Keep the vials in the outer carton in order to protect from light. Single dose pre-filled syringe ▪ Store in a refrigerator (2°C to 8°C). ▪ Do not freeze. ▪ Keep the pre-filled syringes in the outer carton in order to protect from light.	

B. Appendix B Clinical effectiveness and safety

PICOS framework study eligibility

Table B.1 PICOS (population, intervention, comparator, outcomes and study design) criteria used for review selection

Population	▪ those aged ≥80 years ▪ those aged 60-79 years ▪ those aged 18-79 years living in long-term care facilities ▪ those aged ≥6 months living with immunocompromise associated with a suboptimal response to vaccination† ▪ those aged 6 months to 59 years living with underlying medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death‡ ▪ healthcare workers ▪ pregnant adolescents or adults ▪ those aged 18 to 59 years without immunocompromise† or underlying medical conditions‡
Intervention	All antigenically updated COVID-19 vaccines authorised by the European Medicines Agency.
Comparator	No vaccination as defined by study investigators, recognising that some level of background immunity likely exists in the comparator groups either from previous infection or previous vaccination, but where the individual's vaccination status is considered to not be up-to-date.
Outcomes	Effectiveness – main outcomes (laboratory-confirmed) ▪ COVID-19 acute infection ▪ COVID-19-related emergency department visits ▪ COVID-19-related hospitalisation ▪ COVID-19-related intensive care unit admissions ▪ COVID-19-related deaths ▪ Long COVID/post-COVID-19 condition as defined by the World Health Organization§ Safety – main outcomes ▪ serious adverse events†† related to vaccination Safety – additional outcomes ▪ all adverse events including: ○ solicited adverse events – local and systemic reactions ○ unsolicited adverse events – spontaneously reported/other adverse event.
Study design	Systematic review(s) of randomised controlled trials and non-randomised studies with a control group.

†Living with immunocompromise associated with a suboptimal response to vaccination, as defined by study authors.

‡Underlying medical conditions associated with a higher risk of COVID-19 hospitalisation, severe disease or death, as defined by study authors.

§The continuation or development of new symptoms three months after the initial laboratory confirmed diagnosis of SARS-CoV-2 infection, with these symptoms lasting for at least two months with no other explanation.[29]

††An adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a birth defect.[395]

Vaccine effectiveness tables

Older adults

Table B.2 Vaccine effectiveness against symptomatic or medically attended infection among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control studies				
Appaneal 2025[263] Case-control study US 5 September to 30 November 2024 NA	≥65 yrs	Intervention: mRNA KP.2 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a KP.2 vaccine of any kind, regardless of prior COVID-19 vaccination history.	ED or UC visit (aOR) N=12,033 Vaccinated cases: NR/2,616 Vaccinated controls: NR/9,417	VE: 56 (44 to 66) Median 36 days PV (IQR 25 to 49)
			Outpatient visit (aOR), N=6,529 Vaccinated cases: NR/951 Vaccinated controls: NR/5,578	VE: 58 (36 to 73) Median 31 days PV (IQR 20 to 46)
Caffrey 2024[266] Case-control study US 25 September 2023 to 31 January 2024 NA	≥65 yrs	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history	ED or UC visit (without subsequent hospital admission) (aOR) N=26,026 Vaccinated cases: NR/4,827 Vaccinated controls: NR/21,199	VE: 35 (27 to 43) Median 56 days (IQR 36 to 77) PV
			Outpatient visit (without a subsequent ED/UC visit or hospital admission) (aOR) N=13,817 Vaccinated cases: NR/2,119	VE: 24 (9 to 36) Median 53 days (IQR 35 to 76) PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Vaccinated controls: NR/11,698	
Laniece Delaunay 2025[265] Case-control study Croatia, France, Germany, Hungary, Ireland, The Netherlands, Portugal, Spain (Navarre region), Spain (national), Romania and Sweden 1 October 2024 to 9 January 2025 VEBIS	≥60 yrs (median age 66 yrs (IQR 53 to 73) among vaccinated and 63 yrs (IQR 47 to 72) among unvaccinated)	Intervention: mRNA JN.1, KP.2, XBB.1.5, and unspecified strain and unspecified vaccine (received ≥14 days before symptom onset and after the start of the vaccination campaign in their study site). Comparator: Unvaccinated patients were not vaccinated during the campaign or in the 6 months before. People vaccinated on the day of symptom onset were classified as unvaccinated.	Medically attended infection (aoR) N=1,840 14 to 83 days PV: Vaccinated cases: 7/86 Vaccinated controls: 448/1,754 14 to 29 days PV: Vaccinated cases: 2/81 Vaccinated controls: 131/1,437 30 to 59 days PV: Vaccinated cases: 4/83 Vaccinated controls: 225/1,531 14 to 41 days PV: Vaccinated cases: 4/83 Vaccinated controls: 2258/1,531 42 to 83 days PV: Vaccinated cases: 3/82 Vaccinated controls: 219/1,525 14 to 59 days PV: Vaccinated cases: 6/85 Vaccinated controls: 356/1,1,662	VE: 67 (33 to 86) 14 to 83 days PV; median 40 days (IQR 30 to 49) VE: 68 (3 to 93) 14 to 29 days PV; median 19 days (IQR 17 to 20) VE: 59 (0 to 87) 30 to 59 days PV; median 43 days (IQR 40 to 47) VE: 66 (18 to 89) 14 to 41 days PV; median 30 days (IQR 20 to 39) VE: 64 (4 to 90) 42 to 83 days PV; median 51 days (IQR 49 to 62) VE: 65 (25 to 86) 14 to 59 days PV; median 40 days (IQR 26 to 45)
Link-Gelles 2025a[264] Case-control study US	≥65 yrs	Intervention: mRNA KP.2 or protein subunit JN.1 (receipt ≥7 days before the encounter index date)	ED or UC visit (aOR) N=48,685 7 to 119 days PV: Vaccinated cases: 661/4,346	VE: 35 (29 to 41) 7 to 119 days PV; median 57 days (IQR 33 to 82) VE: 36 (28 to 44)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
1 September 2024 to 21 January 2025 VISION		Comparator: Did not receive a mRNA KP.2 or protein subunit JN.1 vaccine, regardless of prior COVID-19 vaccination history.	Vaccinated controls: 12,159/44,339 7 to 59 days PV: Vaccinated cases: 346/4031 Vaccinated controls: 6,410/38,590 60 to 119 days PV: Vaccinated cases: 315/4000 Vaccinated controls: 5,749/37,929	7 to 59 days PV; median 34 days (IQR 21 to 47) VE: 34 (25 to 42) 60 to 119 days PV; median 83 days (IQR 71 to 97)
Link-Gelles 2025b[269] Case-control study US 21 September 2023 to 22 August 2024 VISION	≥65 yrs	Intervention: mRNA or protein subunit XBB.1.5 (excluded if individual received >1 dose). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine (including unvaccinated persons and those who received original monovalent or bivalent COVID-19 vaccines).	ED or UC visit (aOR) N=121,541 7 to 299 days PV Vaccinated cases: 4,036/14,150 Vaccinated controls: 38,215/107,391 7 to 59 days PV Vaccinated cases: 868/10,982 Vaccinated controls: 9,262/78,438 60 to 119 days PV Vaccinated cases: 1,085/11,199 Vaccinated controls: 10,283/79,459 120 to 179 days PV	VE: 25 (22 to 28) 7 to 299 days PV; median 117 days (IQR 62 to 190) VE: 46 (41 to 50) 7 to 59 days PV; median 34 days (21 to 47) VE: 25 (20 to 30) 60 to 119 days PV; median 88 days (73 to 103) VE: 19 (11 to 26) 120 to 179 days PV; median 148 days (133 to 163)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Vaccinated cases: 619/10,733 Vaccinated controls: 8,225/77,401 180 to 299 days PV Vaccinated cases: 1,464/11,578 Vaccinated controls: 10,445/79,621	VE: 2 (-5 to 8) 180 to 299 days PV; median 232 days (204 to 262)
Cohort studies				
Andersen 2025[270] Cohort study US 25 September 2023 to 31 March 2024 NA	≥65 yrs	Intervention: mRNA XBB.1.5 (individuals were considered vaccinated 14 days after receipt of vaccine). Comparator: Did not receive an XBB.1.5 vaccine of any kind.	ED visit (aHR) Vaccinated events 64/226,883 person months at risk Unvaccinated events: 1,717/3,306,086 person-months at risk	VE: 48 (33 to 60) Median 3.9 months PV (IQR 2.2 to 5.1)
Ioannou 2025[271] Cohort study US 2 October 2023 to 10 May 2024 NA	65 to 74 yrs	Intervention: mRNA and protein subunit XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Laboratory-confirmed infection (primarily included medically attended infections) (RR) N=192,911 Vaccinated events: 2,611/92,273.7 person-years Unvaccinated events: 2,675/92,201.0 person-years	VE: 0.2 (-6 to 7) Mean 176 days PV (range 118 to 211)
	≥75 yrs		Laboratory-confirmed infection (primarily included medically attended infections) (RR)	VE: -13 (-18 to 7) Mean 176 days PV (range 118 to 211)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			N=235,743 Vaccinated events: 3,562/113,852.2 person-years Unvaccinated events: 3,255/113,906.5 person-years	
Payne, 2025[272] Cohort study Country: US 17 September 2023 to 13 April 2024 NA	≥65 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive an mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Medically attended infection† (aHR) N=65,978 Vaccinated events: 440/13,108 persons Unvaccinated events: 4,041/52,870 persons	VE: 44 (37 to 51) 7 to 209 days PV; median 152 days
Ward, 2025[273] Cohort study England and Scotland‡ 12 November 2023 to 7 March 2024 Used data from the Winter Coronavirus (COVID-19) Infection Study, a collaboration between the UK Health Security Agency and	≥65 yrs	Intervention: mRNA XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Symptomatic infection (defined as an individual reporting acute respiratory symptoms accompanied by a positive lateral flow test result) (aHR) N=48,642 Vaccinated events: NR Unvaccinated events: NR	VE: 36 (-358 to 91) 0 to 13 days PV VE: 60 (2 to 84) 14 to 34 days PV VE: 33 (1 to 55) 35 to 55 days PV VE: 15 (-8 to 34) 56 to 83 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Office for National Statistics				VE: -7 (-43 to 21) ≥84 days PV
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	≥65 yrs	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Medically attended infection (including hospital admissions, ED/UC visits, doctor's office visits and telemedicine visits) (aHR) N=294,388 Vaccinated events: 5,028/135,955 person-years Unvaccinated events: 4,881/107,640 person-years	VE: 19 (16 to 22) Median 84 days PV (IQR 58 to 101)

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; ARI – acute respiratory infection; CI – confidence interval; COVID-19 – coronavirus disease 2019; ED – emergency department; ESKD – end stage kidney disease; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; RR – risk ratio; UC – urgent care; VE – vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; yrs – years.

*Case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome. Cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

†Defined as having at least one facility claim with COVID-19 diagnosis code or at least two professional claims with COVID-19 diagnosis code on two distinct dates within 21 dates of each other.

‡Study participants in Scotland were excluded as unable to link to vaccination history.

Source: Scott et al.[57]

Table B.3 Vaccine effectiveness against symptomatic or medically attended infection among older adults from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Case-control studies				
Skowronski 2024[396] Case-control study Canada 29 October 2023 to 13 January 2024 Canadian Sentinel Practitioner Surveillance Network	≥65 yrs	Intervention: mRNA or protein subunit XBB.1.5 vaccine. Comparator: Did not receive an XBB.1.5 adapted vaccine.	SARS-CoV-2 infection (self-reported and confirmed by nucleic acid amplification test or rapid antigen test) (aOR)	VE: 52 (10 to 74) adjusted for age group, province and calendar time. Median 5 weeks PV (IQR 3 to 7)
				VE: 46 (-3 to 72) adjusted for age group, province, calendar time, sex and comorbidity. Median 5 weeks PV (IQR 3 to 7)
Link-Gelles 2024b[397] Case-control study US 21 September 2023 until 14 January 2024 ICATT	≥50 yrs	Intervention: monovalent XBB.1.5 vaccine (mixed mRNA and protein sub-unit) Comparator: Unvaccinated during the latest period (September 2023 to January 2024). Secondary analysis comparators included previous receipt of a bivalent dose and	Reporting ≥1 symptom of COVID-19 and testing positive (aOR)	VE: 46 (31 to 58) 7 to 119 days PV; median 50 days (IQR 29 to 77)
				VE: 45 (26 to 60) 7 to 59 days PV; median 32 days (IQR 21 to 45)
				VE: 47 (24 to 62) 60 to 119 days PV; median 81 days (IQR 70 to 91)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
		either being unvaccinated or having only received original COVID-19 vaccines.		
DeCuir 2024[398] Case-control study US September 2023 to January 2024 VISION	≥65 yrs	Intervention: monovalent XBB.1.5 vaccine (mixed mRNA and protein sub-unit vaccines) Comparator: Did not receive an updated vaccine dose during the 2023 vaccination period	ED/UC visits	VE: 45 (41 to 49) 7 to 119 days PV; median 46 days (IQR 27 to 66)
				VE: 49 (44 to 54) 7 to 59 days PV; median 33 days (IQR 21 to 46)
				VE: 37 (29 to 44) 60 to 119 days PV; median 74 days (IQR 66 to 83)
Laniece Delaunay 2024[399] Case-control 10 European study sites across 9 countries (Croatia, France, Germany, Hungary, Ireland, The Netherlands, Portugal, Spain and Spain Navarre region, and Sweden) September 2023 to January 2024 VEBIS primary care	≥50 yrs from one site ≥60 yrs from six sites ≥65 yrs from three sites	Intervention: predominantly XBB.1.5 vaccines (mixed mRNA (99% of vaccines administered being BNT162b2 mRNA vaccine)) and recombinant protein (1%) vaccines) Comparator: Unvaccinated as part of the 2023 autumn vaccination campaign	Medically attended SARS CoV-2 infection	Against any strain VE: 37 (19 to 51) 1 to 14 weeks PV
				Against any strain VE: 45 (26 to 60) 1 to <6 weeks PV
				Against any strain VE: 26 (-3 to 48) 6 to 14 weeks PV
				Against Omicron XBB and sublineages VE: 63 (6 to 88) 1 to 14 weeks PV
				Against Omicron XBB and sublineages VE: 63 (-2 to 90)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				1 to <6 weeks PV
Merdrignac 2024[400] Case-control study 8 study sites from 7 European countries (France, Germany, Hungary, Ireland, The Netherlands, Portugal, Spain and Spain Navarre region) 20 November 2023 to 1 March 2024 (JN.1 predominant period) VEBIS primary care	≥65 yrs only	Intervention: Vaccinated with 2023/24 Autunm vaccine (XBB.1.5 vaccine, mixed mRNA and protein subunit vaccines) Comparator: Unvaccinated referred to those who did not receive a 2023/24 COVID-19 vaccine within 180 days of the start of the 2023/24 vaccination campaign.	Medically attended symptomatic SARS-CoV-2 infection (aOR)	VE: 28 (2 to 48) 1 to 20 weeks PV; median 67 days (IQR 47 to 87)
				VE: 48 (12 to 71) 1 to 5 weeks PV; median 29 days (IQR 20 to 36)
				VE: 23 (-11 to 48) 6 to 11 weeks PV; median 63 days (IQR 53 to 74)
				VE: 5 (-92 to 56) 12 to 20 weeks PV; median 99 days (IQR 90 to 110)
	≥50 yrs one site ≥60 yrs six sites ≥65 yrs one site			VE: 26 (3 to 44) 1 to 20 weeks PV; median 66 days (IQR 47 to 86)
				VE: 51 (20 to 71) 1 to 5 weeks PV; median 29 days (IQR 20 to 36)
				VE: 17 (-15 to 40) 6 to 11 weeks PV; median 63 days (IQR 53 to 74)
				VE: 10 (-64 to 54) 12 to 20 weeks PV; median 99 days (IQR 90 to 110)
Cohort studies				

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Huiberts 2024[401] Cohort study Netherlands 9 October 2023 to 9 January 2024 VAccine Study COvid-19 (VASCO)	60 to 85 yrs	Intervention: mRNA XBB.1.5 adapted vaccine. Comparator: No XBB.1.5 adapted vaccine.	SARS-CoV-2 infection (self-reported; PCR or antigen test) (aHR)	VE: 50 (44 to 56) 1 to 12 weeks PV
				VE: 52 (45 to 58) 1 to 6 weeks PV
				VE: 41 (26 to 52) 7 to 12 weeks PV

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; ED – emergency department; ICATT – Increasing Community Access To Testing; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; UC – urgent care; VE – vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; yrs – years.
Source: Supplemental search.

Table B.4 Vaccine effectiveness against hospitalisation among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control studies				
Caffrey 2024[266] Case-control study US 25 September 2023 to 31 January 2024 NA	≥65 yrs	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive an XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history	Hospitalisation (aOR) N=18,768 Vaccinated cases: NR/3,478 Vaccinated controls: NR/15,290	VE: 41 (32 to 50) Median 54 days PV (IQR 33 to 74)
Levy 2025[268] Case-control study US 24 September 2023 to 21 January 2024 NA	≥65 yrs	Intervention: mRNA XBB.1.5 vaccine Comparator: No previous XBB.1.5 vaccination	Odds of hospitalisation or ED visit versus outpatient visit (aOR) Overall strains N=2,439 Vaccinated cases: 96/1048 Vaccinated controls: 310/1,391 JN.1 strain N=410 Vaccinated cases: 40/174 Vaccinated controls: 94/236 XBB strain N=1,303 Vaccinated cases: 28/568 Vaccinated controls: 117/735	Overall strains: VE: 61 (48 to 71) Median 57 days PV (IQR 39 to 73) JN.1 strain: VE: 48 (14 to 69) Median 57 days PV (IQR 39 to 73) XBB strain: VE: 74 (58 to 84) Median 57 days PV (IQR 39 to 73)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Link-Gelles 2025a[264] Case-control study US 1 September 2024 to 21 January 2025 VISION and IVY	≥65 yrs	Intervention: mRNA KP.2 or protein subunit JN.1 (receipt ≥7 days before the encounter index date) Comparator: Did not receive an mRNA KP.2 or protein subunit JN.1 vaccine, regardless of prior COVID-19 vaccination history.	Hospitalisation (VISION data) (aOR) N=26,219 Overall Vaccinated cases: 232/2,248 Vaccinated controls: 4,773/23,971 7 to 59 days PV Vaccinated cases: 129/2,145 Vaccinated controls: 2,759/21,957 60 to 199 days PV Vaccinated cases: 103/2,119 Vaccinated controls: 2,014/21,212	VE: 45 (36 to 53) 7 to 119 days PV; median 53 days (30 to 77) VE: 42 (30 to 52) 7 to 59 days PV; median 33 days (20 to 46) VE: 48 (36 to 58) 60 to 119 days PV; median 81 days (70 to 94)
			Hospitalisation (IVY data) (aOR) N=1,929 Overall Vaccinated cases: 69/683 Vaccinated controls: 225/1,246 7 to 59 days PV Vaccinated cases: 41/655 Vaccinated controls: 105/1,126 60 to 199 days PV Vaccinated cases: 28/642	VE: 46 (26 to 60) 7 to 119 days PV; median 60 days (31 to 85) VE: 42 (14 to 61) 7 to 59 days PV; median 31 days (20 to 45) VE: 47 (17 to 67)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Vaccinated controls: 120/1,141	60 to 119 days PV; median 85 days (72 to 98)
Link-Gelles 2025b[269] Case-control study US 21 September 2023 to 22 August 2024 VISION	≥65 yrs	Intervention: mRNA or protein subunit XBB.1.5 (excluded if individual received >1 dose). Comparator: Did not receive an mRNA or protein subunit XBB.1.5 vaccine (including unvaccinated persons and those who received original monovalent or bivalent COVID-19 vaccines).	Hospitalisation (aOR) N=72,379 Overall Vaccinated cases: 1,666/7,917 Vaccinated controls: 18,298/64,462 7 to 59 days PV Vaccinated cases: 357/6,608 Vaccinated controls: 4,256/50,420 60 to 119 days PV Vaccinated cases: 434/6,685 Vaccinated controls: 4,684/50,848 120 to 179 days PV Vaccinated cases: 273/6,524 Vaccinated controls: 4,066/50,230 180 to 299 days PV Vaccinated cases: 602/6,853 Vaccinated controls: 5,292/51,456	VE: 31 (27 to 35) 7 to 299 days PV; median 123 days (IQR 63 to 194) VE: 54 (49 to 59) 7 to 59 days PV; median 34 days (IQR 21 to 47) VE: 36 (29 to 42) 60 to 119 days PV; median 88 days (IQR 73 to 104) VE: 21 (10 to 31) 120 to 179 days PV; median 149 days (IQR 134 to 164) VE: 0 (-10 to 10) 180 to 299 days PV; median 230 days (IQR 204 to 261)
Nguyen 2025[274]	≥65 yrs		Hospitalisation (aOR)	VE: 54 (40 to 64)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control study Nine sites across Belgium, Germany, Italy, and Spain 2 October 2023 to 2 April 2024 id.DRIVE†		Intervention: mRNA XBB.1.5 vaccine (at least one dose, regardless of prior COVID-19 vaccine history). Patients who received the vaccination within 14 days prior to SARI symptom onset or ≤12 weeks after receipt of any other COVID-19 vaccine were excluded from the analyses. Comparator: Patients who had not been vaccinated with any COVID-19 vaccine during the 2023–2024 season.	N=1,111 ≥65 yrs Vaccinated cases: 111/239 Vaccinated controls: 547/872 65 to 79 yrs Vaccinated cases: 28/85 Vaccinated controls: 227/405 ≥80 yrs Vaccinated cases: 83/154 Vaccinated controls: 320/467	Median 64 days PV (IQR 49 to 79)
	65 to 79 yrs			VE: 63 (40 to 77) Median 59 days PV (IQR 44 to 73)
	≥80 yrs			VE: 49 (37 to 59) Median 67 days PV (IQR 52 to 81)
Appaneal 2025[263] Case-control study US 5 September to 30 November 2024 NA	≥65 yrs	Intervention: mRNA KP.2 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a KP.2 vaccine of any kind, regardless of prior COVID-19 vaccination history.	Hospitalisation (aOR) N=7,589 Vaccinated cases: NR/706 Vaccinated controls: NR/6,883	VE: 75 (49 to 88) Median 30 days PV (IQR 22 to 43)
Carazo 2025 [275]	≥60 yrs	Intervention: One dose of mRNA XBB.1.5 vaccine.	Hospitalisation (aOR) ≥60 yrs	VE: 70 (31 to 87) 7 to 60 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control study Canada 29 October 2023 to 17 August 2024 NA		Comparator: latest vaccination with an ancestral mRNA monovalent or bivalent booster vaccine dose received during prior vaccination campaign (from July to December 2022).	N=75,960 7 to 60 days PV Vaccinated cases: 6/300 Vaccinated controls: 395/4,694 61 to 121 days PV Vaccinated cases: 14/218 Vaccinated controls: 393/4,692 122 to 182 days PV Vaccinated cases; 49/253 Vaccinated controls: 1,536/5.835 183 to 243 days PV Vaccinated cases: 272/476 Vaccinated controls: 6,620/10,919 244 to 304 days PV Vaccinated cases: 369/573 Vaccinated controls: 4,534/8,833 0 to 10 months PV Vaccinated cases: 2,126/3,482 Vaccinated controls: 52,135/72,478 During XBB period of dominance: NR	VE: 38 (-10 to 65) 61 to 121 days PV VE: 12 (-24 to 38) 122 to 182 days PV VE: 3 (-18 to 21) 183 to 243 days PV VE: -20 (-46 to 1) 244 to 304 days PV VE: 30 (24 to 35) 0 to 10 months PV During XBB period of dominance VE: 54 (46 to 62) During JN.1 period of dominance VE: 23 (12 to 32) During KP.2 period of dominance VE: 1 (-17 to 15)
	60 to 69 yrs			VE: 4 (-18 to 22) 0 to 10 months PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			During JN period of dominance: NR During KP period of dominance: NR	During XBB period of dominance VE: 48 (11 to 69)
			60 to 69 yrs 0 to 10 months PV: NR During XBB period of dominance: NR During JN period of dominance: NR During KP period of dominance: NR	During JN.1 period of dominance VE: -7 (-48 to 23)
				During KP.2 period of dominance VE: -47 (-130 to 6)
	70 to 79 yrs		70 to 79 yrs 0 to 10 months PV: NR During XBB period of dominance: NR During JN period of dominance: NR During KP period of dominance: NR	VE: 33 (24 to 42) 0 to 10 months PV
				During XBB period of dominance VE: 56 (41 to 68)
			≥80 yrs 0 to 10 months PV: NR During XBB period of dominance: NR During JN period of dominance: NR During KP period of dominance: NR	During JN.1 period of dominance VE: 26 (8 to 40)
				During KP.2 period of dominance VE: 10 (-19 to 32)
	≥80 yrs			VE: 34 (26 to 40) 0 to 10 months PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
				During XBB period of dominance VE: 55 (43 to 64)
				During JN.1 period of dominance VE: 29 (15 to 41)
				During KP.2 period of dominance VE: 7 (-16 to 25)
Cohort studies				
Ioannou 2025[271] Cohort study US 2 October 2023 to 10 May 2024 NA	65 to 74 yrs	Intervention: mRNA and protein subunit XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Hospitalisation (RR) 65 to 74 yrs N=192,911 Vaccinated events: 201/93,000.6 person-years Unvaccinated events: 265/92,976.1 person-years ≥75 yrs N=235,743 Vaccinated events: 371/114,839.4 person-years Unvaccinated events: 448/114,806.0 person-years	VE: 16 (-5 to 34) Mean 176 days (range 118 to 211)
	≥75 yrs			VE: 14 (1 to 27) Mean 176 days (range 118 to 211)
Andersen 2025[270]	≥65 yrs	Intervention: mRNA XBB.1.5 (individuals were considered	Hospitalisation (aHR) N=743,124	VE: 47 (28 to 61)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Cohort study US 25 September 2023 to 31 March 2024 NA		vaccinated 14 days after receipt of vaccine). Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Vaccinated events: 44/227,029 person-months Unvaccinated events: 1,207/3,307,824 person-months	Median 3.9 months PV (IQR 2.2 to 5.1)
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥65 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Hospitalisation (aHR) N=65,978 Vaccinated events: 220/13,261 Unvaccinated events: 2,381/52,717	VE: 53 (44 to 62) 7 to 209 days PV; median 153 days
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	≥65 yrs	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Hospitalisation (aHR) N=588,776 Vaccinated events: 441/294,388 Unvaccinated events: 803/294.388	VE: 56 (51 to 61) Median 84 days (IQR 58 to 101)
Andersson 2024[276] Cohort	≥65 yrs 65 to 74 yrs	Intervention: One dose of an mRNA XBB.1.5 vaccine during the study period.	Hospitalisation (RR) ≥65 yrs N=236,261	VE: 58 (50 to 66) 1 to 24 weeks PV VE: 60 (52 to 69)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Denmark, Finland and Sweden 1 October 2023 to 21 April 2024 NA		Comparator: Did not receive a monovalent XBB.1.5-containing COVID-19 vaccine at baseline and continued as unvaccinated during follow-up.	Vaccinated events: 1,085/324,937 person-years Unvaccinated events: 2,635/320,935 person-years 65 to 74 years N=NR Vaccinated events: 226/172,332 person-years Unvaccinated events: 563/171,845 person-years ≥75 yrs N=NR Vaccinated events: 859/152,606 person-years Unvaccinated events: 2,072/149,090 person-years	1 to 24 weeks PV
	≥75 yrs			VE: 58 (48 to 68) 1 to 24 weeks PV
Nunes 2024[277] Cohort Belgium, Denmark, Italy, Navarre (Spain), Norway, Portugal and Sweden 4 December 2023 to 25 February 2024 VEBIS	65 to 79 yrs	Intervention: Receipt of an XBB.1.5 (mRNA and protein subunit) vaccine during the study period. Comparator: Not yet vaccinated. The eligible population included those with primary vaccination series completed at least 180 days ago and who, in the last 90 days, had no vaccine dose administered nor documented SARS-CoV-2 infection or COVID-19 hospitalisation.	Hospitalisation (aHR) 65 to 79 yrs N=14,234,785 Overall Vaccinated events: 908/9,957,896 person-months Unvaccinated events: 1,752/17,500,532 person-months 14 to 89 days Vaccinated events: 813/6,472,961 person-months	VE: 50 (45 to 55) 14 to 179 days PV
				VE: 51 (45 to 56) 14 to 89 days PV
				VE: 47 (32 to 59) 90 to 179 days PV
	≥80 yrs			VE: 41 (35 to 46) 14 to 179 days PV
				VE: 42 (36 to 47) 14 to 89 days PV
				VE: 39 (17 to 54) 90 to 179 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: 1,752/17,500,532 person-months 90 to 179 days Vaccinated events: 91/2,708,455 person-months Unvaccinated events: 1,752/17,500,532 person-months ≥80 yrs N=5,948,837 Overall Vaccinated events: 1,306/4,107,972 person-months Unvaccinated events: 2,117/6,886,612 person-months 14 to 89 days Vaccinated events: 1,167/2,661,954 person-months Unvaccinated events: 2,117/6,886,612 person-months 90 to 179 days Vaccinated events: 139/1,446,776 person-months Unvaccinated events: 2,117/6,886,612 person-months	

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; ARI – acute respiratory infection; CI – confidence interval; COVID-19 – coronavirus disease 2019; IQR – interquartile range; IVY - Investigating Respiratory Viruses in the Acutely Ill Network; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; RR – risk ratio; SARI – severe acute respiratory infection; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; VE: vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; yrs – years.

*Case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome. Cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

†id.DRIVE is a privately funded not-for-profit open public-private partnership.[402]

Source: Scott et al.[57]

Table B.5 Vaccine effectiveness against hospitalisation among older adults from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Case-control studies				
Antunes 2024a[403] Case-control study Spain, Croatia, Ireland, Malta, Navarre region and Portugal 15 February to 31 August 2023 VEBIS	≥60 yrs	Intervention: mRNA or protein subunit adapted bivalent vaccines. Comparator: Received primary series of any monovalent COVID-19 vaccine more than 6 months before the bivalent campaign began.	Hospitalisation at 60-day intervals* *Small sample size precluded VE estimates for 14 to 59 and 300 to 359 days PV (aOR)	VE: 44 (3 to 70) 60 to 119 days PV
				VE: 12 (-16 to 34) 120 to 179 days PV
				VE: 7 (-24 to 29) 180 to 239 days PV
				VE: 11 (-24 to 36) 240 to 299 days PV
			Hospitalisation at 90-day intervals (aOR)	VE: 80 (50 to 94) 14 to 89 days PV
				VE: 15 (-12 to 35) 90 to 179 days PV
				VE: 8 (-19 to 28) 180 to 269 days PV
				VE: 0 (-47 to 31) 270 to 359 days PV
Antunes 2024b[404] Case-control study Belgium, Croatia, Ireland, Lithuania,	60 to 79 yrs	Intervention: Receipt of an XBB.1.5 (mRNA and protein subunit) vaccine after the start of the 2023 autumn	Hospitalisation (aOR)	VE: 44 (23 to 60) 14 to 105 days PV; median 51 days (IQR 34 to 63)
				VE: 59 (20 to 81) 14 to 29 days PV; median 22 days (IQR 18 to 26)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Malta, Navarre region (Spain) and Spain 5 October 2023 to 14 January 2024 VEBIS		vaccination campaign, at least 14 days before symptom onset. Comparator: Did not receive a vaccine during the 2023 autumn vaccination campaign and were either never vaccinated for COVID-19 or received their last COVID-19 vaccination dose at least 180 days prior to the start of the 2023 autumn vaccination campaign.		VE: 42 (13 to 63) 30 to 59 days PV; median 46 days (IQR 38 to 53)
				VE: 36 (-2 to 61) 60 to 105 days PV; median 68 days (IQR 63 to 76)
	≥80 yrs			VE: 52 (36 to 64) 14 to 105 days PV; median 55 days (IQR 37 to 70)
				VE: 76 (53 to 90) 14 to 29 days PV; median 22 days (IQR 18 to 25)
				VE: 55 (34 to 70) 30 to 59 days PV; median 47 days (IQR 39 to 54)
				VE: 39 (10 to 59) 60 to 105 days PV; median 72 days (IQR 67 to 77)
	≥65 yrs			VE: 50 (38 to 60) 14 to 105 days PV; median 53 days (IQR 35 to 68)
				VE: 72 (54 to 85) 14 to 29 days PV; median 22 days (IQR 18 to 26)
				VE: 48 (31 to 62) 30 to 59 days PV; median 46 days (IQR 38 to 53)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 38 (16 to 55) 60 to 105 days PV; median 71 days (IQR 66 to 77)
Antunes 2025[405] Case-control study Hospitals from 8 European countries (Belgium, Germany, Spain and Spain Navarre region, Hungary, Ireland, Lithuania, Malta and Portugal) November 2023 to May 2024 VEBIS Hospital Study	≥65 yrs	Intervention: Received COVID-19 vaccine after roll-out of XBB.1.5 vaccine. For Ireland and Portugal defined as receiving at least third COVID-19 dose after XBB.1.5 roll-out or second dose if primary dose had been Jcovden®. Comparator: Never vaccinated for COVID-19 or last dose ≥180 days prior to 2023/24 vaccination campaign. For Portugal and Ireland, unvaccinated cohort were those with at least primary series vaccination.	Hospitalisation (aOR)	VE: 45 (29 to 58) 14 to 59 days PV; median 45 (IQR 34 to 53)
				VE: 34 (18 to 47) 60 to 119 days PV; median 83 days (IQR 71 to 100)
				VE: -10 (-58 to 24) 120 to 235 days PV; median 154 days (IQR 137 to 178)
	65 to 79 yrs			VE: 47 (22 to 65) 15 to 49 days PV; median 43 days (IQR 33 to 52)
				VE: 33 (6 to 53) 60 to 119 days PV; median 82 days (IQR 69 to 102)
				VE: -1 (-78 to 43) 120 to 234 days PV; median 154 days (IQR 137 to 180)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
	≥80 yrs			VE: 45 (22 to 61) 15 to 49 days PV; median 46 days (IQR 35 to 54)
				VE: 32 (9 to 49) 60 to 119 days PV; median 84 days (IQR 72 to 100)
				VE: -18 (-92 to 27) 120 to 234 days PV; median 154 days (IQR 137 to 177)
DeCuir 2024[398] Case-control study US September 2023 to January 2024 VISION and IVY	≥65 yrs	Intervention: monovalent XBB.1.5 vaccine (mixed mRNA and protein sub-unit vaccines) Comparator: Did not receive an updated vaccine dose during the 2023 vaccination period	Hospitalisation (VISION) (aOR)	VE: 53 (47 to 58) 7 to 119 days PV; median 43 days (IQR 25 to 62)
				VE: 54 (47 to 60) 7 to 59 days PV; median 32 days (IQR 19 to 46)
				VE: 50 (39 to 59) 60 to 119 days PV; median 73 days (IQR 66 to 81)
			Hospitalisation (IVY) (aOR)	VE: 48 (31 to 61) 7 to 119 days PV; median 48 days (IQR 26 to 72)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Kirsebom 2024a[406] Case-control study England 4 September 2023 to 21 January 2024 UKHSA IIS	≥75 yrs	Intervention: mRNA monovalent XBB.1.5 vaccines (BNT162b2 and mRNA-1273) and mRNA bivalent Original/Omicron BA.4-5 Comparator: No autumn 2023 COVID-19 vaccination	Hospitalisation (aOR)	VE: 63 (47 to 74)* 0 to 2 days PV
				VE: 34 (19 to 46) 3 to 8 days PV
				VE: 41 (26 to 53) 9 to 13 days PV
				VE: 50 (42 to 56) 2 to 4 weeks PV
				VE: 46 (39 to 52) 5 to 9 weeks PV
				VE: 36 (27 to 43) 10 to 14 weeks PV
				VE: 13 (-17 to 35) ≥15 weeks PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
	≥65 yrs			VE: 66 (53 to 76)* 0 to 2 days PV
				VE: 31 (17 to 43) 3 to 8 days PV
				VE: 41 (28 to 52) 9 to 13 days PV
				VE: 51 (44 to 56) 2 to 4 weeks PV
				VE: 46 (39 to 51) 5 to 9 weeks PV
				VE: 37 (29 to 43) 10 to 14 weeks PV
				VE: 14 (-12 to 33) ≥15 weeks PV
Kirsebom 2024b[407] Case-control study England	≥75 yrs	Intervention: Comirnaty® mRNA bivalent Original/Omicron BA.4/5†	Hospitalisation (aOR)	VE: 51 (0 to 76)* 0 to 2 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
3 April 2023 to 27 August 2023 UKHSA IIS		Comparator: No Spring 2023 COVID-19 vaccination		VE: 25 (-15 to 51) 3 to 8 days PV
				VE: 56 (25 to 74) 9 to 13 days PV
				VE: 53 (36 to 65) 2 to 4 weeks PV
				VE: 29 (7 to 45) 5 to 9 weeks PV
				VE: 38 (13 to 56) ≥10 weeks PV
	≥75 yrs and not a resident in a LTCF			VE: 59 (9 to 82)* 0to 2 days PV
				VE: 23 (-21 to 51) 3 to 8 days PV
				VE: 55 (22 to 74) 9 to 13 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 51 (33 to 64) 2 to 4 weeks PV
				VE: 29 (7 to 46) 5 to 9 weeks PV
				VE: 39 (14 to 57) ≥10 weeks PV
Rojas-Castro 2025[408] Case-control study Belgium, Germany, Hungary, Ireland, Lithuania, Navarre region (Spain) and Spain 29 September 2024 to 4 May 2025 VEBIS	≥60 yrs	Intervention: mRNA adapted vaccines (adapted for any of the following variants: KP.2, JN.1 or XBB.1.5). One participant had received a protein subunit vaccine. Received a vaccine ≥14 days before symptom onset during the country's autumn 2024 campaign. Comparator: Unvaccinated.	Hospitalisation (aOR)	VE: 32 (12 to 47) 14 to 213 days PV; median 98 days (IQR 54 to 142)
				VE: 42 (15 to 61) 14 to 59 days PV; median 36 days (IQR 21 to 47)
				VE: 32 (-1 to 54) 60 to 119 days PV; 86 days (IQR 76 to 103)
				VE: 36 (2 to 60) 120 to 179 days PV; median 141 days (IQR 130 to 149)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: -43 (-177 to 29) 180 to 213 days PV; median 198 days (IQR 184 to 201)
	60 to 79 yrs			VE: 22 (-13 to 47) 14 to 213 days PV; median 104 days (IQR 56 to 144)
				VE: 40 (-9 to 69) 14 to 59 days PV; median 45 days (IQR 35 to 54)
				VE: 7 (-66 to 50) 60 to 119 days PV; median 88 days (75 to 107)
				VE: 27 (-42 to 65) 120 to 179 days PV; median 144 days (IQR 138 to 147)
				VE: -59 (-310 to 44) 180 to 213 days PV; median 198 days (IQR 184 to 201)
	≥80 yrs			VE: 40 (17 to 57) 14 to 213 days PV; median 94 days (IQR 46 to 138)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 49 (16 to 70) 14 to 59 days PV; median 25 days (IQR 17 to 43)
				VE: 46 (9 to 69) 60 to 119 days PV; median 86 days (IQR 76 to 98)
				VE: 37 (-11 to 66) 120 to 179 days PV; median 138 days (IQR 129 to 152)
				VE: -44 (-249 to 45) 180 to 213 days PV; median 197 days (IQR 188 to 201)
UK Health Security Agency 2024a[409] Case-control study England April 2024 to December 2024 for Spring 2024 campaign Epidemiology of COVID-19 in England report	≥75 yrs	Intervention: mRNA monovalent XBB.1.5 vaccines (BNT162b2 and mRNA-1273) Comparator: No Spring 2024 COVID-19 vaccination	Hospitalisation (aOR)	VE: 44 (36 to 51) 2 to 4 weeks PV
				VE: 41 (35 to 47) 5 to 9 weeks PV
				VE: 32 (24 to 38) 10 to 14 weeks PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 22 (13 to 30) 15 to 19 weeks PV
				VE: 27 (18 to 34) 20 to 24 weeks PV
				VE: 9 (-8 to 23) 25 to 29 weeks PV
				VE: 1 (-23 to 20) ≥30 weeks PV
UK Health Security Agency 2024b[410] Case-control study England April 2024 (long term VE of the autumn 2023 booster) Epidemiology of COVID-19 in England report	≥65 yrs	Intervention: mRNA monovalent XBB.1.5 vaccines (BNT162b2 and mRNA-1273) and mRNA bivalent Original/Omicron BA.4/5 Comparator: No autumn 2023 COVID-19 vaccination	Hospitalisation (aOR)	VE: 32 (11 to 48) 20 to 24 weeks PV
				VE: 25 (15 to 35) 25 to 29 weeks PV
				VE: 12 (4 to 20) ≥30 weeks PV
UK Health Security Agency 2025[411]	≥75 yrs		Hospitalisation (aOR)	VE: 44 (15 to 63) 9 to 13 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Case-control study England January to 3 August 2025 Epidemiology of COVID-19 in England report		Intervention: mRNA monovalent JN.1 vaccines administered from 1 April 2025 to 31 June 2025. ▪ BNT162b2: 14% recipients ▪ mRNA-1273: 86% recipients Comparator: No Spring 2025 COVID-19 vaccination		VE: 49 (36 to 60) 2 to 4 weeks PV
				VE: 55 (44 to 64) 5 to 9 weeks PV
				VE: 35 (14 to 50) 10 to 14 weeks PV
	≥65 yrs	Intervention: mRNA monovalent JN.1 vaccines administered from 3 October 2024. ▪ BNT162b2: 41% recipients ▪ mRNA-1273: 59% recipients Comparator: No autumn 2024 COVID-19 vaccination	Hospitalisation (aOR)	VE: 26 (8 to 41) 9 to 13 days PV
				VE: 34 (24 to 43) 2 to 4 weeks PV
				VE: 37 (28 to 44) 5 to 9 weeks PV
				VE: 43 (34 to 50) 10 to 14 weeks PV
				VE: 40 (30 to 49) 15 to 19 weeks PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 32 (22 to 41) 20 to 24 weeks PV
				VE: 26 (14 to 37) 25 to 29 weeks PV
				VE: 34 (19 to 47) 30 to 34 weeks PV
				VE: 24 (-1 to 43) ≥35 weeks PV
Cohort studies				
ECDC 2024a[412] Cohort study 8 country sites (Belgium, Denmark, Italy, the Netherlands, Norway, Portugal, Spain Navarre region, and Sweden) 1 October 2023 to 25 April 2024 VEBIS-EHR	65 to 79 yrs	Intervention: Vaccinated as part of the 2023/24 autumn campaign with monovalent XBB.1.5 vaccine Comparator: Not vaccinated as part of the 2023/24 autumn campaign but with primary series of vaccination completed previously	Hospitalisation (Random effects meta-analysis) (aHR)	1 October 2023 to 25 November 2023 period VE: 64 (55 to 72) 14 to 89 days PV
				1 November 2023 to 26 December 2023 period VE: 61 (52 to 69) 14 to 89 days PV
				1 December 2023 to 26 January 2024 period VE: 54 (50 to 58) ≥14 days PV
				1 December 2023 to 26 January 2024 period VE: 55 (50 to 60) 14 to 89 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				1 December 2023 to 26 January 2024 period VE: 57 (26 to 75) 90 to 179 days PV
				1 January 2024 to 25 February 2024 period VE: 48 (40 to 55) ≥14 days PV
				1 January 2024 to 25 February 2024 period VE: 49 (41 to 56) 14 to 89 days PV
				1 January 2024 to 25 February 2024 period VE: 41 (20 to 57) 90 to 179 days PV
				1 February 2024 to 25 March 2024 period VE: 32 (3 to 52) ≥14 days PV
				1 February 2024 to 25 March 2024 period VE: 26 (-49 to 63) 14 to 89 days PV
				1 February 2024 to 25 March 2024 period VE: 32 (3 to 53) 90 to 179 days PV
				1 March 2024 to 25 April 2024 period VE: 20 (-48 to 57) ≥14 days PV
				1 March 2024 to 25 April 2024 period

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 26 (-44 to 62) 90 to 179 days PV
	≥80 yrs			1 October 2023 to 25 November 2023 period VE: 65 (56 to 71) 14 to 89 days PV
				1 November 2023 to 26 December 2023 period VE: 59 (52 to 64) 14 to 89 days PV
				1 December 2023 to 26 January 2024 period VE: 48 (45 to 52) ≥14 days PV
				1 December 2023 to 26 January 2024 period VE: 49 (44 to 54) 14 to 89 days PV
				1 December 2023 to 26 January 2024 period VE: 42 (11 to 62) 90 to 179 days PV
				1 January 2024 to 25 February 2024 period VE: 38 (31 to 45) ≥14 days PV
				1 January 2024 to 25 February 2024 period VE: 39 (32 to 46) 14 to 89 days PV
				1 January 2024 to 25 February 2024 period VE: 39 (16 to 56)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				90 to 179 days PV
				1 February 2024 to 25 March 2024 period VE: 35 (21 to 47) ≥14 days PV
				1 February 2024 to 25 March 2024 period VE: 43 (23 to 58) 14 to 89 days PV
				1 February 2024 to 25 March 2024 period VE: 35 (6 to 55) 90 to 179 days PV
				1 March 2024 to 25 April 2024 period VE: 45 (11 to 66) ≥14 days PV
				1 March 2024 to 25 April 2024 period VE: 38 (-23 to 68) 90 to 179 days PV
Humphreys 2025a[413] Cohort study 6 study sites (Belgium, Denmark, Spain Navarre region, Portugal, Italy and Sweden) 1 October 2024 to 25 January 2025	65-79 yrs	Intervention: 2024/25 autumn COVID-19 vaccination (Mixed mRNA vaccines: BNT162b2 JN.1 accounted for 97%, Spikevax® JN.1 accounted for 2.5%, BNT162b2 KP.2 accounted for 0.5%, BNT162b2 XBB.1.5 accounted for 0.1%) Comparator: Not vaccinated during the 2024/25 autumn campaign	Hospitalisation (aHR)	VE: 60 (48 to 70) ≥14 days PV; Median 98 days PV (IQR 82 to 107)
				VE: 59 (51 to 66) 14 to 59 days PV; Median 52 days PV (IQR 45 to 58)
				VE: 59 (-13 to 85) 60 to 119 days PV; Median 99 days PV (IQR 86 to 107)
	≥80 yrs			VE: 58 (48 to 66) ≥14 days PV; Median 100 days PV (IQR 85 to 108)
				VE: 59 (52 to 65)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
VEBIS-EHR				14 to 59 days PV; Median 52 (IQR 45 to 58)
				VE: 54 (22 to 73) 60 to 119 days PV; Median 101 (IQR 87 to 107)
Humphreys 2025b[414] Cohort study 6 study sites (Belgium, Demark, Spain Navarre region, Portugal, Italy and Sweden) 1 June to 25 August 2024 VEBIS-EHR	65 to 79 yrs	Intervention: Autumn 2023 XBB.1.5 vaccine dose (BNT162b2 accounted for 98.4%, mRNA-1273 accounted for 0.8%, Novavax accounted for 0.1%, Other accounted for 0.7%) Comparato: Not vaccinated during the autumn 2023 campaign	Hospitalisation (aHR)	VE: 13 (-12 to 33) ≥14 days PV
				VE: 16 (-52 to 54) 90 to 179 days PV
				VE: 13 (-12 to 33) ≥180 days PV
	≥80 yrs			VE: 7 (-7 to 19) ≥14 days PV
				VE: 13 (-29 to 41) 90 to 179 days PV
				VE: 7 (-7 to 20) ≥180 days PV
Monge 2024[415] Cohort study 7 country sites (Belgium, Denmark, Italy, Spain Navarre region, The Netherlands, Norway, Portugal) October 2023 to November 2023	65 to 79 yrs	Intervention: XBB.1.5 monovalent vaccines (although no recorded cases of protein subunit noted in the paper; 97% recorded as mRNA XBB.1.5 BNT162b2 and 1% XBB.1.5 mRNA-1273) Comparator: Not vaccinated as part of the autumn 2023 vaccination campaign	Hospitalisation (aHR)	Fixed effects estimate VE: 68 (61 to 73) ≥2 weeks PV
				Random effects estimate VE: 67 (58 to 74) ≥2 weeks PV
	≥80 yrs			Fixed effects estimate VE: 67 (62 to 71) ≥2 weeks PV
				Random effects estimate

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
VEBIS-EHR				VE: 66 (57 to 73) ≥2 weeks PV
Ecological study				
van Werkhoven 2024[283] Screening method ecological study Netherlands 9 October to 5 December 2023 National Intensive Care Evaluation (NICE) COVID-19 database	60 to 74 yrs	Intervention: monovalent mRNA BNT162b2 XBB.1.5 vaccine Comparator: The vaccination coverage in the underlying population. The odds of vaccination among cases were compared against the odds of vaccination in the overall population.	Hospitalisation (aRR)	VE: 68 (58 to 76) from 1 to 8 weeks post-vaccination
	75 to 84 yrs			VE: 74 (69 to 78) from 1 to 8 weeks post-vaccination
	≥60 yrs			VE: 71 (67 to 74) from 1 to 8 weeks post-vaccination
	≥85 yrs			VE: 66 (56 to 74) from 1 to 8 weeks post-vaccination

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; aRR – adjusted risk ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; IQR – interquartile range; IVY – Investigating Respiratory Viruses in the Acutely Ill (IVY) Network; LTCF – long-term care facility; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; UKHSA IIS – UK Health Security Agency Immunisation Information System; VE – vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; VEBIS-EHR – Vaccine Effectiveness, Burden and Impact Studies Electronic Health Record; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; yrs – years.

*It was noted by the study authors that the estimate of VE within 0–2 days is likely subject to bias due to deferral of vaccination in individuals who were already aware of their COVID-19 positive status from home lateral flow testing and/or a healthy vaccinee effect in which those with early symptoms of COVID-19 were more unwell than controls and were less likely to be vaccinated.

†Recombinant protein subunit vaccine (VidPrevtyn Beta) was also included as an intervention in the study but as it is now withdrawn only the vaccine effectiveness estimates related to Comirnaty® mRNA bivalent Original/Omicron BA.4/5 were extracted.

Source: Supplemental search.

Table B.6 Vaccine effectiveness against intensive care unit admission among older adults from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
van Werkhoven 2024[283] Screening method ecological study Netherlands 9 October to 5 December 2023 Netherland's National Intensive Care Evaluation (NICE) COVID-19 database	≥60 yrs	Intervention: monovalent mRNA BNT162b2 XBB.1.5 vaccine Comparator: The vaccination coverage in the underlying population. The odds of vaccination among cases were compared against the odds of vaccination in the overall population.	ICU admission (RR) N=92 Vaccinated cases: 8/92 Unvaccinated cases: 84/92	VE: 73 (42 to 88) (1 to 8 weeks follow-up)

Key: CI – confidence interval; ICU – intensive care unit; mRNA – messenger ribonucleic acid; RR – risk ratio; VE – vaccine effectiveness; yrs – years.

*Case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome. Cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

Source: Supplemental search.

Table B.7 Vaccine effectiveness against mortality and composite outcomes among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Mortality				
Cohort studies				
Andersson 2024[276] Cohort Denmark, Finland and Sweden 1 October 2023 to 21 April 2024 NA	≥65 yrs	Intervention: One dose of an mRNA XBB.1.5 vaccine during the study period. Comparator: Did not receive a monovalent XBB.1.5-containing COVID-19 vaccine at baseline and continued as unvaccinated during follow-up.	Death (RR) N=236,793 ≥65 yrs Vaccinated events: 348/326,382 person-years Unvaccinated events: 1,458/322,733 person-years 65 to 74 yrs Vaccinated events: 48/172,688 person-years Unvaccinated events: 181/172,252 person-years ≥75 yrs Vaccinated events: 300/153,694 person-years Unvaccinated events: 1,277/150,481 person-years	VE: 75 (71 to 80) 1 to 24 weeks PV
	65 to 74 yrs			VE: 72 (62 to 81) 1 to 24 weeks PV
	≥75 yrs			VE: 76 (70 to 82) 1 to 24 weeks PV
Ioannou 2025[271] Cohort study US	65 to 74 yrs	Intervention: mRNA and protein subunit XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Death (RR) 65 to 74 yrs N=192,911	VE: 27 (-21 to 59) Mean 176 days (range 118 to 211)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
2 October 2023 to 10 May 2024 NA	≥75 yrs		Vaccinated events: 24/93,057.2 person-years Unvaccinated events: 33/93,054.3 person-years ≥75 yrs N=235,743 Vaccinated events: 84/114,926.9 person-years Unvaccinated events: 108/114,919.0 person-years	VE: 23 (-1 to 45) Mean 176 days (range 118 to 211)
Nunes 2024(277) Cohort Belgium, Denmark, Italy, Navarre (Spain), Norway, Portugal and Sweden 4 December 2023 to 25 February 2024 VEBIS	65 to 79 yrs	Intervention: Receipt of an XBB.1.5 (mRNA and protein subunit) vaccine during the study period. Comparator: Not yet vaccinated. The eligible population included those with primary vaccination series completed at least 180 days ago and who, in the last 90 days, had no vaccine dose administered nor documented SARS-CoV-2 infection or COVID-19 hospitalisation.	Death (aHR) 65 to 79 yrs N=14,234,785 Vaccinated events: 151/7,823,133 person-months Unvaccinated events: 247/15,614,443 person-months	VE: 58 (42 to 69) 14 to 179 days PV
				VE: 59 (41 to 72) 14 to 89 days PV
				VE: 54 (-16 to 82) 90 to 179 days PV
	≥80 yrs		≥80 yrs N=5,948,837 Vaccinated events: 389/3,432,184 person-months	VE: 48 (38 to 57) 14 to 179 days PV
				VE: 51 (42 to 59) 14 to 89 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: 547/6,451,715 person-months	VE: 9 (-86 to 56) 90 to 179 days PV
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥65 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Death (aHR) N=65,978 Vaccinated events: 50/13,346 Unvaccinated events: 607/52,632	VE: 60 (38 to 74) 7 to 209 days PV; median 155 days
Composite outcomes – COVID-19-related hospitalisation or death				
Case-control studies				
Lee 2025[278] Case-control study Canada 24 September 2023 to 1 June 2024 NA	≥65 yrs	Intervention: Two doses of mRNA XBB.1.5 vaccine Comparator: Two or more doses* of a non-XBB.1.5 vaccines ≥6 months prior to the date of SARS-CoV-2 testing.	Hospitalisation or death during period of XBB dominance (aOR) N=7,759 Vaccinated cases: NR Vaccinated controls: NR	VE: 68 (62 to 73) 0 to <3 months PV
			Hospitalisation or death during period of JN.1/KP.2 dominance (aOR) N=11,547 Vaccinated cases: NR Vaccinated controls: NR	VE: 60 (52 to 67) 0 to <3 months PV
Cohort studies				

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Fotakis 2024[279] Cohort study Italy 1 October 2023 to 31 March 2024 NA	≥60 yrs	Intervention: Received seasonal booster of XBB.1.5 vaccine (mRNA or protein subunit). Comparator: Not yet received seasonal booster dose.	Severe hospitalisation or death occurring within 28 days of positive test result (aHR) N=15,558,829 Vaccinated events: NR/13,899,381 Unvaccinated events: NR/1,659,448	VE: 60 (51 to 67) October 2023 to November 2023
			Severe hospitalisation or death occurring within 28 days of positive test result (aHR) N=15,558,829 Vaccinated events: NR/13,899,381 Unvaccinated events: NR/1,659,448	VE: 47 (43 to 51) December 2023 to January 2024
			Severe hospitalisation or death occurring within 28 days of positive test result (aHR) N=15,558,829 Vaccinated events: NR/13,899,381	VE: 36 (21 to 47) February 2024 to March 2024

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome*	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: NR/1,659,448	
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥65 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive an mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Critical illness (hospitalisation with ICU/CCU/MV or death) (aHR) N=65,978 Vaccinated events: 50/13,337 Unvaccinated events: 858/52,641	VE: 51 (34 to 64) 7 to 209 days PV; median 155 days

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; CCU – critical care unit; CI – confidence interval; COVID-19 – coronavirus disease 2019; ESKD – end stage kidney disease; ICU – intensive care unit; mRNA – messenger ribonucleic acid; MV – mechanical ventilation; NA – not applicable; PV – post vaccination; RR – risk ratio; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; VE – vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; yrs – years.

*Case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome. Cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

Source: Scott et al.[57]

Table B.8 Vaccine effectiveness against mortality or composite outcomes among older adults from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Cohort studies				
ECDC 2024a[412] Cohort study 8 country sites (Belgium, Denmark, Italy, the Netherlands, Norway, Portugal, Spain Navarre region, and Sweden) 1 October 2023 to 25 April 2024 VEBIS-EHR	65 to 79 yrs	Intervention: Vaccinated as part of the 2023/24 autumn campaign with monovalent XBB.1.5 vaccine Comparator: Not vaccinated as part of the 2023/24 autumn campaign but with primary series of vaccination completed previously	Mortality (random effects meta-analysis) (aHR)	1 October 2023 to 25 November 2023 VE 67 (43 to 81) 14 to 89 days PV
				1 November 2023 to 26 December 2023 VE: 73 (66 to 79) ≥14 days PV
				1 November 2023 to 26 December 2023 VE: 73 (66 to 80) 14 to 89 days PV
				1 December 2023 to 26 January 2024 VE: 66 (56 to 74) ≥14 days PV
				1 December 2023 to 26 January 2024 VE: 65 (55 to 73) 14 to 89 days PV
				1 January 2024 to 25 February 2024 VE: 53 (24 to 71) ≥14 days PV
				1 January 2024 to 25 February 2024 VE: 55 (28 to 72) 14 to 89 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				1 January 2024 to 25 February 2024 VE: 51 (-26 to 81) 90 to 179 days PV
				1 February 2024 to 25 March 2024 VE: 16 (-190 to 76) ≥14 days PV
				1 February 2024 to 25 March 2024 VE: 28 (-158 to 80) 90 to 179 days PV
				1 March 2024 to 25 April 2024 VE: 36 (-67 to 75) ≥14 days PV
				1 March 2024 to 25 April 2024 VE: 28 (-126 to 77) 90 to 179 days PV
	≥80 yrs			1 October 2023 to 26 November 2023 VE: 67 (41 to 81) 14 to 89 days PV
				1 November 2023 to 26 December 2023 VE: 65 (59 to 70) 14 to 89 days PV
				1 December 2023 to 26 January 2024 VE: 59 (47 to 68) ≥14 days PV
				1 December 2023 to 26 January 2024

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
				VE: 59 (17 to 68) 14 to 89 days PV
				1 December 2023 to 26 January 2024 VE: 62 (16 to 83) 90 to 179 days PV
				1 January 2024 to 25 February 2024 VE: 40 (25 to 51) ≥14 days PV
				1 January 2024 to 25 February 2024 VE: 44 (29 to 58) 14 to 89 days PV
				1 February 2024 to 25 March 2024 VE: 38 (-6 to 64) ≥14 days PV
				1 February 2024 to 25 March 2024 VE: 24 (-76 to 67) 90 to 179 days PV
				1 March 2024 to 25 April 2024 VE: 57 (-44 to 87) ≥14 days PV
				1 March 2024 to 25 April 2024 VE: 55 (-64 to 87) 90 to 179 days PV
Humphreys 2025a[413] Cohort study	65 to 79 yrs	Intervention: 2024/25 autumn COVID-19 vaccination (Mixed	Death (aHR)	VE: 78 (64 to 87) ≥14 days PV; Median 98 days PV (IQR 82 to 107)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
6 study sites (Belgium, Denmark, Spain Navarre region, Portugal, Italy and Sweden) 1 October 2024 to 25 January 2025 VEBIS-EHR		mRNA vaccines: BNT162b2 JN.1 accounted for 97%, Spikevax® JN.1 accounted for 2.5%, BNT162b2 KP.2 accounted for 0.5%, BNT162b2 XBB.1.5 accounted for 0.1%) Comparator: Not vaccinated during the 2024/25 autumn campaign		VE: 82 (68 to 90) 14 to 59 days PV; Median 52 days PV (IQR 45 to 58)
				VE: 74 (45 to 88) 60 to 119 days PV; Median 99 days PV (IQR 86 to 107)
	≥80 yrs			VE: 62 (32 to 79) ≥14 days PV; Median 100 days PV (IQR 85 to 108)
				VE: 60 (31 to 77) 14 to 59 days PV; Median 52 days PV (IQR 45 to 58)
				VE: 69 (40 to 84) 60 to 119 days PV; Median 100 days PV (IQR 87 to 107)
Humphreys 2025b[414] Cohort study 6 study sites (Belgium, Demark, Spain Navarre region, Portugal, Italy and Sweden) 1 June to 25 August 2024 VEBIS-EHR	65 to 79 yrs	Intervention: Autumn 2023 XBB.1.5 vaccine dose (BNT162b2 accounted for 98.4%, mRNA-1273 accounted for 0.8%, Novavax accounted for 0.1%, Other accounted for 0.7%) Comparator: Not vaccinated during the autumn 2023 campaign	Deaths (aHR)	VE: 39 (-7 to 65) ≥14 days PV
				VE: 38 (-12 to 65) ≥180 days PV
	≥80 yrs			VE: 3 (-21 to 23) ≥14 days PV
				VE: 37 (-23 to 68) 90 to 179 days PV
				VE: 3 (-23 to 23) ≥180 days PV
Monge 2024[415] Cohort study 5 country sites (Denmark, Italy, Spain	65 to 79 yrs	Intervention: XBB.1.5 monovalent vaccines (although no recorded cases of protein subunit noted in the paper; 97%	Death (aHR)	Fixed effects estimate VE: 67 (42 to 81) ≥2 weeks PV
				Random effects estimate

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Navarre region, Norway, Portugal) October 2023 to November 2023 VEBIS-EHR		recorded as mRNA XBB.1.5 BNT162b2 and 1% XBB.1.5 mRNA-1273) Comparator: Not vaccinated as part of the autumn 2023 vaccination campaign		VE: 67 (42 to 81) ≥2 weeks PV
	≥80 yrs			Fixed effects estimate VE: 71 (58 to 81) ≥2 weeks PV
				Random effects estimate VE: 72 (51 to 85) ≥2 weeks PV

Key: aHR – adjusted hazard ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; VE – vaccine effectiveness; VEBIS-EHR – Vaccine Effectiveness, Burden and Impact Studies Electronic Health Record; yrs – years.
Source: Supplemental search.

Immunocompromising conditions

Table B.9 Vaccine effectiveness against medically attended infection among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Case-control studies[†]				
Caffrey 2024[(266)] Case-control study US 25 September 2023 to 31 January 2024 NA	≥18 yrs Immunocompromised status defined using an algorithm modified slightly from that described in a landmark study from Greenberg et al.[(416)]	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history.	ED or UC visit (without subsequent hospital admission) N=21,762 Vaccinated cases: NR/3,236 Vaccinated controls: NR/18,526	VE: 34 (22 to 45) Median 52 days PV (IQR 35 to 74)
			Outpatient visit (without a subsequent ED/UC visit or hospital admission) N=8,125 Vaccinated cases: NR/977	VE: 40 (19 to 55) Median 54 days PV (IQR 35 to 77)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Vaccinated controls: NR/7,148	
Cohort studies‡				
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD and one or more additional IC*	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Medically attended infection§ N=34,076 Vaccinated events: 265/ 6,451 Unvaccinated events: 2,219/ 27,625	VE: 31 (19 to 41) 7 to 209 days PV; median 152 days
			Medically attended infection§ N=NR Vaccinated events: 91/612 Unvaccinated events: NR/NR	VE: 50 (35 to 62) 7 to 59 days PV; median 53 days
			Medically attended infection§ N=NR Vaccinated events: 174/5,839 Unvaccinated events: NR/NR	VE: 14 (-5 to 29) 60 to 209 days PV; median 104 days

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
	18 to 64 yrs with ESKD and one or more additional IC*		Medically attended infection§ N=12,076 Vaccinated events: 58/1,301 Unvaccinated events: 736/10,775	VE: 27 (6 to 44) 7 to 209 days PV; median 135 days
	≥65 yrs with ESKD and one or more additional IC* *Defined as having had at least two encounters within 183 days before the index date for one or more of the following conditions: haematologic malignancy, other intrinsic immune conditions or immunodeficiency, solid malignancy, transplant or rheumatologic and or inflammatory disorders.		Medically attended infection§ N=22,000 Vaccinated events: 207/ 5,150 Unvaccinated events: 1,483/16,850	VE: 32 (21 to 42) 7 to 209 days PV; median 153 days
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	≥18 yrs Immunocompromise defined as those with cancer, with primary immunodeficiency, with human immunodeficiency virus (HIV), who have received an organ or a stem	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Medically attended infection (including hospital admissions, ED/UC visits, doctor's office visits and telemedicine visits).	VE: 21 (18 to 24) Median 84 days (IQR 58 to 101)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
	cell transplant, or who are taking drugs that suppress the immune response (within 365 days prior to the index).		N=472,980 Vaccinated events: 4,583/236,490 Unvaccinated events: 4,685/236,490	

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; ED – emergency department; ESKD – end stage kidney disease; IC – immunocompromising condition; ICU – intensive care unit; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; UC – urgent care; VE – vaccine effectiveness; yrs – years.

[†]For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome.

[‡]For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

[§]Defined as having at least one facility claim with COVID-19 diagnosis code or at least two professional claims with COVID-19 diagnosis code on two distinct dates within 21 dates of each other.

Source: Scott et al.[57]

Table B.10 Vaccine effectiveness to prevent hospitalisation among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Case-control studies[†]				
Caffrey 2024[(266)] Case-control study US 25 September 2023 to 31 January 2024 NA	≥18 yrs Immunocompromised status defined using an algorithm modified slightly from that described in a landmark study from Greenberg et al.[(416)]	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history.	Hospitalisation (aOR) N= 10,422 Vaccinated cases: NR/1,507 Vaccinated controls: NR/8,915	VE: 33 (16 to 47) Median 52 days PV (IQR 33 to 73)
Link-Gelles 2024a[(280)] Case-control study US September 2023 to February 2024 VISION	≥18 yrs IC defined using ICD-10 discharge codes for haematological malignancy, solid malignancy, transplant, rheumatologic/inflammatory disorders, other intrinsic immune condition or immunodeficiency.	Intervention: Receipt of 2023-2024 monovalent XBB.1.5 vaccine. Comparator: Have not received the 2023-2024 monovalent XBB.1.5 vaccine, irrespective of the number of previous COVID-19 vaccine doses received (if any).	Hospitalisation (aOR) N=NR Vaccinated cases: 100/ NR Vaccinated controls: 1,281/NR	VE: 38 (23 to 50) 7 to 59 days PV; median 34 days (IQR 21 to 46)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Hospitalisation (aOR) N=NR Vaccinated cases: 95/NR Vaccinated controls: 1,120/NR	VE: 34 (16 to 47) 60 to 119 days PV; median 83 days (IQR 71 to 98)
			Hospitalisation (aOR) N=14,586 Vaccinated cases: 195/1,392 Vaccinated controls: 2,401/13,194	VE: 36 (25 to 46) 7 to 119 days PV; median 56 days (IQR 32 to 81)
Link-Gelles 2025a[264] Case-control study US	≥65 yrs IC defined using ICD-10 discharge codes for haematological malignancy, solid malignancy,	Intervention: Receipt of the 2024-2025 mRNA KP.2 or protein subunit JN.1 (receipt ≥7 days before the encounter index date).	Hospitalisation (aOR) N=8,192 Vaccinated cases: 74/ 598	VE: 40 (21 to 54) 7 to 119 days PV; median 53 days (IQR 31 to 78)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
1 September 2024 to 21 January 2025 VISION	transplant, rheumatologic/inflammatory disorders, other intrinsic immune condition or immunodeficiency).	Comparator: Did not receive the 2024-2025 mRNA KP.2 or protein subunit JN.1 vaccine, regardless of prior COVID-19 vaccination history.	Vaccinated controls: 1,709/ 7,594	
Link-Gelles 2025b[269] Case-control study US 21 September 2023 to 22 August 2024 VISION	≥18 yrs IC defined using ICD-10 discharge codes for haematological malignancy, solid organ malignancy, transplant, rheumatologic/inflammatory disorders, HIV/AIDS and other intrinsic immune condition or immunodeficiency.	Intervention: mRNA or protein subunit XBB.1.5 (excluded if individual received >1 dose). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine (including unvaccinated persons and those who received original monovalent or bivalent COVID-19 vaccines).	Hospitalisation (aOR) N=33,524 Vaccinated cases: 594/2,547 Vaccinated controls: 8,321 /30,977	VE: 20 (12 to 28) 7 to 299 days PV; median 125 days (IQR 66 to 195)
			Hospitalisation (aOR) N=NR Vaccinated cases: 135/NR Vaccinated controls: 1,848/NR	VE: 39 (26 to 49) 7 to 59 days PV; median 34 days (IQR 21 to 46)
			Hospitalisation	VE: 25 (11 to 37)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			(aOR) N=NR Vaccinated cases: 158/NR Vaccinated controls: 2,139/NR	60 to 119 days PV; median 89 days (IQR 74 to 105)
			Hospitalisation (aOR) N=NR Vaccinated cases: 107/NR Vaccinated controls: 1,844/NR	VE: 4 (-19 to 22) 120 to 179 days PV; median 149 days (IQR 134 to 164)
			Hospitalisation (aOR) N=NR Vaccinated cases: 194/NR Vaccinated controls: 2,490/NR	VE: 2 (-16 to 18) 180 to 299 days PV; median 231 days (IQR 203 to 261)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Nguyen 2025[274] Case-control study Nine sites across Belgium, Germany, Italy, and Spain 2 October 2023 to 2 April 2024 id.DRIVE‡	≥18 yrs Outcome reported for those with immunodeficiency or cancer as a composite variable.	Intervention: mRNA XBB.1.5 vaccine (at least one dose, regardless of prior COVID-19 vaccine history). Patients who received the vaccination within 14 days prior to SARI symptom onset or ≤12 weeks after receipt of any other COVID-19 vaccine were excluded from the analyses. Comparator: Patients who had not been vaccinated with any COVID-19 vaccine during the 2023–2024 season.	Hospitalisation (aOR) N= 278 Vaccinated cases: 24 /72 Vaccinated controls: 109/206	VE: 56 (23 to 75) Median 58 days PV (IQR 41 to 71)
Cohort studies§				
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD and one or more additional IC*	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine).	Hospitalisation (aHR) N=34,076 Vaccinated events: 141/6,525	VE: 43 (28 to 54) 7 to 209 days PV; median 152 days

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
		Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Unvaccinated events: 1,295/27,551	
			Hospitalisation (aHR) N=NR Vaccinated events: 50/586 Unvaccinated events: NR/NR	VE: 57 (39 to 70) 7 to 59 days PV; median 53 days
			Hospitalisation (aHR) N=NR Vaccinated events: 91/5,939 Unvaccinated events: NR/NR	VE: 30 (8 to 47) 60 to 209 days PV; median 104 days
	18 to 64 yrs with ESKD and one or more additional IC*		Hospitalisation (aHR) N=12,076 Vaccinated events: 35/1,329	VE: 31 (1 to 52) 7 to 209 days PV; median 138 days

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: 394/10,747	
	≥65 yrs with ESKD and one or more additional IC* *Defined as having had at least two encounters within 183 days before the index date for one or more of the following conditions: haematologic malignancy, other intrinsic immune conditions or immunodeficiency, solid malignancy, transplant or rheumatologic and or inflammatory disorders.		Hospitalisation (aHR) N=22,000 Vaccinated events: 106/5,196 Unvaccinated events: 901/16,804	VE: 45 (33 to 56) 7 to 209 days PV; median 155 days
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	≥18 yrs Immunocompromise defined as those with cancer, with primary immunodeficiency, with human immunodeficiency virus (HIV), who have	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Hospitalisation (aHR) N=472,980 Vaccinated events: 474/236,490	VE: 46 (39 to 52) Median 84 days (IQR 58 to 101)

Study label Study type Country/Region Data collection date Data platform of interest	Population Definition of immunocompromised	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
	received an organ or a stem cell transplant, or who are taking drugs that suppress the immune response (within 365 days prior to the index).		Unvaccinated events: 711/236,490	

Key: aHR – adjusted hazard ratio; AIDS – acquired immune deficiency syndrome; aOR – adjusted odds ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; ED – emergency department; ESKD – end stage kidney disease; HIV – human immunodeficiency virus; IC – immunocompromising condition; ICD-10 – International Statistical Classification of Diseases and Related Health Problems 10th Revision; ICU – intensive care unit; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; SARI – severe acute respiratory infection; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; VE – vaccine effectiveness; yrs – years.

†For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome. id.DRIVE is a privately funded not-for-profit open public-private partnership.(402)

§For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

Source: Scott et al.(57)

Table B.11 Vaccine effectiveness against mortality and composite outcomes among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI)
Mortality				
Cohort studies[†]				
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD and one or more additional IC[*]	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Death (aHR) N=34,076 Vaccinated events: 27/6,575 Unvaccinated events: 339/27,501	VE: 61 (36 to 77) 7 to 209 days PV; median 153 days
			Death (aHR) N=NR Vaccinated events: <11[*]/563 Unvaccinated events: NR/NR	VE: 86 (60 to 95) 7 to 59 days PV; median 53 days
			Death (aHR) N=NR	VE: 40 (-7 to 66) 60 to 209 days PV; median 104 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI)
			Vaccinated events: 21/6,012 Unvaccinated events: NR/NR	
	18 to 64 yrs with ESKD and one or more additional IC*		Death (aHR) N=12,076 Vaccinated events: <11* events out of 1,343 Unvaccinated events: 60/10,733	VE: 60 (-7 to 66) 7 to 209 days PV; median 142 days
	≥65 yrs with ESKD and one or more additional IC* *Defined as having had at least two encounters within 183 days before the index date for one or more of the following conditions: haematologic malignancy, other intrinsic immune conditions or immunodeficiency, solid malignancy, transplant or		Death (aHR) N=22,000 Vaccinated events: 23/5,232 Unvaccinated events: 279/16,768	VE: 61 (40 to 75) 7 to 209 days PV; median 156 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI)
	rheumatologic and or inflammatory disorders.			
Composite outcome – COVID-19 critical illness				
Case-control studies‡				
Link-Gelles 2025b[269] Case-control study US 21 September 2023 to 22 August 2024 VISION	≥18 yrs IC defined using ICD-10 discharge codes for haematological malignancy, solid organ malignancy, transplant, rheumatologic/inflammatory disorders, HIV/AIDS and other intrinsic immune condition or immunodeficiency.	Intervention: mRNA or protein subunit XBB.1.5 (excluded if individual received >1 dose). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine (including unvaccinated persons and those who received original monovalent or bivalent COVID-19 vaccines).	Critical illness§ (aOR) N=23,163 Vaccinated cases: 120/ 507 Vaccinated controls: 8,321/ 22,656	VE: 40 (26 to 51) 7 to 299 days PV; median 125 days (IQR 66 to 195)
			Critical illness§ (aOR) N=NR Vaccinated cases: 28/NR Vaccinated controls: 1,848/NR	VE: 54 (32 to 69) 7 to 59 days PV; median 34 days (IQR 21 to 46)
			Critical illness§ (aOR) N=NR Vaccinated cases: 26/NR	VE: 55 (32 to 70) 60 to 119 days PV; median 89 days (IQR 74 to 105)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI)
			Vaccinated controls: 2,139/ NR	
			Critical illness§ (aOR) N=NR Vaccinated cases: 22/NR Vaccinated controls: 1,844/NR	VE: 25 (-18 to 52) 120 to 179 days PV; median 149 (IQR 134 to 164)
			Critical illness§ (aOR) N=NR Vaccinated cases: 44/NR Vaccinated controls: 2,490/NR	VE: 11 (-25 to 37) 180 to 299 days PV; median 230 days (IQR 203 to 260)
Cohort studies†				
Payne 2025(272) Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD and one or more additional IC*	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine).	Critical illness†† (aHR) N=34,076 Vaccinated events: 50/6,565	VE: 52 (30 to 66) 7 to 209 days PV; median 153 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI)
		Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Unvaccinated events: 498/27,511	
			Critical illness[††] (aHR) N=NR Vaccinated events: 15/586 Unvaccinated events: NR/NR	VE: 65 (35 to 82) 7 to 59 days PV; median 53 days
			Critical illness[††] (aHR) N=NR Vaccinated events: 35/5,997 Unvaccinated events: NR/NR	VE: 39 (5 to 61) 60 to 209 days PV; median 104 days
	18 to 64 yrs with ESKD and one or more additional IC[*]		Critical illness[††] (aHR) N=12,076 Vaccinated events: <11[*]/1,340	VE: 42 (-9 to 70) 7 to 209 days PV; median 142 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI)
			Unvaccinated events: 120/10,736	
	≥65 yrs with ESKD and one or more additional IC* *Defined as having had at least two encounters within 183 days before the index date for one or more of the following conditions: haematologic malignancy, other intrinsic immune conditions or immunodeficiency, solid malignancy, transplant or rheumatologic and or inflammatory disorders.		Critical illness†† (aHR) N=22,000 Vaccinated events: 42/5,225 Unvaccinated events: 378/16,775	VE: 54 (33 to 68) 7 to 209 days PV; median 156 days

Key: aHR – adjusted hazard ratio; AIDS – acquired immune deficiency syndrome; aOR – adjusted odds ratio; CCU – critical care unit; CI – confidence interval; COVID-19 – coronavirus disease 2019; ESKD – end stage kidney disease; HIV – human immunodeficiency virus; IC – immunocompromising condition; ICU – intensive care unit; IQR – interquartile range; mRNA – messenger ribonucleic acid; MV – mechanical ventilation; NA – not applicable; PV – post vaccination; VE – vaccine effectiveness; VISION – Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; yrs – years.

†For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

*Centers for Medicare & Medicaid Services cell suppression policy limited the minimum cell size. Vaccine effectiveness was estimated using the actual number of events

‡For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome.

[§]Defined as admission to the intensive care unit or in-hospital death.
[††]Defined as hospitalisation with ICU/CCU/MV or death.
Source: Scott et al.[57]

Underlying medical conditions

Table B.12 Vaccine effectiveness against medically attended infection among those with underlying conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population Underlying condition	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Case-control studies[†]				
Caffrey 2024[266] Case-control study US 25 September 2023 to 31 January 2024 NA	≥18 yrs Obesity	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive an XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history.	ED or UC visit (without subsequent hospital admission) (aOR) N=32,549 Vaccinated cases: NR/5,779 Vaccinated controls: NR/26,770	VE: 44 (35 to 52) Median 56 days (IQR 36 to 76)
			Outpatient visit (without a subsequent ED/UC visit or hospital admission) (aOR) N=13,048 Vaccinated cases: NR/2,299 Vaccinated controls: NR/10,749	VE: 34 (19 to 47) Median 54 days (IQR 35 to 76)
Cohort studies[‡]				
Payne 2025[272] Cohort study	≥18 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were	Medically attended infection (aHR)	VE: 43 (36 to 50)

Study label Study type Country/Region Data collection date Data platform of interest	Population Underlying condition	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
US 17 September 2023 to 13 April 2024 NA		considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive an mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	N=112,250 Vaccinated events: 90/17,852 Unvaccinated events: 1,159/94,398	7 to 209 days PV; median 150 days
			Medically attended infection (aHR) N=NR Vaccinated events: 34/1,556 Unvaccinated events: NR/NR	VE: 47 (37 to 56) 7 to 59 days PV; median 53 days
			Medically attended infection (aHR) N=NR Vaccinated events: 56/16,296 Unvaccinated events: NR/NR	VE: 40 (30 to 48) 60 to 209 days PV; median 103 days
	18 to 64 yrs with ESKD		Medically attended infection (aHR) N=46,272 Vaccinated events: 12/4,515	VE: 40 (27 to 51) 7 to 209 days PV; median 131 days

Study label Study type Country/Region Data collection date Data platform of interest	Population Underlying condition	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: 301/41,757	
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	≥18 yrs High-risk cohort*	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Medically attended infection (aHR) N=1,532,356 Vaccinated events: 13,039 /766,178 Unvaccinated events: 14,085/766,178	VE: 23 (21 to 24) Median 84 days PV (IQR 58 to 101)

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; ARI – acute respiratory infection; CDC – centers for Disease Control and Prevention; CI – confidence interval; COVID-19 – coronavirus disease 2019; ED – emergency department; ESKD – end stage kidney disease; HIV – human immunodeficiency virus; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; VE – vaccine effectiveness; UC – urgent care; yrs – years.

†For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome.

‡For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

*Underlying medical conditions associated with increased risk of severe COVID-19 outcomes, as defined by the CDC, and immunocompromised individuals, defined as individuals with cancer (based on the Deyo-Charlson comorbidity index cancer list case definition), primary immunodeficiency, HIV, who have received an organ or a stem cell transplant, or who are taking drugs that suppress the immune response (within 365 days prior to index).

Source: Scott et al.[57]

Table B.13 Vaccine effectiveness against hospitalisation among those with underlying conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
Case-control studies[†]				
Caffrey 2024[(266)] Case-control study US 25 September 2023 to 31 January 2024 NA	≥18 yrs Obesity	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history.	Hospitalisation (aOR) N=8,801 Vaccinated cases: NR/1,542 Vaccinated controls: NR/7,259	VE: 50 (36 to 61) 15 to 133 days PV Median 52 days (IQR 33 to 74) PV
Nguyen 2025[(274)] Case-control study Nine sites across Belgium, Germany, Italy, and Spain 2 October 2023 to 2 April 2024 id.DRIVE[‡]	≥18 yrs	Intervention: mRNA XBB.1.5 vaccine (at least one dose, regardless of prior COVID-19 vaccine history). Patients who received the vaccination within 14 days prior to SARI symptom onset or ≤12 weeks after receipt of any other COVID-19 vaccine were excluded from the analyses. Comparator: Patients who had not been vaccinated with any COVID-19 vaccine during the 2023–2024 season.	Hospitalisation, by type of chronic condition: asthma (aOR) N=138 Vaccinated cases: 8/20 Vaccinated controls: 61/118	VE: 56 (25 to 74) Median 61 days PV (IQR 48 to 80)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
			Hospitalisation, by type of chronic condition: Lung disease (aOR) N=509 Vaccinated cases: 45/105 Vaccinated controls: 243/404	VE: 58 (39 to 71) Median 62 days PV (IQR 46 to 76)
			Hospitalisation, by type of chronic condition: Cardiovascular disease (aOR) N=633 Vaccinated cases: 64/148	VE: 64 (46 to 76) Median 64 days PV (IQR 48 to 79)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
			Vaccinated controls: 318/485	
			Hospitalisation, by type of chronic condition: Hypertension (aOR) N=910 Vaccinated cases: 88/198 Vaccinated controls: 439/712	VE: 56 (41 to 67) Median 64 days PV (IQR 49 to 79)
			Hospitalisation, by type of chronic condition: Chronic liver disease (aOR) N=220	VE: 43 (-8 to 70) Median 63 days PV (IQR 48 to 76)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
			Vaccinated cases: 27/58 Vaccinated controls: 107/162	
			Hospitalisation, by type of chronic condition: Renal disease (aOR) N=92 Vaccinated cases: 7/22 Vaccinated controls: 32/70	VE: 66 (50 to 77) Median 66 days PV (IQR 52 to 81)
			Hospitalisation, by type of chronic condition: type 2 diabetes (aOR) N= 404	VE: 43 (-5 to 69) Median 63 days PV (IQR 46 to 78)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
			Vaccinated cases: 45/89 Vaccinated controls: 202/315	
Cohort studies[§]				
Payne 2025[(272)] Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Hospitalisation (aHR) N=33,906 Vaccinated events: 256/17,749 Unvaccinated events: 3,349/94,501	VE: 50 (42 to 58) 7 to 209 days PV; median 151 days
			Hospitalisation (aHR) N=NR Vaccinated events: 98/1,592 Unvaccinated events: NR/NR	VE: 55 (42 to 65) 7 to 59 days PV; median 53 days
			Hospitalisation	VE: 47 (35 to 57)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
			(aHR) N=NR Vaccinated events: 158/16,157 Unvaccinated events: NR/NR	60 to 209 days PV; median 103 days
	18 to 64 yrs with ESKD		Hospitalisation (aHR) N=46,272 Vaccinated events: 36/4,488 Unvaccinated events: 968/41,784	VE: 41 (23 to 55) 7 to 209 days PV; median 135 days
Wilson 2025 [267] Cohort study US 12 September 2023 to 26 January 2024 NA	≥18 yrs High-risk cohort*	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Hospitalisation (aHR) N=1,532,356 Vaccinated events: 1173/766,178	VE: 48 (46 to 53) Median 84 days PV (IQR 58 to 101)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
			Unvaccinated events: 1,969/766,178	

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; ARI – acute respiratory infection; CDC – Centers for Disease Control and Prevention; CI – confidence interval; COVID-19 – coronavirus disease 2019; ESKD – end stage kidney disease; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; SARI – severe acute respiratory infection; VE – vaccine effectiveness; yrs – years.

†For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome. ‡id.DRIVE is a privately funded not-for-profit open public-private partnership.(402)

§For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

*Underlying medical conditions associated with increased risk of severe COVID-19 outcomes, as defined by the CDC, and immunocompromised individuals, defined as individuals with cancer (based on the Deyo-Charlson comorbidity index cancer list case definition), primary immunodeficiency, HIV, who have received an organ or a stem cell transplant, or who are taking drugs that suppress the immune response (within 365 days prior to index)

Source: Scott et al.(57)

Table B.14 Vaccine effectiveness against hospitalisation among those with underlying conditions from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination
Kirsebom 2024a[406] Case-control study England 4 September 2023 to 21 January 2024 UKHSA IIS	18 to 64 yrs and within a clinical risk group*	Intervention: mRNA monovalent XBB.1.5 vaccines (BNT162b2 and mRNA-1273) and mRNA bivalent Original/Omicron BA.4/5 Comparator: No autumn 2023 COVID-19 vaccination	Hospitalisation (aOR)	VE: 63 (47 to 74)¥ 0 to 2 days PV
				VE: 34 (19 to 46) 3 to 8 days PV
				VE: 41 (26 to 53) 9 to 13 days PV
				VE: 50 (42 to 56) 2 to 4 weeks PV
				VE: 46 (39 to 52) 5 to 9 weeks PV
				VE: 36 (27 to 43) 10 to 14 weeks PV
				VE: 13 (-17 to 35) ≥15 weeks PV

Key: aOR – adjusted odds ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; ESKD – end stage kidney disease; LTCF – long-term care facility; mRNA – messenger ribonucleic acid; PV – post vaccination; UKHSA – UK Health Security Agency; UKHSA IIS – UK Health Security Agency Immunisation Information System; VE – vaccine effectiveness; yrs – years.

*Clinical risk groups as defined in tables 3 and 4 of the UKHSA Green Book COVID-19 chapter and include comorbidities, pregnancy and residing in a LTCF

¥Noted by authors that this estimate is likely subject to bias due to deferral of vaccination in individuals who were already aware of their COVID-19 positive status from home lateral flow testing and/or a healthy vaccinee effect in which those with early symptoms of COVID-19 were more unwell than controls and were less likely to be vaccinated.

Source: Supplemental search.

Table B.15 Vaccine effectiveness against mortality among those with underlying conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
COVID-19 related mortality				
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive an mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Death (aHR) N=112,250 Vaccinated events: 52/17,865 Unvaccinated events: 737/94,385	VE: 59 (41 to 72) 7 to 209 days PV; median 151 days
			Death (aHR) N=NR Vaccinated events: 19/1,545 Unvaccinated events: NR/NR	VE: 71 (46 to 84) 7 to 59 days PV; median 53 days
			Death (aHR) N=NR	VE: 51 (24 to 69) 60 to 209 days PV; median 104 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Vaccinated events: 33/16,320 Unvaccinated events: NR/NR	
	18 to 64 yrs with ESKD		Death (aHR) N=46,272 Vaccinated events: <11*/4,519 Unvaccinated events: 130/41,753	VE: 58 (1 to 82) 7 to 209 days PV; median 135 days
COVID-19 related critical illness				
Payne 2025[272] Cohort study US 17 September 2023 to 13 April 2024 NA	≥18 yrs with ESKD	Intervention: mRNA or protein subunit XBB.1.5 (individuals were considered vaccinated 7 days after receipt of vaccine). Comparator: Did not receive an mRNA or protein subunit XBB.1.5 vaccine, regardless of prior COVID-19 vaccination history.	Critical illness† (aHR) N=112,250 Vaccinated events: 90/17,852	VE: 49 (32 to 61) 7 to 209 days PV; median 151 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: 1,159/94,398	
			Critical illness† (aHR) N=NR Vaccinated events: 34/1,556 Unvaccinated events: NR/NR	VE: 54 (29 to 71) 7 to 59 days PV; median 53 days
			Critical illness† (aHR) N=NR Vaccinated events: 56/16,296 Unvaccinated events: NR/NR	VE: 44 (21 to 61) 60 to 209 days PV; median 104 days
	18 to 64 yrs with ESKD		Critical illness† (aHR) N=46,272	VE: 39 (-3 to 64) 7 to 209 days PV; median 135 days

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
			Vaccinated events: 12/4,515 Unvaccinated events: 301/41,757	

Key: aHR – adjusted hazard ratio; CCU – critical care unit; CI – confidence interval; COVID-19 – coronavirus disease 2019; ESKD – end stage kidney disease; ICU – intensive care unit; mRNA – messenger ribonucleic acid; MV – mechanical ventilation; NA – not applicable; PV – post vaccination; VE – vaccine effectiveness; yrs – years.

Note: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

*Centers for Medicare & Medicaid Services cell suppression policy limits the minimum cell size. Vaccine effectiveness was estimated using the actual number of events.

†Defined as hospitalisation with ICU/CCU/MV or death

Source: Scott et al.[57]

Health care workers

Table B.16 Vaccine effectiveness against infection among healthcare workers from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Kirwan 2024[281] Cohort study UK October 2023 to March 2024 data from the UK SIREN study	Healthcare workers, 91% aged 35 to 64 yrs	Intervention: Monovalent XBB.1.5 or bivalent/original BA.4/5 Comparator: Waned booster from previous vaccination.	Moderate infection* (aHR) N=4,203 Vaccinated events: 88/1,412 Unvaccinated events: 175/2,791	VE: 40 (20 to 55) 6 months follow-up
		Intervention: Monovalent XBB.1.5 Comparator: Waned booster from previous vaccination.	Moderate infection* (aHR) N=3,932 Vaccinated events: 63/1,141 Unvaccinated events: 175/2,791	VE: 47 (28 to 62) 6 months follow-up
		Intervention: Bivalent/original BA.4/5 Comparator: Waned booster from previous vaccination.	Moderate infection* (aHR) N=3,071 Vaccinated events: 25/280 Unvaccinated events: 175/2,791	VE: 7 (-44 to 40) 6 months follow-up

Key: aHR – adjusted hazard ratio; CI – confidence interval; PV – post vaccination; SIREN – Sarscov2 Immunity & REinfection EvaluatioN; VE – vaccine effectiveness; yrs – years.
Note: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.
*Moderate infection was defined as COVID-19 related infection with clinically relevant symptoms such as influenza-like illness or acute respiratory illness lasting 5 or more days, or any sick leave.
Source: Scott et al.[57]

Table B.17 Vaccine effectiveness against infection among healthcare workers from the supplemental search

Study label Study type Country/Region Data collection date: Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness range % (95% CI) Time post-vaccination (PV)
Savulescu 2024[284] Cohort study 7 European countries (Estonia, Ireland, Italy, Latvia, Portugal, Romania, Spain) October 2023 to May 2024 VEBIS healthcare worker cohort	Hospital-based healthcare workers from 13 hospitals in 7 countries. N=1,305 (100%) 18-34 yrs: 264 (20%) 35-39 yrs: 144 (11%) 40-44 yrs: 190 (15%) 45-49 yrs: 229 18%) 50-54 yrs: 196 (15%) 55+ yrs: 282 (22%)	Intervention: Any COVID-19 vaccine dose during the autumn 2023 campaign (82% of the 300 vaccinated cohort received XBB.1.5 adapted vaccines, 18% received non XBB.1.5 adapted vaccines) Comparator: Unvaccinated referred to those who did not receive a vaccine dose during the autumn 2023 campaign	Symptomatic infection (aHR)	VE: 17 (-40 to 51) 7 to 149 days PV
			Any SARS-CoV-2 infection (asymptomatic or symptomatic) (aHR)	VE: 24 (-29 to 55) 7 to 59 days PV
				VE: 39 (-43 to 74) 60 to 119 days PV
				VE: -2 (-114 to 52) 120 to 149 days PV

Key: aHR – adjusted hazard ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; PV – post vaccination; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; VE – vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; yrs – years.
Source: Supplemental search.

General population aged 18 to 59 years

Table B.18 Vaccine effectiveness against medically attended infection among those in the general population aged 18 to 59 years from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case control studies[†]				
Caffrey 2024[266] Case-control study US 25 September 2023 to 31 January 2024 NA	18 to 64 yrs	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive a XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history	ED/UC visits (aOR) N=35,950 Vaccinated cases: NR/6,417 Vaccinated controls: NR/29,533	VE: 48 (37 to 57) Median 54 days PV (IQR 35 to 74)
			Outpatient (aOR) N=13,175 Vaccinated cases: NR/2,599 Vaccinated controls: NR/10,576	VE: 34 (14 to 50) Median 51 days PV (IQR 33 to 75)
Link-Gelles 2025a[264] Case-control study US 1 September 2024 to 21 January 2025	18 to 64 yrs	Intervention: mRNA KP.2 or protein subunit JN.1 (receipt ≥7 days before the encounter index date) Comparator: Did not receive a mRNA KP.2 or protein subunit JN.1 vaccine,	ED/UC visits (aOR) N=88,858 Vaccinated cases: 253/6,113	VE: 30 (20 to 39) 7 to 119 days PV

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
VISION		regardless of prior COVID-19 vaccination history.	Vaccinated controls: 5,953/82,745	
			ED/UC visits (aOR) N=NR Vaccinated cases: 134/NR Vaccinated controls: 3,379/NR	VE: 36 (23 to 46) 7 to 59 days PV
			ED/UC visits (aOR) N=NR Vaccinated cases: 119/NR Vaccinated controls: 2,574/NR	VE: 21 (5 to 35) 60 to 119 days PV
Link-Gelles 2025b[269] Case-control study US 21 September 2023 to 22 August 2024 VISION	18 to 64 yrs (without immunocompromise)	Intervention: mRNA or protein subunit XBB.1.5 (excluded if individual received >1 dose). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine (including unvaccinated persons and those who received original monovalent or bivalent COVID-19 vaccines).	ED/UC visits (aOR)* N=200,443 Vaccinated cases: 1,893/21,053 Vaccinated controls: 21,762/179,390	aVE: 22 (18 to 26) 7 to 299 days PV; median 116 days PV (59 to 187)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			ED/UC visits (aOR)* N=NR Vaccinated cases: 360/NR Vaccinated controls: 5,592/NR	aVE: 55 (49 to 59) 7 to 59 days PV; median 34 days PV (20 to 47)
			ED/UC visits (aOR)* N=NR Vaccinated cases: 436/NR Vaccinated controls: 5,849/NR	aVE: 29 (22 to 36) 60 to 119 days PV; median 88 days PV (74 to 104)
			ED/UC visits (aOR)* N=NR Vaccinated cases: 256/NR Vaccinated controls: 4,715/NR	aVE: 22 (11 to 31) 120 to 179 days PV; median 147 days PV (133 to 163)
			ED/UC visits (aOR)* N=NR	aVE: -24 (-34 to -14) 180 to 299 days PV; median 230 days PV (203 to 260)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Vaccinated cases: 841/NR Vaccinated controls: 5,606/NR	
Cohort studies‡				
Ioannou 2025[271] Cohort study US 2 October 2023 to 10 May 2024 NA	18 to 64 yrs	Intervention: mRNA and protein subunit XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	SARS-CoV-2 infection (primarily medically attended but not exclusively) (RR) N=157,266 Vaccinated events: 1,855/73,893.2 person-years Unvaccinated events: 2,016/73,804.8 person-years	VE: 9 (2 to 15) Mean 176 days PV (range 118 to 211)
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	18 to 49 yrs	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Medically attended COVID-19 infection (aHR) N=890,686 Vaccinated events: 4,980/445,343	VE: 28 (25 to 30) Median 84 days PV (IQR 58 to 101)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Unvaccinated events: 6,042/445,343	
	50 to 64 yrs		Medically attended COVID-19 infection (aHR) N=1,064,028 Vaccinated events: 8,261/532,014 Unvaccinated events: 9,146/532,014	VE: 25 (23 to 27) Median 84 days PV (IQR 58 to 101)

Key: aHR – adjusted hazard ratio; aOR – adjusted odds ratio; ARI – acute respiratory infection; aVE – adjusted vaccine effectiveness; CI – confidence interval; COVID-19 – coronavirus disease 2019; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; RR – risk ratio; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; VE – vaccine effectiveness; VISION – Virtual SARS-CoV-2, yrs – years.
†For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome.
*Adjusted for age, race and ethnicity, sex, geographic region and calendar time.
‡For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.
Source: Scott et al.[57]

Table B.19 Vaccine effectiveness against medically attended infection among those in the general population aged 18 to 59 yrs from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control studies				
DeCuir 2024[398] Case-control study US September 2023 to January 2024 VISION	18 to 64 yrs	Intervention: monovalent XBB.1.5 vaccine (mixed mRNA and protein sub-unit vaccines) Comparator: Did not receive an updated vaccine dose during the 2023 vaccination period	ED/UC visits (aOR)	VE: 50 (45 to 55) 7 to 119 days PV; Median 42 days PV (IQR 24 to 62)
				VE: 52 (45 to 58) 7 to 59 days PV; Median 31 days PV (IQR 19 to 45)
				VE: 45 (34 to 55) 60 to 119 days PV; Median 73 days PV (IQR 66 to 83)
Link-Gelles 2024b[397] Case-control study US 21 September until 14 January ICATT	18 to 49 yrs	Intervention: monovalent XBB.1.5 vaccine (mixed mRNA and protein sub-unit) Comparator: Unvaccinated during the latest period (September 2023 to January 2024). Secondary analysis comparators included previous receipt of a bivalent dose and either being unvaccinated or having only received original COVID-19 vaccines.	Reporting ≥1 symptom of COVID-19 and testing positive (aOR)	VE: 57 (48 to 65) 7 to 119 days PV; median 53 days PV (IQR 30 to 74)
				VE: 64 (53 to 73) 7 to 59 days PV; median 32 days PV (IQR 19 to 46)
				VE: 48 (61 to 60) 60 to 119 days PV; median 77 days PV (IQR 67 to 89)
Skowronski 2024[396] Case-control study Canada	12 to 64 yrs	Intervention: mRNA or protein subunit XBB.1.5 vaccine.	SARS-CoV-2 infection (self-reported and	VE: 47 (7 to 70) adjusted for age group, province and calendar time. Median 5 weeks PV (IQR 3 to 8)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
29 October 2023 to 13 January 2024 Canadian Sentinel Practitioner Surveillance Network		Comparator: Did not receive an XBB.1.5 adapted vaccine.	confirmed by nucleic acid amplification test or rapid antigen test) (aOR)	
Cohort studies				
Huiberts 2024[401] Cohort study Netherlands 9 October 2023 to 9 January 2024 VAccine Study COvid-19 (VASCO)	18 to 59 yrs	Intervention: mRNA XBB.1.5 adapted vaccine. Comparator: No XBB.1.5 adapted vaccine.	SARS-CoV-2 infection (self-reported; PCR or antigen test) (aHR)	VE: 41 (23 to 56) 1 to 12 weeks PV
				VE: 40 (20 to 56) 1 to 6 weeks PV
				VE: 47 (-6 to 73) 7 to 12 weeks PV
			Symptomatic SARS-CoV-2 infections only	VE: 35 (10 to 52) 1 to 12 weeks PV

Key: aOR – adjusted odds ratio; aHR – adjusted hazard ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; ICATT – Increasing Community Access To Testing; IQR – interquartile range; mRNA – messenger ribonucleic acid; PV – post vaccination; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; VE – vaccine effectiveness; VISION – Virtual SARS-CoV-2, yrs – years.
Source: Supplemental search.

Table B.20 Vaccine effectiveness against hospitalisation among those in the general population aged 18 to 59 years from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control studies[†]				
Caffrey 2024[266] Case-control study US 25 September 2023 to 31 January 2024 NA	18 to 64 yrs	Intervention: mRNA BNT162b2 XBB.1.5 (receipt of vaccine at least 14 days before ARI encounter). Comparator: Did not receive an XBB.1.5 vaccine of any kind, regardless of prior COVID-19 vaccination history	Hospitalisation (aOR) N=5,438 Vaccinated cases: NR/1,083 Vaccinated controls: NR/4,355	VE: 58 (33 to 73) Median 50 days PV (IQR 34 to 67)
Link-Gelles 2025b[269] Case-control study US 21 September 2023 to 22 August 2024 VISION	18 to 64 yrs	Intervention: mRNA or protein subunit XBB.1.5 (excluded if individual received >1 dose). Comparator: Did not receive a mRNA or protein subunit XBB.1.5 vaccine (including unvaccinated persons and those who received original monovalent or bivalent COVID-19 vaccines).	Hospitalisation (aOR) N=35,303 Vaccinated cases: 234/2,229 Vaccinated controls: 4,015/33,074	VE: 15 (2 to 27) Overall, 7 to 299 days PV: Median 120 days PV (IQR 62 to 188)
			Hospitalisation (aOR) N=NR Vaccinated cases: 60/NR Vaccinated controls: 945/NR	VE: 31 (10 to 47) 7 to 59 days PV: Median 33 days (IQR 21 to 46)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			Hospitalisation (aOR) N=NR Vaccinated cases: 52/NR Vaccinated controls: 1,061/NR	VE: 33 (11 to 50) 60 to 119 days PV: Median 89 days (IQR 75 to 104)
			Hospitalisation (aOR) N=NR Vaccinated cases: 33/NR Vaccinated controls: 903/NR	VE: 21 (-12 to 45) 120 to 179 days PV: Median 148 days (IQR 135 to 164)
			Hospitalisation (aOR) N=NR Vaccinated cases: 89/NR Vaccinated controls: 1,106/NR	VE: -31 (-66 to -4) 180 to 299 days PV: Median 229 days (IQR 201 to 259)
Nguyen 2025[274] Case-control study Nine sites across Belgium, Germany, Italy, and Spain	18 to 64 yrs	Intervention: mRNA XBB.1.5 vaccine (at least one dose, regardless of prior COVID-19 vaccine history). Patients who received the vaccination within 14	Hospitalisation (aOR) N=314 Vaccinated cases: 9/69	VE: 57% (19 to 77) Median 56 days PV (IQR 38 to 78)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
2 October 2023 to 2 April 2024 id.DRIVE‡		days prior to SARI symptom onset or ≤12 weeks after receipt of any other COVID-19 vaccine were excluded from the analyses. Comparator: Patients who had not been vaccinated with any COVID-19 vaccine during the 2023–2024 season.	Vaccinated controls: 54/245	
Cohort studies§				
Ioannou 2025[271] Cohort study US 2 October 2023 to 10 May 2024 NA	18 to 64 yrs	Intervention: mRNA and protein subunit XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Hospitalisation (RR) N=157,266 Vaccinated events: 78/74,430.1 person-years Unvaccinated events: 110/74,416.9 person-years	VE: 30 (3 to 48) Mean 176 days PV (range 118 to 211)
Wilson 2025[267] Cohort study US 12 September 2023 to 26 January 2024 NA	18 to 49 yrs	Intervention: mRNA-1273 XBB.1.5 vaccination (from 12 September 2023 through 31 December 2023). Comparator: Did not receive a 2023-2024 COVID-19 vaccine.	Hospitalisation (aHR) N=890,686 Vaccinated events: 378/445,343 Unvaccinated events: 682/445,343	VE: 51 (45 to 57) Median 84 days PV (IQR 58 to 101)
	50 to 64 yrs		Hospitalisation	VE: 47% (42 to 52)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
			(aHR) N=1,064,028 Vaccinated events: 679/532,014 Unvaccinated events: 1,075/532,014	Median 84 days PV (IQR 58 to 101)

Key: aOR – adjusted odds ratio; aHR – adjusted hazard ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; IQR – interquartile range; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; RR – risk ratio; SARI – severe acute respiratory infection; VE – vaccine effectiveness; VISION – Virtual SARS-CoV-2, yrs – years.

†For case-control studies: Vaccinated cases refer to test-positive vaccinated persons with outcome over total test-positive persons with outcome. Vaccinated controls refer to test-negative vaccinated persons with outcome over total test-negative persons with outcome. N= total test-positive persons plus total test-negative persons with outcome.

‡id.DRIVE is a privately funded not-for-profit open public-private partnership.[402]

§For cohort studies: Vaccinated events refer to vaccinated persons with outcome over total vaccinated persons (or person-years where specified). Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.

Source: Scott et al.[57]

Table B.21 Vaccine effectiveness against hospitalisation among those in the general population aged 18 to 59 yrs from the supplemental search

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Case-control studies				
Antunes 2024b[404] Case-control study Belgium, Croatia, Ireland, Lithuania, Malta, Navarre region (Spain) and Spain 5 October 2023 to 14 January 2024 VEBIS	18 to 59 yrs	Intervention: Receipt of an XBB.1.5 (mRNA and protein subunit) vaccine after the start of the 2023 autumn vaccination campaign, at least 14 days before symptom onset. Comparator: Did not receive a vaccine during the 2023 autumn vaccination campaign and were either never vaccinated for COVID-19 or received their last COVID-19 vaccination dose at least 180 days prior to the start of the 2023 autumn vaccination campaign.	Hospitalisation (OR)	VE: 49 (-28 to 84) 14 to 105 days PV; median 47 days (IQR 34 to 63)
DeCuir 2024[398] Case-control study US September 2023 to January 2024 VISION	18 to 64 yrs	Intervention: monovalent XBB.1.5 vaccine (mixed mRNA and protein sub-unit vaccines) Comparator: Did not receive an updated vaccine dose during the 2023 vaccination period	Hospitalisation (aOR)	VE: 43 (20 to 59) 7 to 119 days PV; median 38 days PV (IQR 22 to 58)
				VE: 42 (14 to 61) 7 to 59 days PV; median 30 days PV (IQR 19 to 44)
				VE: 45 (-6 to 71) 60 to 119 days PV; median 74 days PV (IQR 67 to 81)

Key: aOR – adjusted odds ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; IQR – interquartile range; mRNA – messenger ribonucleic acid; OR – odds ratio; PV – post vaccination; VE – vaccine effectiveness; VEBIS – Vaccine Effectiveness, Burden and Impact Studies; VISION – Virtual SARS-CoV-2, yrs – years.
Source: Supplemental search.

Table B.22 Vaccine effectiveness against death among those in the general population aged 18 to 59 years from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Vaccine effectiveness % (95% CI) Time post-vaccination (PV)
Ioannou 2025[271] Cohort study US 2 October 2023 to 10 May 2024 NA	18 to 64 yrs	Intervention: mRNA and protein subunit XBB.1.5 Comparator: Did not receive an XBB.1.5 vaccine of any kind.	Death (RR) N=157,266 Vaccinated events: 1/74,451.0 person-years Unvaccinated events: 16/74,449.5 person-years	VE: 84 (21 to 100) Mean 176 days PV (range 118 to 211)

Key: CI – confidence interval; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; RR – risk ratio; VE – vaccine effectiveness.
Note: Vaccinated events refer to vaccinated persons with outcome over total vaccinated person-years. Unvaccinated events refer to unvaccinated persons with outcome over total unvaccinated persons. N = total vaccinated plus unvaccinated persons.
Source: Scott et al.[57]

Vaccine safety tables

Older adults

Table B.23 Guillain-Barré syndrome risk among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Nasreen 2025[285] Self-controlled case series 14 study sites (African COVID-19 Vaccine Safety Surveillance system, South Africa, Australia (Victoria, New South Wales), Canada (British Columbia, Ontario), Denmark, Finland, Indonesia, Republic of Korea, Spain (Catalonia, Valencia), UK 1 December 2019 to 9 August 2023 Global Vaccine Data Network	Adults ≥65 yrs	Intervention: COVID-19 mRNA vaccination. Risk period day 1 to 42 PV Comparator: Unexposed period day 43 to 64 PV	GBS	RI: 0.87 (0.52 to 1.47)
		Intervention: BNT162b2 mRNA vaccination. Risk period day 1 to 42 PV Comparator: Unexposed period day 43 to 64 PV		RI: 0.39 (0.08 to 1.80)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; GBS – Guillain-Barré syndrome; mRNA – messenger ribonucleic acid; PV – post vaccination; RI – relative incidence; yrs – years.
*Data points estimated using https://plotdigitizer.com/app.
Source: Scott et al.[57]

Table B.24 Myocarditis and pericarditis risk among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Le Vu 2024[286] Case-control study France 27 December 2020 to 30 November 2022 National Health Data (France)	≥50 yrs	Intervention exposure: BNT162b2 vaccination Control non-exposed: Unvaccinated Case: Myocarditis Control: Patients without myocarditis	Myocarditis	OR Dose 1: 1.4 (0.7 to 2.9) Dose 2: 0.84 (0.40 to 1.8) Dose 3: 2.0 (1.1 to 3.8)
		Intervention exposure: mRNA-1273 vaccination Control non-exposed: Unvaccinated Case: Myocarditis Control: Patients without myocarditis		OR Dose 1: 1.0 (0.20 to 5.3) Dose 2: 2.0 (0.46 to 8.7) Dose 3: 3 (1.2 to 7.8)
Xu 2025[287] Cohort study Sweden 27 December 2020 to 31 December 2022 Register based large scale national population study to monitor COVID-19 vaccination effectiveness and safety	Adults ≥76 yrs	Intervention: Any COVID-19 vaccine dose (mRNA vaccines included BNT162b2 and mRNA-1273, viral vector vaccine include AZD1222/ChAdOx1) Comparator: No COVID-19 vaccination	Myopericarditis* (1 to 6 weeks after vaccine dose)	HR Dose 1: 1.88 (1.28 to 2.76) Dose 2: 3.32 (2.41 to 4.67) Dose 3: 1.93 (1.08 to 3.54)
	Adults 66 to 75 yrs			HR Dose 1: 1.27 (0.87 to 1.82) Dose 2: 1.85 (1.35 to 2.57) Dose 3: 1.60 (0.02 to 2.49)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; mRNA – messenger ribonucleic acid; OR – odds ratio; yrs – years.
*Data points estimated using https://plotdigitizer.com/app.
Source: Scott et al.[57]

Table B.25 Stroke risk among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chemaitelly 2024[288] Case-control study Qatar 1 December 2020 to 11 April 2023 National Data	≥60 yrs	Intervention exposure: COVID-19 vaccination Control unexposed: No vaccination Case: Stroke Controls: control individuals without stroke	Any stroke	OR: 0.84 (0.63 to 1.12)
Xiang 2024[289] Cohort study Country: UK 8 December 2020 to 31 March 2021 UK Biobank Data and Electronic Health Records	Adults 50 to 87 yrs	Intervention: COVID-19 vaccination with one or two doses or BNT162b2 and or ChAdOx1nCoV-19 vaccines Comparator: No vaccination	Stroke resulting in hospitalisation after at least one dose of either vaccine	HR: 0.18 (0.13 to 0.25)
		Intervention: COVID-19 vaccination with one or two doses of BNT162b2 only Comparator: No vaccination		HR: 0.17 (0.11 to 0.27)
Xu 2024[290] Self-controlled case series US 1 September 2022 and 31 March 2023 Kaiser Permanente Southern California	Adults ≥65 yrs	Intervention: COVID-19 bivalent mRNA BNT162b2 vaccination. Risk interval was 1 to 42 days after vaccination Comparator: Person time outside of the risk intervals served as the control interval	Ischaemic stroke 1 to 42 days after vaccination	RI 1 to 42 days PV: 0.96 (0.79 to 1.17)
		Intervention: COVID-19 bivalent mRNA-1273 vaccination. Risk interval was 1 to 42 days after vaccination		RI 1 to 42 days PV: 0.9 (0.72 to 1.13)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
		Comparator: Person time outside of the risk intervals served as the control interval		
Xu 2025[287] Cohort study Sweden 27 December 2020 to 31 December 2022 Register based large scale national population study to monitor COVID-19 vaccination effectiveness and safety	Adults ≥76 yrs	Intervention: Any COVID-19 vaccine dose (mRNA vaccines included BNT162b2 and mRNA-1273, viral vector vaccine include AZD1222) Comparator: No COVID-19 vaccination	Stroke* (1 to 6 weeks after vaccine dose)	HR Dose 1: 0.94 (0.87 to 1.01) Dose 2: 0.93 (0.86 to 0.99) Dose 3: 0.71 (0.63 to 0.80)
	Adults 66 to 75 yrs			HR Dose 1: 0.88 (0.77 to 0.99) Dose 2: 0.88 (0.77 to 1.02) Dose 3: 0.74 (0.63 to 0.88)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; mRNA – messenger ribonucleic acid; OR – odds ratio; PV – post vaccination; RI – relative incidence; yrs – years.
*Data points estimated using https://plotdigitizer.com/app
Source: Scott et al.[57]

Table B.26 Venous thromboembolism risk among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Choi 2024[291] Self-controlled case series South Korea February to December 2021 National Health Insurance Data	Adults 65 to 74 yrs	Intervention: COVID-19 vaccination. Risk period 0 to 21 days after vaccine doses. A pre-risk period was 21 days before vaccination. Comparator: Control period ≥22 days before vaccination and 22 days after each dose	Thromboembolic events	IRR Pre-risk period: 0.42 (0.25 to 0.71) Risk period 0 to 21 days PV: 1.16 (0.53 to 1.42)
	Adults ≥75 yrs			IRR Pre-risk period: 0.38 (0.27 to 0.53) Risk period 0-21 days PV: 0.88 (0.69 to 1.13)
Xiang 2024[289] Cohort study UK 8 December 2020 to 31 March 2021 UK Biobank Data and Electronic Health Records	Adults 50 to 87 yrs	Intervention: COVID-19 vaccination with one or two doses or BNT162b2 and or ChAdOx1nCoV-19 vaccines	Venous thromboembolism resulting in hospitalisation after at least one dose of either vaccine	HR: 0.43 (0.27 to 0.67)
		Intervention: COVID-19 vaccination with one or two doses of BNT162b2 only Comparator: No vaccination		HR: 0.45 (0.27 to 0.76)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; mRNA – messenger ribonucleic acid; PV – post vaccination; IRR – incidence rate ratio; yrs – years.
*Data points estimated using https://plotdigitizer.com/app
Source: Scott et al.[57]

Table B.27 Risk of composite safety outcomes among older adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Ip 2024[292] Cohort study England 8 December 2020 to 23 January 2022 NHS England Secure Data Environment	Adults 60 to 79 yrs	Intervention: Dose 1 and 2 of mRNA BNT162b2 vaccine and booster mRNA BNT162b2 vaccine Comparator: Unvaccinated control	Composite venous outcome including pulmonary embolism, intracranial venous thrombosis, portal vein thrombosis and lower limb deep vein thrombosis	HR Week 1: 0.61 (0.51 to 0.73) Weeks 2: 0.56 (0.47 to 0.68) Weeks 3-4: 0.54 (0.47 to 0.62) Weeks 5-12: 0.46 (0.40 to 0.52) Weeks 13-24: 0.48 (0.38 to 0.59)
	Adults ≥80 yrs			HR Week 1: 0.44 (0.36 to 0.55) Weeks 2: 0.54 (0.44 to 0.65) Weeks 3-4: 0.46 (0.40 to 0.54) Weeks 5-12: 0.42 (0.37 to 0.48) Weeks 13-24: 0.35 (0.29 to 0.43)
	Adults 60 to 79 yrs	Intervention: Dose 1 and 2 of mRNA BNT162b2 vaccine and booster mRNA-1273 vaccine Comparator: Unvaccinated control		HR Weeks 1-4: 0.39 (0.28 to 0.56) Weeks 5-24: 0.44 (0.30 to 0.65)
	Adults ≥80 yrs			Weeks 1-4: 0.52 (0.30 to 0.90) Weeks 5-24: 0.31 (0.15 to 0.65)
	Adults 60 to 79 yrs	Intervention: Dose 1 and 2 of mRNA BNT162b2 vaccine and booster mRNA BNT162b2 vaccine Comparator: Unvaccinated control	Composite arterial outcome including acute myocardial infarction, ischaemic stroke, and other arterial embolism.	HR Week 1: 0.67 (0.62 to 0.73) Weeks 2: 0.79 (0.73 to 0.86) Weeks 3-4: 0.77 (0.72 to 0.82) Weeks 5-12: 0.73 (0.69 to 0.78) Weeks 13-24: 0.68 (0.61 to 0.75)
	Adults ≥80 yrs			HR Week 1: 0.65 (0.60 to 0.70)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
				Weeks 2: 0.69 (0.64 to 0.75) Weeks 3-4: 0.71 (0.67 to 0.76) Weeks 5-12: 0.68 (0.64 to 0.72) Weeks 13-24: 0.63 (0.58 to 0.68)
	Adults 60 to 79 yrs	Intervention: Dose 1 and 2 of mRNA BNT162b2 vaccine and booster mRNA-1273 vaccine Comparator: Unvaccinated control		Week 1-4: 0.70 (0.61 to 0.82) Weeks 5-24: 0.65 (0.55 to 0.78)
	Adults ≥80 yrs			HR Week 1: 0.81 (0.54 to 1.22) Weeks 2: 0.95 (0.65 to 1.40) Weeks 3-4: 0.68 (0.49 to 0.96) Weeks 5-12: 0.67 (0.51 to 0.87) Weeks 13-24: 0.94 (0.23 to 3.85)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; mRNA – messenger ribonucleic acid; yrs – years.
*Data points estimated using https://plotdigitizer.com/app.
Source: Scott et al.[57]

Immunocompromising conditions

Table B.28 Anaphylaxis risk among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chen 2024[293] Self controlled case series England December 2020 to 11 April 2022 NA	≥12 yrs with immunocompromise	Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Anaphylaxis	IRR Dose 1: 1.06 (0.59 to 1.89) Dose 2: 0.91 (0.43 to 1.95) Dose 3: 1.19 (0.48 to 2.98)
		Intervention: BNT162b2 mRNA vaccine dose. Comparator:*		IRR Dose 1: 1.47 (0.65 to 3.32) Dose 2: 1.66 (0.60 to 4.60) Dose 3: 0.87 (0.29 to 2.58)
		Intervention: mRNA-1273 mRNA vaccine dose. Comparator:*		IRR Dose 3: 6.87 (1.64 to 28.72) (Based on n=5 cases)

Key: CI – confidence interval; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; NA – not applicable; yrs – years.
Intervention risk windows were 1 to 28 days after vaccination.
*Comparator baseline period comprised >28 days prior to vaccine dose and >28 days after vaccine dose.
Source: Scott et al.[57]

Table B.29 Guillain-Barré syndrome risk among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Nasreen 2025[285] Self-controlled case series 14 study sites (African COVID-19 Vaccine Safety Surveillance system, South Africa, Australia (Victoria, New South Wales), Canada (British Columbia, Ontario), Denmark, Finland, Indonesia, Republic of Korea, Spain (Catalonia, Valencia), UK 1 December 2019 to 9 August 2023 Global Vaccine Data Network	Immunocompromised adults	Intervention: COVID-19 mRNA vaccination. Risk period day 1 to 42 PV Comparator: Unexposed period day 43 to 64 PV	GBS	RI: 0.78 (0.54 to 1.14)
Chen 2024[293] Self-controlled case series England 1 December 2020 to 11 April 2022 NA	≥12 yrs with immunocompromise	Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Risk windows were 1 to 28 days after vaccination. Comparator: baseline period comprised >28 days prior to vaccine dose and >28 days after vaccine dose	GBS	IRR Dose 1: 2.22 (0.46 to 10.73)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; GBS – Guillain-Barré syndrome; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; NA – not applicable; PV – post vaccination; RI – relative incidence; yrs – years.
Source: Scott et al.[57]

Table B.30 Myocarditis or pericarditis risk among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chen 2024[293] Self-controlled case series England 1 December 2020 to 11 April 2022 NA	≥12 yrs with immunocompromise	Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Myocarditis	IRR Dose 1: 0.43 (0.12 to 1.54) Dose 2: 0.56 (0.14 to 2.21)
			Pericarditis	IRR Dose 1: 0.62 (0.26 to 1.48) Dose 2: 0.95 (0.47 to 1.95) Dose 3: 0.91 (0.29 to 2.80)
		Intervention: mRNA vaccine BNT162b2. Comparator:*		IRR Dose 1: 0.86 (0.49 to 0.89) Dose 2: 0.95 (0.32 to 2.78) Dose 3: 0.82 (0.25 to 2.74)

Key: CI – confidence interval; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; NA – not applicable; yrs – years.
Note: Intervention risk windows were 1 to 28 days after vaccination.
*Comparator baseline period comprised >28 days prior to vaccine dose and >28 days after vaccine dose.
Source: Scott et al.[57]

Table B.31 Stroke risk among those with immunocompromising conditions from the index review

Study label Study type/Region Country Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chen 2024[293] Self-controlled case series England 1 December 2020 to 11 April 2022 NA	≥12 yrs with immunocompromise	Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Ischaemic stroke	IRR Dose 1: 0.68 (0.56 to 0.82) Dose 2: 0.83 (0.70 to 0.98) Dose 3: 0.74 (0.60 to 0.91)
		Intervention: mRNA vaccine BNT162b2. Comparator:*		IRR Dose 1: 0.68 (0.53 to 0.89) Dose 2: 0.84 (0.67 to 1.05) Dose 3: 0.75 (0.61 to 0.93)
		Intervention: mRNA vaccine mRNA-1273. Risk windows were 1 to 28 days after vaccination. Comparator:*		IRR Dose 3: 0.48 (0.18 to 1.30)
		Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Haemorrhagic stroke	IRR Dose 1: 0.50 (0.25 to 0.98) Dose 2: 0.52 (0.28 to 0.98) Dose 3: 0.90 (0.50 to 1.63)
		Intervention: mRNA vaccine BNT162b2. Comparator:*		IRR Dose 1: 0.22 (0.07 to 0.70) Dose 2: 0.39 (0.15 to 1.00) Dose 3: 0.90 (0.49 to 1.65)
		Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Any Stroke and TIA	IRR Dose 1: 0.71 (0.59 to 0.84) Dose 2: 0.81 (0.69 to 0.96)

Study label Study type/Region Country Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
				Dose 3: 0.77 (0.63 to 0.94)
		Intervention: mRNA vaccine BNT162b2. Comparator:*		IRR Dose 1: 0.71 (0.55 to 0.91) Dose 2: 0.80 (0.64 to 1.00) Dose 3: 0.79 (0.65 to 0.96)
		Intervention: mRNA vaccine mRNA-1273. Comparator:*		IRR Dose 3: 0.51 (0.20 to 1.30)

Key: CI – confidence interval; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; NA – not applicable; TIA – transient ischemic attack; yrs – years.

Note: Intervention risk windows were 1 to 28 days after vaccination.

*Comparator baseline period comprised >28 days prior to vaccine dose and >28 days after vaccine dose.

Source: Scott et al.[57]

Table B.32 Immune thrombocytopenic purpuria risk among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chen 2024[293] Self-controlled case series England 1 December 2020 to 11 April 2022 NA	≥12 yrs with immunocompromise	Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Immune thrombocytopenic purpuria	IRR Dose 1: 1.17 (0.81 to 1.68) Dose 2: 0.97 (0.67 to 1.39) Dose 3: 1.24 (0.79 to 1.95)
		Intervention: mRNA vaccine BNT162b2. Comparator:*		IRR Dose 1: 1.03 (0.63 to 1.71) Dose 2: 1.04 (0.66 to 1.66) Dose 3: 1.14 (0.72 to 1.82)

Key: CI – confidence interval; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; NA – not applicable; yrs – years.
Note: Intervention risk windows were 1 to 28 days after vaccination.
*Comparator baseline period comprised >28 days prior to vaccine dose and >28 days after vaccine dose.
Source: Scott et al.[57]

Table B.33 Venous thromboembolism risk among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chen 2024[293] Self-controlled case series England 1 December 2020 to 11 April 2022 NA	≥12 yrs with immunocompromise	Intervention: mRNA vaccine (BNT162b2, mRNA-1273) or adenoviral vector vaccine (ChAdOx1). Comparator:*	Venous Thromboembolism	IRR Dose 1: 0.74 (0.63 to 0.87) Dose 2: 0.72 (0.60 to 0.86) Dose 3: 0.70 (0.56 to 0.87)
		Intervention: mRNA vaccine BNT162b2. Comparator:*		IRR Dose 1: 0.66 (0.53 to 0.84) Dose 2: 0.61 (0.47 to 0.78) Dose 3: 0.70 (0.56 to 0.87)
		Intervention: mRNA vaccine mRNA-1273. Comparator:*		IRR Dose 3: 0.66 (0.29 to 1.54)

Key: CI – confidence interval; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; NA – not applicable; yrs – years.
Note: Intervention risk windows were 1 to 28 days after vaccination.
*Comparator baseline period comprised >28 days prior to vaccine dose and >28 days after vaccine dose.
Source: Scott et al.[57]

Table B.34 Immune-related adverse events among those with immunocompromising conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Fabbri 2025[294] Cohort study US 27 November 2021 to 31 March 2024 National Drug Agency	Patients with advanced non-small cell lung cancer Mean age 68.8 yrs (SD 8.4)	Intervention: mRNA bivalent booster vaccination Comparator: No booster vaccination	Immune-related adverse events	HR Any Grade: 0.91 (0.43 to 1.91) Grade 1-2: 0.60 (0.27 to 1.37) Grade 3: 4.16 (0.81 to 21.33)

Key: CI – confidence interval; HR – hazard ratio; mRNA – messenger ribonucleic acid; NA – not applicable; yrs – years.
Source: Scott et al.[57]

Underlying medical conditions

Table B.35 Guillain-Barré syndrome risk among those with underlying medical conditions adults from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Guillain-Barré syndrome				
Nasreen 2025[285] Self-controlled case series 14 study sites (African COVID-19 Vaccine Safety Surveillance system, South Africa, Australia (Victoria, New South Wales), Canada (British Columbia, Ontario), Denmark, Finland, Indonesia, Republic of Korea, Spain (Catalonia, Valencia), UK 1 December 2019 to 9 August 2023 Global Vaccine Data Network	Adults with a comorbidity	Intervention: COVID-19 mRNA vaccination. Risk period day 1 to 42 PV Comparator: Unexposed period day 43 to 64 PV	GBS	RI: 0.85 (0.55 to 1.32)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; GBS – Guillain-Barré syndrome; mRNA – messenger ribonucleic acid; RI – relative incidence.

Source: Scott et al.[57]

Table B.36 Stroke risk among adults with underlying medical conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Stroke				
Byoun 2024[295] Cohort study South Korea Not specified, patients experienced health events during 2021. Health Insurance Data	Patients with Moyamoya disease	Intervention: Any COVID-19 vaccine (mRNA vaccines BNT162b2 and mRNA-1273, adenoviral vector vaccine ChAdOx1 nCoV-19, viral vector vaccine Jcovden®, and protein subunit vaccine Novavax) Comparator: No vaccination	Stroke-related hospital admission	OR: 0.17 (0.13 to 0.22)
Chemaitelly 2024[288] Case-control study Qatar 1 December 2020 to 11 April 2023 National Data	Those with 1 coexisting condition*	Intervention exposure: COVID-19 vaccination (mRNA vaccines BNT162b2, mRNA-1273, and bivalent mRNA 1273.214, adenoviral vector vaccine ChAdOx1 nCoV-19) Control unexposed: No vaccination Case: Stroke Controls: control individuals without stroke	Any stroke	OR: 0.93 (0.61 to 1.42)
	Those with 2 coexisting conditions*			OR: 0.84 (0.55 to 1.27)
	Those with 3 coexisting conditions*			OR: 0.64 (0.47 to 0.88)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; OR – odds ratio.
*Coexisting conditions included 39 classifications of conditions and included any factors influencing health status and contact with health services.
Source: Scott et al.[57]

Table B.37 Thromboembolic events among those with underlying medical conditions from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Choi 2024[291] Self-controlled case series South Korea February to December 2021 National Health Insurance Data	≥12 yrs with a diagnosis of atrial fibrillation/flutter	Intervention: COVID-19 vaccination (mRNA vaccines BNT162b2 or mRNA-1273, or viral vector vaccines ChAdOx1 nCoV-19 or Ad.26.COV2.S).* Comparator: *	Thromboembolic events	IRR Pre-risk period: 0.38 (0.29 to 0.50) Risk period 0 to 21 days PV: 0.93 (0.77 to 1.12)
		Intervention: COVID-19 vaccination with mRNA vaccine BNT162b2. * Comparator: *		IRR Pre-risk period: 0.38 (0.26 to 0.54) Risk period 0 to 21 days PV: 0.74 (0.56 to 0.97)
		Intervention: COVID-19 vaccination with mRNA vaccines mRNA-1273. * Comparator: *		IRR Pre-risk period: 1.15 (0.37 to 3.58) Risk period 0 to 21 days PV: 1.17 (0.35 to 3.85) Based on <5 cases

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; IRR – incidence rate ratio; mRNA – messenger ribonucleic acid; OR – odds ratio; yrs – years.

*Intervention: risk period 0 to 21 days after vaccine doses; pre-risk period was 21 days before vaccination. Comparator: Control period ≥22 days before vaccination and 22 days after each dose.

Source: Scott et al.[57]

Pregnant individuals

Table B.38 Risk of stillbirth or foetal loss among pregnant populations from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Spontaneous abortion, stillbirths or other mortality outcomes					
Sheth 2025[296] Case-control study US 19 January 2021 to 27 October 2021 Vaccine Safety Datalink	Pregnant patients aged 16 to 49 yrs	Intervention exposure: All COVID-19 vaccines approved for use in the US, received during pregnancy. Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Spontaneous abortion Control: Live births	Spontaneous abortion† (foetal loss between 6 and less than 20 weeks of gestation)	SAB: 17/296 Live birth: 105/592	aOR: 0.85 (0.56 to 1.30)
		Intervention exposure: BNT162b2 vaccine only during pregnancy. Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Spontaneous abortion Control: Live births		SAB: 26/275 Live birth: 59/546	aOR 0.97 (0.57 to 1.66)
		Intervention exposure: mRNA-1273 vaccine only received during pregnancy. Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Spontaneous abortion. Control: Live births		SAB: 18/267 Live birth: 40/527	aOR: 0.59 (0.29 to 1.19)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Denoble 2024(297) Case-control study US 14 February 2021 to 27 February 2022 Vaccine Safety Datalink	Pregnant patients aged 16 to 49 yrs	Intervention exposure: All COVID-19 vaccines approved for use in the US, received during pregnancy. Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Stillbirths Control: Live births	Stillbirth‡	Stillbirths: 106/276 Live births: 323/822	aOR: 1.02 (0.76 to 1.37)
		Intervention exposure: Janssen vaccine (viral vector vaccine) received during pregnancy. Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Stillbirths Control: Live births		Stillbirths: 7/276 Live births: 15/822	Not estimable due to small sample size
		Intervention exposure: mRNA-1273 (mRNA) vaccine received during pregnancy. Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Stillbirths Control: Live births		Stillbirths: 39/276 Live births: 114/822	aOR: 1.00 (0.69 to 1.43)
		Intervention exposure: BNT162b2 (mRNA) vaccine received during pregnancy.		Stillbirths: 60/276 Livebirths: 194/822	aOR: 1.00 (0.69 to 1.43)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		Comparator non-exposed: No COVID-19 vaccination during pregnancy Case: Stillbirths Control: Live births			
Mensah 2024[298] Case-control study England 16 April 2021 to 31 March 2022 Maternity Services Data Set (MSDS) antenatal booking records linked to Hospital Episodes Statistics database and National Immunisation Management System (NIMS)	Pregnant individuals aged 18 to 50 yrs	Intervention exposure: COVID-19 vaccine at least one dose received during pregnancy. Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (Stillbirth, neonatal and perinatal deaths) Control: Did not experience the outcome of interest	Stillbirth§	Stillbirths: 401/1848 Livebirths: 1717/7254	OR: 0.90 (0.76 to 1.07)
			Neonatal deaths**	Deaths: 110/506 Alive: 413/2043	OR: 1.27 (0.91 to 1.77)
			Perinatal deaths**	Deaths: 422/1872 Alive: 1686/7337	OR: 0.98 (0.83 to 1.16)
		Intervention exposure: BNT162b2 vaccination during pregnancy Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (Stillbirth, neonatal and perinatal deaths). Control: Did not experience the outcome of interest	Stillbirth§	Stillbirths: 256/1620 Live births: 1164/6344	OR: 0.85 (0.69 to 1.05)
			Neonatal deaths**	Deaths: 76/438 Alive: 260/1802	OR: 1.32 (0.89 to 1.97)
			Perinatal deaths**	Deaths: 276/1872 Alive: 1117/7337	OR: 0.94 (0.78 to 1.14)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		Intervention exposure: mRNA-1273 vaccination during pregnancy. Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (Stillbirth, neonatal and perinatal deaths). Control: Did not experience the outcome of interest	Stillbirth§	Stillbirths: 92/1620 Livebirths: 375/6344	OR: 0.97 (0.71 to 1.32)
			Neonatal deaths**	Deaths: 26/438 Alive: 104/1802	OR: 1.37 (0.76 to 2.48)
			Perinatal deaths**	Deaths: 98/1872 Alive: 389/7337	OR: 1.12 (0.84 to 1.49)
		Intervention exposure: ChAdOx1-S vaccination during pregnancy Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (Stillbirth, neonatal and perinatal deaths). Control: Did not experience the outcome of interest	Stillbirth§	Stillbirths: 53/1620 Livebirths: 177/6344	OR: 0.98 (0.64 to 1.50)
			Neonatal deaths**	Deaths: 8/438 Alive: 49/1802	OR: 0.88 (0.32 to 2.40)
			Perinatal deaths**	Deaths: 48/1872 Alive: 180/7337	OR: 1.08 (0.71 to 1.63)
Suseeladevi 2024(299) Cohort study England 25 May 2021 to 28 October 2022	Pregnant individuals aged 18 to 45 yrs	Intervention: COVID-19 vaccination (viral vector vaccine ChAdOx1-S and mRNA vaccine BNT162b2) received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Stillbirth††	Vaccinated: 115/53,060 Unvaccinated: 375/133,405	HR: 0.86 (0.67 to 1.10)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
EHR data within National Health Service England Secure Data Environment		Intervention: COVID-19 vaccination with viral vector vaccine ChAdOx1-S received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination		Vaccinated: 65/24,490 Unvaccinated: 375/133,405	HR: 1.02 (0.75 to 1.38)
		Intervention: COVID-19 vaccination with mRNA vaccine BNT162b2 received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination		Vaccinated: 50/27,760 Unvaccinated: 375/133,405	HR: 0.72 (0.52 to 1)
Tamir-Hostovsky 2024[300] Case-control study Israel May 2020 to October 2021 NA	Preterm infants born between 24 and <35 wGA and admitted to NICU	Intervention: mRNA BNT162b2 vaccination during pregnancy. Comparator: no COVID-19 vaccination during pregnancy matched controls	Death before discharge	Vaccinated: 1/78 Unvaccinated: 2/78	NR

Key: aOR – adjusted odds ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; ICU – intensive care unit; mRNA – messenger ribonucleic acid; n – number of events; N – total denominator; NA – not applicable; NICU – neonatal intensive care unit; NR – not reported; OR – odds ratio; SAB – spontaneous abortion; wGA – weeks' gestational age; yrs – years.

Notes:

*For case control studies presented groups sizes by outcome status (yes, no); for cohort studies presented groups sizes by exposure status (vaccinated, unvaccinated)

†Adjusted using study week and maternal age as cubic splines, and race and ethnicity and neighbourhood poverty as main effects.

‡Adjusted for study week, maternal age, COVID-19 disease during pregnancy, race and ethnicity, study site, smoking, pregestational diabetes, hypertension, and obesity.

§Stillbirths adjusted for mother's age, pregnancy gestational length, ethnicity, region, IMD, complex social factors, disability parity, gestational age at first antenatal appointment, previous adverse outcomes in pregnancy, comorbidities, healthcare worker occupation, risk of COVID-19 complication, COVID-19 infection in pregnancy.
**Neonatal deaths and perinatal deaths adjusted for mother's age, pregnancy gestational length, ethnicity, region, IMD, complex social factors, disability parity, previous adverse outcomes in pregnancy, comorbidities, healthcare worker occupation, risk of COVID-19 complication, COVID-19 infection in pregnancy
††Adjusted for maternal age, calendar month of pregnancy, ethnicity, region, level of deprivation, smoking status, parity, prior stillbirth, history of COVID-19 diagnosis, JCVI priority group and comorbidities.
Source: Scott et al.[57]

Table B.39 Risk of low birthweight, preterm birth or low Apgar scores among pregnant populations and preterm infants from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Mensah 2024[298] Case-control study England 16 April 2021 to 31 March 2022 Maternity Services Data Set (MSDS) antenatal booking records linked to Hospital Episodes Statistics database and National Immunisation Management System (NIMS)	Pregnant individuals aged 18 to 50 yrs	Intervention exposure: COVID-19 vaccine at least one dose received during pregnancy. Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (low birthweight, premature birth. Control: Did not experience the outcome of interest	Low birthweight (<2.5Kg)†	Yes: 4425/20945 No: 10705/45941	OR: 0.86 (0.79 to 0.93)
			Premature birth (<37 wGA)‡	Yes: 10815/38502 No: 31600/103783	OR: 0.89 (0.85 to 0.92)
			Low Apgar score (<7 at 5 mins)	Yes: 1080/4547 No: 5339/21208	OR: 0.89 (0.80 to 0.98)
		Intervention exposure: BNT162b2 vaccination during pregnancy. Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (low birthweight, premature birth, during perinatal period).	Low birthweight (<2.5Kg)†	Yes: 3928/20128 No: 9136/44270	OR: 0.89 (0.82 to 0.97)
			Premature birth (<37 wGA)‡	Yes: 6330/37152 No: 19179/100617	OR: 0.86 (0.83 to 0.90)
			Low Apgar score (<7 at 5 mins)	Yes: 671/4169 No: 3402/19701	OR: 0.89 (0.79 to 1.00)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		Control: Did not experience the outcome of interest			
		Intervention exposure: mRNA-1273 vaccination during pregnancy Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (low birthweight, premature birth, during perinatal period). Control: Did not experience the outcome of interest	Low birthweight (<2.5Kg)†	Yes: 1168/20128 No: 2914/44270	OR: 0.80 (0.70 to 0.92)
			Premature birth (<37 wGA)‡	Yes: 1989/37152 No: 6576/100617	OR: 0.86 (0.81 to 0.93)
			Low Apgar score (<7 at 5 mins)	Yes: 281/4169 No: 1326/19701	OR: 0.92 (0.77 to 1.08)
		Intervention exposure: ChAdOx1-S vaccination during pregnancy. Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (low birthweight, premature birth, during perinatal period).	Low birthweight (<2.5Kg)†	Yes: 1350/37152 No: 3035/100617	OR: 0.96 (0.83 to 1.10)
			Premature birth (<37 wGA)‡	Yes: 2495/37152 No: 5844/100617	OR: 0.98 (0.92 to 1.05)
			Low Apgar score (<7 at 5 mins)	Yes: 128/4169 No: 610/19701	OR: 0.86 (0.68 to 1.10)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		Control: Did not experience the outcome of interest			
Suseeladevi 2024[299] Cohort study England 25 May 2021 to 28 October 2022 EHR data within National Health Service England Secure Data Environment	Pregnant individuals aged 18 to 45 yrs	Intervention: COVID-19 vaccination (viral vector vaccine ChAdOx1-S and mRNA vaccine BNT162b2) received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Preterm§ (24 to <32 wGA)	Vaccinated: 44,15/53,060 Unvaccinated: 8,435/133,405	HR: 0.74 (0.63 to 0.88)
			Preterm§ (32 to 36 wGA)		HR: 0.98 (0.93 to 1.03)
		Intervention: COVID-19 vaccination with viral vector vaccine ChAdOx1-S received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Preterm§ (24 to <32 wGA)	Vaccinated: 2,005/24,490 Unvaccinated: 8,435/133,405	HR: 0.72 (0.58 to 0.91)
			Preterm§ (32 to 36 wGA)		HR: 1.02 (0.95 to 1.08)
		Intervention: COVID-19 vaccination with mRNA vaccine BNT162b2 received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Preterm§ (24 to <32 wGA)	Vaccinated: 2,325/27,760 Unvaccinated: 8,435/133,405	HR: 0.79 (0.65 to 0.97)
			Preterm§ (32 to 36 wGA)		HR: 0.93 (0.87 to 0.99)
		Intervention: COVID-19 vaccination (viral vector vaccine	Small for gestational age§ (24 to <32 wGA)	Vaccinated: 1,725/53,060	HR: 0.87 (0.61 to 1.25)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		ChAdOx1-S and mRNA vaccine BNT162b2) received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Small for gestational age§ (32 to 36 wGA)	Unvaccinated: 5,510/133,405	HR: 1.00 (0.80 to 1.25)
			Small for gestational age§ (>36 wGA)		HR: 0.94 (0.88 to 1.00)
		Intervention: COVID-19 vaccination with viral vector vaccine ChAdOx1-S received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Small for gestational age§ (24 to <32 wGA)	Vaccinated: 795/24,490 Unvaccinated: 5,510/133,405	HR: 0.96 (0.61 to 1.52)
			Small for gestational age§ (32 to 36 wGA)		HR: 1.05 (0.79 to 1.4)
			Small for gestational age§ (>36 wGA)		HR: 0.93 (0.85 to 1.01)
		Intervention: COVID-19 vaccination with mRNA vaccine BNT162b2 received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination	Small for gestational age§ (24 to <32 wGA)	Vaccinated: 905/27,760 Unvaccinated: 5,510/133,405	HR: 0.85 (0.53 to 1.34)
			Small for gestational age§ (32 to 36 wGA)		HR: 0.97 (0.73 to 1.3)
			Small for gestational age§ (>36 wGA)		HR: 0.93 (0.86 to 1.01)
Kim 2025[301] Cohort study South Korea 1 February 2022 and 31 December 2022	Pregnant individuals aged 20 to 49 yrs	Intervention: mRNA BNT162b2 or mRNA-1273 vaccination during pregnancy. Comparator: No COVID-19 vaccine received during pregnancy	Preterm births	Vaccinated: 55.4 (50.7 to 60.1) per 1,000 births Unvaccinated: 66.4 (63.9 to 68.9) per 1,000 births	aOR: 0.83 (0.75 to 0.91)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Korean Disease Control and Prevention Agency-COVID19-National Health Insurance data					
Hall 2025(302) Cohort study US 1 January 2021 and 31 December 2021 Department of Defense Birth and Infant Health Research programme	Pregnant US military service members	Intervention: mRNA BNT162b2, mRNA-1273 or Ad26.COV2-S (viral vector) vaccination during pregnancy. Comparator: No COVID-19 vaccine received during pregnancy	Preterm birth** (<37 wGA)	Vaccinated: 170/2867 Unvaccinated: 331/4317	HR: 1.02 (0.83 to 1.26)
			Small for gestational age** (<10th percentile)	Vaccinated: 118/2867 Unvaccinated: 175/4317	HR: 1.01 (0.78 to 1.30)
			Low birthweight** (<2500g)	Vaccinated: 131/2867 Unvaccinated: 257/4317	HR: 1.01 (0.80 to 1.28)
		Intervention: mRNA BNT162b2 vaccination during pregnancy.	Preterm birth** (<37 wGA)	Vaccinated: 110/1715 Unvaccinated: 331/4317	HR: 1.12 (0.88 to 1.42)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		Comparator: No COVID-19 vaccine received during pregnancy	Small for gestational age** (<10th percentile)	Vaccinated: 68/1715 Unvaccinated: 175/4317	HR: 0.95 (0.70 to 1.29)
			Low birthweight** (<2500g)	Vaccinated: 72/1715 Unvaccinated: 257/4317	HR: 0.90 (0.67 to 1.22)
		Intervention: mRNA-1273 vaccination during pregnancy. Comparator: No COVID-19 vaccine received during pregnancy	Preterm birth** (<37 wGA)	Vaccinated: 52/969 Unvaccinated: 331/4317	HR: 0.84 (0.60 to 1.16)
			Small for gestational age** (<10th percentile)	Vaccinated: 44/969 Unvaccinated: 175/4317	HR: 1.11 (0.76 to 1.60)
			Low birthweight**(<2500g)	Vaccinated: 53/969 Unvaccinated: 257/4317	HR: 1.14 (0.82 to 1.59)
Tamir-Hostovsky 2024[300] Case-control study Israel May 2020 to October 2021 NA	Preterm infants born between 24 and <35 wGA and admitted to NICU	Intervention: mRNA BNT162b2 vaccination during pregnancy. Comparator: no COVID-19 vaccination during pregnancy	Small for gestational age	Vaccinated: 8/78 Unvaccinated: 8/78	NR
			Apgar below 7 at 5 minutes	Vaccinated: 0/78 Unvaccinated: 3/78	NR

Key: aOR – adjusted odds ratio; CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; ICU – intensive care unit; mRNA – messenger ribonucleic acid; n – number of events; N – total denominator; NA – not applicable; NICU – neonatal intensive care unit; NR – not reported; OR – odds ratio; wGA – weeks' gestational age; yrs – years.
*For case control studies presented groups sizes by outcome status (yes, no); for cohort studies presented groups sizes by exposure status (vaccinated, unvaccinated).
†Low birthweight adjusted for mother's age, pregnancy gestational length, ethnicity, region, IMD, complex social factors, disability, parity, gestational age at first antenatal appointment, previous adverse outcomes in pregnancy, comorbidities, healthcare worker occupation, risk of COVID-19 complication, COVID-19 infection in pregnancy.
‡Premature birth adjusted for ethnicity, region, IMD, complex social factors, disability, parity, gestational age at first antenatal appointment, previous adverse outcomes in pregnancy, comorbidities, healthcare worker occupation, risk of COVID-19 complication, COVID-19 infection in pregnancy.
§Adjusted for maternal age, calendar month of pregnancy, ethnicity, region, level of deprivation, smoking status, parity, prior stillbirth, history of COVID-19 diagnosis, JCVI priority group and comorbidities.
**Adjusted estimates included SARS-CoV-2 infection in pregnancy and inverse probability of treatment weights, which balanced groups in terms of birthing parent age at conception, month of conception, race and ethnicity, marital status, military rank, military service branch, military occupation, and four pre-pregnancy comorbidities (obesity, asthma, tobacco use, SARS-CoV-2 infection).
Source: Scott et al.[57]

Table B.40 Risk of venous thromboembolism or ICU admission among pregnant populations from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Mensah 2024[298] Case-control study England 16 April 2021 to 31 March 2022 Maternity Services Data Set (MSDS) antenatal booking records linked to Hospital Episodes Statistics database and National Immunisation Management System (NIMS)	Pregnant individuals aged 18 to 50 yrs	Intervention exposure: COVID-19 vaccine at least one dose received during pregnancy. Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (venous thromboembolism, and ICU admission during perinatal period). Control: Did not experience the outcome of interest	Venous thromboembolism†	Yes: 23/295 No: 127/1446	OR: 0.82 (0.43 to 1.56)
			ICU admission‡	Yes: 924/4880 No: 5578/22973	OR: 0.85 (0.76 to 0.95)
		Intervention exposure: BNT162b2 vaccination during pregnancy Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (venous thromboembolism, and ICU admission during perinatal period). Control: Did not experience the outcome of interest	Venous thromboembolism†	Yes: 8/243 No: 84/1257	OR: 0.33 (0.11 to 0.99)
			ICU admission‡	Yes: 629/4453 No: 3647/20658	OR: 0.88 (0.77 to 1.00)
		Intervention exposure: mRNA-1273 vaccination during pregnancy	Venous thromboembolism†	Yes: 6/243 No: 20/1257	OR: 1.14 (0.34 to 3.83)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
		Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (Stillbirth, neonatal and perinatal deaths, low birthweight, premature birth, venous thromboembolism, and ICU admission during perinatal period). Control: Did not experience the outcome of interest	ICU admission‡	Yes: 159/4453 No: 1396/20658	OR: 0.65 (0.52 to 0.81)
		Intervention exposure: ChAdOx1-S vaccination during pregnancy Comparator non-exposed: Unvaccinated participants or those who received the vaccine after delivery. Case: outcomes of interest (Stillbirth, neonatal and perinatal deaths, low birthweight, premature birth, venous thromboembolism, and ICU admission during perinatal period). Control: Did not experience the outcome of interest	Venous thromboembolism†	Yes: 9/243 No: 23/1257	OR: 1.11 (0.39 to 3.18)
			ICU admission‡	Yes: 134/4453 No: 535/20658	OR: 1.11 (0.86 to 1.45)
Suseeladevi 2024[299] Cohort study England	Pregnant individuals aged 18 to 45 yrs	Intervention: COVID-19 vaccination (viral vector vaccine ChAdOx1-S and mRNA vaccine BNT162b2) received before estimated pregnancy start date.	Venous thromboembolism§	Vaccinated: 105/52,295 Unvaccinated: 195/133,630	HR: 1.27 (0.95 to 1.69)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
25 May 2021 to 28 October 2022 EHR data within National Health Service England Secure Data Environment		Comparator: No prior COVID-19 vaccination			
		Intervention: COVID-19 vaccination with viral vector vaccine ChAdOx1-S only received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination		Vaccinated: 65/24,545 Unvaccinated: 195/133,630	HR: 1.54 (1.1 to 2.16)
		Intervention: COVID-19 vaccination with mRNA vaccine BNT162b2 only received before estimated pregnancy start date. Comparator: No prior COVID-19 vaccination		Vaccinated: 40/27,935 Unvaccinated: 195/133,630	HR: 1.02 (0.7 to 1.5)
Hall 2025[302] Cohort study US 1 January 2021 and 31 December 2021 Department of Defense Birth and Infant Health Research programme	Pregnant US military service members	Intervention: mRNA BNT162b2, mRNA-1273 or Ad26.COV2-S (viral vector) vaccination during pregnancy. Comparator: No COVID-19 vaccine received during pregnancy	NICU admission** (within 28 days of birth)	Vaccinated: 224/2867 Unvaccinated: 383/4317	RR: 0.90 (0.75 to 1.07)
		Intervention: mRNA BNT162b2 vaccination during pregnancy. Comparator: No COVID-19 vaccine received during pregnancy		Vaccinated: 145/1715 Unvaccinated: 383/4317	RR: 0.99 (0.80 to 1.21)
		Intervention: mRNA-1273 vaccination during pregnancy. Comparator: No COVID-19 vaccine received during pregnancy		Vaccinated: 68/969 Unvaccinated: 383/4317	RR: 0.79 (0.60 to 1.03)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; ICU – intensive care unit; mRNA – messenger ribonucleic acid; n – number of events; N – total denominator; NICU – neonatal intensive care unit; OR – odds ratio; RR – risk ratio; yrs – years.

*For case control studies presented groups sizes by outcome status (yes, no); for cohort studies presented groups sizes by exposure status (vaccinated, unvaccinated)
†Venous thromboembolism adjusted for mother's age, pregnancy gestational length, ethnicity, risk of COVID-19 complication, parity, previous adverse outcomes in pregnancy, comorbidities.
‡ICU admission adjusted for mother's age, pregnancy gestational length, ethnicity, risk of COVID-19 complication, parity, previous adverse outcomes in pregnancy, comorbidities, previous adverse outcomes in pregnancy, region, IMD, complex social factors, disability, gestational age at first antenatal appointment, healthcare worker occupation, COVID-19 infection in pregnancy.
§Adjusted for maternal age, calendar month of pregnancy, ethnicity, region, level of deprivation, smoking status, parity, prior stillbirth, history of COVID-19 diagnosis, JCVI priority group and comorbidities.
**Adjusted estimates included SARS-CoV-2 infection in pregnancy and inverse probability of treatment weights, which balanced groups in terms of birthing parent age at conception, month of conception, race and ethnicity, marital status, military rank, military service branch, military occupation, and four pre-pregnancy comorbidities (obesity, asthma, tobacco use, SARS-CoV-2 infection).
Source: Scott et al.[57]

Table B.41 Risk of congenital anomalies of infants born to pregnant populations or preterm infants from the index review

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Jorgensen 2024[303] Cohort study Canada 16 October 2021 to 1 May 2023 Linked health administrative databases analysed at the Institute for Clinical Evaluative Sciences	Pregnant individuals aged 12 to 50 yrs	Intervention: mRNA COVID-19 vaccine received in the first trimester (BNT162b2 or mRNA-1273) Comparator: No COVID-19 vaccine before or during pregnancy	Major congenital anomalies† (medically, surgically or cosmetically significant and diagnosed during admission or ≤28 days after birth)	Vaccinated: 832/34,181 Unvaccinated: 927/34,951	Adjusted prevalence ratio: 0.89 (0.79 to 1.01)
		Intervention: mRNA BNT162b2 only received in the first trimester Comparator: No COVID-19 vaccine before or during pregnancy		Vaccinated: 587/23,345 Unvaccinated: 927/34,951	Adjusted prevalence ratio: 0.91 (0.80 to 1.04)
		Intervention: mRNA-1273 only received in the first trimester Comparator: No COVID-19 vaccine before or during pregnancy		Vaccinated: 221/10,102 Unvaccinated: 927/34,951	Adjusted prevalence ratio: 0.88 (0.65 to 1.21)
Kim 2025[301] Cohort study Canada 1 February 2022 and 31 December 2022	Pregnant individuals aged 20 to 49 yrs	Intervention: mRNA BNT162b2 and mRNA-1273 vaccination during pregnancy	Congenital malformations‡ (EUROCAT definitions)	Vaccinated: 76.1 (70.6 to 81.6) per 1,000 births	aOR: 0.95 (0.87 to 1.04)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Participant event data (n/N)*	Effect estimate (95% CI)
Korean Disease Control and Prevention Agency-COVID19-National Health Insurance data		Comparator: No COVID-19 vaccine received during pregnancy		Unvaccinated: 80.5 (77.6 to 83.4) per 1,000 births	
Tamir-Hostovsky 2024[300] Case-control study Israel May 2020 to October 2021 NA	Preterm infants born between 24 and <35 wGA and admitted to NICU	Intervention: mRNA BNT162b2 vaccination during pregnancy. Comparator: no COVID-19 vaccination during pregnancy	Major congenital anomalies	Vaccinated: 4/78 Unvaccinated: 3/78	NR

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; EUROCAT – European Surveillance of Congenital Anomalies classification; mRNA – messenger ribonucleic acid; n – number of events; N – total denominator; NA – not applicable; NICU – neonatal intensive care unit; NR – not reported; yrs – years.

*For case control studies presented groups sizes by outcome status (yes, no); for cohort studies presented groups sizes by exposure status (vaccinated, unvaccinated).

†Adjusted with stabilised inverse probably of treatment weights; covariates included month and year of conception, maternal age, parity, use of assisted reproductive technology, pre-existing maternal medical conditions (asthma, hypertension, heart disease, diabetes mellitus, epilepsy, autoimmune disease, and immunosuppression), maternal influenza vaccination during the 2019-20 or 2020-21 influenza seasons (as a proxy for health behaviour), maternal outpatient opioid prescription during the first trimester of pregnancy, neighbourhood level income, neighbourhood level proportion of the population who self-identify as a visible minority, Public Health Unit region, and rural residence.

*‡Adjusted for women's age, residential area (Seoul capital area or not), employment, income, disability, month of conception, pre-pregnancy obesity and smoking, and SARS-CoV-2 infection.

Source: Scott et al.[57]

General population aged 18 to 59 years

Table B.42 Guillain-Barré syndrome safety data from the index review among adults aged 18 to 59 years

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Nasreen 2025[285] Self-controlled case series 14 study sites (African COVID-19 Vaccine Safety Surveillance system, South Africa, Australia (Victoria, New South Wales), Canada (British Columbia, Ontario), Denmark, Finland, Indonesia, Republic of Korea, Spain (Catalonia, Valencia), UK 1 December 2019 to 9 August 2023 Global Vaccine Data Network	Adults 18 to 64 yrs	Intervention: COVID-19 mRNA vaccination. Risk period day 1 to 42 PV Comparator: Unexposed period day 43 to 64 PV	GBS	RI: 0.78 (0.55 to 1.11)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; GBS – Guillain-Barré syndrome; mRNA – messenger ribonucleic acid; RI – relative incidence; yrs – years.
*Data points estimated using https://plotdigitizer.com/app
Source: Scott et al.[57]

Table B.43 Myocarditis and myopericarditis safety data from the index review among adults aged 18 to 59 years

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Le Vu 2024[286] Case-control study France 27 December 2020 to 30 November 2022 National Health Data (France)	12 to 29 yrs	Intervention exposure: BNT162b2 vaccination Control non-exposed: Unvaccinated Case: Myocarditis Control: Patients without myocarditis	Myocarditis	OR Dose 1: 2.0 (1.4 to 2.9) Dose 2: 11.0 (8.6 to 13) Dose 3: 6.2 (4.5 to 8.6)
	30 to 49 yrs			OR Dose 1: 2.5 (1.5 to 4.0) Dose 2: 5.2 (3.5 to 7.8) Dose 3: 2.5 (1.4 to 4.7)
	12 to 29 yrs	Intervention exposure: mRNA-1273 vaccination Control non-exposed: Unvaccinated Case: Myocarditis Control: Patients without myocarditis	Myocarditis	OR Dose 1: 1.3 (0.36 to 4.5) Dose 2: 38 (23 to 64) Dose 3: NR
	30 to 49 yrs			OR Dose 1: 3.6 (1.5 to 8.9) Dose 2: 20 (12 to 34) Dose 3: 5 (2.8 to 8.8)
Xu 2025[287] Cohort study Sweden 27 December 2020 to 31 December 2022 Register based large scale national population study to monitor COVID-19 vaccination effectiveness and safety	18 to 25 yrs	Intervention: Any COVID-19 vaccine dose (mRNA vaccines included BNT162b2 and mRNA-1273, viral vector vaccine included AZD1222) Comparator: No COVID-19 vaccination	Myopericarditis	HR* Dose 1: 0.97 (0.60 to 1.58) Dose 2: 1.08 (0.66 to 1.80) Dose 3: 1.88 (0.78 to 4.54)
	41 to 65 yrs			HR* Dose 1: 1.00 (0.77 to 1.32) Dose 2: 1.00 (0.76 to 1.34) Dose 3: 0.72 (0.5 to 1.05)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; mRNA – messenger ribonucleic acid; OR – odds ratio; yrs – years.
*Data points estimated using https://plotdigitizer.com/app
Source: Scott et al.
(57)

Table B.44 Safety data from the index review reporting stroke among adults aged 18 to 59 years

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Chemaitelly 2024[288] Case-control study Qatar 1 December 2020 to 11 April 2023 National Data	<40 yrs	Intervention exposure: COVID-19 vaccination Control unexposed: No vaccination Case: Stroke Controls: control individuals without stroke	Any stroke	OR: 1.41 (0.91 to 2.19)
	40 to 59 yrs			OR: 0.8 (0.66 to 0.96)
Xu 2025[287] Cohort study Sweden 27 December 2020 to 31 December 2022 Register based large scale national population study to monitor COVID-19 vaccination effectiveness and safety	41 to 65 yrs	Intervention: Any COVID-19 vaccine dose (mRNA vaccines included BNT162b2 and mRNA-1273, viral vector vaccine included AZD1222) Comparator: No COVID-19 vaccination	Stroke* (1 to 6 weeks after vaccine dose)	HR Dose 1: 0.89 (0.79 to 1.01) Dose 2: 0.81 (0.71 to 0.93) Dose 3: 0.63 (0.53 to 0.75)

Key: CI – confidence interval; COVID-19 – coronavirus disease 2019; HR – hazard ratio; mRNA – messenger ribonucleic acid; OR – odds ratio; yrs – years.
*Data points estimated using https://plotdigitizer.com/app
Source: Scott et al.[57]

Table B.45 Safety data from the index review reporting composite outcomes among adults aged 18 to 59 years

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
Ip 2024[292] Cohort study England 8 December 2020 to 23 January 2022 NHS England Secure Data Environment	Adults <40 yrs	Intervention: Dose 1 and 2 of mRNA BNT162b2 vaccine and booster mRNA 12-73 vaccine Comparator: Unvaccinated control	Composite venous outcome including pulmonary embolism, intracranial venous thrombosis, portal vein thrombosis and lower limb deep vein thrombosis	HR Weeks 1-4: 0.94 (0.61 to 1.45) Weeks 5-24: 0.85 (0.37 to 1.94)
	Adults 40 to 59 yrs			HR Weeks 1-4: 0.60 (0.39 to 0.93) Weeks 5-24: 0.57 (0.35 to 0.93)
	Adults <40 yrs		Composite arterial outcome including acute myocardial infarction, ischaemic stroke, and other arterial embolism.	HR Weeks 1-4: 0.38 (0.21 to 0.69) Weeks 5-24: 0.19 (0.07 to 0.53)
	Adults 40 to 59 yrs			HR Week 1: 0.63 (0.42 to 0.94) Weeks 2: 0.96 (0.68 to 1.34) Weeks 3-4: 0.83 (0.63 to 1.09) Weeks 5-12: 0.79 (0.61 to 1.01) Weeks 13-24: 13.78 (1.83 to 103.78)
	Adults <40 yrs	Intervention: Dose 1, 2 and booster of mRNA BNT162b2 vaccine Comparator: Unvaccinated control	Composite venous outcome including pulmonary embolism, intracranial venous thrombosis, portal vein thrombosis and lower limb deep vein thrombosis	HR Week 1: 0.61 (0.35 to 1.09) Weeks 2: 1.01 (0.64 to 1.59) Weeks 3-4: 0.90 (0.62 to 1.30) Weeks 5-12: 0.99 (0.71 to 1.37) Weeks 13-24: 0.74 (0.32 to 1.75)
	Adults 40 to 59 yrs			HR Week 1: 0.85 (0.63 to 1.14) Weeks 2: 0.65 (0.47 to 0.91) Weeks 3-4: 0.72 (0.57 to 0.92)

Study label Study type Country/Region Data collection date Data platform of interest	Population	Intervention Comparator	Outcome	Effect estimate (95% CI)
				Weeks 5-12: 0.66 (0.54 to 0.79) Weeks 13-24: 0.60 (0.42 to 0.86)
	Adults <40 yrs		Composite arterial outcome including acute myocardial infarction, ischaemic stroke, and other arterial embolism.	HR Week 1: 0.71 (0.40 to 1.29) Weeks 2: 1.02 (0.60 to 1.75) Weeks 3-4: 0.71 (0.45 to 1.12) Weeks 5-12: 1.17 (0.79 to 1.73) Weeks 13-24: 1.04 (0.44 to 2.45)
	Adults 40 to 59 yrs			HR Week 1: 0.67 (0.56 to 0.80) Weeks 2: 0.78 (0.66 to 0.92) Weeks 3-4: 0.85 (0.75 to 0.96) Weeks 5-12: 0.79 (0.71 to 0.87) Weeks 13-24: 0.70 (0.56 to 0.88)

Key: CI – confidence interval; HR – hazard ratio; mRNA – messenger ribonucleic acid; yrs – years.
*Data points estimated using https://plotdigitizer.com/app
Source: Scott et al.[57]

Quality appraisal table

Table B.46 AMSTAR 2 assessment of critical domains for index review

Critical domain	Yes (Y) / No (N)	Comments
Item 2: Protocol registered before commencement of the review	Y	Prospectively registered on PROSPERO and deviations were addressed
Item 4: Adequacy of the literature search	N	The publication did not provide information on grey literature searches, forward/backward citation searching nor trial or study registries
Item 7: Justification for excluding individual studies	N	A list of excluded systematic reviews and meta-analyses is provided in supplementary appendix table S12. A PRISMA flow diagram was provided which provides a high level summary of the reasons for exclusion overall, but not for individual studies.
Item 9: Risk of bias from individual studies being included in the review	Y	The Risk of Bias assessments were described in the supplementary appendix.
Item 11: Appropriateness of meta-analytical methods	Y	The review authors used DerSimonian-Laird random effects model. VE estimates were only eligible if there were three or more studies of the study design contributing data on the same population type for the same vaccine category. For safety outcomes analysis was restricted to the same vaccine product due to previously reported product-specific differences in safety outcomes. If studies only provided unadjusted effect estimates, they were not included in the meta analysis.
Item 13: Risk of bias when interpreting the results of the review	Y	The authors acknowledge the potential for publication bias to have led to an overrepresentation of novel findings while underrepresenting confirmatory studies. The authors acknowledged that the RoB assessment tools do not necessarily capture all potential sources of bias that may impact the interpretation of the study results. The authors noted that the observational studies that were rated as having a low risk of bias attempted to control for known confounders with robust design and analytic methods
Item 15: Assessment of presence and likely impact of publication bias	N	The authors noted that publication bias may influence which questions were prioritised during brief assessment

Critical domain	Yes (Y) / No (N)	Comments
		windows, potentially overrepresenting novel findings while underrepresenting confirmatory studies.
Overall	**Critically Low**	More than one critical flaw with or without non-critical weakness: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

Pharmacovigilance tables

Comirnaty®

Table B.47 The most frequent adverse events among single dose Comirnaty® vaccine recipients aged 12 years and older

Vaccine strain	Adverse event	Frequency (%)
Original N= 25651 participants aged 16 years and older	Injection site pain Fatigue Headache Myalgia Chills Arthralgia Pyrexia and injection site swelling	>80 >60 >50 >40 >30 >20 >10
Original N= 305 participants aged 56 years and older	Injection site pain Fatigue Headache Myalgia and chills	>60 >40 >20 >10
Original/Omicron BA.4-5 N= 726 participants aged 12 years and older	Injection site pain Fatigue Myalgia Chills Arthralgia	>60 >50 >40 >10 >10
XBB.1.5 N= 412 participants aged 12 years and older	Injection site pain Fatigue Headache Myalgia, diarrhoea, arthralgia, chills and injection site swelling	>50 >30 >20 >10
JN.1 N= 216 participants aged 12 years and older	Injection site pain Fatigue Headache Myalgia, chills and injection site swelling	>60 >30 >20 >10
KP.2 N= 102 participants aged 18 years and older	Injection site pain Fatigue Headache and myalgia	>50 >40 >20

Source: European Medicines Agency[7]

Spikevax®

Table B.48 The most frequent adverse events among Spikevax® single dose vaccine recipients

Vaccine strain	Adverse event	Frequency (%)
Original N=30351 participants aged 18 years and older	Injection site pain Fatigue Headache Myalgia Arthralgia Chills Nausea/Vomiting Axillary swelling/tenderness Fever Injection site swelling Redness	92 70 64.7 61.5 46.4 45.4 23 19.8 15.5 14.7 10
Original/Omicron BA.4-5 N=437 participants aged 18 years and older	Noted to be similar to that of the original vaccine series	NR
Original/Omicron BA.4-5 N=511 participants aged 18 years and older	Noted to be similar to that of the original vaccine series	NR
XBB.1.5 N=50 participants aged 18 years and older	Noted to be similar to that of the original vaccine series and original/omicron BA.4-5 booster	NR

Source: European Medicines Agency[53]

mCombriax®

Table B.49 The most frequent adverse events among mCombriax® vaccine recipients

Vaccine strain	Adverse event	Frequency (%)
Quadrivalent Influenza and COVID-19 mRNA Combination Vaccine (SARS-CoV-2 Omicron XBB.1.5)	Injection site pain	75.8
	Fatigue	55.9
	Myalgia	54.8
	Headache	47.5
	Arthralgia	44.6
	Chills	38.2
	Lymphadenopathy	22.5
	Nausea and vomiting	15.7
	Pyrexia	13.2

Source: European Medicines Agency [307]

Nuvaxovid®

Table B.50 The most frequent adverse events among Nuvaxovid® vaccine recipients

Vaccine strain	Adverse event	Frequency (%)
Original primary series Participants aged 18 years and older	Injection site tenderness Injection site pain Fatigue Myalgia Headache Malaise Arthralgia Nausea and vomiting	75 62 53 51 50 41 24 14
Original booster dose Participants aged 18 years and older	Injection site tenderness Injection site pain Fatigue Muscle pain Headache Malaise Joint pain	73 61 53 52 46 41 26
Original overall Participants aged 65 and older	Increased incidence of hypertension in vaccinated participants compared with placebo during the three days post-vaccination	Vaccine group: n=46 (1%) Placebo group: n=22 (0.6%)
BA.5 booster	Injection site tenderness Injection site pain Fatigue Headache Myalgia Malaise	>50 >30 >30 >20 >20 >10

Source: European Medicines Agency[56]

Bimervax®

Table B.51 The most frequent adverse events among Bimervax® vaccine recipients

Spikevax® vaccine strain	Adverse event	Frequency (%)
Original Participants aged 18 years and older	Injection site pain Headache Fatigue Myalgia	82.9 30.9 31.1 20.7
Heterodimer B.1.351 and B.1.1.7 Participants aged 18 years and older	Injection site pain Headache Fatigue	79.9 25.0 25.0
XBB.1.16	Injection site pain Headache Fatigue Myalgia	68.1 23.4 19.6 13.6
LP.8.1	Noted to be inferred from the safety data of the earlier vaccine strains	

Source: European Medicines Agency[55]

Overall frequency of known adverse reactions

Table B.52 Adverse reactions from COVID-19 vaccines as per Summary of Product Characteristics

Vaccine	System organ class	Frequency	Adverse reaction
Comirnaty®	Blood and lymphatic system disorders	Common ≥100 to <10	Lymphadenopathy
Spikevax®		Very common ≥10	
Nuvaxovid®		Uncommon≥1000 to <100	
Bimervax®		Common ≥100 to <10	
mCombriax®		Very common ≥10	
Comirnaty®	Immune system disorders	Uncommon ≥1000 to <100	Hypersensitivity reactions (rash, pruritus)
Spikevax®		Not known	
Comirnaty®		Rare ≥10000 to <1000	Hypersensitivity reactions (urticaria, angioedema)
Spikevax®		Not known	
Comirnaty®		Not known	Anaphylaxis
Spikevax®		Rare ≥10000 to <1000	
Nuvaxovid®		Not known	
Comirnaty®	Metabolism and nutrition disorders	Uncommon ≥1000 to <100	Decreased appetite
Spikevax®		Very common ≥10	
Comirnaty®	Psychiatric disorders	Uncommon ≥1000 to <100	Insomnia
Spikevax®		Not reported	
Comirnaty®		Not reported	Irritability/crying
Spikevax®		Very common ≥10	
Comirnaty®	Nervous system disorders	Very common ≥10	Headache
Spikevax®		Very common ≥10	
Nuvaxovid®		Very common ≥10	
Bimervax®		Very common ≥10	
mCombriax®		Very common ≥10	
Comirnaty®		Uncommon ≥1000 to <100	Dizziness, Lethargy
Spikevax®		Uncommon ≥1000 to <100	Dizziness
Bimervax®		Uncommon ≥1000 to <100	Dizziness, somnolence
Comirnaty®		Not reported	Sleepiness
Spikevax®		Very common ≥10	
Comirnaty®		Rare ≥10000 to <1000	Acute peripheral facial paralysis

Vaccine	System organ class	Frequency	Adverse reaction
Spikevax®		Rare ≥10000 to <1000	
Comirnaty®		Not known	Paraethesia, hypoaesthesia
Spikevax®		Rare ≥10000 to <1000	
Nuvaxovid®		Not known	
Bimervax®		Rare ≥10000 to <1000	
Comirnaty®	Cardiac disorders	Very rare <10000	Myocarditis, Pericarditis
Spikevax®		Very rare <10000	
Nuvaxovid®		Not known	
Bimervax®		Not known	Pericarditis
Comirnaty®	Gastrointestinal disorders	Very common ≥10	Diarrhoea
Spikevax®		Common ≥100 to <10	
Bimervax®		Common ≥100 to <10	
mCombriax®		Uncommon ≥1000 to <100	
Comirnaty®		Common ≥100 to <10	Nausea, vomiting*
Spikevax®		Very common ≥10	
Nuvaxovid®		Very common ≥10	
Bimervax®		Common ≥100 to <10	
mCombriax®		Very common ≥10	
Comirnaty®		Not reported	Abdominal pain
Spikevax®		Uncommon ≥1000 to <100	
Bimervax®		Rare ≥10000 to <1000	Abdominal pain, odynophagia
Comirnaty®	Skin and subcutaneous tissue disorder	Uncommon ≥1000 to <100	Hyperhidrosis, night sweats
Spikevax®		Not reported	
Comirnaty®		Not known	Erythema multiforme
Spikevax®		Rare ≥10000 to <1000	
Nuvaxovid®		Uncommon ≥1000 to <100	
Bimervax®		Rare ≥10000 to <1000	
Comirnaty®		Listed above as immune system disorder	Rash
Spikevax®		Common ≥100 to <10	

Vaccine	System organ class	Frequency	Adverse reaction
Nuvaxovid®		Uncommon ≥1000 to <100	
Bimervax®		Rare ≥10000 to <1000	
Comirnaty®		Listed above as immune system disorder	Urticaria
Spikevax®		Uncommon ≥1000 to <100	
Nuvaxovid®		Uncommon ≥1000 to <100	
Bimervax®		Rare ≥10000 to <1000	
Comirnaty®		Not reported	Mechanical urticaria, chronic urticaria
Spikevax®		Not known	
Nuvaxovid®		Uncommon ≥1000 to <100	Pruritus
Bimervax®		Uncommon ≥1000 to <100	
Bimervax®		Rare ≥10000 to <1000	Cold sweats
Comirnaty®	Musculoskeletal and connective tissue disorders	Very common ≥10	Arthralgia, myalgia
Spikevax®		Very common ≥10	
Nuvaxovid®		Very common ≥10	
mCombriax®		Very common ≥10	
Bimervax®		Very common ≥10	Myalgia
Bimervax®		Uncommon ≥1000 to <100	Arthralgia
Comirnaty®		Uncommon ≥1000 to <100	Pain in extremity
Spikevax®		Not reported	
Comirnaty®	Reproductive system and breast disorders	Not known	Heavy menstrual bleeding
Spikevax®		Not known	
Comirnaty®	General disorders and administration site conditions	Very common ≥10	Injection site pain, fatigue, chills, pyrexia, injection site swelling
Spikevax®		Very common ≥10	Injection site pain, fatigue, chills, pyrexia, injection site swelling, injection site erythema
Nuvaxovid®		Very common ≥10	Injection site tenderness, injection site pain, fatigue, malaise
Bimervax®		Very common ≥10	Injection site pain, fatigue
mCombriax®		Very common ≥10	Injection site pain, fatigue, chills, pyrexia
Comirnaty®		Common ≥100 to <10	Injection site redness

Vaccine	System organ class	Frequency	Adverse reaction
Spikevax®		Common ≥100 to <10	Injection site urticaria, injection site rash, delayed injection site reaction
Nuvaxovid®		Common ≥100 to <10	Injection site redness, injection site swelling, pyrexia, pain in extremity
Bimervax®		Common ≥100 to <10	Injection site swelling, injection site erythema, injection site induration, pyrexia, axillary pain
mCombriax®		Common ≥100 to <10	Injection site swelling, injection site erythema
Comirnaty®		Uncommon ≥1000 to <100	Asthenia, malaise, injection site pruritus
Spikevax®		Uncommon ≥1000 to <100	Injection site pruritus
mCombriax®		Uncommon ≥1000 to <100	
Nuvaxovid®		Uncommon ≥1000 to <100	Injection site pruritus, chills
Bimervax®		Uncommon ≥1000 to <100	Asthenia, Chills, Malaise, Injection site pruritus
Comirnaty®		Not known	Extensive swelling of vaccinated limb, facial swelling
Spikevax®		Rare ≥10000 to <1000	Facial swelling
		Not known	Extensive swelling of vaccinated limb
Nuvaxovid®		Rare ≥10000 to <1000	Injection site warmth
Bimervax®		Rare ≥10000 to <1000	Injection site bruising, injection site hypersensitivity
Nuvaxovid®	Vascular disorders	Uncommon ≥1000 to <100	Hypertension

*For Comirnaty®, vomiting very common for pregnant women ≥18 years and IC patients 5 to 18 years

Source: European Medicines Agency[7, 53, 55, 56, 307]

C. Appendix C Economic Evaluation

Appendix C.1 Model parameters

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Epi parameters					
COVID-19 risk parameters					
Incidence covid19_age group 5_current	0.2051%	0.1851%	0.2261%	Beta	Health Protection Surveillance Centre (HPSC)
Incidence covid19_age group 6_current	0.2932%	0.2647%	0.3233%	Beta	
Incidence covid19_age group 7_current	0.4564%	0.4119%	0.5032%	Beta	
Incidence covid19_age group 8_current	0.8154%	0.7359%	0.8989%	Beta	
Incidence covid19_age group 9_current	1.5854%	1.4308%	1.7478%	Beta	
Incidence ED_age group 5_current	0.0723%	0.0653%	0.0797%	Beta	
Incidence ED_age group 6_current	0.1040%	0.0939%	0.1147%	Beta	
Incidence ED_age group 7_current	0.1564%	0.1411%	0.1724%	Beta	
Incidence ED_age group 8_current	0.2620%	0.2365%	0.2889%	Beta	
Incidence ED_age group 9_current	0.4465%	0.4030%	0.4922%	Beta	
Incidence hospitalisation_age group 5_current	0.0806%	0.0728%	0.0889%	Beta	
Incidence hospitalisation_age group 6_current	0.1188%	0.1072%	0.1309%	Beta	
Incidence hospitalisation_age group 7_current	0.1971%	0.1779%	0.2173%	Beta	
Incidence hospitalisation_age group 8_current	0.3785%	0.3415%	0.4172%	Beta	
Incidence hospitalisation_age group 9_current	0.7304%	0.6591%	0.8052%	Beta	
Incidence covid19 death_age group 5_current	0.0016%	0.0014%	0.0018%	Beta	
Incidence covid19 death_age group 6_current	0.0059%	0.0053%	0.0065%	Beta	
Incidence covid19 death _age group 7_current	0.0066%	0.0059%	0.0072%	Beta	
Incidence covid19 death_age group 8_current	0.0211%	0.0191%	0.0233%	Beta	
Incidence covid19 death_age group 9_current	0.0759%	0.0685%	0.0837%	Beta	
Incidence covid19_age group 5_counterfactual_ESTIMATED	0.2136%			Fixed	
Incidence covid19_age group 6_counterfactual_ESTIMATED	0.3054%			Fixed	
Incidence covid19_age group 7_counterfactual_ESTIMATED	0.4754%			Fixed	
Incidence covid19_age group 8_counterfactual_ESTIMATED	0.8493%			Fixed	
Incidence covid19_age group 9_counterfactual_ESTIMATED	1.7856%			Fixed	
Incidence ED_age group 5_counterfactual_ESTIMATED	0.0780%			Fixed	
Incidence ED_age group 6_counterfactual_ESTIMATED	0.1122%			Fixed	
Incidence ED_age group 7_counterfactual_ESTIMATED	0.1687%			Fixed	
Incidence ED_age group 8_counterfactual_ESTIMATED	0.2826%			Fixed	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Incidence ED_age group 9_counterfactual_ESTIMATED	0.5438%			Fixed	
Incidence hospitalisation_age group 5_counterfactual_ESTIMATED	0.0887%			Fixed	
Incidence hospitalisation_age group 6_counterfactual_ESTIMATED	0.1307%			Fixed	
Incidence hospitalisation_age group 7_counterfactual_ESTIMATED	0.2169%			Fixed	
Incidence hospitalisation_age group 8_counterfactual_ESTIMATED	0.4164%			Fixed	
Incidence hospitalisation_age group 9_counterfactual_ESTIMATED	0.9369%			Fixed	
Incidence covid19 death_age group 5_counterfactual_ESTIMATED	0.0019%			Fixed	
Incidence covid19 death_age group 6_counterfactual_ESTIMATED	0.0071%			Fixed	
Incidence covid19 death_age group 7_counterfactual_ESTIMATED	0.0079%			Fixed	
Incidence covid19 death_age group 8_counterfactual_ESTIMATED	0.0255%			Fixed	
Incidence covid19 death_age group 9_counterfactual_ESTIMATED	0.1128%			Fixed	
Mortality parameters					
Life expectancy_age group 5 (years)	22			Fixed	Central Statistics Office (CSO) - Irish Life Tables (weighted average for age group)[337]
Life expectancy_age group 6 (years)	18			Fixed	
Life expectancy_age group 7 (years)	14			Fixed	
Life expectancy_age group 8 (years)	11			Fixed	
Life expectancy_age group 9 (years)	4			Fixed	
Resource use parameters					
Probability GP visit for covid19					
Probability GP visit for covid19_age group 5	1			Fixed	Assumed given notified case
Probability GP visit for covid19_age group 6	1			Fixed	
Probability GP visit for covid19_age group 7	1			Fixed	
Probability GP visit for covid19_age group 8	1			Fixed	
Probability GP visit for covid19_age group 9	1			Fixed	
Frequency of GP visit for covid19					
Frequency of GP visit for covid19_age group 5	2	1	3	Gamma	Assumed the same as Respiratory Syncytial Virus (RSV) and as reported in 2026 Health Technology Assessment [356]
Frequency of GP visit for covid19_age group 6	2	1	3	Gamma	
Frequency of GP visit for covid19_age group 7	2	1	3	Gamma	
Frequency of GP visit for covid19_age group 8	4	1	6	Gamma	
Frequency of GP visit for covid19_age group 9	4	1	6	Gamma	
Frequency of GP visit for long covid					

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Frequency of GP visit for long covid_age group 5	5	1	9	Gamma	(351, 352)
Frequency of GP visit for long covid_age group 6	5	1	9	Gamma	
Frequency of GP visit for long covid_age group 7	5	1	9	Gamma	
Frequency of GP visit for long covid_age group 8	5	1	9	Gamma	
Frequency of GP visit for long covid_age group 9	5	1	9	Gamma	
Probability prescription medication prescribed by GP for COVID-19					
Probability medication prescribed by GP for covid19_age group 5	18.1%	16.3%	19.9%	Beta	Primary Care Reimbursement Service (PCRS) Personal Communisation: Paxlovid® Prescription Data
Probability medication prescribed by GP for covid19_age group 6	15.8%	14.3%	17.5%	Beta	
Probability medication prescribed by GP for covid19_age group 7	15.1%	13.6%	16.6%	Beta	
Probability medication prescribed by GP for covid19_age group 8	12.5%	11.3%	13.8%	Beta	
Probability medication prescribed by GP for covid19_age group 9	8.5%	7.7%	9.4%	Beta	
Probability GP visit card					
Probability GP visit card_age group 5	4.0%			Fixed	Health Service Executive (HSE): PCRS eligibility February 2026(350)
Probability GP visit card_age group 6	4.1%			Fixed	
Probability GP visit card_age group 7	40.8%			Fixed	
Probability GP visit card_age group 8	26.1%			Fixed	
Probability GP visit card_age group 9	26.1%			Fixed	
Probability medical card					
Probability medical card_age group 5	29.0%			Fixed	HSE: PCRS eligibility February 2026(350)
Probability medical card_age group 6	36.7%			Fixed	
Probability medical card_age group 7	52.7%			Fixed	
Probability medical card_age group 8	73.9%			Fixed	
Probability medical card_age group 9	73.9%			Fixed	
Probability post hospitalisation step-down care after COVID-19					
Probability post hospitalisation step-down care_age group 5	0.0%	0.0%	0.0%	Beta	Hospital InPatient Enquiry (HIPE) Discharge Data for Primary Diagnosis COVID-19 2024, by discharge destination
Probability post hospitalisation step-down care_age group 6	0.7%	0.6%	0.9%	Beta	
Probability post hospitalisation step-down care_age group 7	0.4%	0.3%	0.5%	Beta	
Probability post hospitalisation step-down care_age group 8	0.3%	0.2%	0.4%	Beta	
Probability post hospitalisation step-down care_age group 9	1.0%	0.8%	1.3%	Beta	
Probability post hospitalisation care LTCF after COVID-19					
Probability post hospitalisation short-term care LTCF_age group 5	0.3%	0.2%	0.3%	Beta	
Probability post hospitalisation short-term care LTCF_age group 6	0.7%	0.5%	0.8%	Beta	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Probability post hospitalisation short-term care LTCF_age group 7	0.6%	0.5%	0.8%	Beta	HIPE Discharge Data for Primary Diagnosis COVID-19 2024, by discharge destination
Probability post hospitalisation short-term care LTCF_age group 8	0.7%	0.6%	0.9%	Beta	
Probability post hospitalisation short-term care LTCF_age group 9	1.5%	1.2%	1.8%	Beta	
Probability post hospitalisation long-term care LTCF_age group 5	1.4%	1.2%	1.8%	Beta	
Probability post hospitalisation long-term care LTCF_age group 6	3.7%	3.0%	4.4%	Beta	
Probability post hospitalisation long-term care LTCF_age group 7	3.4%	2.8%	4.1%	Beta	
Probability post hospitalisation long-term care LTCF_age group 8	3.9%	3.2%	4.7%	Beta	
Probability post hospitalisation long-term care LTCF_age group 9	8.0%	6.5%	9.7%	Beta	
Length of stay post hospitalisation step-down care after COVID-19					
Length of stay (weeks) post hospitalisation step-down care_age group 5	6	2	10	Gamma	Expert opinion[137]
Length of stay (weeks) post hospitalisation step-down care_age group 6	6	2	10	Gamma	
Length of stay (weeks) post hospitalisation step-down care_age group 7	6	2	10	Gamma	
Length of stay (weeks) post hospitalisation step-down care_age group 8	6	2	10	Gamma	
Length of stay (weeks) post hospitalisation step-down care_age group 9	6	2	10	Gamma	
Length of stay post hospitalisation short-term nursing home care after COVID-19					
Length of stay (weeks) post hospitalisation short-term care_age group 5	6	2	10	Gamma	Assumed as above for step-down care
Length of stay (weeks) post hospitalisation short-term care_age group 6	6	2	10	Gamma	
Length of stay (weeks) post hospitalisation short-term care_age group 7	6	2	10	Gamma	
Length of stay (weeks) post hospitalisation short-term care_age group 8	6	2	10	Gamma	
Length of stay (weeks) post hospitalisation short-term care_age group 9	6	2	10	Gamma	
Length of stay post hospitalisation long-term nursing home care after COVID-19					
Length of stay (weeks) post hospitalisation long-term care_age group 5	129	107	151	Gamma	[147]
Length of stay (weeks) post hospitalisation long-term care_age group 6	129	107	151	Gamma	
Length of stay (weeks) post hospitalisation long-term care_age group 7	129	107	151	Gamma	
Length of stay (weeks) post hospitalisation long-term care_age group 8	129	107	151	Gamma	
Length of stay (weeks) post hospitalisation long-term care_age group 9	129	107	151	Gamma	
Probability long COVID					
Probability of long covid19_age group 5	0.85%	0.69%	1.03%	Beta	Chapter 3 Epidemiology
Probability of long covid19_age group 6	0.85%	0.69%	1.03%	Beta	
Probability of long covid19_age group 7	0.85%	0.69%	1.03%	Beta	
Probability of long covid19_age group 8	0.85%	0.69%	1.03%	Beta	
Probability of long covid19_age group 9	0.85%	0.69%	1.03%	Beta	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Frequency of clinic for long covid					
Frequency (each year) of clinic visit for long covid_age group 5	2	1	4	Gamma	Personal communication
Frequency (each year) of clinic visit for long covid_age group 6	2	1	4	Gamma	
Frequency (each year) of clinic visit for long covid_age group 7	2	1	4	Gamma	
Frequency (each year) of clinic visit for long covid_age group 8	2	1	4	Gamma	
Frequency (each year) of clinic visit for long covid_age group 9	2	1	4	Gamma	
Cost parameters					
Direct medical costs – COVID-19					
Cost of GP visit for covid19_public	€56.06	€45.41	€67.81	Gamma	(353)
Cost of prescription medication for covid19 public_age group 5	€871	€705	€1,053	Gamma	HSE Prescribing Guidelines - Treatment for people at the highest risk from COVID-19 and PCRS data(354)
Cost of prescription medication for covid19 public_age group 6	€871	€705	€1,053	Gamma	
Cost of prescription medication for covid19 public_age group 7	€871	€705	€1,053	Gamma	
Cost of prescription medication for covid19 public_age group 8	€871	€705	€1,053	Gamma	
Cost of prescription medication for covid19 public_age group 9	€871	€705	€1,053	Gamma	
Cost of prescription medication for covid19 public_BIA_age group 5	€883	€715	€1,068	Gamma	HSE Prescribing Guidelines - Treatment for people at the highest risk from COVID-19 and PCRS data(354)
Cost of prescription medication for covid19 public_BIA_age group 6	€883	€715	€1,068	Gamma	
Cost of prescription medication for covid19 public_BIA_age group 7	€883	€715	€1,068	Gamma	
Cost of prescription medication for covid19 public_BIA_age group 8	€883	€715	€1,068	Gamma	
Cost of prescription medication for covid19 public_BIA_age group 9	€883	€715	€1,068	Gamma	
Cost of ED for covid19_age group 5	€520	€421	€629	Gamma	Healthcare Pricing Office (HPO) and HIPE - personal communication
Cost of ED for covid19_age group 6	€520	€421	€629	Gamma	
Cost of ED for covid19_age group 7	€520	€421	€629	Gamma	
Cost of ED for covid19_age group 8	€520	€421	€629	Gamma	
Cost of ED for covid19_age group 9	€520	€421	€629	Gamma	
Cost of hospitalisation for severe covid19_age group 5	€6,638	€5,377	€8,030	Gamma	Average cost per episode of care estimated from HIPE Diagnosis Related Group (DRG) cost data and HPSC Notified Hospitalisation data(357)
Cost of hospitalisation for severe covid19_age group 6	€6,955	€5,634	€8,413	Gamma	
Cost of hospitalisation for severe covid19_age group 7	€7,586	€6,145	€9,177	Gamma	
Cost of hospitalisation for severe covid19_age group 8	€7,532	€6,101	€9,111	Gamma	
Cost of hospitalisation for severe covid19_age group 9	€7,518	€6,090	€9,094	Gamma	
Cost (per week) of post hospitalisation step-down care_age group 5	€2,010	€1,628	€2,431	Gamma	(358)
Cost (per week) of post hospitalisation step-down care_age group 6	€2,010	€1,628	€2,431	Gamma	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Cost (per week) of post hospitalisation step-down care_age group 7	€2,010	€1,628	€2,431	Gamma	
Cost (per week) of post hospitalisation step-down care_age group 8	€2,010	€1,628	€2,431	Gamma	
Cost (per week) of post hospitalisation step-down care_age group 9	€2,010	€1,628	€2,431	Gamma	
Cost (per week) of post hospitalisation short-term LTCF care_age group 5	€1,658	€1,343	€2,006	Gamma	Estimated
Cost (per week) of post hospitalisation short-term LTCF care_age group 6	€1,658	€1,343	€2,006	Gamma	
Cost (per week) of post hospitalisation short-term LTCF care_age group 7	€1,658	€1,343	€2,006	Gamma	
Cost (per week) of post hospitalisation short-term LTCF care_age group 8	€1,658	€1,343	€2,006	Gamma	
Cost (per week) of post hospitalisation short-term LTCF care_age group 9	€1,658	€1,343	€2,006	Gamma	
Cost (per week) of post hospitalisation long-term LTCF care_age group 5	€1,213	€983	€1,467	Gamma	(359)
Cost (per week) of post hospitalisation long-term LTCF care_age group 6	€1,213	€983	€1,467	Gamma	
Cost (per week) of post hospitalisation long-term LTCF care_age group 7	€1,213	€983	€1,467	Gamma	
Cost (per week) of post hospitalisation long-term LTCF care_age group 8	€1,213	€983	€1,467	Gamma	
Cost (per week) of post hospitalisation long-term LTCF care_age group 9	€1,213	€983	€1,467	Gamma	
Proportion of post hospitalisation long-term LTCF care cost paid by HSE	69%	54%	82%	Beta	(359)
Cost of long covid clinic (per visit)_age group 5	€242	€196	€293	Gamma	HPO HIPE Personal Communication - cost of outpatient case
Cost of long covid clinic (per visit)_age group 6	€242	€196	€293	Gamma	
Cost of long covid clinic (per visit)_age group 7	€242	€196	€293	Gamma	
Cost of long covid clinic (per visit)_age group 8	€242	€196	€293	Gamma	
Cost of long covid clinic (per visit)_age group 9	€242	€196	€293	Gamma	
Quality of life parameters					
Baseline utility_age group 5	0.90730			Fixed	(341)
Baseline utility_age group 6	0.87900			Fixed	
Baseline utility_age group 7	0.87900			Fixed	
Baseline utility_age group 8	0.84100			Fixed	
Baseline utility_age group 9	0.84100			Fixed	
Baseline utility_lt_care_age group 5	0.80800			Fixed	Estimated - assumed the difference in baseline utility (0.091) between those aged ≥80yrs in the general population and those residing in nursing homes was the same across all age groups in the model.
Baseline utility_lt_care_age group 6	0.78800			Fixed	
Baseline utility_lt_care_age group 7	0.78800			Fixed	
Baseline utility_lt_care_age group 8	0.75000			Fixed	
Baseline utility_lt_care_age group 9	0.75000			Fixed	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
					Difference of 0.091 is based on a baseline utility of 0.76 for those aged ≥80yrs residing in a nursing home from a Swedish study.[340]
QALY_loss_covid19_GP_age_group_5	0.0045	0.0022	0.0076	Gamma	(332-336)
QALY_loss_covid19_GP_age_group_6	0.0045	0.0022	0.0076	Gamma	
QALY_loss_covid19_GP_age_group_7	0.0045	0.0022	0.0076	Gamma	
QALY_loss_covid19_GP_age_group_8	0.0045	0.0022	0.0076	Gamma	
QALY_loss_covid19_GP_age_group_9	0.0045	0.0022	0.0076	Gamma	
QALY_loss_covid19_ED_age_group_5	0.0110	0.0054	0.0186	Gamma	(332-336)
QALY_loss_covid19_ED_age_group_6	0.0111	0.0054	0.0186	Gamma	
QALY_loss_covid19_ED_age_group_7	0.0110	0.0054	0.0185	Gamma	
QALY_loss_covid19_ED_age_group_8	0.0110	0.0054	0.0185	Gamma	
QALY_loss_covid19_ED_age_group_9	0.0110	0.0054	0.0185	Gamma	
QALY_loss_covid19_hospitalisation_age_group_5	0.0176	0.0099	0.0274	Gamma	(332-336)
QALY_loss_covid19_hospitalisation_age_group_6	0.0176	0.0099	0.0274	Gamma	
QALY_loss_covid19_hospitalisation_age_group_7	0.0175	0.0099	0.0273	Gamma	
QALY_loss_covid19_hospitalisation_age_group_8	0.0175	0.0099	0.0273	Gamma	
QALY_loss_covid19_hospitalisation_age_group_9	0.0175	0.0098	0.0272	Gamma	
QALY_loss_covid19_sd_care_age_group_5	0.1907	0.1545	0.2307	Gamma	(339)
QALY_loss_covid19_sd_care_age_group_6	0.1808	0.1464	0.2187	Gamma	
QALY_loss_covid19_sd_care_age_group_7	0.1808	0.1464	0.2187	Gamma	
QALY_loss_covid19_sd_care_age_group_8	0.1618	0.1311	0.1957	Gamma	
QALY_loss_covid19_sd_care_age_group_9	0.1618	0.1311	0.1957	Gamma	
QALY_loss_covid19_st_care_age_group_5	0.1907	0.1545	0.2307	Gamma	(339)
QALY_loss_covid19_st_care_age_group_6	0.1808	0.1464	0.2187	Gamma	
QALY_loss_covid19_st_care_age_group_7	0.1808	0.1464	0.2187	Gamma	
QALY_loss_covid19_st_care_age_group_8	0.1618	0.1311	0.1957	Gamma	
QALY_loss_covid19_st_care_age_group_9	0.1618	0.1311	0.1957	Gamma	
Utility_covid19_lt_care_age_group_5	0.5165	0.4661	0.5694	Gamma	
Utility_covid19_lt_care_age_group_6	0.5165	0.4661	0.5694	Gamma	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Utility_covid19_lt_care_age_group_7	0.5165	0.4661	0.5694	Gamma	Assumed the same as utility of step-down patients reported by McCarthy et al. 2024[339]
Utility_covid19_lt_care_age_group_8	0.5165	0.4661	0.5694	Gamma	
Utility_covid19_lt_care_age_group_9	0.5165	0.4661	0.5694	Gamma	
Utility_long_covid19_age_group_5	0.4900	0.4422	0.5402	Gamma	[338]
Utility_long_covid19_age_group_6	0.4900	0.4422	0.5402	Gamma	
Utility_long_covid19_age_group_7	0.4900	0.4422	0.5402	Gamma	
Utility_long_covid19_age_group_8	0.4900	0.4422	0.5402	Gamma	
Utility_long_covid19_age_group_9	0.4900	0.4422	0.5402	Gamma	
Immunisation programme parameters					
Immunisation programme cost parameters					
Cost of vaccine	€75	€61	€91	Gamma	Estimated based on international published prices
Cost of vaccine administration	€25	€20	€30	Gamma	Assumed based on other adult vaccination programmes
Cost of storage and distribution (per annum)	€600,000	€486,024	€725,801	Gamma	National Immunisation Office (NIO)
Cost of pick and pack (per single dose pack)	€1.39	€1.13	€1.68	Gamma	
Cost of public health information campaign (adult programme)	€500,000	€405,020	€604,834	Gamma	
Cost of training (development of module)	€50,000	€40,502	€60,483	Gamma	
Cost of programme management (maintenance IT system for recording and monitoring uptake)	€100,000	€81,004	€120,967	Gamma	NIO - assumed maintenance cost is 10% of capital cost
Cost of programme manager	€140,251	€113,609	€169,657	Gamma	[348]
Eligible population					
Eligible population_age group 5 (BIA - year 1)	312,500			Fixed	[327]
Eligible population_age group 6 (BIA - year 1)	271,100			Fixed	
Eligible population_age group 7 (BIA - year 1)	228,300			Fixed	
Eligible population_age group 8 (BIA - year 1)	184,700			Fixed	
Eligible population_age group 9 (BIA - year 1)	231,800			Fixed	
Immunisation coverage					
Immunisation coverage_age group 5_counterfactual	33.2%			Fixed	[329, 342, 343]
Immunisation coverage_age group 6_counterfactual	33.2%			Fixed	
Immunisation coverage_age group 7_counterfactual	33.2%			Fixed	
Immunisation coverage_age group 8_counterfactual	33.2%			Fixed	
Immunisation coverage_age group 9_dose_1_counterfactual	60.8%			Fixed	

Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Immunisation coverage_age group 9_dose_2_counterfactual	32.3%			Fixed	
Immunisation coverage_age group 5	33.2%	30.0%	36.5%	Beta	
Immunisation coverage_age group 6	33.2%	30.0%	36.5%	Beta	
Immunisation coverage_age group 7	33.2%	30.0%	36.5%	Beta	
Immunisation coverage_age group 8	33.2%	30.0%	36.5%	Beta	
Immunisation coverage_age group 9_dose_1	60.8%	54.8%	66.7%	Beta	
Immunisation coverage_age group 9_dose_2	32.3%	29.2%	35.5%	Beta	
Immunisation coverage_ltcf_1	74.2%	66.6%	81.1%	Beta	
Immunisation coverage_ltcf_2	76.4%	68.5%	83.5%	Beta	
Immunisation coverage_immunocompromise_dose_1	18.2%	16.5%	20.0%	Beta	
Immunisation coverage_immunocompromise_dose_2	14.6%	13.2%	16.1%	Beta	
Immunisation coverage_high_risk	23.6%	21.3%	26.0%	Beta	
Immunisation coverage_hcw	8.7%	7.9%	9.6%	Beta	
Immunisation coverage_pregnant	6.5%	5.9%	7.2%	Beta	
Immunisation coverage_others	3.6%	3.3%	4.0%	Beta	
Relative risk with vaccination					
Relative risk covid19_adult_vaccine_60-64y (1-VE)	0.880	0.841	0.920	Log Normal	Estimated by meta-regression analysis using data reported in Chapter 4
Relative risk covid19_adult_vaccine_65-69y (1-VE)	0.880	0.841	0.920	Log Normal	
Relative risk covid19_adult_vaccine_70-74y (1-VE)	0.880	0.841	0.920	Log Normal	
Relative risk covid19_adult_vaccine_75-79y (1-VE)	0.880	0.841	0.920	Log Normal	
Relative risk covid19_adult_vaccine_≥80y (1-VE) ESTIMATED	0.816	0.758	0.879	Estimated	
Relative risk covid19_adult_vaccine_≥80y_1_dose (1-VE)	0.880	0.841	0.920	Log Normal	
Relative risk covid19_adult_vaccine_≥80y_2_dose (1-VE)	0.759	0.684	0.842	Log Normal	
Relative risk covid19_ED (1-VE)	0.781	0.702	0.868	Log Normal	
Relative risk covid19_ED_≥80y (1-VE) ESTIMATED	0.706	0.630	0.790	Estimated	
Relative risk covid19_ED_≥80y_1_dose (1-VE)	0.781	0.702	0.868	Log Normal	
Relative risk covid19_ED_≥80y_2_dose (1-VE)	0.639	0.566	0.722	Log Normal	
Relative risk covid19_hospitalisation (1-VE)	0.725	0.678	0.777	Log Normal	
Relative risk covid19_hospitalisation_≥80y (1-VE) ESTIMATED	0.638	0.593	0.685	Estimated	
Relative risk covid19_hospitalisation_≥80y_1_dose (1-VE)	0.725	0.678	0.777	Log Normal	
Relative risk covid19_hospitalisation_≥80y_2_dose (1-VE)	0.560	0.518	0.604	Log Normal	
Relative risk covid19_mortality (1-VE)	0.481	0.328	0.705	Log Normal	
Relative risk covid19_mortality_≥80y (1-VE) ESTIMATED	0.463	0.324	0.661	Estimated	
Relative risk covid19_mortality_≥80y_1_dose (1-VE)	0.481	0.328	0.705	Log Normal	
Relative risk covid19_mortality_≥80y_2_dose (1-VE)	0.447	0.321	0.623	Log Normal	

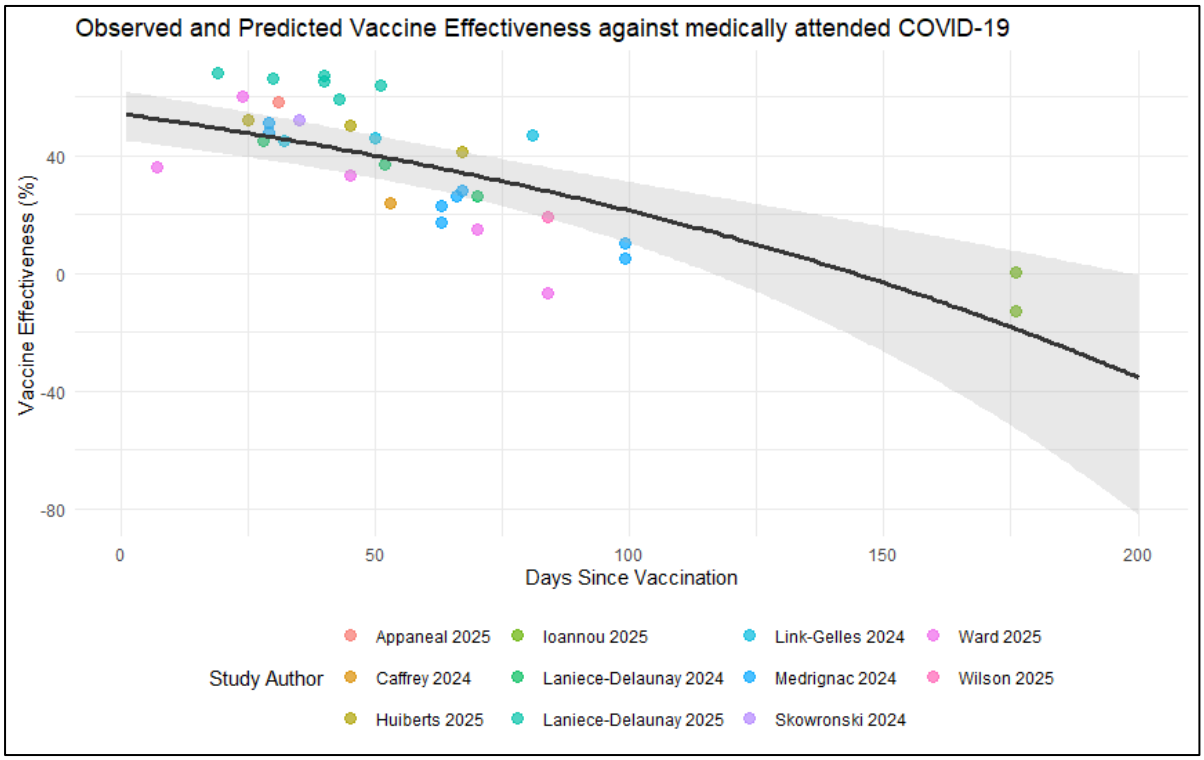
Immunisation adverse events parameters

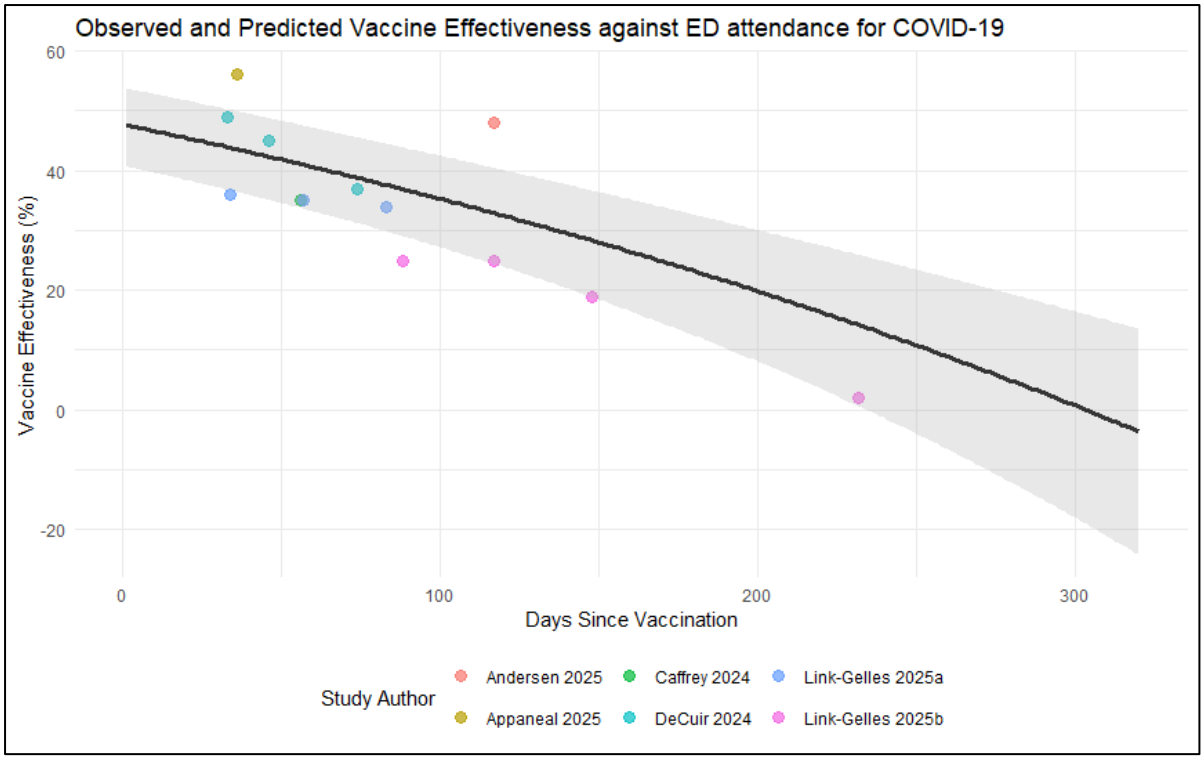
Description	Deterministic	Lower Range	Upper Range	Distribution	Source
Probability of solicited severe adverse event (≥Grade 3)	2.6%	1.9%	3.4%	Beta	(332)
QALY_loss_covid19_vax_ae_age_group_5	0.0013	0.0007	0.0020	Gamma	Assumed equivalent of 2 days QALY loss for a notified case of COVID-19
QALY_loss_covid19_vax_ae_age_group_6	0.0013	0.0007	0.0020	Gamma	
QALY_loss_covid19_vax_ae_age_group_7	0.0013	0.0007	0.0020	Gamma	
QALY_loss_covid19_vax_ae_age_group_8	0.0013	0.0007	0.0020	Gamma	
QALY_loss_covid19_vax_ae_age_group_9	0.0013	0.0007	0.0020	Gamma	
Other parameters					
VAT	23.0%			Fixed	(361)
Discount rate_costs	4%	3%	5%	Beta	(324)
Discount rate_QALYs	4%	3%	5%	Beta	

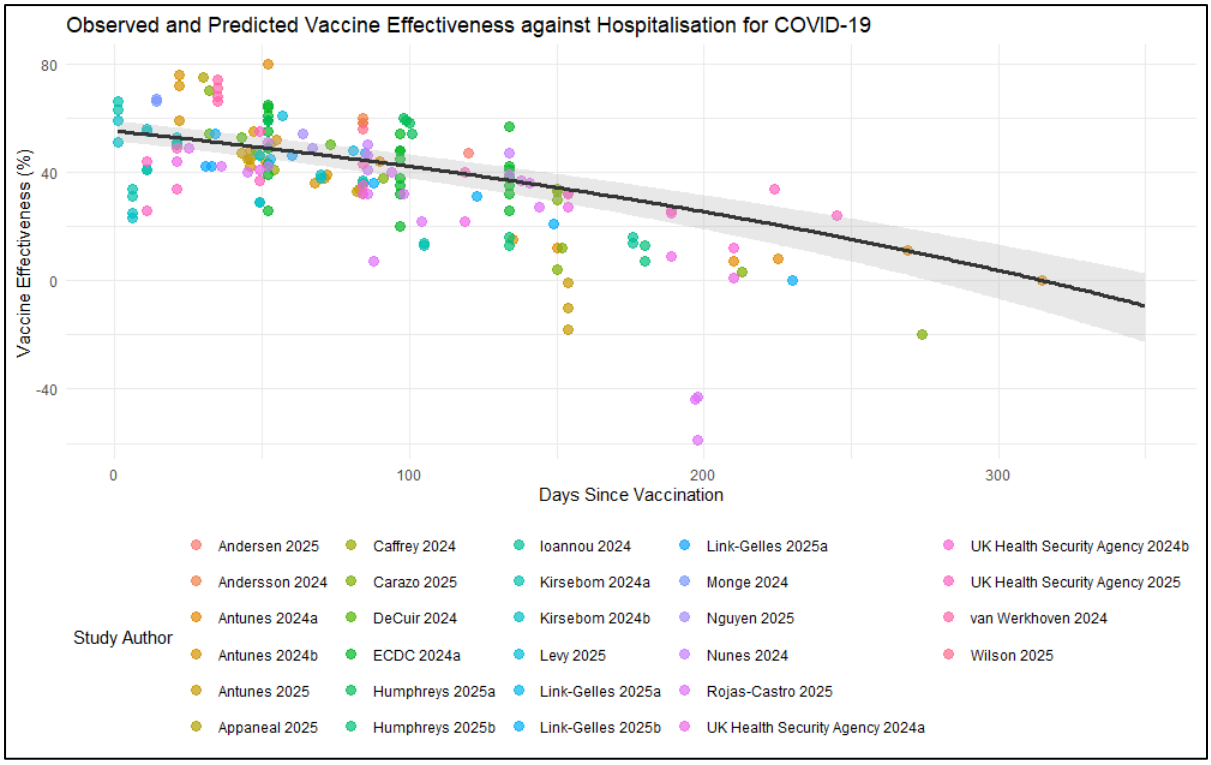
Key: ae – adverse event; BIA – budget impact analysis; ED – emergency department; hcw – health and care worker; lt – long-term; ltcf – long-term care facility; QALY - quality-adjusted life year; sd – step-down; st – short-term; VAT – value-added tax; VE – vaccine effectiveness.

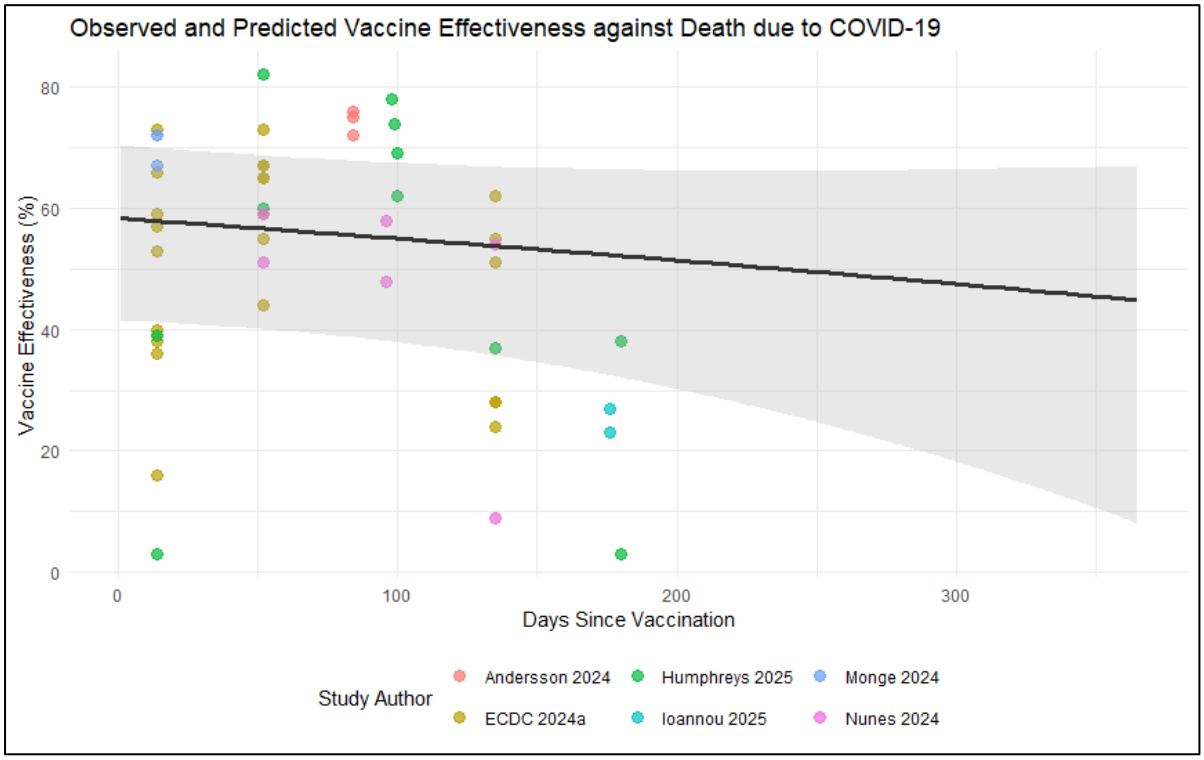
Note: age group 5: 60-64yrs; age group 6: 65-69yrs; age group 7: 70-74yrs; age group 8: 75-79yrs: age group 9: 80yrs and older.

Appendix C.2 Observed and predicted (using metafor package in R) vaccine effectiveness against COVID-19 outcomes over time

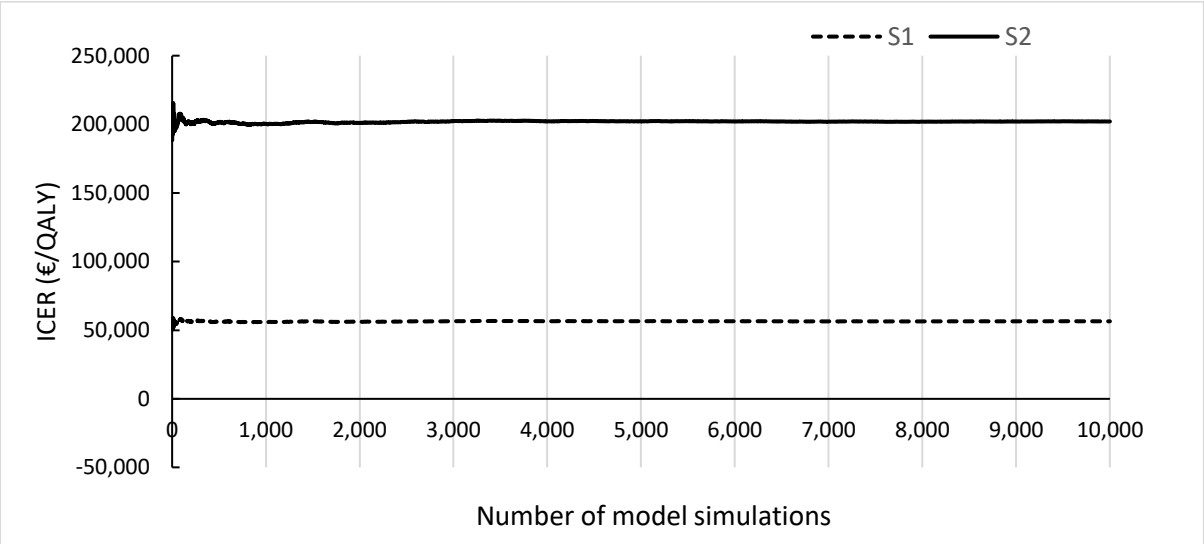





Observed and Predicted Vaccine Effectiveness against Hospitalisation for COVID-19
Vaccine Effectiveness (%)
80
40
0
-40
0
100
200
300
Days Since Vaccination
Study Author
Andersen 2025
Andersson 2024
Antunes 2024a
Antunes 2024b
Antunes 2025
Appaneal 2025
Caffrey 2024
Carazo 2025
DeCuir 2024
ECDC 2024a
Humphreys 2025a
Humphreys 2025b
Ioannou 2024
Kirsebom 2024a
Kirsebom 2024b
Levy 2025
Link-Gelles 2025a
Link-Gelles 2025b
Link-Gelles 2025a
Monge 2024
Nguyen 2025
Nunes 2024
Rojas-Castro 2025
UK Health Security Agency 2024a
UK Health Security Agency 2024b
UK Health Security Agency 2025
van Werkhoven 2024
Wilson 2025


Observed and Predicted Vaccine Effectiveness against Death due to COVID-19
Vaccine Effectiveness (%)
80
60
40
20
0
0
100
200
300
Days Since Vaccination
Study Author
Andersson 2024
ECDC 2024a
Humphreys 2025
Ioannou 2025
Monge 2024
Nunes 2024

Appendix C.3 Convergence testing for COVID-19 vaccination strategies



Key: ICER - incremental cost-effectiveness ratio; QALY – quality-adjusted life year; S1 – Strategy 1: 2-dose 80 years and above; S2 - Strategy 2: 2-dose 80 years and above and 1-dose 60 to 79 yrs old.

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