Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Potential impact of different testing scenarios to reduce the duration of restriction of movements and or number of tests for close contacts of a COVID-19 case

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About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children, Equality, Disability, Integration and Youth, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.

- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.

- **Regulating health services —** Regulating medical exposure to ionising radiation.

- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.

- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.

- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.

- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

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List of abbreviations used in this report

CI	confidence interval
COVID-19	Coronavirus disease 2019
HIQA	Health Information and Quality Authority
HSE	Health Service Executive
HTA	health technology assessment
NPHET	National Public Health Emergency Team
rRT-PCR	real time reverse transcription-polymerase chain reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SCOPI	Study to investigate COVID-19 Infection in People Living in Ireland
WHO	World Health Organization

Update of analysis - Potential impact of different testing scenarios to reduce the duration of restriction of movements and or number of tests for close contacts of a COVID-19 case

Key points

- National testing strategies for SARS-CoV-2 have changed during the course of the pandemic to reflect both test capacity and demand for testing. In May 2020, following significant increases in testing capacity, testing was expanded to a standard practice whereby close contacts were offered two tests (first test - 'day zero', day of identification; second test - 'day seven' since last exposure) for the purposes of onward contact tracing with the aim to contain the pandemic.
- Since late December 2021, there has been a significant increase in the incidence of COVID-19 with test demand exceeding available capacity. To mitigate risk within the community, testing of symptomatic individuals was prioritised. Therefore, unless symptomatic, close contacts in the community were not tested.
- Irrespective of testing, standard practice in Ireland has been that close contacts should restrict their movements for 14 days from their last exposure event. That is, receipt of a 'not detected' test result does not impact the recommended duration. While this approach minimises the risk of onward transmission, it can pose significant societal challenges such as resourcing of essential services and impact on population mental health.
- Earlier analysis underpinning advice to NPHET published on 4 November 2020, modelled the potential impact of a number of different testing scenarios to reduce the duration of restricted movements from 14 days for close contacts. This present report serves as an update to that analysis considering the standard approach and 10 alternative scenarios which reduce the duration of restricted movements and or the number of tests conducted. Given current, and future potential, disease trajectories and testing constraints, two-test and single-test regimens are considered alongside no universal testing of close contacts. These scenarios can be grouped as:

- Mitigation phase – high incidence and or limited testing capacity, so that requirement for testing greatly exceeds available capacity. Within the community, prioritise testing of symptomatic individuals. Scenarios modelled include no universal testing of close contacts (that is, individuals are only tested if symptomatic) and different durations of restriction of movements.

- Containment phase - some constraints in testing capacity relative to the requirement for testing. For close contacts, scenarios modelled include a number of single-test strategies with different durations of restriction of movements.

- Containment phase - no constraints in testing capacity relative to the requirement for testing. For close contacts, scenarios modelled include a number of two-test strategies with different durations of restriction of movements.

- Parameter estimates for the model were gathered from the recent literature, previous HIQA evidence summaries, and Irish data sources. The outcomes of interest from the model, included estimates of potential benefits (reduced person-days in restricted movements), potential risks (increased infectious person-days in the community), and organisational implications (number of tests conducted).

- Two scenarios examined no universal testing of close contacts in the community; that is, only symptomatic individuals are tested. Relative to standard practice in Ireland:
  - Ending of restriction of movements on day 14 in this context results in an increase of 194 (95% CI: 101 to 318) infectious person-days in the community per 1,000 close contacts.
  - Ending on day 10 in this context results in an increase of 336 (95% CI: 203 to 493) infectious person-days in the community per 1,000 close contacts. However, a considerable benefit is seen with a reduction of 2,198 person-days (95% CI: -2,631 to -1,720) in restricted movements.

- Five scenarios examined reducing the number of tests for close contacts from two to one. Compared to standard practice in Ireland:
  - All single test scenarios lead to a reduction of approximately 383 to 397 tests completed per 1,000 close contacts.

- A scenario of a single test taken five days since last exposure, with ending the period of restricted movements on day 14 since last exposure would provide similar number of person-days in restricted movements and infectious person-days in the community.
- A single test on day five, with ending the period of restricted movements 10 days since last exposure would lead to a substantial reduction in the burden of person-days in restricted movements (-1,715 days, 95% CI (-2,191 to -1,194), but may increase the risk in terms of infectious person-days in the community (20 days, 95% CI: -14 to 61) per 1,000 close contacts.

- Three of the alternative scenarios considered two-test regimens. Relative to standard practice in Ireland:
  - On balance, the scenario, which included ending the period of restricted movements on receipt of 'not detected' test result from a test conducted on day 10 since last exposure, leads to an estimated reduction in the burden of person-days in restricted movements (-607 person-days, 95%CI: -972 to -193) while maintaining similar rates of infectious person-days in the community (1 person-day, 95% CI: -27 to 23) per 1,000 close contacts.
  - In terms of the number of tests completed, the above scenario could result in a mean increase of 227 tests (95% CI: 194 to 258) per 1,000 close contacts. This increase is associated with a longer interval between the first and second tests increasing the number of individuals eligible for a second test.
  - The other scenarios modelled, one which involved an end of restricted movements after ten days irrespective of the day seven test result or the other scenario which ended restriction of movements on receipt of a day seven 'not detected' result, were noted to have larger benefits in terms of reduced burden of person-days in restricted movements, but had a higher risk in terms of infectious days in the community.

- Overall, the results within this report must be considered against what constitutes an acceptable level of risk relative to standard practice in the context of:
  - the current and future disease trajectories

- possible broader public and mental health considerations
- the capacity to resource essential services.

- The estimates presented in this report are underpinned by a range of assumptions and data from a point in time. Substantial changes in how and when close contacts are identified, and the extent to which they attend for testing, will impact on the relative benefits and harms of the modelled scenarios.

Update of analysis - Potential impact of different testing scenarios to reduce the duration of restriction of movements and or number of tests for close contacts of a COVID-19 case

The Health Information and Quality Authority (HIQA) has developed a series of evidence syntheses to inform advice from HIQA to the National Public Health Emergency Team (NPHET). This evidence synthesis relates to the following policy question outlined by NPHET:

"What is the potential impact of different testing scenarios to reduce the duration of restriction of movements and or reduce the number of tests for close contacts of a COVID-19 case?"

This report summarises a modelling exercise to estimate the potential impact of specific testing scenarios to reduce the duration of restriction of movements and or reduce the number of tests for close contacts of a COVID-19 case, relative to the standard of practice in Ireland. The present report serves as an update to a report, and subsequent NPHET advice, published 4 November 2020.[(1)] This update incorporates data reflective of the current context of the COVID-19 pandemic in Ireland and assesses a number of specific testing scenarios outlined by NPHET with respect to test demand relative to testing capacity. These scenarios include two-test strategies reflective of unconstrained testing (that is, testing capacity that exceeds demand with no constraints at any point in the process), single test strategies reflective of constrained testing, and strategies with no universal testing of close contacts in the community reflective of significantly constrained testing within a mitigation phase.

Methods

A modelling exercise was undertaken to estimate the potential impact of a reduction in the duration of the restriction of movements and or a reduction in tests based on pre-specified scenarios. Below is a summary of the four key elements underpinning the model: population, outcomes, scenarios considered and parameter estimates.

Population and setting

This modelling exercise considers close contacts of a confirmed COVID-19 case. In the context of close contacts, all settings (for example, household and non-household) are considered relevant. The model does not consider individuals with potential travel-related exposure.

Outcomes of interest

The model estimates the following three clinical and organisational outcomes of interest to the policy question, relative to the base case comparator of the standard of practice in Ireland:

- total number of person-days of restricted movements
- total number of person-days for infected individuals not in restricted movements
- number of tests conducted.

Base case analysis and testing scenarios

As a base case analysis, the model considers the standard of practice in Ireland (comparator), and a reduction in the duration of restricted movements and or reduction in the number of tests based on 10 alternative scenarios. These scenarios are summarised in Table 1, and outlined in full below, segregated as strategies involving two tests, a single test, or no universal testing for close contacts.

- Scenario one (comparator): the base case scenario is the standard practice in Ireland; this standard reflects a containment phase of the pandemic with relatively controlled disease levels and sufficient testing capacity. For close-contact exposure, a restriction of movements for a period of 14 days from last contact with the confirmed COVID-19 case is recommended. Close contacts of a confirmed COVID-19 case are identified and tested as soon as possible, preferably on the same day of identification, representing a 'day zero' test. Of note, this 'day zero' reflects the time of identification and contact, it is not reflective of time since exposure. If a 'not detected' test is returned, a follow-up test is conducted seven days since the last identified exposure to the confirmed case ('day seven' test). If the 'day zero' and 'day seven' test fall within 24 hours of each other, the second test is not

conducted. The results of these tests have no effect on the duration of the restriction of movements, with an individual who returns two negative ('not detected') tests asked to continue to restrict their movements for the full 14-day period.

Scenarios involving two-tests

For all three scenarios which examined two-test regimens, individuals who do not attend their second test are asked to continue to restrict their movements for the full 14-day period:

- Scenario two: ending the period of restricted movements of an individual on day 10 since last exposure, on receipt of a 'not detected' RT-PCR test result from the test conducted seven days post-exposure ('day seven' test).
- Scenario three: ending the period of restricted movements of an individual, on receipt of a 'not detected' RT-PCR test result from the test conducted seven days post-exposure ('day seven' test).
- Scenario four: replacing the 'day seven' test with a test on day 10 since last exposure ('day 10' test), with ending of the period of restricted movements on receipt of a 'not detected' result from this second test.

Scenarios involving a single test

- Scenario five: removing the 'day seven' RT-PCR test, and ending the period of restricted movements on day 14 since last exposure if the RT-PCR test on 'day zero' returns a 'not detected' result.
- Scenario six: removing the 'day seven' RT-PCR test, and ending the period of restricted movements on day 10 since last exposure if the RT-PCR test on 'day zero' returns a 'not detected' result.
- Scenario seven: removing the 'day seven' RT-PCR test, and ending the period of restricted movements on day seven since last exposure if the RT-PCR test on 'day zero' returns a 'not detected' result.
- Scenario eight: replacing the 'day zero' and 'day seven' RT-PCR tests with a single test taken on day five since last exposure ('day five' test), with ending of the period of restricted movements on day 14 since last exposure, conditional on a 'not detected' result received.
- Scenario nine: replacing the 'day zero' and 'day seven' RT-PCR tests with a single test taken on day five since last exposure ('day five' test), with ending of the period of restricted movements on day 10 since last exposure, conditional on a 'not detected' result received.

Scenarios with no universal testing of close contacts

For the two scenarios which do not include the universal testing of close contacts, individuals are only tested if they become symptomatic:

- Scenario ten: no universal testing of close contacts, and restriction of movements for 10 days.
- Scenario eleven: no universal testing of close contacts, and restriction of movements for 14 days.

Table 1. Scenarios considered within model

Scenario	First test*	Second test^	End of restriction of movements+
1 (comparator)	Day 0 - RT-PCR	Day 7 - RT-PCR	Day 14
Two-test scenarios			
2	Day 0 - RT-PCR	Day 7 - RT-PCR	Day 10
3	Day 0 - RT-PCR	Day 7 - RT-PCR	On receipt of ND Day 7 result
4	Day 0 - RT-PCR	Day 10 - RT-PCR	On receipt of ND Day 10 result
Single test scenarios			
5	Day 0 - RT-PCR		Day 14
6	Day 0 - RT-PCR		Day 10
7	Day 0 - RT-PCR		Day 7
8	Day 5 - RT-PCR		Day 14
9	Day 5 - RT-PCR		Day 10
No universal testing scenarios			
10			Day 10
11			Day 14

Key: ND- Not Detected; RT-PCR- real time reverse transcription polymerase chain reaction; *First test on 'Day zero' indicates time of contact identification and testing, it does not infer time since exposure, ^Second test infers time since last exposure to a COVID-19 case, +End of restriction of movements infers time since last exposure to a COVID-19 case

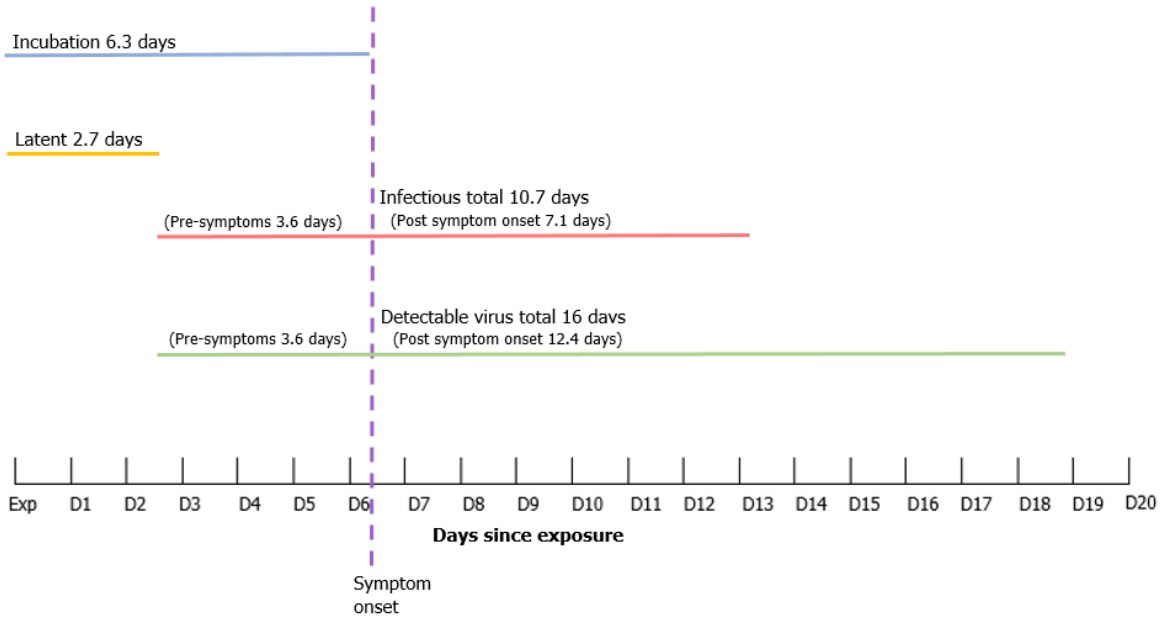
Model parameters

The model required a range of input parameters that describe disease, person, testing, and organisational factors. Parameter estimates are typically defined by statistical distributions that reflect the uncertainty in their true values. A number of the parameter estimates outlined below have been updated since the previous report was published; taking account of up-to-date data to appropriately reflect the current situation in Ireland.(1)

Disease factors

A summary of the parameter estimates for each relevant disease factor is provided in Table 2. Figure 1 illustrates the key disease parameter estimates for an average symptomatic COVID-19 case.

Figure 1. Disease parameter estimates for an average symptomatic COVID-19 case



- Incubation period

  The incubation period denotes the period from exposure to symptom onset. It is frequently reported as the time from last known exposure. The incubation period is not used explicitly in the model, but rather used along with the latent period to determine the infectious period prior to symptom onset. The estimate of the incubation period is derived from a systematic review of relevant studies.(2)

- Latent period

  The latent period is the period from exposure to becoming infectious. During this period the individual is asymptomatic or pre-symptomatic and will not transmit the infection to others. There are very limited data to support an estimate of the latent period, and as such there is substantial uncertainty around the estimate.

- Duration of infectiousness (pre-symptom onset)

  The period prior to becoming symptomatic when an infected individual's viral load is sufficient to transmit infection to others. Managing the period during which an individual is infectious is critical to controlling transmission of SARS-

CoV-2. It is assumed that a person will not test positive prior to the infectious period. The pre-symptomatic infectious period is modelled as the difference between the incubation time and the latent period.

- Duration of infectiousness (post-symptom onset)

  This denotes the period that an infected individual is infectious after symptom onset. It was assumed in the model that symptomatic individuals would self-isolate and thereby minimise the onward transmission of COVID-19. Asymptomatic individuals were assumed to have an equivalent period during which they were infectious, but not symptomatic. Furthermore, the model accounts for a reduction in the number of infectious individuals over time. While it was assumed that a person was equally likely to transmit COVID-19 throughout the infectious period, it is highly likely that the profile of infectivity changes over time. This is partly implicit in the data, as the duration of infectivity is estimated from an evidence of transmission over time. The available data also suggest that a disproportionate amount of transmission occurs before symptom onset, but this may be a reflection of reduced opportunity after symptom onset due to self-isolation of the index case. The reduced opportunity to transmit is explicit in the model as we assume all symptomatic and test-detected cases adhere to self-isolation. This is consistent with the results of a recent Irish audit which reported 96.6% adherence to self-isolation with the majority of non-adherence related to leaving the house for exercise or to attend a medical appointment.[3]

- Detectable virus (post-infectious state)

  While viral load and detectability increase rapidly at the start of infection, viral load diminishes slowly over time at the end of the infection.[4] As such, an individual tested late in the infection cycle may return a positive test result, but no longer be infectious.

- Proportion of close contacts infected

  In determining the impact of different strategies of testing and restricted movements, it is essential to consider the risk of infection in the target population. With a low likelihood of infection, the benefit to harm balance of some control measures will shift. With a very low risk, for example, a large group of people will be required to restrict movements with little gain in terms of reduced infection. Conversely, in a group with a high risk of infection there will be a substantial health gain from restricted movements. In this model,

the probability that a close contact of a confirmed case is infected was inferred from Irish contact tracing data from December 2020.

- Proportion of asymptomatic infections

  Infected individuals may experience a range of symptoms of varying severity. Some individuals will experience no notable symptoms at all, and therefore may be unaware that they are infected unless detected through testing. Asymptomatic individuals can, however, transmit disease, creating challenges for the control of transmission. The parameter values here are based on the findings of a systematic review,[5] and are consistent with the proportion of asymptomatic cases estimated in an Irish sero-prevalence study.[6]

Three parameters were considered subject to substantial uncertainty: the proportion of close contacts that are infected, the latent period and the pre-symptomatic infectious period. The model was initially run with those three parameters allowed to vary substantially within plausible ranges. The parameter values from simulations that produced plausible outputs for numbers of tests conducted and positivity rates were used to re-estimate the parameters. The latent period and pre-symptomatic infectious periods were constrained to sum to the incubation period as estimated from a range of studies.[2]

Table 2. Parameter estimates for disease factors

Parameter	Description	Source(s)	Estimate
Latent period	The time duration (in days) from exposure to becoming infectious.	HIQA evidence summary of incubation period combined with LSHTM modelling estimate of latent period.[2, 7]	Mean: 2.7 95% CI (1.0 to 6.0)
Duration of infectiousness (pre-symptomatic)	The time duration (in days) from becoming infectious to symptom onset.	HIQA evidence summary of duration of infectiousness[8] combined with LSHTM modelling estimate of latent period.[7]	Mean: 3.6 95% CI (0.8 to 10.6)
Duration of infectiousness (symptomatic)	The time duration (in days) from symptom onset to no longer being infectious. Adjusted for proportional reduction in infectious individuals over time.	HIQA evidence summary of duration of infectiousness.[8] Singanayagam et al.[9]	Mean: 7.1 95% CI (2.8 to 11.5)
Percentage of close contacts infected	The percentage of close contacts who subsequently test positive for SARS-CoV-2 RNA.	HSE COVID-19 CMP data	Mean: 18% 95% CI (16% to 21%)
Percentage of asymptomatic infections	The percentage of all infected cases which remain asymptomatic (that is they do not show symptoms at any point). The confidence bounds are based on the reported prediction interval in the underlying study.	Buitrago-Garcia et al.[5]	Mean: 31% 95% CI (24% to 38%)

Key: LSHTM London School of Hygiene and Tropical Medicine

Person factors

A summary of the parameter estimates for each relevant person factor is provided in Table 3.

- Adherence to testing

  An important aspect of managing contact tracing is identifying those who have been infected with COVID-19. Identification is contingent on testing or through symptomatic presentation. In the most recent data available, the uptake of testing on 'day zero' is almost identical to the uptake of 'day seven' tests.

- Estimated proportion of individuals adherent to restriction of movements

  Individuals may adhere to restriction of movements, but not avail of testing. There are limited international or Irish data that examine adherence to restricting movements. Some of the evidence available has taken a strict two-

part approach to measuring adherence, with individuals considered to be either fully adherent or not at all. Such a narrow definition is unrealistic in practice, and we have assumed that the majority of people asked to restrict movements will enter into the spirit of the request as far as is possible. On the basis that more than 80% of individuals avail of the first test, we have assumed that 90% of close contacts are compliant with restricting movements at the outset. This is consistent with the findings of a recent Irish audit which reported 86.6% compliance with restriction of movements for the period between notification of close contact status and the first test; the majority of those reporting non-compliance left the house to take exercise or to purchase essential items like groceries or medicines.[3] Based on international evidence, it was assumed in the earlier analysis that adherence to restriction of movements declines over time to an average of 65% ten days following exposure.[10] However, given the higher uptake of second tests in recent months likely influenced by public health measures in place (see Table 3), the adherence to restriction of movements on day ten was increased to 75% in this updated analysis. It was assumed that all those who become symptomatic or are test-detected will self-isolate. It was also assumed that adherence to restriction of movements is unaffected by attendance at testing. That is, a person who adheres to restriction of movements will do so irrespective of attending testing.

The adherence to restriction of movements was modelled as a curve of waning adherence connecting between initial adherence and adherence on day ten, with extrapolation out to day 14 (Figure 2). Substantial uncertainty was applied to account for the very limited data available on adherence to restriction of movements, particularly among those who return a 'not detected' test result.

It was assumed that adherence to restriction of movement wanes from date of last exposure, meaning that the likelihood of a close contact adhering to restriction of movement will be lower if they are first contacted on day five rather than day four, for example. A scenario analysis was used to examine the alternative assumption that adherence wanes from the date on which a close contact is first notified of the need to restrict movements. That is, for example, the likelihood of adherence on day six is the same for all individuals first notified of being a close contact on day six or earlier.

Figure 2. Proportion of close contacts adherent to restriction of movements by days since last exposure

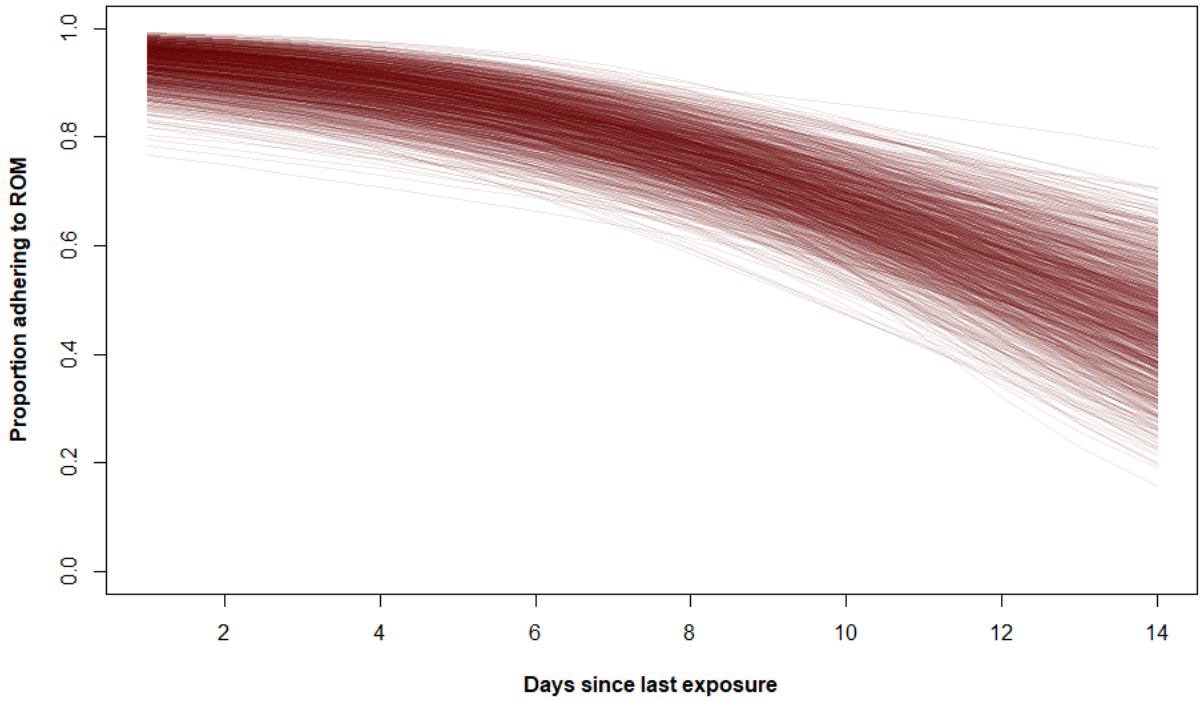


Table 3. Parameter estimates for person factors

Parameter	Description	Source(s)	Estimate*
Uptake of first test	The proportion of close contacts that present for 'Day zero' testing	HSE COVID-19 CMP data	Mean: 83% 95% CI (81% to 86%)
Uptake of second test (in eligible individuals)	The proportion of close contacts that present for 'Day seven' testing.	HSE COVID-19 CMP data	Mean: 83% 95% CI (81% to 85%)

*Estimates rounded to nearest whole number

Test factors

A summary of the parameter estimates for each relevant test factor is provided in Table 4.

- Sensitivity and specificity of RT-PCR testing for SARS-CoV-2

  RT-PCR is generally considered the gold standard for detection of SARS-CoV-2. As such, there are challenges to assessing the diagnostic test accuracy of the test. While high sensitivity and specificity are achievable, accuracy is affected by the stage of infection and the quality of the sample, among other factors. At early or late stages of infection, the viral load may be insufficient to trigger a positive test result. Swabbing from a single site or issues with

storage and transportation of swabs can also impact on diagnostic test accuracy. For modelling purposes we adopted an average sensitivity of 90%, but allowed wide uncertainty to explore the impact on the results.

Table 4. Parameter estimates for test factors

Parameter	Description	Source(s)	Estimate
Clinical sensitivity of RT-PCR testing for SARS-CoV-2	Proportion of individuals with COVID-19 correctly identified as infected with SARS-CoV-2 by RT-PCR testing, subject to pre-analytical factors.	HIQA Rapid HTA of diagnostic tests;[11] inferred as high sensitivity when appropriate pre-analytical time factors satisfied.	Mean: 90% 95% CI (83% to 95%)
Clinical specificity of RT-PCR testing for SARS-CoV-2	Proportion of individuals who do not have COVID-19 correctly identified as negative by RT-PCR testing for SARS-CoV-2.	HIQA Rapid HTA of diagnostic tests;[11] inferred as high.	Mean: 99% 95% CI (98% to 100%)

Organisational factors

A summary of the parameter estimates for each relevant organisational factor is provided in Table 5.

- Time lag between exposure to 'day zero' test referral

  Although referred to as the 'day zero' test, it is in reality the first test and referral may occur up to ten days or more after exposure. Data from the contact management programme provided evidence on the range of days on which referral for the first test was undertaken. Based on the same principle, while 'day five' tests in the single-test strategies occur no earlier than five days post exposure, this test could occur up to ten days or more post exposure.

- Time lag between referral and test appointment

  There can be a substantial lag between referral and attendance at a test centre. Using data from the SwiftQueue appointment management system for October to December 2020, 43% of people referred attend for COVID-19 testing on the day of referral, 46% the following day, and the remaining 11% attend two or more days after referral. Some individuals attend a week or more after referral.

- Time lag between test and result

After a sample is collected from an individual, there is an average lag of 1.5 days to receiving the test results for a 'not detected' result, and a lag of 2.1 days for a positive result. The lag arises for a variety of reasons, including the time taken for transportation to the laboratory and processing. The longer lag for positive tests relates to additional validation steps.

- Capacity for RT-PCR testing

  The capacity to carry out RT-PCR testing was not explicitly included in the model, but used for considering the logistical feasibility of different testing scenarios. Capacity for RT-PCR is in excess of 100,000 tests per week including additional off-shore testing capacity.

Table 5. Parameter estimates for the testing process

Parameter	Description	Source(s)	Estimate*
Time lag between exposure to 'Day zero' test referral^	The time period (in days) from the point of exposure to COVID-19 case and the close contact having 'day zero' test.	HSE COVID-19 CMP data.	Mean 3.3 95% CI (1.0 to 7.0)
Time lag between test referral and test appointment	The time period (in days) from test referral to test attendance.	Estimated from HSE SwiftQueue data (months October, November, December).	Mean 0.82 95% CI (0.0 to 4.0)
Time lag between test and 'not detected' result	The time period (in days) from specimen collection from the close contact and informing the individual of a 'not detected' test result.	Estimated from HSE Testing and Tracing data.	Mean 1.5 95% CI (1.0 to 3.0)
Time lag between test and positive result	The time period (in days) from specimen collection from the close contact and informing the individual of a positive test result.	Estimated from HSE Testing and Tracing data.	Mean 2.1 95% CI (1.0 to 3.0)

^Twenty-three percent of close contacts are classified as being in continuous exposure and the lag to 'day zero' is zero days. While this correctly describes date of last contact, it does not necessarily reflect time since infection. For the base case, it was assumed that the time lag for those in continuous contact would follow the same distribution as for those not in continuous contact.

* Data from contact tracing reflect activity in October to December 2020

Model structure

A natural history model was used that simulates individuals from the initial call to notify them of being a close contact of a confirmed case, through to reaching day 14 since exposure. Close contacts were classified into a series of mutually exclusive states based on the progression of infection (Figure 3). Close contacts with undetected disease could also adhere to restriction of movements or not, in which case it is assumed they are moving freely in the community. After the infectious period is complete there is an extended period during which the viral load was sufficiently high that a case can return a positive test result. The model did not use explicit transition probabilities, as transitions were based on the duration of each period, which could be shortened through testing or a close contact ceasing to adhere to restriction of movements. While a close contact could cease adhering to restriction of movements, the model assumed that they would adhere to self-isolation if informed of a positive test result. Close contacts that were not infected had three states: uninfected and observing restriction of movements, uninfected and not observing restriction of movements, and self-isolating having received a false-positive test result.

The model was structured as a series of functions. One function was used to generate the parameter values for use in the model. Parameters were split into individual-level and simulation-level variables. Individual-level parameters captured the variability in infection characteristics across cases. Simulation-level parameters captured population-level variables, such as test uptake and test performance. A separate function took the generated parameter data as an input and estimated the number of close contacts in each state by days since exposure.

The model generated 20,000 close-contacts, with a cohort of 1,000 randomly sampled for each simulation. For each of the modelled scenarios, individuals could change states in different ways depending on the timing and accuracy of testing.

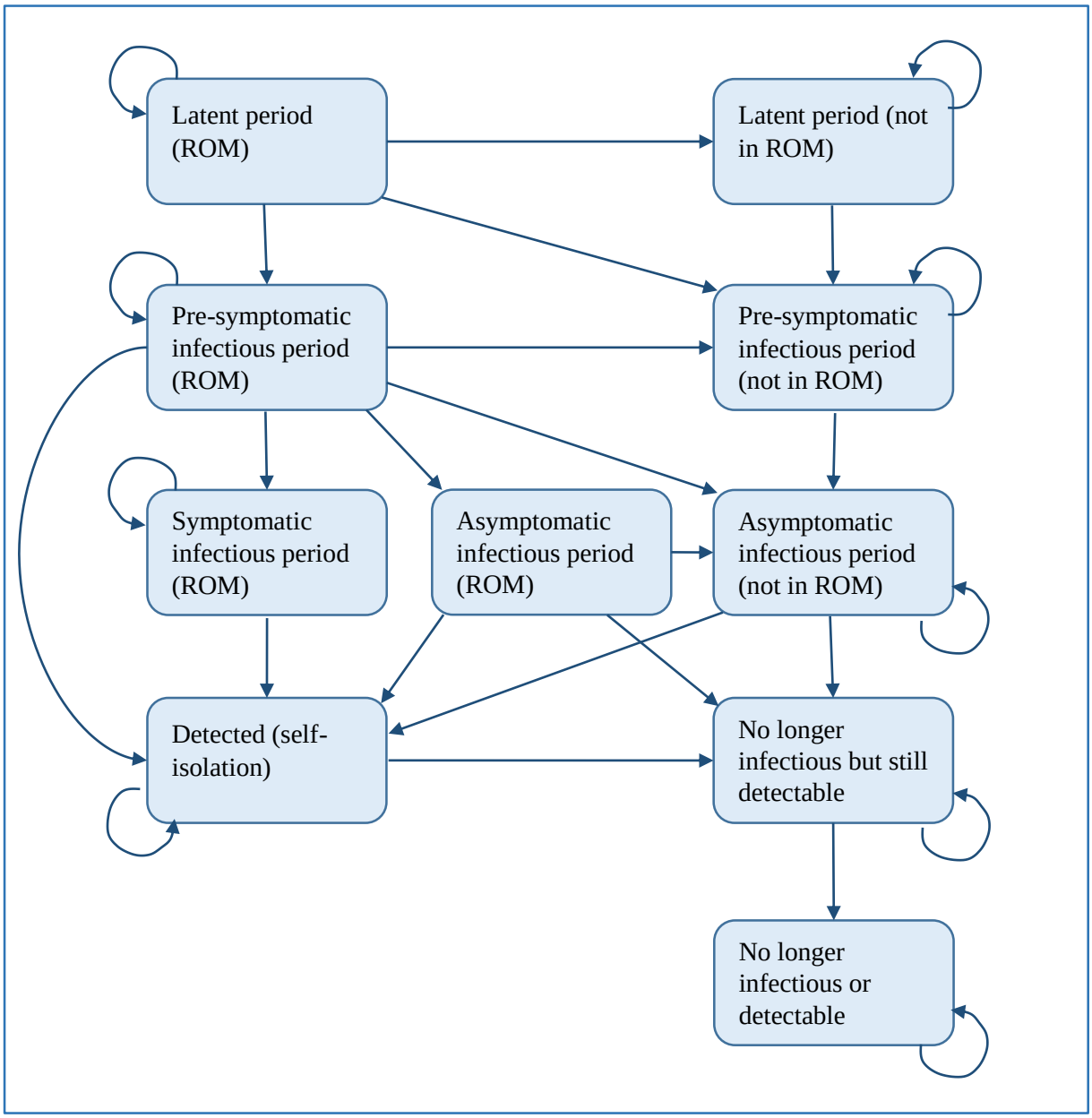
As previously noted, the so-called 'day zero' tests can occur at any point after last exposure, although the 95% confidence interval runs from two to 10 days following last exposure. It was assumed that a second test, that is, the 'day seven' test would not be conducted unless it arose more than a day after the first test. A test is intended to occur on the stated day or as soon as possible after that day, unless the close contact was already tested in the 24 hours before that day.

Individuals that become symptomatic, but have not been referred for a test through contact tracing were assumed to get tested and or be clinically diagnosed outside of the contact tracing system. Once symptomatic, cases were assumed to self-isolate. Asymptomatic cases could only be test identified if referred for testing by contact tracing. It was assumed that not all individuals would restrict movements. Any testing strategy that reduces identification of cases is likely to lead to an increase in

infectious person-days in the community due to undetected cases that do not adhere to restriction of movement.

All computations were carried out in R (4.0.2). Results are presented for a hypothetical cohort of 1,000 close contacts. The model allowed parameters to vary for all the outlined parameters. A series of sensitivity analyses were conducted to test structural assumptions in the model. A validation exercise was conducted to compare the modelled outputs for the standard practice of RT-PCR tests on days zero and seven, coupled with end of restriction of movements on day 14. The outcomes for validation were the number of tests conducted and the positivity rate. Details of the model validation are provided in Appendix 1, with full details of the parameters used provided in Appendix 2.

Figure 3. State transition model for infected close contacts



Key: ROM Restriction of movements

Results

Model results

The results of this analysis are presented by each of the three relevant outcomes considering each scenario. Results are presented for a hypothetical cohort of 1,000 close contacts and are presented separately for scenarios involving two tests, a single test, or no universal testing. Details of additional outcomes are provided in Appendix 3.

Strategies involving two tests

The three scenarios which involve two-test strategies are:

- Scenario two: ending the period of restricted movements of an individual on day 10 since last exposure, on receipt of a 'not detected' RT-PCR test result from the test conducted seven days post-exposure ('day seven' test).
- Scenario three: ending the period of restricted movements of an individual, on receipt of a 'not detected' RT-PCR test result from the test conducted seven days post-exposure ('day seven' test).
- Scenario four: replacing the 'day seven' test with a test on day 10 since last exposure ('day 10' test), with ending of the period of restricted movements on receipt of a 'not detected' result from this second test.

Person-days in restricted movements

The total number of person-days in restricted movements is a measure of the burden of the control measure. The highest burden of restricted movements, 9,376 days per 1,000 close contacts of a confirmed case, is under the comparator strategy of 14 days in restricted movements irrespective of test results (Table 6). The lowest burden (of 6,823 days) is for scenario three; that is, a RT-PCR first test on 'day zero' and an RT-PCR test on day seven with release from restriction of movements on a 'not detected' test result.

Table 6. Total person days in restricted movements (per 1,000 close contacts of confirmed cases): two-test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	9,376	(8,410 to 10,288)	-	-
2	7,721	(7,004 to 8,346)	-1,655	(-2,146 to -1,142)
3	6,823	(6,214 to 7,375)	-2,553	(-3,179 to -1,899)
4	8,769	(7,907 to 9,486)	-607	(-944 to -233)

Note shading indicates scenario with lowest burden in terms of person days in restricted movements

Person-days of infectious individuals in community

Increased risk can arise through an earlier end of restricted movements for individuals who are yet to become symptomatic or those who will remain asymptomatic.

The more time an infectious individual is in the community, the greater the risk of onward transmission, and as such it can be interpreted as a measure of risk.

As shown in Table 7, the lowest risk relative to standard practice is scenario four, with a potential increase of one infectious person-day in the community per 1,000 close contacts (95%CI: -27 to 27). That is, an RT-PCR first test on 'Day zero' with an RT-PCR test on day 10 with release from restriction of movements on receipt of day 10 test result.

Table 7. Total person days for infected individuals not in restricted movements (per 1,000 close contacts of confirmed cases): two-test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	222	(119 to 352)	-	-
2	239	(127 to 370)	17	(2 to 37)
3	254	(141 to 389)	32	(7 to 67)
4	222	(118 to 353)	1	(-27 to 27)

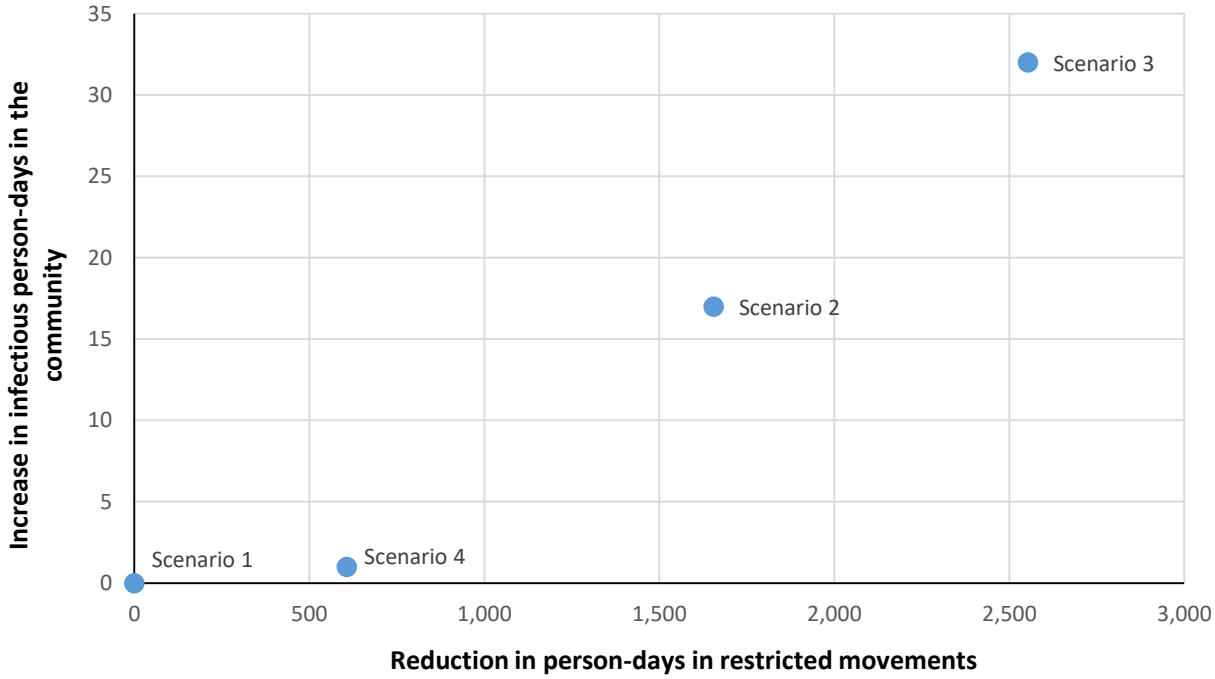
Note shading indicates scenario with lowest risk in terms of infectious person days in community

Person days in restricted movements versus infectious person-days in community

To provide a balanced view of the above results it is useful to consider these two estimates simultaneously. Figure 4 below presents each scenario plotted with respect to the estimated number of person-days in restricted movements and the estimated infectious person-days in the community upon ending the restriction of movements. On balance, it can be seen that relative to the comparator, scenario 4

provides the largest benefit (in terms of reduced number of person-days in restricted movements), relative to a decreased risk (in terms of infectious days in the community).

Figure 4. Increase in infectious person-days in the community versus reduction in person-days in restricted movements: two-test strategies



Number of tests carried out

Alternative strategies will have implications for the number of tests carried out. Of the scenarios modelled, the highest number of tests (1,445) are generated by scenario 4. This is the only scenario of the two-test scenarios in which the second test occurs on 'Day 10' rather that 'Day seven'. Within standard practice, individuals are not referred for a second test if it falls within 24 hours of their first test; an increase in the time between these two tests is estimated to increase the number of individuals eligible for a second test.

Table 8. Total tests performed as part of contact tracing (per 1,000 close contacts of confirmed cases): two-test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	1,218	(1,172 to 1,267)	-	-
2	1,218	(1,172 to 1,267)	-	-
3	1,218	(1,172 to 1,267)	-	-
4	1,445	(1,387 to 1,504)	227	(194 to 258)

Sensitivity analysis

A series of sensitivity analyses were carried out to explore the impact of structural and certain parameter assumptions in the model (Table 9). The analyses were limited to the comparison of scenarios one and four. Benefits are the reduction in person-days in restricted movements; harms are expressed as the increase in infectious person-days in the community. Across all of the sensitivity analyses carried out, scenario four generally leads to a reduction in person-days in restricted movements with varying, but small, effects on harm estimates.

Table 9. Scenario four relative to scenario one: impact of sensitivity analyses

Sensitivity analysis	Benefits*	Harms*
Main analysis	607	1
Average adherence to restriction of movements 65% on day 10	323	8
Uptake of second test at 53%	881	3
Adherence curve applies from first day of contact tracing	983	4
Test appointment always on day after referral	490	-2
No adjustment to day 0 for those in continuous exposure	685	7
Lower proportion asymptomatic (20%)	606	-1
Test results always on day after test	607	1
Sensitivity of RT-PCR is 95%	608	2

*Benefits infers reduction in person-days in restricted movements relative to standard practice. Harms infers increase in infectious person-days in the community relative to standard practice.

Strategies involving single test

The five scenarios which involve a single test strategy are:

- Scenario five: removing the 'day seven' RT-PCR test, and ending the period of restricted movements on day 14 since last exposure if the RT-PCR test on 'day zero' returns a 'not detected' result.
- Scenario six: removing the 'day seven' RT-PCR test, and ending the period of restricted movements on day 10 since last exposure if the RT-PCR test on 'Day zero' returns a 'not detected' result.
- Scenario seven: removing the 'day seven' RT-PCR test, and ending the period of restricted movements on day seven since last exposure if the RT-PCR test on 'day zero' returns a 'not detected' result.
- Scenario eight: replacing the 'day zero' and 'day seven' RT-PCR tests with a single test taken on day five since last exposure ('day five' test), with ending of the period of restricted movements on day 14 since last exposure, conditional on a 'not detected' result received.
- Scenario nine: replacing the 'day zero' and 'day seven' RT-PCR tests with a single test taken on day five since last exposure ('day five' test), with ending of the period of restricted movements on day 10 since last exposure, conditional on a 'not detected' result received.

Person-days in restricted movements

The total number of person-days in restricted movements is a measurement of the burden caused by the control measure. The highest burden of restricted movements, 9,376 days per 1,000 close contacts of a confirmed case, is under the standard strategy of 14 days irrespective of test results (Table 10). The lowest burden (of 5,970 days) is for scenario seven; an RT-PCR first test on 'day zero' with release from restriction of movements on day seven contingent on a 'not detected' test result.

Table 10. Total person days in restricted movements (per 1,000 close contacts of confirmed cases): single test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	9,376	(8,410 to 10,288)	-	-
5	9,295	(8,290 to 10,233)	-81	(-151 to -31)
6	7,548	(6,838 to 8,190)	-1,828	(-2,301 to -1,321)
7	5,970	(5,479 to 6,475)	-3,406	(-4,078 to -2,706)
8	9,354	(8,377 to 10,262)	-23	(-77 to 21)
9	7,662	(6,941 to 8,294)	-1,715	(-2,191 to -1,194)

*shading indicates scenario with lowest burden in terms of person days in restricted movements

Person-days of infectious individuals in community

As shown in Table 11, in terms of infectious person-days in the community, the highest total risk is seen with scenario seven (incremental increase of 163 days relative to standard practice); an RT-PCR test on 'day zero' with end of restricted movements on day seven contingent on a 'not detected' test result. The lowest risk is seen with standard practice and with scenario eight (no increase relative to standard practice); that is, RT-PCR test on day five with end of restriction of movements on day 14.

Table 11. Total person days for infected individuals not in restricted movements (per 1,000 close contacts of confirmed cases): single test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	222	(119 to 352)	-	-
5	258	(139 to 404)	36	(8 to 73)
6	314	(185 to 463)	92	(46 to 146)
7	385	(243 to 552)	163	(91 to 245)
8	222	(118 to 359)	0	(-27 to 30)
9	242	(132 to 379)	20	(-14 to 61)

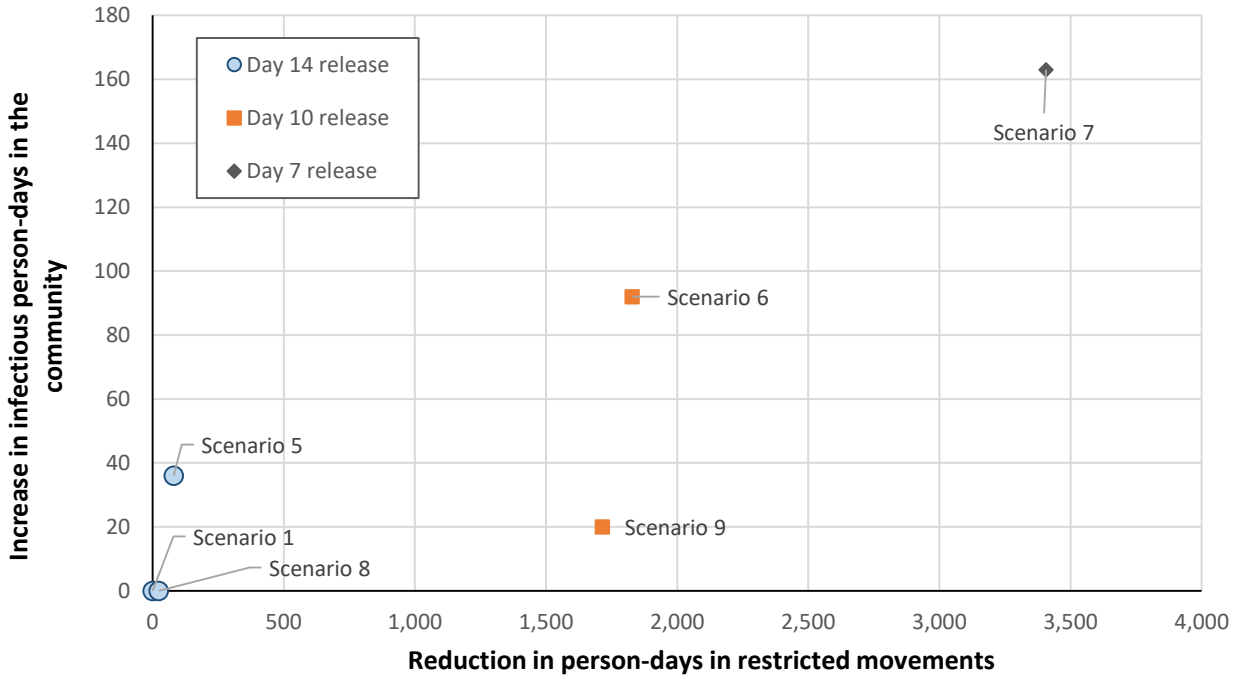
*shading indicates scenario with lowest additional risk in terms of infectious person days in community

Person days in restricted movements versus infectious person-days in community

Figure 5 below presents each scenario plotted with respect to the estimated number of person-days in restricted movements and the estimated infectious person-days in the community upon ending the restriction of movements. On balance, it can be

seen that relative to the comparator, scenario eight provides similar benefit (in terms of number of person-days in restricted movements) with minimal change in risk (in terms of increased infectious days in the community).

Figure 5. Increase in infectious person-days in the community versus reduction in person-days in the restricted movements: single test strategies



Number of tests carried out

As shown in Table 12, of the single test scenarios modelled, there is little difference seen between the scenarios involving 'day zero' test (scenarios 5, 6 and 7) versus those with a 'day five' test (scenarios 8 and 9), with all leading to a reduction of approximately 383 to 397 tests per 1,000 close contacts.

Table 12. Total tests performed as part of contact tracing (per 1,000 close contacts of confirmed cases): single test strategies

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	1,218	(1,172 to 1,267)	-	-
5	835	(804 to 865)	-383	(-419 to -350)
6	835	(804 to 865)	-383	(-419 to -350)
7	835	(804 to 865)	-383	(-419 to -350)
8	821	(790 to 852)	-397	(-432 to -364)
9	821	(790 to 852)	-397	(-432 to -364)

Sensitivity analysis

A series of sensitivity analyses were carried out to explore the impact of structural and certain parameter assumptions in the model (Table 13). The analyses were limited to the comparison of scenarios one and eight. The measures of benefits and harms are clearly sensitive to assumptions, although it should be remembered that the magnitude of effect is small in all cases – scenarios one and eight are almost indistinguishable in terms of benefits and harms. The main notable difference is when there is a low uptake of the 'day seven' test. A single test on 'day five' with a high uptake reduced the infectious person days in the community relative to a strategy with low uptake of a 'day seven' test, but also leads to an increase in the number of person days in restriction of movement.

Table 13. Scenario eight relative to scenario one: impact of sensitivity analyses

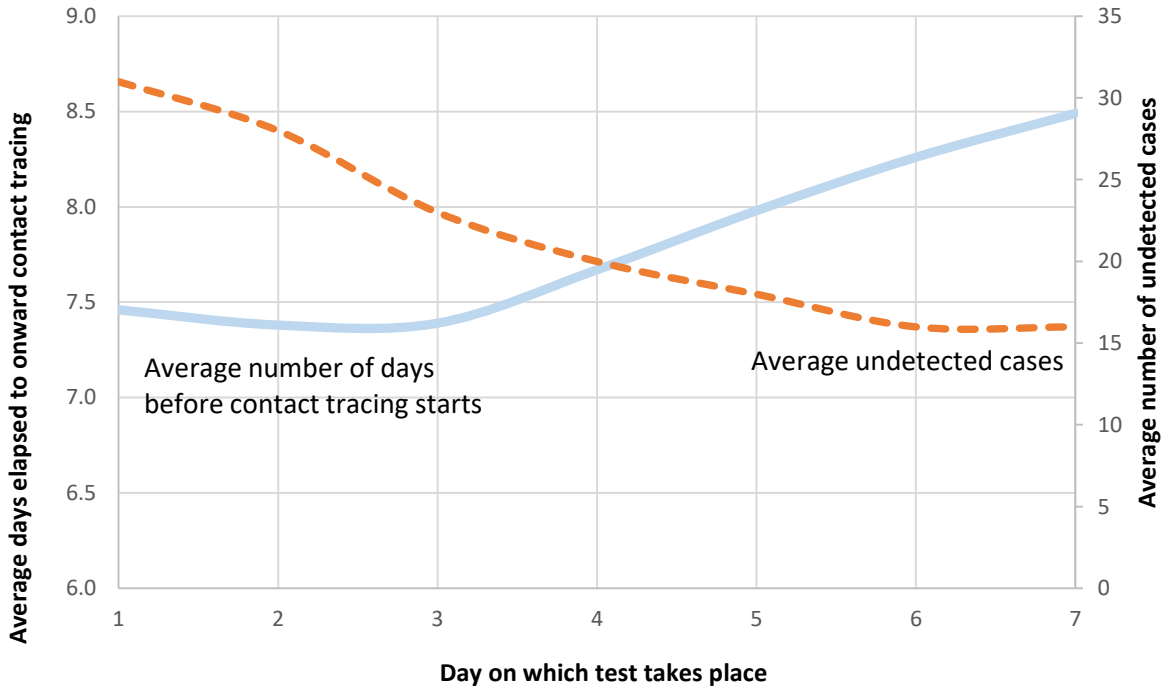
Sensitivity analysis	Benefits*	Harms*
Main analysis	23	0
Average adherence to restriction of movements 65% on day 10	44	0
Uptake of second test at 53%	-46	-28
Adherence curve applies from first day of contact tracing	3	-1
Test appointment always on day after referral	12	-3
No adjustment to day 0 for those in continuous exposure	23	3
Lower proportion asymptomatic (20%)	26	3
Test results always on day after test	23	0
Sensitivity of RT-PCR is 95%	21	-1

*Benefits suggest a reduction in person-days in restricted movements relative to standard practice. Harms suggest an increase in infectious person-days in the community relative to standard practice.

Threshold analysis of choice of day for single test

An analysis was undertaken to determine the impact of choice of day for a single test on the time to onward contact tracing and on the number of undetected cases (Figure 6). The average time to onward contact tracing is minimised with a single test on day three. The average number of undetected cases is minimised if testing occurs on days five, six or seven. By testing on day five rather than day three, the average lag to onward contact tracing is increased by one day.

Figure 6. Threshold analysis of choice of day for single test (per 1,000 close contacts)



Strategies involving no universal testing of close contacts

The two scenarios which do not involve universal testing of close contacts are:

- Scenario ten: no universal testing of close contacts, and restriction of movements for 10 days.
- Scenario eleven: no universal testing of close contacts, and restriction of movements for 14 days.

Person-days in restricted movements

The total number of person-days in restricted movements is a measure of the burden of the control measure. The highest burden of restricted movements, 9,376 days per 1,000 close contacts of a confirmed case, is under the standard strategy of 14 days restricted movements irrespective of test results (Table 12). Two alternative scenarios were modelled: in both cases it was assumed that there would be no universal testing of close contacts, with ending of restricted movements on day 10 (scenario 10) or day 14 (scenario 11).

A small reduction is seen in scenario 11; the reduction is viewed as a consequence of the level of adherence expected to overall restricted movements. As it is assumed that not all individuals will be adherent to restriction of movement unless they receive a positive test result, any strategy that reduces the number of detected cases will also reduce the number of total person days in restriction of movement. In the absence of universal testing, individuals that are asymptomatic will not be test detected. The lowest burden (of 7,178 days) is for scenario 10; end of restriction of movements on day 10, with an estimated reduction of 2,198 days relative to standard practice.

Table 12. Total person days in restricted movements (per 1,000 close contacts of confirmed cases): no universal testing

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	9,376	(8,410 to 10,288)	-	-
10	7,178	(6,377 to 7,838)	-2,198	(-2,631 to -1,720)
11	9,058	(7,908 to 10,098)	-318	(-532 to -156)

*shading indicates scenario with lowest burden in terms of person days in restricted movements

Person-days of infectious individuals in community

As shown in Table 13, in terms of infectious person-days in the community, both scenarios which do not include universal testing of close contacts result in an increased risk, with scenario 10, end of restriction of movements on day 10, exhibiting the highest risk overall (incremental increase of 336 days relative to standard practice).

Table 13. Total person-days for infected individuals not in restricted movements (per 1,000 close contacts of confirmed cases): no universal testing

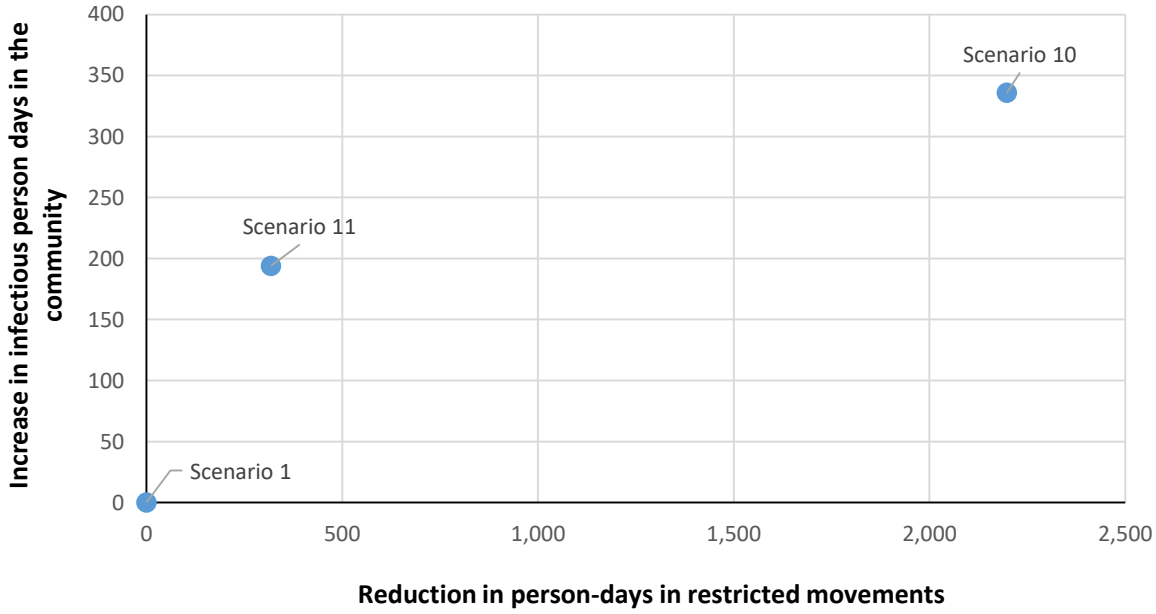
Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	222	(119 to 352)	-	-
10	558	(363 to 805)	336	(203 to 493)
11	416	(249 to 631)	194	(101 to 318)

*shading indicates scenario with lowest additional risk in terms of infectious person days in community

Person days in restricted movements versus infectious person-days in community

Figure 7 below presents each of the two scenarios, and the standard of practice, plotted with respect to the estimated number of person-days in restricted movements and the estimated infectious person-days in the community upon ending the period of restriction of movements. It can be seen that relative to standard practice, scenario 10 and scenario 11 both result in an increase in risk. This increase in risk is more marked for scenario 10 (end of restricted movements on day 10), but this strategy also provides the largest benefit in terms of reduced person-days in restricted movements.

Figure 7. Increase in infectious person-days in the community versus reduction in person-days in the restricted movements: no universal testing strategies



Number of tests carried out

As shown in Table 14, of the two scenarios without universal testing, both naturally result in a substantial reduction in the number of tests conducted (mean reduction of 1,128 relative to standard practice). Symptomatic close contacts are factored into the model as being referred for testing, with 134 tests estimated to be completed by this cohort.

Table 14. Total tests performed (per 1,000 close contacts of confirmed cases): no universal testing

Scenario	Referred as part of contact tracing				Symptomatic referral	
	Total		Incremental		Total	Incremental
	Mean	95% CI	Mean	95% CI		
1 (comparator)	1,218	(1,172 to 1,267)	-	-	45	(29 to 64)
10	0	(0 to 0)	-1,218	(-1,267 to -1,172)	134	(97 to 173)
11	0	(0 to 0)	-1,218	(-1,267 to -1,172)	134	(97 to 173)

Sensitivity analysis

A series of sensitivity analyses were carried out to explore the impact of structural and certain parameter assumptions in the model (Table 14). The analyses were limited to the comparison of scenarios one and eleven. The measures of benefits and harms are clearly sensitive to assumptions within the model.

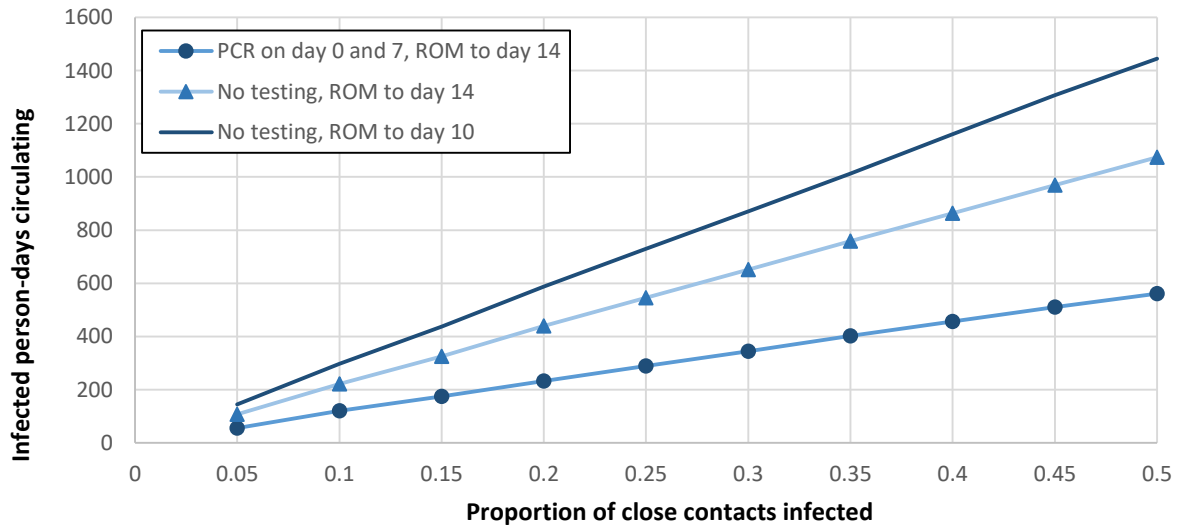
Table 14. Scenario eleven relative to scenario one: impact of sensitivity analyses

Sensitivity analysis	Benefits*	Harms*
Main analysis	318	194
Average adherence to restriction of movements 65% on day 10	420	240
Uptake of second test at 53%	250	166
Adherence curve applies from first day of contact tracing	179	149
Test appointment always on day after referral	315	200
No adjustment to day 0 for those in continuous exposure	253	146
Lower proportion asymptomatic (20%)	609	484
Test results always on day after test	318	194
Sensitivity of RT-PCR is 95%	328	203

*Benefits suggest a reduction in person-days in restricted movements relative to standard practice. Harms suggests an increase in infectious person-days in the community relative to standard practice.

A threshold analysis was undertaken to examine the impact on infectious person days in the community of different levels of infection in close contacts. The main analysis assumed approximately 18% of close contacts of a confirmed case to be infected. There is a linear increase in the infectious person days in the community with an increase in the proportion of individuals infected (Figure 8). The proportionate increase is consistent with a strategy of no testing, with release from restriction of movement after ten days since last exposure leading to a 255% increase in infectious person days in the community relative to standard practice; no testing with release from restriction of movement 14 days after last exposure leads to a 190% increase. Even at low levels of infection, the absolute increase in infectious person days in the community can be substantial.

Figure 8. Impact of the proportion close contacts infected on infectious person-days in the community: no universal testing strategies



Limitations

Context of data

The model incorporates parameter data in a manner intended to capture uncertainty in the true values. While variability across patients is modelled, there is an averaging effect in aggregating results to a group level. The data are a mixture of international and Irish-specific estimates and reflect what is known at this point in time. It is evident that there have been quite substantial shifts over time in the demographic characteristics of those infected with SARS-CoV-2 in Ireland. Data from contact tracing reflect activity in October to December 2020, which include periods of substantial demand due to high incidence of COVID-19. It is assumed that the disease parameters used in the model apply to the demographic group represented in the contact tracing data. It is also important to acknowledge that the contact tracing data reflect the conditions of the time. Adherence to restriction of movements and uptake of tests are influenced by the incidence of COVID-19 and the public health measures in place. This changing pattern may have a substantial impact over time on the estimates presented within this report.

Data quality

The model included numerous parameters. The data supporting the parameter estimates came from a wide range of heterogeneous sources. Some were derived from observational studies which were not always designed to estimate the parameter of interest.

A key distinction that frequently occurs is the difference between the last date of exposure and the date of exposure that lead to the infection. The difference between the two may be a matter of a day or two, but that becomes important in understanding the latent period, incubation period and critically, the point at which an infected individual becomes infectious.

It is also important to note that the available data describes the course of infectious individuals in a wide range of settings and population groups, not all of which may be applicable to an Irish setting. While characteristics of the infection itself should perhaps be similar across populations, those aspects that are affected by human behaviour could vary immensely. Of particular relevance are adherence to control measures and testing. The model presented here used uncertainty around parameter estimates to explore uncertainty in the relative effects of the different scenarios modelled.

Infectivity

An important consideration in the spread of COVID-19 is the period and magnitude of infectivity in an index case. The estimates of duration of infectivity implicitly acknowledge that viral load declines over time to the extent that an individual may

no longer be infectious, but can still test positive with RT-PCR. It is plausible that peak infectiousness may occur early in the infection, as demonstrated by the proportion of onward infections that occur prior to symptom onset.[12] However, it is worth considering that the propensity to infect and the opportunity to infect are distinct, and that symptomatic cases will typically self-isolate, reducing the opportunity to transmit disease. The reported data likely reflect the fact that both propensity and opportunity to infect decreases over time. In the absence of data on the magnitude of infectiousness, we have modelled uniform infectiousness for an individual over the period for which they are considered infectious. In the event that infectiousness is greater prior to and at the point of symptom onset, than after symptom onset, the model may be impacted through the overestimation of the benefits of 'day 10' testing, relative to 'day seven'. However, in the absence of good supporting data, we have taken a conservative approach and assumed that propensity to infect is constant, but the opportunity is reduced by restricted movements or self-isolation.

Uptake and adherence

The extent to which close contacts adhere to restricted movements and can avail of the offered tests is clearly a significant factor. We assumed that adherence to restriction of movements is initially high and wanes over time. The initial high adherence is confirmed by an audit of restriction of movements among close contacts and cases identified through the contact tracing service.[3] The uptake of the so-called 'day zero' test indicates a large proportion of people present for testing, and may be reflective of a high willingness to follow guidance.

Uptake for the 'day seven' test is high at present - and is similar to the uptake for the 'day zero' test. The high uptake for the second test reported in recent contract tracing data (approximately 83%) is in contrast to earlier data that indicated a lower uptake used in the first iteration of this model (approximately 57%). The changes in uptake must be considered within context – it is possible that uptake of testing is higher when incidence is higher and during a period of lockdown. Another aspect to consider is that the demographics of cases and close contacts has changed over time, and is likely to continue changing. The balance of benefits and harms associated with adhering to restricted movements will be interpreted differently by people depending on their perception of the risk of poor outcomes and the impact on daily activities, such as work.

Another important consideration is the potential for uptake of testing to be higher in people who are symptomatic or pauci-symptomatic. That is, people with some symptoms would be more likely to attend for testing in the belief that they may be infected. They may also have a shorter lag between referral and their testing appointment as they seek to expedite finding out if they are infected. This would

certainly impact on the movements of contacts through the system and when they may be test detected.

Characterisation of the pathway

Describing the management pathway of close contacts of confirmed cases is challenging. There is substantial variation across individuals in terms of when they are identified, when and whether they attend for the 'day zero' test, whether they present for a second test, and how long it takes to get test results.

It is not possible at this point to determine the extent to which there are associations between different characteristics. For example, is it possible to predict which cases are unlikely to present for 'day seven' testing based on the interactions up to 'day seven'. It is also a dynamic situation because of changes to the system, such as reductions in the time from testing to the receipt of results, or capacity constraints on the numbers of contacts that can be followed up. We have attempted to characterise the management pathway based on recent activity in the contact management programme, but acknowledge that the findings from this point in time may no longer be applicable if there are substantive changes to the contact management programme.

Correlation between variables

As the various parameter estimates were each derived independently, we have assumed that they are not correlated. That is, that an individual with a long latent period may also have a long pre-symptomatic infectious period. Certain correlations could be important, such as if asymptomatic cases had a longer infectious period, as this would imply that in the absence of being test-detected or adhering to restricted movements that they could infect many individuals. In terms of future research and potentially to aid understanding of individuals described as superspreaders, it would be useful for studies to consider the extent to which infection characteristics are correlated.

Calibration of model

The model was developed to simulate the progression of infection in infected close contacts, attendance for testing and adherence to restriction of movement. It was possible to compare the performance of the model against observed data for certain outcomes such as number of individuals tested and the proportion positive. One parameter for which there were limited supporting data were the proportion of close contacts that were infected. There was also substantial uncertainty about the duration of the latent period. These parameters were treated as unknowns in a calibration exercise to identify estimates that would lead to plausible model outputs.

Based on calibration, it was found that the proportion infected was likely to have been in excess of 18% for the period analysed (first three weeks of December). In

addition, it was found that a shorter estimate for the latent period resulted in more plausible outputs. While this may imply that the latent period is shorter than the available evidence suggests, it could also be indicative that the date of last exposure may not be a good measure of day of transmission for infected cases. That is, some close contacts may have had two or more consecutive days of exposure to the confirmed case and that transmission may have occurred prior to the last day of exposure. A shorter latent period obtained through calibration may therefore be acting as an adjustment for how date of exposure is measured.

Modelled scenarios

A selected group of potential testing scenarios were modelled in this report. Particularly for scenarios involving testing, it is important to acknowledge that a given sequence of tests may not be logistically feasible or may offer very little benefit. In particular, for two-test strategies there needs to be sufficient lag between the tests to allow for turnaround of results and to take into account the lag between referral and test appointments. As such, tests on days five and seven, for example, would not be practical.

Contextualisation of results

Overall, the update of this analysis highlights a number of key points for consideration:

- Of the two-test options assessed, at a population level, the use of testing on 'day zero' and 'day 10' with end of restriction of movements on receipt of a 'not detected' test result from the second test would, on balance, present the largest potential reduction in risk (in terms of infectious person-days in the community) relative to an increase in benefit (in terms of reduced person-days in restricted movements) compared to standard practice in Ireland.
    - Per 1,000 close contacts, this scenario infers a reduction of 607 (95% CI: -944 to -233) person-days in restricted movements with no significant increase in infectious person-days in the community, relative to standard practice (1 person-day, 95% CI: -27 to 27).
    - For a hypothetical cohort of 1,000 COVID-19 cases, assuming an average of three close contacts per case, this would equate to a reduction of approximately 1,821 person-days in restricted movements and an increase of three infectious person-days in the community.
- For scenarios involving a single test, the use of a 'day five' test with end of restricted movements on day 14 was most similar to standard practice in Ireland.
    - Per 1,000 close contacts, estimates for this scenario result in no significant change in benefits or harms relative to standard practice (-23 person-days in restricted movements, 95% CI: -77 to 21; 0 infectious person-days in the community, 95% CI: -27 to 30).
- Of the two-test options, the above scenario of adopting a 'day 10' test in lieu of the 'day seven' test is associated with an increase in the total number of tests conducted (approximately 227 tests (95% CI: 194 to 258) per 1,000 close contacts). This increase is due a higher proportion of individuals eligible for a second test because of the longer interval between it and the 'Day zero' test. The use of a single-test strategy results in a reduction of approximately 383 to 397 tests per 1,000 close contacts irrespective of the day on which the test is conducted.
- Consistently during the pandemic, the majority of cases identified through contact tracing have been detected through the 'day zero' test, with a much smaller proportion identified with the 'day seven' test. A change to the timing of the first test, such as moving it to 'day five', will delay detection of cases with consequent implications for onward contact tracing. However, testing on

'day five' is associated with the lowest number of undetected cases relative to earlier testing days.

- Relative to standard practice, a reduction in the duration of restricted movements based on a 'not detected' test result could lead to an increased residual risk of infection. Therefore, if a strategy is adopted that increases residual risk, it should be accompanied by additional public health guidance including the requirement for ongoing physical distancing (and additional precautions in terms of contact with vulnerable populations), hand hygiene, and respiratory etiquette.
- If considering a reduction in duration of restricted movements based on testing, attention needs to be paid to the impact on certain groups such as vulnerable individuals or those in high-risk settings, in which any increased risk of onward infection may not be acceptable.
- An increase in risk compared with standard practice was observed in both scenarios in which there was no universal testing of close contacts:
    - Ending of restriction of movements on day 14 in this context infers an increase of 194 (95% CI: 101 to 318) infectious person-days in the community per 1,000 close contacts. For a hypothetical cohort of 1,000 COVID-19 cases assuming an average of three close contacts per case, this would equate to an increase of approximately 582 infectious person-days in the community.
    - Ending of restriction of movements on day 10 in this context infers an increase of 336 (95% CI: 203 to 493) infectious person-days in the community per 1,000 close contacts. However, this scenario is associated with a mean reduction of 2,198 person-days in restricted movements. For a hypothetical cohort of 1,000 COVID-19 cases assuming an average of three close contacts per case, this would equate to an increase of approximately 1,008 infectious person-days in the community and a reduction of 6,594 person-days in restricted movements.
- The data used in the model for characterising disease progression were based on studies that were published prior to the recent identification of two variants of SARS-CoV2 (B.1.1.7 and B.1.351) which may possess higher transmissibility than other circulating strains. Sequencing in Ireland suggests a trend for an increasing proportion of cases being attributed to these new variants. It is unclear whether the new variants are associated with a different profile of progression of infection. Of particular importance are the latent period, pre-symptomatic infectious period and likelihood of being

symptomatic. If, for example, the new variants were associated with a longer incubation period, then early cessation of restriction of movements without testing could increase the risk of onward infection.

- Overall, the results presented within this report should be considered with regards to what constitutes an acceptable level of risk relative to standard practice in the context of the current and future disease trajectory, possible broader public and mental health considerations, and the capacity to resource essential services.
- The estimates presented in this report are underpinned by a range of assumptions and data from a point in time. Important factors such as uptake of testing and proportion close contacts infected are continuously changing in response to incidence, testing capacity and the public health measures in place. Substantial changes in how and when close contacts are identified, and the extent to which they attend for testing, will impact on the relative benefits and harms of the modelled scenarios.

Appendix 1- Model validation

The model developed for this report was intended to simulate the process of testing close contacts of confirmed cases of COVID-19 in Ireland. The model required a wide range of parameters, some of which relate to individuals and others that reflect the organisational aspects.

The course of infection in individuals was simulated based on international data on period of infectiousness and incubation period, from which the length of latent period was inferred. Those parameters are subject to substantial uncertainty and variability across individuals. Some of the key parameters, such as the proportion of cases that are asymptomatic, are equally associated with degrees of uncertainty.

Parameters that describe the process are also subject to uncertainty and reflect the conditions at a point in time. For example, the uptake of the second test has varied substantially over time.

In validating the model, we compared certain key model outputs against the reported values from contact tracing to determine if the model was broadly accurate. The main model used uptakes rates that reflected an average over three weeks in December 2020. For the validation exercise, we used directly comparable figures for the available data. Outputs were compared for 'day zero' and 'day seven' testing (Tables A1.1 and A1.2).

For 'day zero' testing, the model provides a very accurate estimate of the main outputs. The number tested is accurate because the uptake figure is directly supplied to the model. The percentage positive is modelled based on disease parameters and an assumption that infected cases will become symptomatic no more than a day before being referred for testing.

Table A1.1 Comparing contact tracing and model outputs for 'Day zero' testing

Measure	Service	Model	
		Mean	95% CI
Referred	1,000	1,000	
Tested	830	835	(804 to 865)
Positive (%)	13.4	12.4	(9.0 to 16.0)

For 'day seven' testing, the model is less accurate. It predicts a higher number to be referred for testing, although the number tested is accurate. This is because within the model, people may become symptomatic and seek testing before their referred appointment comes up. The percentage positive is also an over-estimate. There may

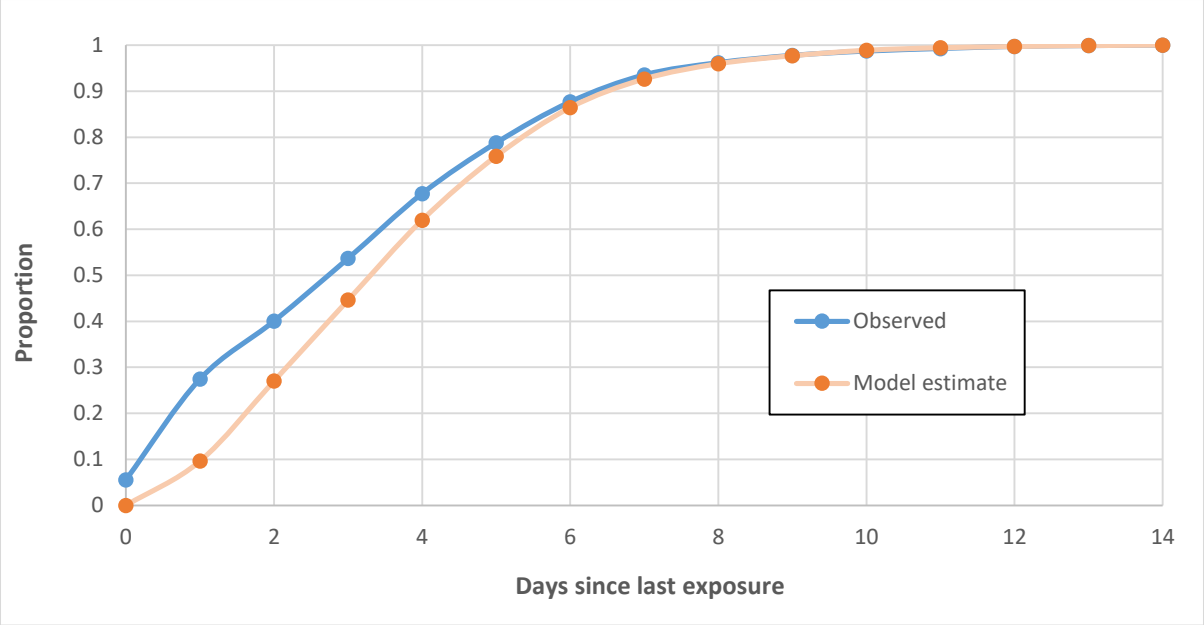
be a variety of reasons for this, such as the assumption of the actual proportion infected potentially being too high. An over-estimate of the number of positive cases will potentially result in an under-estimate of the number of infectious person-days in the community. In practical terms, the over-estimate means that per 1,000 close contacts, the model predicts 31 positive cases detected at 'day seven' whereas in reality it is fourteen. Relative to the 182 infected individuals simulated in the model, it is a small contribution.

Table A1.2 Comparing contact tracing and model outputs for 'Day seven' testing

Measure	Service	Model	
		Mean	95% CI
Referred	366	529	(495 to 562)
Tested	307	383	(350 to 419)
Positive (%)	4.5	8.2	(5.2 to 12.3)

The other data for validating the model relates to the day on which close contacts are tested (Figure A1.1).

Figure A1.1 Cumulative 'Day zero' tests completed by days since last exposure



The estimates from the model are substantially different for the first two days which is due to the fact that the model does not treat a case in continuous exposure as being identified on day zero, but rather that exposure occurred at some point prior to being identified as a close contact. As part of model validation, the model was run with day zero cases being treated as day zero. This resulted in the outputs underestimating positivity at 'day zero' testing and over-estimating positivity at 'day seven' testing. The model also substantially overestimated the number of people tested on 'day seven'. These findings suggest that people in continuous exposure who are infected are likely to have been infected prior to being identified as a close contact and referred for 'day zero' testing.

Appendix 2 – Model parameters

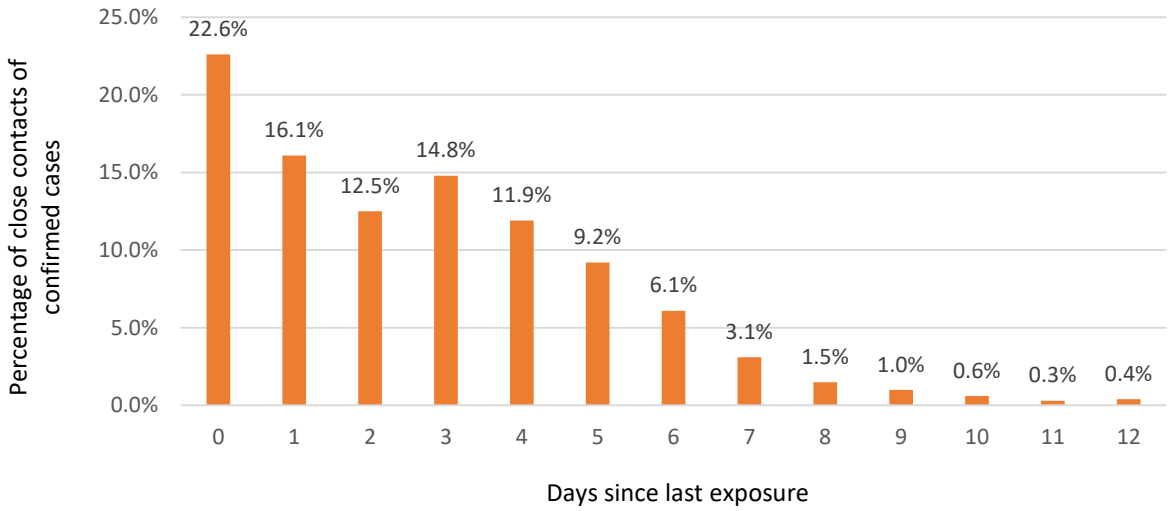
This appendix provides the details of the parameters used in the model. The main parameters were defined by statistical distributions (Table A2.1).

Table A2.1 Details of parameter distributions

Parameter	Distribution	Definition
Latent period (days)	Log-normal	0.881; 0.458
Pre-symptomatic infectious period (days)	Log-normal	1.024; 0.678
Symptomatic infectious period (days)	Weibull	3.493; 7.903
Proportion close contacts infected	Beta	154.4; 695.6
Proportion symptomatic	Beta	115.02; 51.68
Proportional uptake of 'Day 0' test	Beta	832; 168
Proportional uptake of second test	Beta	837; 173
Adherence to restriction of movements at outset	Beta	45; 5
Adherence to restriction of movements on day 10	Beta	37.5, 12.5
Sensitivity of RT-PCR	Beta	90; 10
Specificity of RT-PCR	Beta	990; 10

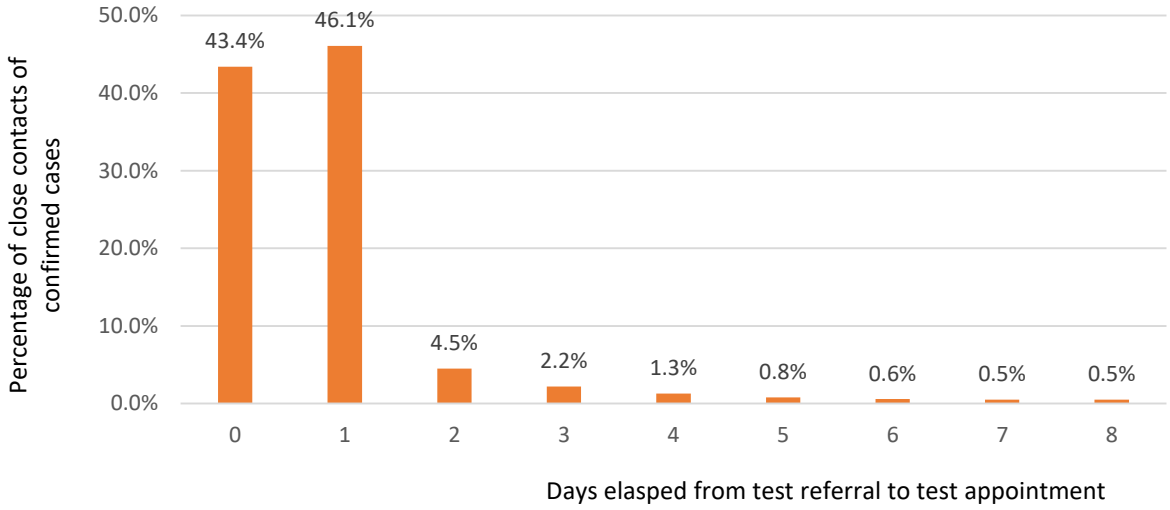
The lag from last date of exposure to being contacted by contact tracing was sampled. The sampling probabilities were derived from contact tracing data (Figure A2.1).

Figure A2.1 Sampling weights for lag to 'Day zero'



The lag from day of test referral to day of test appointment was also sampled. The sampling probabilities were derived from HSE SwiftQueue data (Figure A2.2).

Figure A2.2 Sampling weights for lag from test referral to appointment



The lag from test appointment to receipt of a 'not detected' test result could be one, two or three days and was sampled with probabilities of 0.55, 0.40 and 0.05, respectively. For a positive test result, the sampling weights were 0.20, 0.50 and 0.30 for one, two and three days, respectively.

Appendix 3- Modelled outcomes

This appendix includes all of the modelled outcomes for each scenario.

Table A3.1 True-positives by testing scenario (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	134	(100 to 172)	-	-
2	134	(100 to 172)	0	(0 to 0)
3	134	(100 to 172)	0	(0 to 0)
4	127	(94 to 163)	-7	(-17 to 2)
5	103	(75 to 134)	-31	(-46 to -20)
6	103	(75 to 134)	-31	(-46 to -20)
7	103	(75 to 134)	-31	(-46 to -20)
8	130	(97 to 167)	-5	(-18 to 7)
9	130	(97 to 167)	-5	(-18 to 7)
10	0	(0 to 0)	-134	(-172 to -100)
11	0	(0 to 0)	-134	(-172 to -100)

Table A3.2 False-positives by testing scenario (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	9	(3 to 19)	-	-
2	9	(3 to 19)	-	-
3	9	(3 to 19)	-	-
4	12	(3 to 23)	2	(-4 to 9)
5	6	(1 to 13)	-3	(-9 to 0)
6	6	(1 to 13)	-3	(-9 to 0)
7	6	(1 to 13)	-3	(-9 to 0)
8	8	(2 to 16)	-3	(-8 to -2)
9	7	(1 to 14)	-3	(-8 to -2)
10	0	(0 to 0)	-9	(-19 to -3)
11	0	(0 to 0)	-9	(-19 to -3)

Table A3.3 Number of undetected cases by testing scenario (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	16	(8 to 27)	-	-
2	16	(8 to 27)	0	(0 to 0)
3	16	(8 to 27)	0	(0 to 0)
4	14	(6 to 23)	-3	(-8 to 2)
5	31	(18 to 46)	14	(7 to 23)
6	31	(18 to 46)	14	(7 to 23)
7	31	(18 to 46)	14	(7 to 23)
8	18	(8 to 29)	1	(-4 to 7)
9	18	(8 to 29)	1	(-4 to 7)
10	61	(39 to 89)	45	(27 to 67)
11	61	(39 to 89)	45	(27 to 67)

Table A3.4 Average days since exposure on which cases are identified [and contact tracing can be initiated]

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	7.73	(7.37-8.10)	-	-
2	7.73	(7.37-8.10)	0.00	(0.00-0.00)
3	7.73	(7.37-8.10)	0.00	(0.00-0.00)
4	8.00	(7.56-8.42)	0.27	(0.05-0.49)
5	7.46	(7.07-7.85)	-0.28	(-0.46--0.12)
6	7.46	(7.07-7.85)	-0.28	(-0.46--0.12)
7	7.46	(7.07-7.85)	-0.28	(-0.46--0.12)
8	7.98	(7.69-8.31)	0.25	(-0.06-0.57)
9	7.98	(7.69-8.31)	0.25	(-0.06-0.57)
10	7.78	(7.32-8.23)	0.05	(-0.37-0.49)
11	7.78	(7.32-8.23)	0.05	(-0.37-0.49)

Table A3.5 Number of referred tests completed by testing scenario (per 1,000 close contacts of confirmed cases)

Scenario	Total		Incremental (relative to comparator)	
	Mean	95% CI	Mean	95% CI
1 (comparator)	1,218	(1,172-1,267)	-	-
2	1,218	(1,172-1,267)	0	(0-0)
3	1,218	(1,172-1,267)	0	(0-0)
4	1,445	(1,387-1,504)	227	(194-258)
5	835	(804-865)	-383	(-419--350)
6	835	(804-865)	-383	(-419--350)
7	835	(804-865)	-383	(-419--350)
8	821	(790-852)	-397	(-432--364)
9	821	(790-852)	-397	(-432--364)
10	0	(0-0)	-1,218	(-1,267--1,172)
11	0	(0-0)	-1,218	(-1,267--1,172)

Note: this table is limited to tests carried out on foot of a referral from the contact tracing service. It does not include tests carried out on individuals that became symptomatic before referral or after referral if not detected during testing.

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