ROYAL COLLEGE OF PHYSICIANS OF IRELAND

National Immunisation Advisory Committee

COVID-19 VACCINATION
AFTER LABORATORY CONFIRMED COVID-19 INFECTION

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About NIAC

NIAC includes representatives from the RCPI, its Faculties and Institutes, the RCSI, the ICGP, the National Immunisation Office, the Nursing and Midwifery Board of Ireland, the Infectious Diseases Society of Ireland, the Travel Medicine Society, the National Virus Reference Laboratory and lay members. Meetings are also attended by representatives from the Department of Health and the HSE, Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

This group of experts meet to consider new evidence about vaccines and provide advice to the Chief Medical Officer and the Department of Health. The Department and the Minister for Health make policy decisions on vaccines which are implemented by the HSE.

https://www.rcpi.ie/policy-and-advocacy/national-immunisation-advisory-committee/

Executive summary

The National Immunisation Advisory Committee (NIAC) was requested by the Department of Health (DOH) to monitor any new scientific evidence that that a single dose of a COVID-19 mRNA vaccine may induce a long-lasting immune response in those with previous confirmed SARS-CoV-2 infections and second dose may not be required, with a view to updating the current immunisation schedule as appropriate for individuals who have had a SARS-CoV-2 laboratory confirmed infection.

A small number of studies demonstrated that those with prior COVID-19 infection who had a single dose of a mRNA COVID-19 vaccine had a similar antibody response to those with no prior infection after two doses of COVID-19 vaccine. Previous infection effectively acts as a booster, similar to the second dose in those with no prior COVID-19 infection.

There is some evidence that people aged 50 years and older do not have the same antibody response as people under 50 years of age.

Those who are immunocompromised due to disease or treatment require two doses due to their less robust immune response.

There is evidence of immunity post COVID-19 infection for at least 6-8 months.

Although the evidence relates to mRNA vaccines, it is based on immunological priming with subsequent boosting, thus it is reasonable to infer that these findings can be applied to viral vector vaccines.

NIAC has developed the following recommendations:

Recommendation 1

For those who have had a previous laboratory confirmed COVID-19 infection within 6 months:

- aged 50 years and older should receive a full COVID-19 vaccine schedule
- aged under 50 years and immunocompromised should receive a full COVID-19 vaccine schedule
- aged under 50 years and immunocompetent: a single dose of COVID-19 vaccine is sufficient and they should then be considered fully vaccinated

Recommendation 2

Those who have had laboratory confirmed COVID-19 infection within 6 months after a first dose of COVID-19 vaccine should complete the course

This advice will be kept under review in light of the emerging variants of concern and assessment of vaccine efficacy against such variants.

National Immunisation Advisory Committee
Request for advice

On 31 March 2021, the Department of Health (DOH) asked the National Immunisation Advisory Committee (NIAC) to consider the following:

"*there is emerging evidence that a single dose of a COVID-19 mRNA vaccine may induce a long-lasting immune response in those with previous confirmed SARS-CoV-2 infections and second dose may not be required*"

NIAC was requested to "*continue to monitor any new scientific evidence that may emerge on this issue, with a view to updating the current immunisation schedule as appropriate for individuals who have had a SARS-CoV-2 laboratory confirmed infection*."

Background

NIAC issued recommendations on 10 March 2021 for COVID-19 vaccination of individuals following positive PCR or antigen test for COVID-19.

At that time, there was evidence that infection is followed by a period of immunity to COVID-19 for at least six months. The possibility of reinfection remained but appeared to be a rare event and would likely present as an asymptomatic or mild infection. There was a paucity of evidence regarding those aged 65 and older and those under 65 years who are immunocompromised.

The consequent NIAC recommendations and immunisation guidelines for COVID-19 stated that:

- for all age groups, vaccination should be deferred until clinical recovery from COVID-19 and for at least four weeks after diagnosis or symptom onset, or from the first PCR or antigen positive specimen in those who are asymptomatic
- for those aged under 65 years, who are not immunocompromised, COVID-19 vaccination may be deferred for up to six months after diagnosis, symptom onset, or from the first PCR or antigen positive specimen.

Evidence

There is evidence of sustained immunity for at least 6-8 months following COVID-19 infection.

There is good evidence that those with prior COVID-19 infection who subsequently received a single dose of COVID-19 mRNA vaccine had a similar antibody response to those individuals with no prior infection after two doses of COVID-19 vaccine. There is some evidence that those with prior COVID-19 infection who subsequently had a second dose of COVID-19 vaccine have no additional boosting of their antibody response. There is limited evidence that those 50 years of age and older do not have as good an antibody response as people under 50 years of age.

References	Study	Results	Conclusion
Abu-Jabal et al Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021 Published February 2021 *Eurosurveillance* doi:https://doi.org/10.2807/1560-7917.es.2021.26.6.2100096	Prospective Cohort Study (Israel) n=514 participants (n=475 elicited an immune response post vaccination) HCWs who received one dose of BNT162b2 mRNA vaccine. Stratified by age, ethnicity, gender and previous exposure to SARS-Cov-2 Outcome measures: Number of immune responders and Mean concentration of anti-SARS-CoV2-spike-IgG antibodies 21 days after 1 dose of BNT162b2 mRNA Vaccine IgG titres measured pre and 21 days post vaccination with BNT162b2 mRNA vaccine	Post-vaccination IgG levels among those with evidence of previous infection were much higher than those with no evidence of previous infection (GMC 573 vs 61.5)	Vaccinating individuals with evidence of prior COVID-19 infection with one dose of vaccine led to a boost response, achieving IgG titres approximately one order of magnitude higher compared with naïve individuals.

Ebinger et al Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2 Published April 2021 *Nature Medicine* doi:https://doi.org/10.1038/s41591-021-01325-6	Prospective cohort (USA) 981 HCW vaccine recipients, including 78 with prior SARS-CoV-2 infection, provided baseline (pre-vaccine) samples; 525 (35 with prior infection) provided samples after dose 1; and 239 (11 with prior infection) provided samples after dose 2. 217 individuals (ten with prior infection) provided blood samples at all three time points	Spike-specific IgG antibody levels and ACE2 antibody binding inhibition responses elicited by a single vaccine dose in individuals with prior SARS-CoV-2 infection (n = 35) were similar to those seen after two doses of vaccine in individuals without prior infection (n = 228)	Individuals previously infected with SARS-CoV-2 developed vaccine-induced antibody responses after a single dose of the BNT162b2 (Pfizer–BioNTech) mRNA vaccine similar to antibody responses seen after a two-dose vaccination course administered to infection-naive individuals.
Gobbi et al Antibody Response to the BNT162b2 MRNA COVID-19 Vaccine in Subjects with Prior SARS-CoV-2 Infection Published March 2021 *Viruses* doi: https://doi.org/10.3390/v13030422	Prospective cohort (Italy) Six healthcare workers who contracted SARS-CoV-2, nine control subjects without a previous infection Antibody response to the BNT162b2 mRNA COVID-19 vaccine in those with and without prior infection with COVID-19	A rapid increase in antibodies was observed one week after the first dose in all subjects with pre-existing immunity which seemed to act as a booster. Neutralizing antibody titres 7 days after the first vaccine dose in previously infected individuals were not significantly different from those observed in naïve subjects 7 days after the second vaccine dose	In previously infected people, a single dose of the vaccine might be sufficient to induce an effective antibody response
Goel et al Distinct antibody and memory B cell responses in SARA-CoV-2 naïve and	Prospective cohort (USA) 44 people. 33 SARS-CoV2 naïve and 11 SARS-CoV2 recovered subjects.	In Naïve: Primary vaccination induced a significant increase in SARS-CoV-2 specific antibodies that was enhanced by the booster dose.	Data consistent with need for a two dose mRNA vaccine schedule in naïve individuals

recovered individuals following mRNA vaccination Preprint March 06, 2021 *MedRxiv* doi: https://doi.org/10.1101/2021.03.03.21252872	Individuals who received SARS-CoV2 mRNA vaccines (Pfizer BNT162b2 or Moderna mRNA-1273) In 11 individuals infection was 65-275 days prior to vaccination	Required second dose to achieve detectable antibodies against the B1.353 variant. In Recovered: Similar levels achieved in recovered individuals after a single dose. No additional increase in antibody level following the second dose. Negative correlation between post-boost memory T cells and age	Age a key variable in mRNA vaccine -induced immunity COVID recovered individuals may only require a single dose of vaccine
Jeewandara et al. Antibody and T cell responses to a single dose of the AZD1222/Covishield vaccine in previously SARS-CoV-2 infected and naïve health care workers in Sri Lanka Preprint April 13, 2021. *medRxiv* doi:https://doi.org/10.1101/2021.04.09.21255194	Real time assessment (Sri Lanka) Assessed antibody and T cell responses 633 HCW, 607naive and 26 recovered, med age 41 (21- 81 yrs) who received the AZD1222/Covishield (AstraZeneca) vaccine during late January/early February including immune responses generated by these vaccines against the variants of concern (B.1.1.7 and B.1.351).	Following a single dose of the vaccine, those who had past COVID-19 had significantly higher antibody titres than naïve individuals.	A single dose of AZD 1222 vaccine in previously exposed individuals not only significantly increased their antibodies including for some variants.
Krammer et al Robust spike antibody responses and increased reactogenicity in	Cross sectional (USA) 13 subjects who had documented infection with SARS-CoV-2 and 19	The antibody titres of vaccinees with pre-existing immunity are 10-20 times higher after one dose of vaccine than those of naïve vaccines	A single dose of mRNA vaccine elicits very rapid immune responses in seropositive individuals comparable to or exceeding that

seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine Preprint February 01, 2021. *MedRxiv* doi: https://doi.org/10.1101/2021.01.29.21250653	subjects who were SARS-CoV-2-naive. Individuals with and without documented pre-existing SARS-CoV-2 who received their first vaccine dose in 2020		found in naïve individuals who received two vaccinations
Manisty et al Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals Published February 2021 *The Lancet* doi:https://doi.org/10.1016/S0140-6736(21)00501-8	Nested case-control analysis (UK) 51 participants of COVIDsortium. 24 with previous PCR positive for COVID-19. 27 seronegative Healthcare workers followed 19-29 days The effect of one dose of BNT162b2 (Pfizer/ BioNTech) vaccine in those who were previously infected with COVID-19 compared to those who were seronegative for previous infection	Among previously uninfected, seronegative individuals, anti-S titres after one vaccine dose were comparable to peak anti-S titres in individuals with a previous natural infection who had not yet been vaccinated. Among those with a previous SARS-CoV-2 infection, vaccination increased anti-S titres more than 140-fold from peak pre-vaccine levels. This increase appears to be at least one order of magnitude greater than reported after a conventional prime-boost vaccine strategy.	Suggest prioritising the booster dose (i.e the second dose) for those with no prior evidence of infection. Suggest role for serologic testing prior to vaccination.
Samanovic et al Analysis of COVID-19 HIPE data, March to July 2020: Using data to	Prospective Cohort Study (USA) 13 subjects who had documented infection with SARS-CoV-2 and 19		Individuals with documented prior infection had 20 times the antibody response of naïve subjects after the first vaccine dose. Conversely naïve

inform health service planning in the COVID-19 era Poor Antigen-Specific Responses to the Second BNT162b2 MRNA Vaccine Dose in SARS-CoV-2-Experienced Individuals. Preprint February 2021 *MedRxiv* doi:https://doi.org/10.1101/2021.02.07.21251311	subjects who were SARS-CoV-2-naive. All subjects received two doses of the BNT162b2 mRNA vaccine and immune responses assessed at approximate intervals before and after each dose of vaccine		subjects had over 10 times the antibody response to the second vaccine suggesting little additional benefit of second dose to those previously infected.
Tré-Hardy et al Reactogenicity, Safety and Antibody Response, after One and Two Doses of mRNA-1273 in Seronegative and Seropositive Healthcare Workers Published: March 31, 2021 *Journal of Infection* doi:https://doi.org/10.1016/j.jinf.2021.03.025	Prospective Cohort Study (Italy) n=160 (seropositive=36) HCWs who received two doses of mRNA-1273 vaccine Antibody response +local/systemic side effects up to 2 weeks post 2nd dose	Seropositive HCWs had their antibody levels boosted by the first dose but no additional boosting effect was observed after the second injection. Seronegative participants required two doses of vaccine to achieve the same antibody levels as seropositive individuals	Consider reserving the second dose for seronegative individuals prior to vaccination, as the additional protective effect of the second dose has yet to be demonstrated in seropositive individuals

Limitations

All studies related to mRNA vaccines and had a small number of participants with limited follow up of approximately one month.

Most studies were carried out prior to the emergence of variants of concern.

International Practice

European Centre for Disease Prevention and Control

Recommendations for COVID-19 vaccination in individuals previously infected with SARS-CoV2

Recommendation	Country(countries)
Full vaccination schedule	Belgium, Croatia, Cyprus, Czechia, Denmark, Finland, Germany, Ireland, Latvia, Lithuania, Luxembourg, Malta, Poland, Romania, Sweden
One dose	Austria, Estonia, France, Italy, Norway, Spain, Slovakia
No dose	Iceland
Under discussion	Portugal

EEA countries with one dose schedule after previous SARS CoV-2 infection

Country	Recommendation
Austria	One dose after six to eight months following infection
Estonia	One dose from one week up to six months after recovery
France	One dose for immunocompetent people
Norway	One dose three months after recovery from laboratory confirmed infection
Slovakia	One dose after three months following infection (for all vaccines available, but the decision is up to the doctor and patient)
Spain	One dose after six months in people under 55 years previously infected (with the recommended vaccine according to each population group)

Overview of the implementation of COVID-19 vaccination strategies and vaccine deployment plans in the EU/EEA

France, Haute Autorité de Santé (HAS)

SARS-CoV-2 vaccination strategy - Vaccination of people with a history of Covid-19

Switzerland, Federal Office of Public Health

The second dose of COVID-19 vaccine can be waived in those not in a vulnerable group with previous COVID-19 and a strong medically confirmed systemic reaction after the first dose of vaccine (e.g. by family physician or the person in charge of the vaccination centre).

Recommandations de vaccination avec des vaccins à ARNm contre le COVID-19 in French

Discussion

A small number of studies examined a single dose COVID-19 vaccine strategy for those with prior COVID-19 infection. They demonstrated that those with prior COVID-19 infection who had a single dose of a mRNA COVID-19 vaccine had a similar antibody response to those with no prior infection after two doses of COVID-19 vaccine. Previous infection could be analogous to immune priming and so the first vaccine dose effectively acts as a booster, similar to the second dose in those with no prior COVID-19 infection.

Evidence suggests that those with prior COVID-19 infection who had a second dose of COVID-19 vaccine have no appreciable boost in terms of antibody response following the second dose.

Limitations of the studies include small number of participants, short follow up of approximately one month, and they were carried out prior to the emergence of variants of concern.

There is some evidence that people aged 50 years and older do not have the same antibody response as people under 50 years of age.

Those who are immunocompromised due to disease or treatment will require two doses due to their less robust immune response.

There is evidence of immunity post COVID-19 infection for 6-8 months.

Although the evidence relates to mRNA vaccines, it is based on immunological priming with subsequent boosting, thus it is reasonable to infer that these findings can be applied to viral vector vaccines.

Those who have had laboratory confirmed COVID-19 infection after a first dose of COVID-19 vaccine should complete the course. Serological testing for prior infection is not recommended for decision-making about vaccination.

NIAC Recommendations

This advice will be kept under review in light of the emerging variants of concern and assessment of vaccine efficacy against such variants.

Recommendation 1

For those who have had a previous laboratory confirmed COVID-19 infection within 6 months:

- aged 50 years and older, immunocompetent and immunocompromised, should receive a full COVID-19 vaccine schedule
- aged under 50 years and immunocompromised should receive a full COVID-19 vaccine schedule
- aged under 50 years and immunocompetent: a single dose of COVID-19 vaccine is sufficient and they should then be considered fully vaccinated

Recommendation 2

Those who have had laboratory confirmed COVID-19 infection within 6 months after a first dose of COVID-19 vaccine should complete the course

These recommendations are based on current data and are subject to ongoing review.

DOH will be informed of any changes.

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Amendments

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