

National Immunisation Advisory Committee (NIAC)

RECOMMENDATIONS REGARDING BOOSTER DOSES OF COVID-19 VACCINE FOR THOSE AGED 60 TO 79 YEARS

NIAC | 22.10.2021

1. About NIAC

NIAC membership 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 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.

NIAC meets to consider new evidence about vaccines and provide advice to the Chief Medical Officer (CMO) and the Department of Health (DOH). The Department and the Minister for Health make policy decisions on vaccines which are implemented by the HSE.

Recommendations

These recommendations reflect current evidence and will be reviewed when more information becomes available.

- 1. All unvaccinated or incompletely vaccinated people eligible for COVID-19 vaccine are strongly encouraged to complete a primary vaccination course.
- 2. Everyone must continue to observe all recommended public health and social measures to limit COVID-19 exposure. Booster doses will not immediately contribute to outbreak management or take the place of public health and social measures.
- 3. A booster dose of Comirnaty is recommended for all those aged 60 to 79 years who have completed their primary course with any COVID-19 vaccine. This is in addition to previous NIAC recommendations: <u>Additional doses of COVID-19 vaccine for those with immunocompromise</u> and <u>Booster doses of COVID-19 vaccine for those aged 80 years and older and aged 65 and older in long term care facilities.</u>

The booster dose should be given after an interval of six months (or at least five months) following the last dose of any authorised COVID-19 vaccine, or any time thereafter. It can be given at the same time or at any interval before or after seasonal influenza vaccine.

As previously recommended, if a person in a group for whom a booster dose is recommended has had laboratory confirmed COVID-19 infection after a completed primary vaccine course (i.e., a breakthrough infection), the booster dose should be delayed for at least six months after the COVID-19 infection was diagnosed.

2. Executive summary

- Globally, COVID-19 vaccines are a scarce resource; recommendation for booster vaccines must be based on need and evidence driven.
- NIAC fully supports the Government's commitment to global vaccine equity and took into account vaccine supply and the potential for donation to low-and-middle income countries in these recommendations.
- Access to and completion of a primary vaccine series by countries is an essential prerequisite to controlling the SARS-CoV-2 pandemic on a global basis. Until global control is achieved, all countries remain at risk.
- The most effective way to prevent hospitalisation, severe illness and death related to COVID-19 is to ensure that all eligible people are fully vaccinated. In the US, those who are unvaccinated are 10 times more likely to require hospitalisation than those fully vaccinated. In Ireland, those who are unvaccinated account for 70% of COVID-19 ICU admissions from April to October 2021.
- Overall, high levels of vaccine effectiveness (VE) against hospitalisation, severe disease and death have been sustained throughout the Alpha and Delta periods for at least five to six months.
- There is attenuation of protection against infection over time since primary vaccination, with some increase in hospitalisation and severe illness, although overall good protection against severe disease is sustained.
- Vaccination rates are very high in Ireland, especially in those aged 60 years and older (97% or higher). However, the incidence of breakthrough infections requiring hospitalisation has increased in fully vaccinated older people. Vaccinated older people are much less likely to require hospitalisation but if they do, they carry the same risk of severe disease and death as the unvaccinated.
- Available data on booster vaccination with an mRNA vaccine following a primary viral vector or mRNA vaccine course show similar safety to that reported for the primary series, and booster doses were found to be highly immunogenic.
- Booster doses with an mRNA vaccine have not shown unexpected patterns with regard to short term safety when administered at least five months after an mRNA primary vaccine course.
- In Israel, booster Comirnaty vaccination together with public health and social measures have been shown to extend protective benefits, reversing COVID-19 disease incidence trends and reducing rates of hospitalisation.
- On 4 October 2021, the European Medicines Agency (EMA) stated that a booster dose (third dose) of Comirnaty may be considered in individuals 18 years of age and older.

- NIAC will continue to examine new evidence regarding the durability of protection of the primary vaccine series in other groups. These groups include:
 - those younger than 60 years of age with comorbidities (other than those who are immunocompromised as recommendations previously issued).
 - frontline healthcare workers (HCWs) (recognising their vital role in providing essential health services. Currently, there is no evidence of increased hospitalisation or death in fully vaccinated HCWs. There is evidence to suggest that VE for symptomatic disease in HCWs is the same as the general population.

3. Background

On 22 June 2021, NIAC received a request from the DOH for advice on the need for booster vaccines in the National COVID-19 Vaccination Programme.

On 19 July 2021, NIAC advised the CMO that COVID-19 booster vaccines were likely to be required by some people. Groups mentioned for initial priority consideration were:

- Those aged 16 years and older with immunocompromise associated with a suboptimal response to vaccines (as listed in Chapter 5a, Table 5.2)
- Residents of long-term care facilities (LTCFs) aged 65 and older
- Those aged 80 years and older
- Frontline healthcare workers

On 25 August 2021, the CMO asked if NIAC had "any further advice in relation to the requirement for additional doses of vaccine, with particular reference to the priority groups identified in your previous advice".

On 30 August 2021, NIAC issued <u>recommendations</u> regarding an additional COVID-19 vaccine dose for those with immunocompromise associated with a suboptimal response to vaccines.

On 7 September 2021, NIAC issued <u>recommendations</u> regarding booster doses of COVID-19 vaccine for those aged 80 years and older and those aged 65 and older in long term care facilities.

On 18 October 2021, NIAC issued <u>an overview of recommendations</u> regarding booster doses of COVID-19 vaccine for those aged 60 to 79 years. This document provides the evidence and rationale for these recommendations.

4. COVID-19: situation in Ireland, October 2021

In Ireland, vaccination rates are very high, especially in those aged 60 years and older. However, it is estimated there remain 300,000 unvaccinated or incompletely vaccinated adults in Ireland (Figure 1). (1)

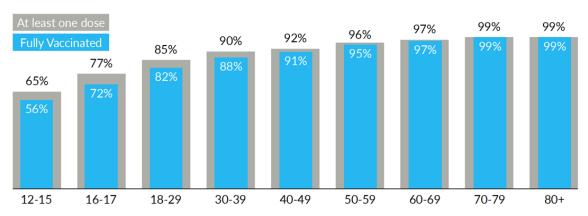


Figure 1: COVID-19 Vaccine uptake by age group. 30 September 2021 Source: High-Level Task Force

The vaccination campaign has been very successful in preventing severe COVID-19, hospitalisations, ICU admission and death particularly in the older age cohorts. This is clearly evidenced by the age specific rates for hospitalisation, ICU admission and death for waves 1 and 4 (Table 1). (2)

Table 1: Age specific rates for COVID-19 hospitalisations, ICU admission and death. 14 October 2021 Source: HPSC CIDR.

	Age specific rate/100,000				
Age	60 -69 years		70 – 79 years		
COVID-19 related	Wave 1*	Wave 4*	Wave 1*	Wave 4*	
Hospitalisation	107	67	324	183	
ICU admission	27	14	22	14	
Death	25	8	315	42	

*Wave 1: all cases notified until 1 August 2020, wave 4: 26 June - 13 October 2021

However, in these highly vaccinated cohorts, aged 60 - 79 years, COVID-19 continues to present a serious challenge. These age cohorts accounted for 47% of all COVID hospitalisations and 42% of all COVID-19 ICU admissions from 27 June to 10 October 2021 (Figure 2).

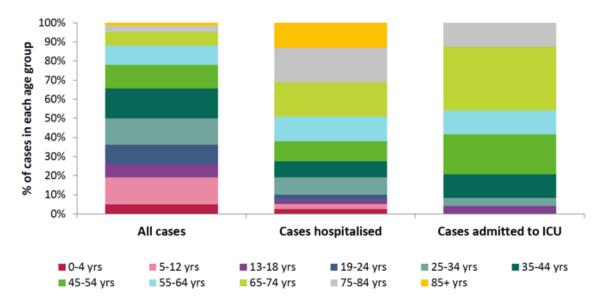
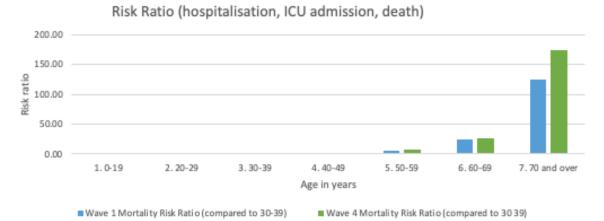


Figure 2: Percentage of confirmed cases of COVID-19 notified in Ireland by age group, all cases, hospitalisations and ICU admissions (up to midnight 11 October 2021). Source: HPSC

Of 321 cases admitted to ICU between 26 June and 14 October 2021, 136 (42%) were aged 60 and older (source: HPSC CIDR extract 14 October 2021). As shown in Figure 3, the risk of COVID-19 related hospital admission increases with age, trending slightly higher with respect to the reference age group (30 - 39) in wave 4 compared to wave 1. (2)

Figure 3: Relative risk of hospitalisation, ICU admission and death by age and wave (reference group those aged 30 - 39 years) 13 October 2021. Source: HPSC CIDR



Of those admitted to ICU, 80% were unvaccinated or incompletely vaccinated and 20% were laboratory confirmed COVID-19 infection 14 days or more after a completed primary vaccine course (i.e., a breakthrough infection). However, a higher proportion of those aged 60 and older admitted to ICU were fully vaccinated compared to younger age groups. The median age of breakthrough infections requiring ICU admission between 01 April 2021 and 09 October 2021 was 67 years, mean 66 years, (range 30 to 88). (3)

5. Global and national equity

NIAC is conscious of the global demands on vaccine supplies and recognises that facilitating vaccination on a global level is not only important on a humanitarian and global equity basis, but essential to limit the threat of COVID-19 to our own population.

Access to and completion of a primary vaccine series by countries is an essential prerequisite to controlling the SARS-CoV-2 pandemic on a global basis. Until global control is achieved, all countries remain at risk.

NIAC fully supports the Government's commitment to global vaccine equity and took into account vaccine supply and the potential for donation to low-and middle-income countries in these recommendations.

6. Rationale for booster doses

The rationale for booster doses has been outlined in a previous <u>recommendation</u>. In the context of these recommendations, booster COVID-19 vaccine doses may be needed because of waning immunity following primary vaccination.

The rationale for booster doses may differ by vaccine product, disease epidemiology, risk group, and vaccine coverage rates.

There are data with consistent themes that can help inform current decisions. There is no agreed level of antibody that correlates with protection. Khoury et al have identified that neutralising antibodies (NAs) are an important correlate of protection although other mechanism including cellular immunity may also have an important protective role, particularly against severe disease. (4) Feng et al showed that higher anti-spike IgG, anti-RBD IgG and NA were all associated with a lower risk of symptomatic disease. (5) Shields et al reported that reinfection rates were higher in those seronegative despite previous infection. (6)

These studies and others indicate that lower antibody levels are associated with a lesser protective effect, and higher antibody levels are associated with lower risk of symptomatic disease. Boosting of antibody responses in the event of waning immunity might be anticipated to extend the duration of protection.

It is possible that a new vaccine-resistant variant may emerge which could result in need for a booster dose with a modified vaccine.

7. COVID-19 vaccination

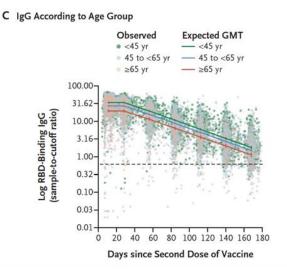
Duration of protection

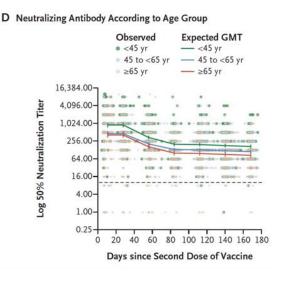
Immunity generally lasts for at least nine to 12 months following natural infection (HIQA report on duration of immunity, October 2021). Reinfection is uncommon within that timeframe, with rates ranging from 0 - 5.9%. The risks of reinfection are highest in those with immunocompromise, those aged 65 years and older and those who are seronegative at baseline.

A Danish population study carried out before variants came to prominence reported that protection against repeat infection, at 47.1%, was substantially lower in those aged 65 and older than that that observed overall (78.8%) and was no different in HCW than in the overall population. (7)

A study in Israel showed that NAs can persist for at least six to eight months following vaccination but that waning of NAs does occur (Figure 4). (8) The negative correlation of initial antibody response with age, coupled with time dependent waning following vaccination, may increase the age-related susceptibility of those fully vaccinated to breakthrough infection. (9, 10)

Figure 4. Distribution of antibodies by age, six months after receipt of the second dose of Comirnaty vaccine. Source: Levin E et al.

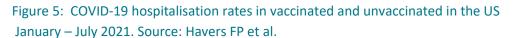


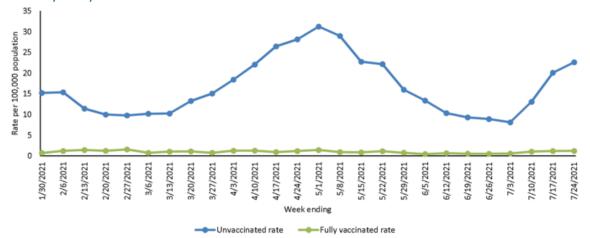


Vaccine effectiveness

COVID-19 vaccines are highly effective in protecting against symptomatic disease, hospitalisation and severe illness caused by the Alpha and preceding variants. Protection is less reliably achieved in those with immunocompromise. (11)

A US study of breakthrough infections found that high levels of vaccine effectiveness (VE) against hospitalisation, severe disease and death are sustained for at least five to six months. Fully vaccinated persons admitted with COVID-19 were older compared with unvaccinated persons and were more likely to have three or more underlying medical conditions. From 24 January -24 July 2021, cumulative hospitalisation rates were 17 times higher in unvaccinated persons compared with vaccinated persons (423 cases per 100,000 population compared with 26 per 100,000 population, respectively). Cumulative hospitalisation rates for unvaccinated compared with vaccinated persons were 23 times higher for those aged 18-49, 22 times higher for those aged 50-64 and 13 times higher for those aged 65 and older. For 27 June – 24 July 2021, the Delta period, overall hospitalisation rates were at least 10 times higher in unvaccinated persons compared with vaccinated persons for all age groups across all weeks (Figure 5). (12)





Fully vaccinated older people had higher risks of hospitalisation compared to younger age groups (Table 2). (12)

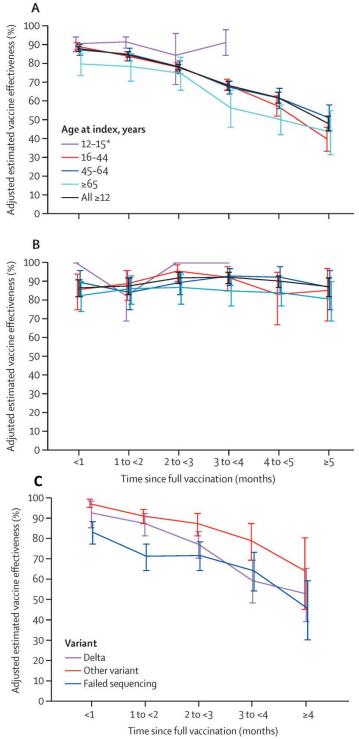
Table 2: Demographics of a representative sample of hospitalised adults aged \geq 18 years with laboratory-confirmed COVID-19-associated hospitalisation admitted January 1–June 30, 2021, by vaccination status in 13 US States. Source: Havers FP et al.

Characteristics	Adults ≥ 18 years	Unvaccinated (weighted %)	Vaccinated >14 days prior to positive test (weighted %)	Partially vaccinated (weighted %)	Fully vaccinated (weighted %)
Total*	35,766	30,967 (87.6)	1791 (5.0)	1753 (4.4)	1253 (3.0)
Age group (median, IQR)	60 (46-72)	58 (45-70)	69 (59-80)	71 (61-82)	72 (63 –81)
18-49 years	10,929	10,342 (95.1)	285 (2.4)	197 (1.4)	155 (1.2)
50-64 years	10,407	9,265 (90.9)	507 (4.0)	396 (3.5)	239 (1.6)
65-74 years	6,686	5,573 (82.9)	401 (6.9)	400 (5.8)	312 (4.4)
75-84 years	4,788	3,692 (79.4)	343 (6.1)	428 (7.4)	325 (7.1)

In most EU/EEA countries, including Ireland, the Delta variant is the predominant circulating strain. The Delta variant is characterised by very high transmissibility with an estimated reproduction rate of between five and eight. While VE against SARS-CoV-2 infection may decline over time, VE against hospitalisation and severe disease is sustained for at least six months, remaining high in the general population. (13, 14)

A large retrospective cohort study in the US found that, for those fully vaccinated, VE of Comirnaty was 73% against infection and 90% against hospitalisation. VE against infection declined from 88% during the first month after full vaccination to 47% after 5 months. VE against the Delta variant was 93% during the first month after full vaccination but declined to 53% after four months. VE against non-delta variants the first month after full vaccination was 97% but waned to 67% at four to five months. VE against hospitalisation with Delta variant for all ages was 93% up to six months. The authors concluded that reduction in effectiveness against SARS-CoV-2 infections over time was likely primarily due to waning rather than Delta escaping vaccine protection (Figure 6). (14)

Figure 6. Adjusted estimated vaccine effectiveness against SARS CoV2 infection (A), hospital admission (B), and variant (C). Source: Tartoff S et al.



In a US study carried out by Grannis & al between June and August 2021 reported a significantly lower (VE) (76% vs. 89%) for adults aged 75 years or older compared with those aged less than 75 years. (15)

A Portuguese study of COVID-19 related hospitalisation and deaths in older adults from February to August 2021 reported that VE against hospitalisation was 94% and 82% for those 65-79 and over 80 years old respectively, with no evidence of waning 3 months after dose two. VE against death was 96% and 81% in these two age groups. A significant limitation in this study is the short duration of follow-up. (16)

In Qatar a large observational study identified that induced protection against SARS-CoV-2 infection appeared to wane rapidly following its peak after the second dose, but protection against hospitalisation and death persisted at a robust level for 6 months after the second dose. Of note similar VE over time was observed for those aged under 60 years compared to those aged 60 years and older, although effectiveness was slightly lower for those aged 60 years and older. (17)

A large study in England of those aged 16 and older reported that VE against symptomatic Delta infection peaked in the early weeks after the second dose and then fell beyond 20 weeks to 69.7% for Comirnaty and 47.3% for Vaxzevria. For Comirnaty, effectiveness beyond 20 weeks against hospitalisation fell to 77%, and effectiveness against death fell to 90.4%. For Vaxzevria, effectiveness beyond 20 weeks against hospitalisations fell to 47.3%, and effectiveness against death fell to 78.7%. Greater waning was observed among those aged 65 years and older in a clinically extremely vulnerable group and 40-64-years old with underlying medical conditions compared to healthy adults. Waning effectiveness was greater for those aged 65 years and older compared to those aged 40-64 years (Table 3). (13)

Vaccine	Age group (Years)	Week 1 VE (%)	Week 20+ VE (%)
Comirnaty	16 - 39	93	N/A
	40 - 64	88	76
	65+	92	55
Spikevax	16 - 39	95	N/A
	40 - 64	94	N/A
	65+	N/A	N/A
Vaxzevria	16 - 39	62	N/A
	40 - 64	57	58
	65+	64	37

Table 3: Vaccine effectiveness against Delta symptomatic disease among individuals with twodoses of Comirnaty, Spikevax or Vaxzevria in England at 1 week, and beyond 20 weeks.Source: Andrews N et al.

Waning against hospitalisation was less pronounced (Figure 7).

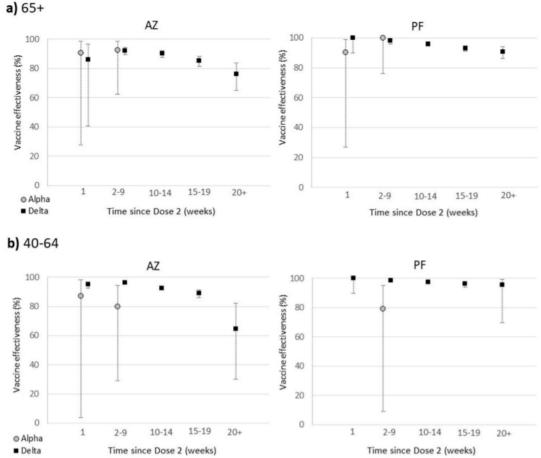


Figure 7: Vaccine effectiveness against hospitalisation by age group in those who received two doses of Vaxzevria (AZ) or Comirnaty (PF) in England. Source: Andrews N et al.

In Israel data from all SARS-CoV-2 infections in Israel between 11 July and 31 July 2021 were analysed. People aged 60 years or older who were fully vaccinated with Comirnaty in March 2021 were 1.7 times more protected against severe COVID-19 compared to those who were fully vaccinated in January 2021. (18)

Mizrahi et al. compared the incidence rates of breakthrough infections in HCWs aged 16 years and older vaccinated with Comirnaty early or late in their program. The longer the interval after vaccination, the lower the risk of breakthrough infection. A limitation of this study is that those who were first vaccinated were those most at risk of infection, which may have contributed to the higher infection rate. (19) There is attenuation of protection against infection over time since primary vaccination with some increase in hospitalisation and severe illness, greater in older age groups, although overall good protection against severe disease is sustained. (13)

Delta breakthrough infections have been reported to be associated with similar viral burden in both vaccinated and unvaccinated. (20) Data indicates vaccinated and unvaccinated persons infected with Delta have similar levels of viral RNA and culturable virus detected. However, a more rapid decline is seen in viral RNA and culturable virus in fully vaccinated individuals compared with those who remain unvaccinated. (21-23)

In Israel, booster Comirnaty vaccination together with public health and social measures have been shown to extend protective benefits, reversing COVID-19 disease incidence trends and reducing rates of hospitalisation (Figure 8). (24)

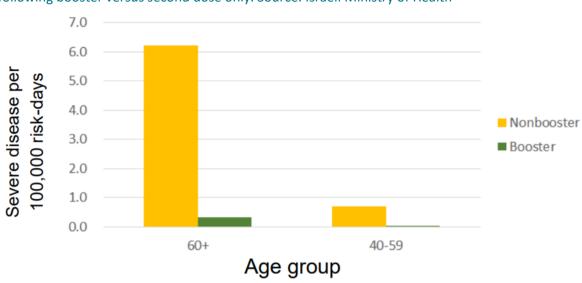


Figure 8: Absolute rates of severe COVID-19 disease* per 100,000 risk-days by age group, 12+ days following booster versus second dose only. Source: Israeli Ministry of Health

*Severe disease (NIH definition): resting respiratory rate more than 30 breaths per minute or O_2 saturation less than 94% or PaO_2/FiO_2 less than 300

Bar-On et al. evaluated those aged over 60 years who had received their first two doses of Comirnaty at least five months earlier. Twelve or more days after receiving a third dose, participants were about 19.5 times less likely to have severe COVID-19 than were people in the same age group who were not given a third dose (Figure 9). A study limitation is the short follow up period. (24)

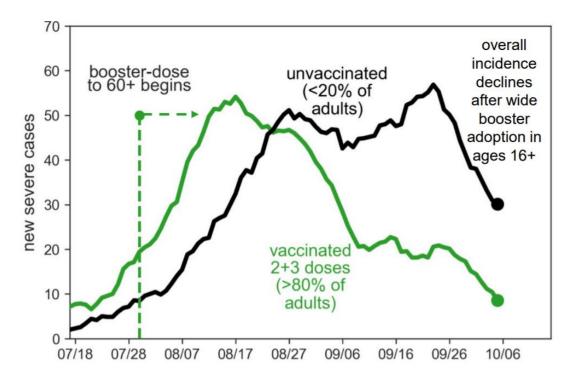


Figure 9: Number of new severe COVID-19 cases by date. Source: Israeli Ministry of Health

The relative contributions of waning immunity, circulation of the more transmissible Delta variant, viral load and relaxation of public health and social measures to community transmission and the increase in case numbers are uncertain. The likelihood is that waning immunity represents a particular vulnerability for defined patient groups including those aged 60 and older.

All recommended public health and social measures to limit COVID-19 exposure must be observed. Booster doses will not contribute immediately to outbreak management or take the place of public health and social measures.

Safety of booster COVID-19 vaccination

On 4 October 2021, the <u>EMA</u> stated that a booster dose (third dose) of Comirnaty may be considered in individuals 18 years of age and older. The safety and immunogenicity of a booster dose (third dose) of Comirnaty in individuals 65 years of age and older is based on safety and immunogenicity data in adults 18 to 55 years of age who received their booster dose approximately 6 months after receiving Dose 2.

Booster doses with Comirnaty have not shown any unexpected patterns with regard to short term safety when administered at least five months after an mRNA primary vaccine course. (25)

The Israeli Health Ministry shared findings of their population-based booster programme at the Vaccines and Related Biological Products Advisory Committee meeting of the US Federal Drug Administration on 14-15 October 2021. Overall, 3.7 million booster doses of Comirnaty have been administered to those aged 16 and older with 1.2 million doses given to those aged 60 years and older. No initial safety concerns have been identified with a similar profile but lower rate of systemic and local reactions than after first or second doses. (26) The potential risk of myocarditis following an mRNA booster dose is yet to be characterised and will be closely monitored.

Wu et al reported the results of a preliminary evaluation of Spikevax and a reduced dose Spikevax vaccine assessing immunogenicity against the less sensitive Beta strain. In the study, a half dose (50 microgram) booster was given 5.9 to 7.5 months after receipt of the second vaccine dose to participants aged 27 to 76 years. The vaccines were found to have a favourable safety profile consistent with the known safety profile of Spikevax and to be immunogenic. There were significant increases in neutralising titres against wild-type, Beta and Gamma variants with neutralising titres against wild-type exceeding those following the primary immunisation. (27)

The EMA is evaluating more recent data that a lower dose may suffice as a booster dose for Spikevax. Until this is authorised, it is preferable that Comirnaty would be given as a booster vaccine.

Timing and selection of booster doses

The safety and immunogenicity of a booster dose of Comirnaty was based on data in adults 18 to 55 years of age who showed a rise in antibody levels when a booster dose was given approximately 6 months after the second dose. On the basis of this data, the EMA concluded that booster doses may be considered at least 6 months after the second dose for people aged 18 years and older. The data showed that the booster doses were given at a range of 4.8 to 8.0 months after receiving Dose 2. (28)

Most of the evidence regarding booster vaccination relates to the use of an mRNA vaccine. There are limited data on the use of adenoviral vector booster vaccines. The results of heterologous studies carried out as primary or booster immunisation indicate that an adenoviral vector vaccine followed by an mRNA vaccine is safe and immunogenic. (29)

Based on the data above, a booster dose of Comirnaty should be given after an interval of six months (or at least five months) following the last dose of any authorised COVID-19 vaccine, or any time thereafter.

Co-administration

NIAC has previously advised that COVID-19 vaccines and other vaccines including seasonal influenza vaccine may be administered at the same time or at any interval.

This is consistent with recommendations from CDC and the UK and results from the UK ComFluCOV study which showed that administering an influenza vaccine at the same time as a second dose of a COVID-19 vaccine produced no safety concerns and preserved the immune response to both vaccines. (30)

8. International recommendations

Booster doses of an mRNA, heterologous or homologous COVID-19 vaccine are recommended for older individuals in different age groups in the following countries (Table 4):

Country	Age	Vaccine
Austria	65 and older	mRNA ¹
Belgium	65 and older	mRNA ¹
Bulgaria	65 and older	Heterologous vaccine
Denmark	65 and older	mRNA
Estonia	65 and older	mRNA ¹
Finland	30 and older	Homologous vaccine
Germany	70 and older ²	Heterologous vaccine
Hungary	65 and older	Heterologous vaccine
Iceland	60 and older	Heterologous vaccine
Israel	16 and older	mRNA
Latvia	65 and older	Homologous vaccine
Lithuania	18 and older	mRNA ¹
Norway	65 and older	mRNA
Malta	65 and older	Heterologous vaccine
Romania	65 and older	mRNA ¹
Slovenia	65 and older	Heterologous vaccine
Spain	70 and older	mRNA ¹
UK	50 and older	mRNA ¹
US	65 and older	mRNA

Table 4: COVID-19 booster vaccine recommendations by country, age group and type of vaccine [information accessed 19 October 2021]

¹ regardless of the primary course

² those over 60 can get a booster if recommended by their doctor on a case-by-case basis

Most countries have selected an interval of six months since completion of the primary vaccine schedule. In Estonia, it is eight months. In Germany a six-month interval is recommended if the primary series was with an mRNA vaccine and a four-week interval after COVID-19 vaccine Janssen. Belgium recommends a six-month interval if the primary series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval after COVID-19 vaccine Janssen. Belgium recommends a six-month interval if the primary series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with a mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was with an mRNA vaccine and a four-week interval series was week interval series was we

9. Conclusions

COVID-19 related hospitalisation and severe illness can be prevented by optimising the protection afforded by vaccination. This can be achieved by encouraging and facilitating unvaccinated or incompletely vaccinated people eligible for COVID-19 vaccine to complete a primary vaccination course.

Although vaccination rates are very high in Ireland, especially in those aged 60 years and older (97% or higher), the incidence of breakthrough infections requiring hospitalisation has increased in fully vaccinated older people. Vaccinated older people are much less likely to require hospitalisation but if they do, they carry the same risk of severe disease and death as the unvaccinated. A higher proportion of those aged 60 and older admitted to ICU between 25 June and 13 October 2021 had a breakthrough infection compared to younger age groups

Booster vaccination is safe and immunogenic and the EMA has stated that the EMA stated that a booster dose of Comirnaty may be considered in individuals 18 years of age and older. It is preferable that Comirnaty would be given as a booster vaccine until a booster dose of Spikevax is authorised.

Booster vaccination for those at increased risk for breakthrough infection i.e., those aged 60 and older will optimise their protection. It is essential that all recommended public health and social measures to limit COVID-19 exposure are observed. Booster doses will not immediately contribute to outbreak management nor take the place of public health and social measures.

NIAC continues to examine new evidence regarding the durability of protection of the primary vaccine series in other groups. These groups include those younger than 60 years of age with comorbidities (other than those who are immunocompromised) and healthcare workers (HCWs) recognising their vital role in providing essential health services. Currently, there is no evidence of increased hospitalisation or death in fully vaccinated HCWs. There is evidence to suggest that VE for symptomatic disease in HCWs is the same as the general population.

10. Recommendations

These recommendations reflect current evidence and will be reviewed when more information becomes available.

- 1. All unvaccinated or incompletely vaccinated people eligible for COVID-19 vaccine are strongly encouraged to complete a primary vaccination course.
- 2. Everyone must continue to observe all recommended public health and social measures to limit COVID-19 exposure. Booster doses will not immediately contribute to outbreak management or take the place of public health and social measures.
- 3. A booster dose of Comirnaty is recommended for all those aged 60 to 79 years who have completed their primary course with any COVID-19 vaccine. This is in addition to previous NIAC recommendations: <u>Additional doses of COVID-19 vaccine for those with immunocompromise</u> and Booster doses of COVID-19 vaccine for those aged 80 years and older and aged 65 and older in long term care facilities

The booster dose should be given after an interval of six months (or at least five months) following the last dose of any authorised COVID-19 vaccine, or any time thereafter. It can be given at the same time or at any interval before or after seasonal influenza vaccine.

As previously recommended, if a person in a group for whom a booster dose is recommended has had laboratory confirmed COVID-19 infection after a completed primary vaccine course (i.e., a breakthrough infection), the booster dose should be delayed for at least six months after the COVID-19 infection was diagnosed.

References

- 1. High Level Task Force. COVID-19 Vaccination Uptake. As yet unpublished; 2021.
- 2. Health Protection Surveillance Centre. Computerised Infectious Disease Reporting; 2021 Up to midnight on 13th October 2021. <u>https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/surveillance/</u>
- HPSC Epidemiology Team. Vaccination status of COVID-19 cases admitted to ICU in Ireland between April 1st 2021 and October 16th 2021. Health Protection Surveillance Centre; 2021 extracted on 2021.10.18 <u>https://www.hpsc.ie/az/respiratory/coronavirus/novelcoronavirus/surveillance/vaccinationstatusweeklyreports/Vaccination%20Status%20of%20ICU%20admissions.pdf</u>
- Khoury DS, Cromer D, Reynaldi A, Schlub TE, Wheatley AK, Juno JA, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nature Medicine. 2021;27(7):1205-11. <u>https://doi.org/10.1038/s41591-021-01377-8</u>
- 5. Feng S, Phillips DJ, White T, Sayal H, Aley PK, Bibi S, et al. Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection. Nature Medicine. 2021. https://www.nature.com/articles/s41591-021-01540-1
- Shields AM, Faustini SE, Kristunas CA, Cook AM, Backhouse C, Dunbar L, et al. Longitudinal protection following natural SARS-CoV-2 infection and early vaccine responses: insights from a cohort of community based dental health care professionals. medRxiv. 2021:2021.02.24.21252368. <u>https://doi.org/10.1101/2021.02.24.21252368</u>
- 7. Hansen CH, Michlmayr D, Gubbels SM, Mølbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. The Lancet. 2021;397(10280):1204-12. <u>https://doi.org/10.1016/S0140-6736(21)00575-4</u>
- Naaber P, Tserel L, Kangro K, Sepp E, Jürjenson V, Adamson A, et al. Dynamics of antibody response to BNT162b2 vaccine after six months: a longitudinal prospective study. The Lancet Regional Health – Europe. <u>https://www.thelancet.com/pdfs/journals/lanepe/PIIS2666-7762(21)00185-X.pdf</u>
- Bates TA, Leier HC, Lyski ZL, Goodman JR, Curlin ME, Messer WB, et al. Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples. JAMA. 2021;326(9):868-9. <u>https://jamanetwork.com/journals/jama/fullarticle/2782428</u>
- 10. Levin EG, Lustig Y, Cohen C, Fluss R, Indenbaum V, Amit S, et al. Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months. New England Journal of Medicine. 2021. <u>https://www.nejm.org/doi/full/10.1056/NEJMoa2114583</u>

- 11. Oliver S. Data and clinical considerations for additional doses in immunocompromised people. 2021. <u>https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/07-COVID-Oliver-508.pdf</u>
- Havers FP, Pham H, Taylor CA, Whitaker M, Patel K, Anglin O, et al. COVID-19-associated hospitalizations among vaccinated and unvaccinated adults ≥18 years – COVID-NET, 13 states, January 1 – July 24, 2021. medRxiv. 2021:2021.08.27.21262356. <u>https://doi.org/10.1101/2021.08.27.21262356</u>
- 13. Andrews N, Tessier E, Stowe J, Gower C, Kirsebom F, Simmons R, et al. Vaccine effectiveness and duration of protection of Comirnaty, Vaxzevria and Spikevax against mild and severe COVID-19 in the UK. medRxiv. 2021:2021.09.15.21263583. https://www.medrxiv.org/content/10.1101/2021.09.15.21263583v2
- 14. Tartof SY, Slezak JM, Fischer H, Hong V, Ackerson BK, Ranasinghe ON, et al. Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. The Lancet. 2021;398(10309):1407-16. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02183-8/fulltext
- Grannis SJ, Rowley EA, Ong TC, Stenehjem E, Klein NP, DeSilva MB, et al. Interim Estimates of COVID-19 Vaccine Effectiveness Against COVID-19-Associated Emergency Department or Urgent Care Clinic Encounters and Hospitalizations Among Adults During SARS-CoV-2 B.1.617.2 (Delta) Variant Predominance - Nine States, June-August 2021. MMWR Morb Mortal Wkly Rep. 2021;70(37):1291-3. <u>http://dx.doi.org/10.15585/mmwr.mm7037e2</u>
- 16. Nunes B, Rodrigues AP, Kislaya I, Cruz C, Peralta-Santos A, Lima J, et al. mRNA vaccine effectiveness against COVID-19-related hospitalisations and deaths in older adults: a cohort study based on data linkage of national health registries in Portugal, February to August 2021. Eurosurveillance. 2021;26(38):2100833. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.38.2100833
- Chemaitelly H, Tang P, Hasan MR, AlMukdad S, Yassine HM, Benslimane FM, et al. Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar. New England Journal of Medicine. 2021. <u>https://doi.org/10.1101/2021.07.19.21260808</u>
- 18. Goldberg Y, Mandel M, BarOn Y et al, Waning immunity of the BNT162b2 vaccine: A nationwide study from Israel. 2021. https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1
- Mizrahi B, Lotan R, Kalkstein N, Peretz A, Perez G, Ben-Tov A, et al. Correlation of SARS-CoV-2 Breakthrough Infections to Time-from-vaccine; Preliminary Study. medRxiv. 2021:2021.07.29.21261317. <u>https://www.medrxiv.org/content/10.1101/2021.07.29.21261317v1</u>

- 20. Pouwels KB, Pritchard E, Matthews PC, Stoesser N, Eyre DW, Vihta K-D, et al. Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. medRxiv. 2021:2021.08.18.21262237. <u>https://doi.org/10.1101/2021.08.18.21262237</u>
- Chia PY, Xiang Ong SW, Chiew CJ, Ang LW, Chavatte J-M, Mak T-M, et al. Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine-breakthrough infections: a multi-center cohort study. medRxiv. 2021:2021.07.28.21261295. <u>https://www.medrxiv.org/content/10.1101/2021.07.28.21261295v1</u>
- Riemersma KK, Grogan BE, Kita-Yarbro A, Halfmann PJ, Segaloff HE, Kocharian A, et al. Shedding of Infectious SARS-CoV-2 Despite Vaccination. medRxiv.
 2021:2021.07.31.21261387. https://doi.org/10.1101/2021.07.31.21261387
- Christensen PA, Olsen RJ, Long SW, Subedi S, Davis JJ, Hodjat P, et al. Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas. medRxiv. 2021:2021.07.19.21260808. <u>https://doi.org/10.1101/2021.07.19.21260808</u>
- Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Freedman L, Kalkstein N, et al. Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. New England Journal of Medicine. 2021;385(15):1393-400. https://www.nejm.org/doi/full/10.1056/NEJMoa2114255
- 25. Mofaz M, Yechezkel M, Guan G, Brandeau ML, Patalon T, Gazit S, et al. Self-reported and physiological reactions to the third BNT162b2 mRNA COVID-19 (booster) vaccine dose. medRxiv. 2021:2021.09.15.21263633. https://www.medrxiv.org/content/10.1101/2021.09.15.21263633v2
- 26. Vaccines and Related Biological Products Advisory Committee Meeting Presentation. Meeting Presentation. Israel Minitry of Health; 2021 October 14-15, 2021. <u>https://www.fda.gov/media/153086/download</u>
- Wu K, Choi A, Koch M, Ma L, Hill A, Nunna N, et al. Preliminary Analysis of Safety and Immunogenicity of a SARS-CoV-2 Variant Vaccine Booster. medRxiv.
 2021:2021.05.05.21256716.
 https://www.medrxiv.org/content/10.1101/2021.05.05.21256716v1
- 28. European Medicines Agency. Comirnaty INN-COVID-19 mRNA Vaccine (nucleosidemodified), Summary of Product Characteristics. 2021 Product Information as approved by CHMP on 14 October 2021; pending translations and endorsement by the European Commission. <u>https://www.ema.europa.eu/en/documents/product-information/comirnaty-eparproduct-information_en.pdf</u>

- Atmar RL, Lyke KE, Deming ME, Jackson LA, Branche AR, El Sahly HM, et al. Heterologous SARS-CoV-2 Booster Vaccinations – Preliminary Report. medRxiv. 2021:2021.10.10.21264827. https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v2
- Lazarus R, Baos S, Cappel-Porter H, Carson-Stevens A, Clout Clout M, Culliford L, et al. The Safety and Immunogenicity of Concomitant Administration of COVID-19 Vaccines (ChAdOx1 or BNT162b2) with Seasonal Influenza Vaccines in Adults: A Phase IV, Multicentre Randomised Controlled Trial with Blinding (ComFluCOV). Preprint. 2021. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3931758

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