National Immunisation Advisory Committee (NIAC)

RECOMMENDATIONS REGARDING BOOSTER DOSES OF COVID-19 VACCINE FOR THOSE AGED 16 TO 49 YEARS

NIAC |25.11.2021

UPDATED 26.11.2021

About NIAC

NIAC membership includes representatives from the Royal College of Physicians of Ireland, its Faculties and Institutes, the Royal College of Surgeons of Ireland the Irish College of General Practitioners, 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 observers from the Department of Health, the Health Service Executive. Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

NIAC considers new evidence about vaccines and provides 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.

Amendments 26.11.21

Recommendation Number 3 Page 3 and page 19	In addition to prior recommendations, in next order of priority, a booster dose of an mRNA vaccine is recommended for • all pregnant women aged 16 years and older • all those aged 40 - 49 years who received any COVID-19 vaccine including COVID-19 vaccine Janssen • those aged 16 - 39 years, who received an mRNA vaccine in descending order by age cohort; 30 - 39 years, 20 - 29 years and 16 -19 years • those aged 16 - 29 years who received COVID-19 vaccine Janssen can be offered a booster vaccine in parallel with those aged 30 - 39 years. *Deleted text – bullet 2 'l0 year age cohort' and bullet 4 'with the exception of Janssen recipients' and 'irrespective of their age'* New text in blue, deleted text in red.

Recommendations

1. All those who are unvaccinated or incompletely vaccinated are strongly recommended to complete a primary COVID-19 vaccination course. Booster doses are strongly recommended for those eligible. Seasonal influenza vaccine can be given at the same time to those for whom it is recommended.

2. All must continue to observe all recommended public health and social measures. The use of masks, physical distancing, hand hygiene, and ventilation of indoor spaces are key to reducing transmission of SARS-CoV-2. Booster vaccines will not immediately contribute to outbreak management and do not take the place of public health and social measures.

3. Priority for booster vaccines must be given to those at highest risk of severe COVID-19 breakthrough infection i.e., those in the older age cohorts and those with underlying conditions. Booster vaccines should be offered to those in previously recommended groups before progression to the younger age cohorts.

   In addition to prior recommendations, in next order of priority, a booster dose of an mRNA vaccine is recommended for

- all pregnant women aged 16 years and older
- all those aged 40 - 49 years who received any COVID-19 vaccine including COVID-19 vaccine Janssen
- those aged 16 - 39 years, who received an mRNA vaccine in descending order by age cohort; 30 - 39 years, 20 - 29 years and 16 -19 years
- those aged 16 - 29 years who received COVID-19 vaccine Janssen can be offered a booster vaccine in parallel with those aged 30 - 39 years.

4. For those aged 30 years and older, a full dose of Comirnaty (0.3ml/30 micrograms) or a half dose of Spikevax (0.25ml/50 micrograms) should be given six months (or at least five months for operational reasons) or longer following completion of a primary two dose course of any COVID-19 vaccine.

   For those aged 16 to 29 years, a full dose of Comirnaty (0.3ml/30 micrograms) should be given six months (or at least five months for operational reasons) or longer following completion of a primary two dose course of any COVID-19 vaccine.

   Recipients of COVID-19 vaccine Janssen should receive an mRNA booster dose after a minimum interval of three months.

5. Those who have a breakthrough infection following a primary vaccination course should defer booster vaccination for at least six months following infection onset.

6. If an mRNA vaccine is contraindicated, consideration can be given to boosting with an authorised non-mRNA vaccine following an individual benefit-risk assessment.

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

1. Executive summary

- Access to and completion of a primary COVID-19 vaccine series in all countries is an essential prerequisite to control the global SARS-CoV-2 pandemic. Until worldwide control is achieved, all countries remain at risk.
- In Ireland, COVID-19 vaccine uptake is very high, yet numbers of infection, hospitalisation, severe disease and death have increased. The rate of hospitalisation of unvaccinated people is substantially higher than in those who are fully vaccinated. However, as vaccination rates are so high, the proportion of those vaccinated who are admitted to hospital is increasing.
- The high transmissibility of the Delta variant, waning of immunity following vaccination, increasing socialisation and the time lapse since vaccination have contributed to the surge in new infections and increased the risk of severe disease in those with underlying conditions.
- The primary aim of the booster campaign is to protect against severe breakthrough infection.
- Age and underlying conditions are the most important determinants of risk of severe breakthrough infection.
- Pregnancy is a risk factor for severe illness and adverse outcomes related to COVID-19.
- Booster vaccination is associated with a substantial reduction in the rate of severe illness in those aged 40 to 49 years and also a reduction in confirmed infection across the age groups.
- As the effectiveness of the single dose COVID-19 vaccine Janssen vaccine is less robust than vaccines with a two dose schedule, offering an earlier booster vaccine may help to control the surge in case numbers in younger people.
- Heterologous boosting following single dose COVID-19 vaccine Janssen is more immunogenic than homologous boosting and so is recommended.
- Booster doses of mRNA vaccines have not shown any unexpected short term safety concerns. The risk of myocarditis or other rare adverse reaction following an mRNA booster dose has yet to be characterised and will be closely monitored. As a precaution, Comirnaty is the recommended booster vaccine for those aged 16 to 29 years.
- NIAC continues to examine new evidence regarding COVID-19 vaccination of younger children and durability of protection of the primary vaccine series in other groups, e.g., the immunocompromised who received an additional dose and those aged 12 to 15 years.

2. Background

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

- Those aged 16 years and older with immunocompromise associated with a suboptimal response to vaccines (as listed in Chapter 5a COVID-19, Table 5a.2 of the Immunisation Guidelines for Ireland.)
- Residents of long-term healthcare facilities aged 65 years and older
- Those aged 80 years and older
- Frontline healthcare workers

On 30 August 2021, NIAC issued recommendations regarding an additional COVID-19 vaccine dose for those aged 12 years and older with immunocompromise associated with a suboptimal response to vaccines.

On 7 September 2021, NIAC issued recommendations regarding a booster dose of COVID-19 vaccine for those aged 80 years and older and those aged 65 and older in long term healthcare facilities.

On 18 October 2021, NIAC issued an overview of recommendations regarding a booster dose of COVID-19 vaccine for those aged 60 to 79 years. The evidence and rationale for these recommendations was issued on 22 October and updated on 29 October 2021.

On 1 November 2021, NIAC issued an overview of recommendations regarding a booster dose of COVID-19 vaccine for healthcare workers (HCWs).

On 3 November 2021, NIAC updated recommendations regarding selection, dose and timing of booster doses of COVID-19 vaccine.

On 15 November 2021, NIAC issued recommendations regarding a booster dose for healthcare workers, those aged 16 to 59 years with underlying conditions and all those living in residential healthcare facilities, and those aged 50 to 59 years.

This document provides the evidence and rationale for recommending a booster dose of COVID-19 vaccine for pregnant women aged 16 and older, those aged 40 to 49 years and those aged 16 to 39 years, including those who received COVID-19 vaccine Janssen.

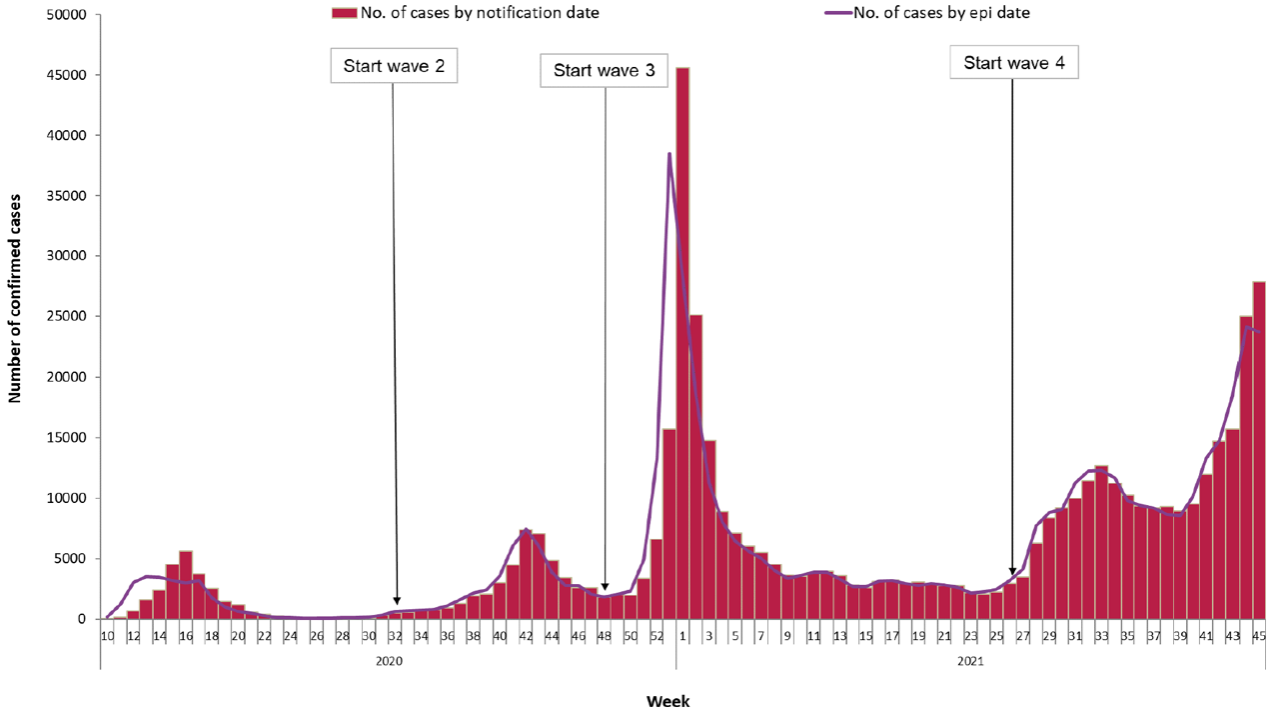
3. COVID-19 situation in Ireland

Vaccination is the most effective way to prevent hospitalisations, severe illness and death related to COVID-19. Thus, it is important to ensure that all eligible people are fully vaccinated. In Ireland, more than 75% of the total population and 92% of those aged 16 years and older are fully vaccinated.

As of 16 November 2021, 7.4 million doses of COVID-19 vaccine have been administered, excluding booster vaccines i.e., 3.7 million first doses, 3.6 million second doses and approximately 236,000 single dose vaccines. (source: Ireland COVID-19 Data Hub, accessed 22 November 2021) One third of the single dose COVID-19 vaccines Janssen were administered to those aged 50 to 59 years, and two thirds to those aged 18 to 49 years.

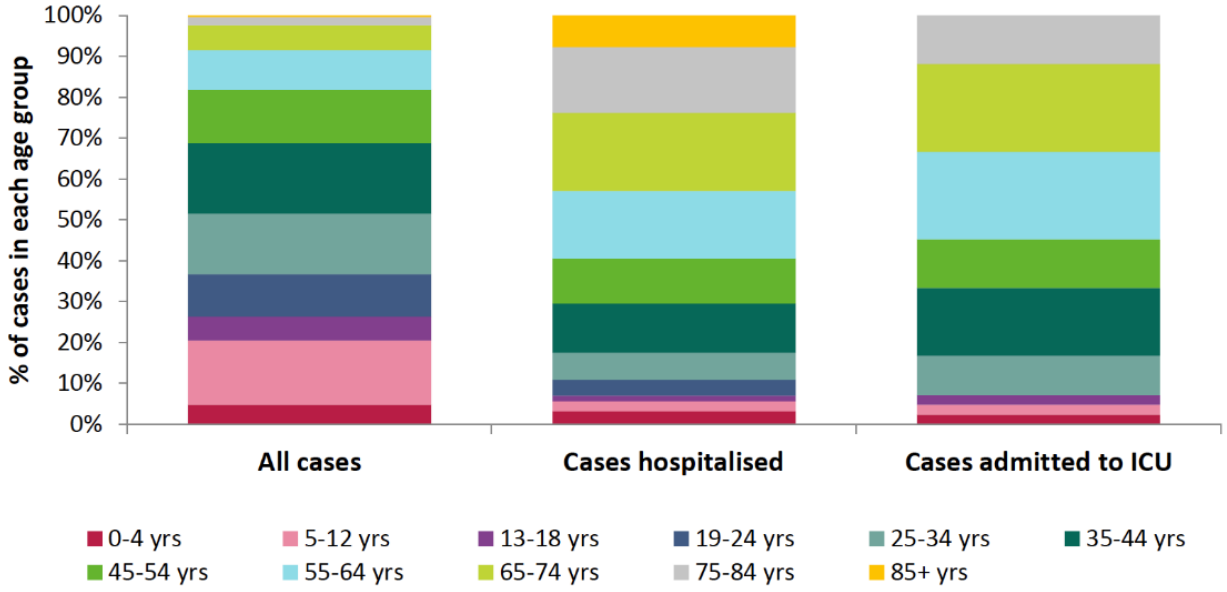
Ireland is currently undergoing a surge in case numbers despite the high vaccine uptake (Figure 1). This is due to the confluence of a number of factors, including the high transmissibility Delta variant, waning of immunity and the opening up of society with an increase in socialisation.

Figure 1: Number of confirmed cases of COVID-19 by notification week from March 2020 15 November 2021 Source: HPSC



There have been 56,562 confirmed cases notified in Ireland from 5 to 18 November 2021. The median age of cases was 34 years, with high case numbers in the younger age cohorts [1]. While the likely driver of this rise is increased social mixing in the context of the high transmissibility of the Delta variant, waning of immunity over time and variability in vaccine specific effectiveness against infection combine to facilitate transmission. Age, immune status, and the presence of underlying conditions are the main factors in determining the severity of breakthrough disease. In the two weeks 5 to 18 November 2021, 70% of hospitalisations and 66% ICU admission were in those aged 45 and older. (Figure 2).

Figure 2: Percentage of confirmed cases of COVID-19 notified in Ireland from 5 to 18 November 2021, by age group, all cases, hospitalisations, and ICU admissions Source: HPSC



The percentage of younger people being admitted to ICU has increased between wave one and wave four. In wave four, 20% of people aged under 55 years admitted to ICU had no underlying condition compared to 10% in waves two and three (Table 1).

Table 1: Summary of cases of COVID-19 admitted to ICU in Ireland (irrespective of vaccination status) Source: HPSC

Age group	Number (and percentage) of total COVID-19 admissions			
	Wave 1 (n=436)	Wave 2 (n=170)	Wave 3 (n=972)	Wave 4 (n=476)
15-24 years	5 (1.1)	2 (1.8)	16 (1.6)	13 (2.7)
25-34 years	15 (3.4)	2 (1.2)	36 (3.7)	44 (9.2)
35-44 years	36 (8.3)	14 (8.2)	80 (8.2)	70 (14.7)
45-54 years	91 (20.9)	19 (11.2)	178 (18.3)	92 (19.3)

The percentage of pregnant women being admitted to ICU has increased between wave one and wave four. One pregnant woman was admitted to ICU in wave one compared to 19 in wave four. Of the 19 cases admitted to ICU, 10 did not have an underlying condition. Eighteen cases (95%) reported not having received a vaccine and one case (5%) reported having received one dose of a two dose vaccine regimen prior to admission to ICU. [2]

4. 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.

While ensuring that recommendations for booster COVID-19 vaccine doses are evidence based, as articulated by Dr Tedros Ghebreyesus, Director General of the World Health Organization, NIAC agrees that "the key is to make sure that the vulnerable will be protected and the key is to make sure that the number of cases will not overwhelm the healthcare capacity".

5. Booster vaccination in the general population aged 16 to 49 years

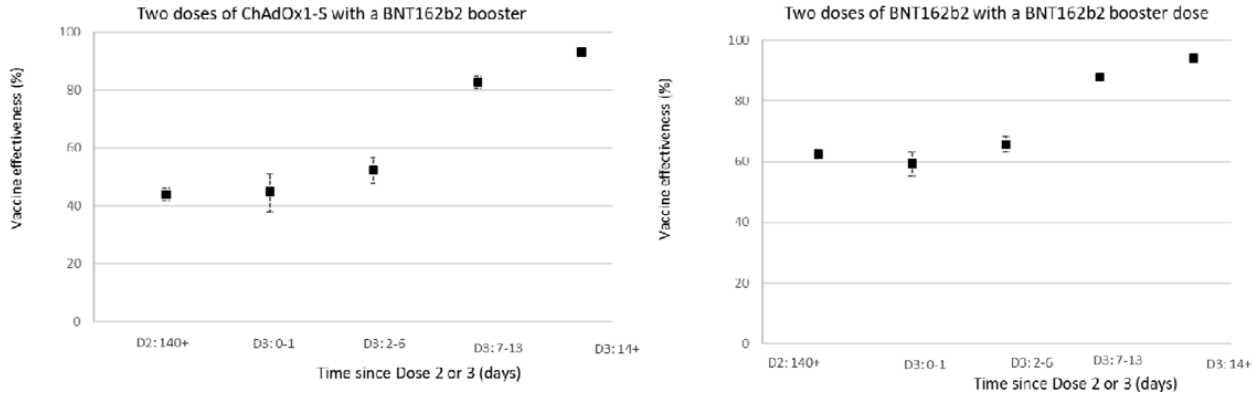
The risks of risk of severe COVID-19, hospitalisation and ICU admission are lower in younger people, but are not negligible. The presence of an underlying condition increases the risk of severe COVID-19 and booster vaccination has been recommended for those identified in this category. For all, there remains a residual risk, that decreases with age, of severe COVID-19 even in those with no risk factors. This risk will increase as the force of infection in the community remains high and as time from initial primary vaccination schedule elapses. While the benefits of vaccination against hospitalisation and deaths have been sustained for at least six months for all European Medicines Agency (EMA) authorised vaccines, [3-6] the risk of breakthrough infections and symptomatic disease increases over time. [5,7,8]

While pregnant women are at no higher risk of contracting SARS-CoV-2, those that do are at higher risk of severe disease and adverse outcomes.

Booster vaccination reduces the incidence of breakthrough infections, symptomatic disease and severe illness in those aged 50 years and older. [9,10]

Vaccine effectiveness against confirmed symptomatic disease increased from 44% and 63% at least at 140 days post dose two of Vaxzevria and Comirnaty respectively to 93 and 94% respectively after dose three. (Figure 3) [10]

Figure 3: Vaccine effectiveness estimates for at least 140 days post dose two (no booster) or for time intervals post dose three (booster) according to primary course. Unvaccinated as baseline. Source: Andrews et al.



Administration of booster vaccination to those aged 16 years and older in Israel has had a very significant beneficial effect. The rate of confirmed infection in those aged 16 to 49 years in the booster group was at least 10 times less than those who had not been boosted, although follow up was less than three months. [11]

The primary aim of the vaccination programme is to protect against severe COVID -19 hospitalisation and death. Secondary aims include reduction of risk of infection and transmission in the population, to maintain healthcare capacity and to help minimise disruption to society and the economy.

Wider booster vaccination in reducing the risk of breakthrough infection and transmission could help to curb future surges of infection.

The duration of protection after booster vaccination is uncertain. However, given the high levels of antibodies achieved and based on experience with other vaccines, it may extend longer than the after a primary vaccination course.

Booster vaccinations are not a replacement for public health and social measures.

6. Vaccine effectiveness

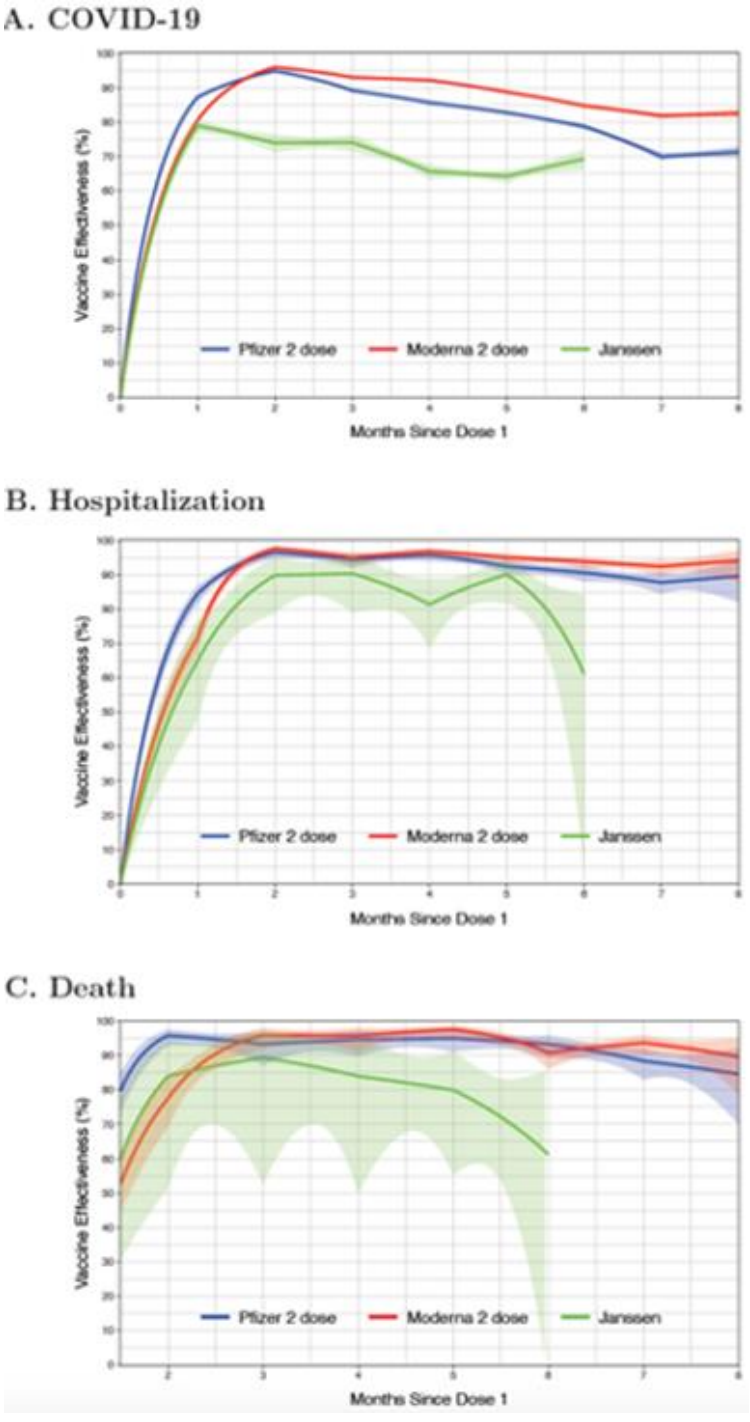
COVID-19 vaccine Janssen

The phase 3 study of COVID-19 vaccine Janssen reported vaccine efficacy of 76% against severe disease and 66% against all symptomatic infection.[12] This is lower than that reported for the mRNA vaccines. In a population based study in Puerto Rico, VE peaked at 90%, 87% and 58%, and declined to about 70%, 60% and 30% for Spikevax, Comirnaty and COVID-19 vaccine Janssen respectively.[13]

While waning immunity is a feature of COVID-19 vaccines, this coupled with the initial lower efficacy of the single dose COVID-19 Janssen vaccine may make recipients more susceptible to breakthrough infections.

In a real world effectiveness study, Lin et al. showed that the VE of COVID-19 vaccine Janssen was similar to that of the two mRNA vaccines one month after vaccination and then starts to decline. (Figure 4)

Figure 4: Vaccine Effectiveness of Comirnaty, Spikevax, and COVID-19 vaccine Janssen in reducing the risks of COVID-19 disease (A) hospitalisation (B) and death (C) in North Carolina, 13 December 2020 - 8 September 8, 2021. Source: Lin et al.



Vaccine effectiveness against hospitalisation and deaths continues to remain stable in the majority of studies up to nine months after completion of the primary series. [8]

While the COVID-19 vaccine Janssen as a single dose vaccine offered high levels of protection against hospitalisation and death, the mRNA vaccines were more durable in reducing the risk of COVID-19. Studies have found that VE against symptomatic disease declines for all COVID-19 vaccines. (ECDC, 2021) The decline was greatest for COVID-19 Janssen which started from a lower base. [7,8,13]

A study from Spain of close contacts of those with breakthrough infection showed VE against transmission of 59% for Comirnaty, 70% for Spikevax and 23% for COVID-19 vaccine Janssen.[14]

In the Netherlands de Gier found that the VE of full vaccination of the index case against transmission to unvaccinated and fully vaccinated household contacts was 63% and 40% respectively. That was in addition to the direct protection of vaccination of contacts against infection.[15]

As the protection of the single dose COVID-19 vaccine Janssen against infection declines more rapidly than vaccines with a two dose schedule (Cohn et al), offering an earlier booster vaccine may help to control the surge in case numbers in younger people whose lifestyle, work and living conditions may increase their social mixing.

Delta variant

The Delta variant is characterised by very high transmissibility with an estimated basic reproduction rate of between five and eight. A household transmission study in a largely unvaccinated population found that the odds of subsequent transmission from a Delta variant was 70% higher than from Alpha cases. [16]

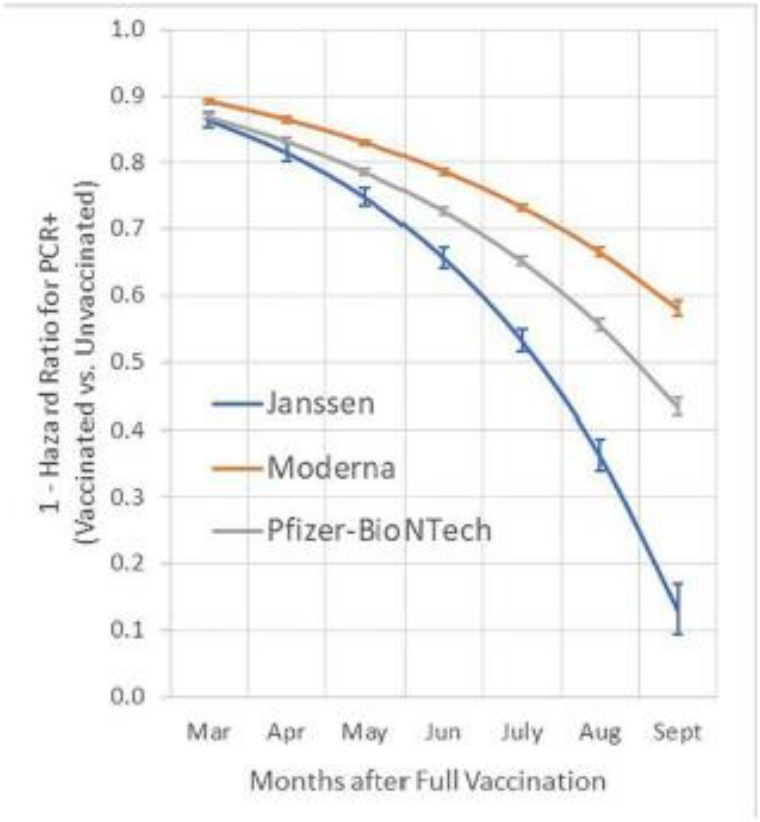
Delta breakthrough infections are associated with a similar viral burden in both vaccinated and unvaccinated people. Duration of viral shedding and culture positivity with breakthrough Delta infection exceeds that of Alpha infection with duration of positivity increasing with time from vaccination. [17,18] Some studies show that levels of culturable virus and duration of viral shedding are reduced in the vaccinated with breakthrough infection. [19]

Vaccination reduces transmission, although less with Delta than with Alpha infection [20]. While antibody levels can decline over time, VE against hospitalisation and severe disease is sustained for at least six months in the general population[16] In the Netherlands, De Gier found VE of the index case in preventing transmission to unvaccinated household contacts was 63%, lower than that with Alpha infection at 73%. [15]

Several studies have shown that the Delta variant has been associated with some decline in VE of EMA authorised COVID-19 vaccines [4,21,22]. Reduction in VE is more evident against infection and symptomatic disease than against hospitalisation and death.

COVID-19 vaccine Janssen showed the greatest decline in VE against infection as the Delta variant emerged in the US (Figure 5) [7]

Figure 5: Time dependent vaccine effectiveness against SARS-CoV-2 infection as estimated from Cox proportional hazards models. Source: Cohn et al



Note: VE effectiveness estimated corrected for misclassification of vaccination status are presented on this slide. Uncorrected VE are 64-69% for COVID-19 infection and 68 -75% for COVID-19 related hospitalisation

In the Netherlands, 161 breakthrough infections were identified in a population of 24,706 HCWs immunised with mRNA or adenoviral vector vaccine. The Delta variant was identified in most cases. One third had received COVID-19 vaccine Janssen but they accounted for 44% of breakthrough infections. [19]

7. Booster vaccination

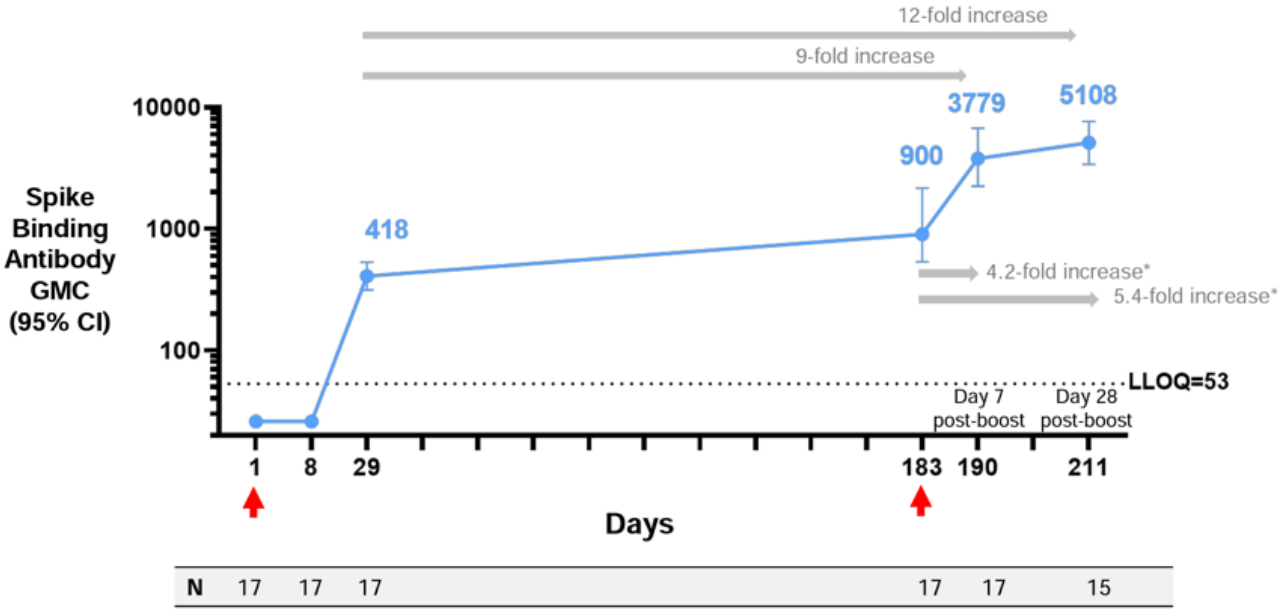
Both homologous and heterologous vaccines schedules have been shown to be highly immunogenic.

Homologous boosting after COVID- 19 vaccine Janssen

Additional vaccine doses may be required because of a suboptimal response to a primary vaccine course, waning immunity or reduced protection against variant strains. A single dose of COVID-19 vaccine Janssen achieves lower overall VE compared with the mRNA vaccines. Effectiveness can be significantly augmented by a second vaccine dose.[23]

The addition of a second dose is highly immunogenic with boosting at six months associated with a 9 to 12-fold increase in antibodies and was more potent than boosting at two months. Boosting at six months increased the breath of response including against variants of concern. [24] (Figure 6).

Figure 6: Spike binding antibodies after a six month booster COVID-19 vaccine Janssen by time (Source: FDA briefing)



No unexpected safety signals have been identified following a second dose of COVID-19 vaccine given up to six months after the first dose**.**

Heterologous boosting after COVID- 19 vaccine Janssen

In a clinical trial in the U.S., adults who received one of three authorised COVID-19 vaccines at least 12 weeks prior to enrolment received a booster with one of three vaccines (full dose Spikevax, COVID-19 vaccine Janssen, or Comirnaty) in nine different combinations. The results showed that homologous or heterologous booster vaccination was highly immunogenic and that reactogenicity was similar to the primary reported series. [25]

In the Netherlands, a randomised controlled trial in HCWs vaccinated with COVID-19 vaccine Janssen compared the reactogenicity and immunogenicity of homologous or heterologous boosting with either Comirnaty or Spikevax with no boosting. Homologous and heterologous booster vaccination resulted in an increase in SARS-CoV-2-specific binding antibodies, neutralising antibodies and T-cell responses when compared to single COVID-19 vaccine Janssen vaccination. In comparison with the homologous boost, the increase was significantly larger in heterologous regimens with the mRNA-based vaccines. Spikevax boosting was most immunogenic and was associated with higher reactogenicity.

As the immunogenicity is greater after heterologous boosting this is the preferred option.
The duration of protection that a booster dose affords is uncertain. However, given the high levels of antibodies achieved and based on experience with other vaccines, it is reasonable to expect that it might extend longer than that following a primary vaccine series.

Safety of mRNA booster vaccination

In Israel over 3.7 million booster doses of Comirnaty have been administered to those aged 16 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.

Booster doses of 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. Current data for Spikevax also indicate that the pattern of side effects after the booster is similar to that after the second dose.

In heterologous booster studies with Covid-19 vaccine Janssen and mRNA vaccines, reactogenicity was generally similar between heterologous and homologous boosts and compared to the primary series and no new safety concerns were identified. [25,26]

In Scandinavia and France, preliminary data indicate that the rate of myocarditis is higher in males aged 16 to 29 years receiving a full dose of Spikevax as a second dose in the primary vaccine series, compared to those receiving Comirnaty. The risk of rare adverse reactions, including myocarditis, is being further characterised and closely monitored. While the EMA assesses the data, as a precaution Comirnaty is recommended as a booster for all in this age group.

Age and timing of mRNA booster vaccination

The EMA stated that a booster dose of Comirnaty (0.3ml, full dose) may be considered in those aged 18 years and older. The safety and immunogenicity of a booster dose of Comirnaty was based on data in those aged 18 to 55 years who showed a rise in antibody levels when a booster dose was given approximately six months (range 4.8 to 8.0 months) after the second dose.

The EMA stated that a booster dose of Spikevax (0.25ml, half the dose of the primary schedule) may be considered in those aged 18 years and older. The safety and immunogenicity of a booster dose of Spikevax was based on data in those aged 18 years and older who showed a rise in antibody levels when a booster dose was given at least six months (range six to nine months) after the second dose.

The EMA concluded that booster doses of Comirnaty and Spikevax may be considered at least six months after the second dose for those aged 18 years and older.

Real world evidence from Israel [11] and preliminary data from a randomised control trial of participants aged 16 and over, supports the safety and effectiveness of Comirnaty booster vaccines in those 16 years and older. As no unexpected safety concerns have been identified in those aged 16 and 17 years, it is reasonable to include this age group in these recommendations.

NIAC recommends that a full dose of Comirnaty (0.3ml/30 micrograms) or half dose of Spikevax (0.25ml/50 micrograms) should be given after an interval of six months or longer following completion of the primary course of any two dose COVID-19 vaccine. A minimum interval of five months may be used for operational reasons.

COVID-19 vaccine Janssen recipients should receive an mRNA booster dose after an interval of three months. This is because the VE of this single dose vaccine is less robust than the vaccines with a two dose schedule.

Co-administration

COVID-19 vaccines and other vaccines including live and non-live seasonal influenza vaccines may be administered at the same time or at any interval.

This is consistent with recommendations from CDC, Canada and the UK.

8. International recommendations

Table 2: COVID-19 booster vaccine recommendations by country. Source: DOH [information accessed 23 November 2021]

Country	Recommendation for booster by age	Specific recommendation for booster by receipt of COVID-19 Vaccine Janssen
Austria	12 and older	√
Belgium	12 and older[1]	
Croatia	65 and older	√
Denmark	65 and older	√
Estonia	18 and older	
Finland	30 and older	
France	40 and older	√
Germany	18 and older	√
Hungary	18 and older[2]	
Iceland	60 and older[3]	√
Israel	12 and older	
Italy	60 and older[4]	
Latvia	50 and older	√
Lithuania	18 and older	√
Luxembourg	75 and older	√
Netherlands	60 and older	
Norway	18 and older	√
Malta	60 and older[5]	
Poland	18 and older	
Romania	18 and older	
Slovakia	55 and older[5]	
Slovenia	70 and older	√
Spain	60 and older	√
Canada	18 and older	
UK	40 and older [6]	
US	18 and older	√

[1] to be discussed 27 November 2021
[2] everyone will receive a booster according to their registration
[3] everyone over 16 years will be offered a booster
[4] 40 and older from 1 December 2021
[5] will be offered to all of the population
[6] JCVI reviewing case for 18 and older

9. Conclusions

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

Ireland is undergoing a surge in case numbers across all ages, despite high vaccination rates. This is due to a number of factors, including the highly transmissible Delta variant, waning of immunity over time and the opening up of society with an increase in socialisation. These factors increase the risk of breakthrough infections, transmission and perpetuation of the infection transmission cycle.

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.

Booster vaccines are one component in the fight to suppress COVID-19 infections in the community. Their main role is to protect against hospitalisation, severe COVID-19 and death. As age and underlying conditions are the most important determinants of risk of severe breakthrough infection, priority for booster vaccines must be given to these groups as previously recommended.

While pregnant women are at no higher risk of contracting SARS-CoV-2, those that do are at higher risk of severe disease and adverse outcomes and they should avail of a booster vaccination at the earliest opportunity.

Booster vaccination in Israel has led to substantial reductions in the rate of severe illness in those aged 40 to 49 years and this cohort should be prioritised next.

A secondary but important role of booster vaccines is their ability to reduce the risk of transmission of the virus. Boosting antibody levels has been shown to reduce breakthrough infections and the transmission risk in all age groups.

While all COVID-19 vaccines have good effectiveness against symptomatic COVID-19, protection afforded by COVID-19 vaccine Janssen is lower than that of the mRNA vaccines. Antibody levels after COVID-19 vaccine Janssen are substantially lower that those after a two dose vaccine series. Given the accepted correlation of antibody levels with protection against infection, it is likely that boosting the antibody levels will have a considerable impact in reducing the rate of symptomatic COVID-19.

As the protection of the single dose COVID-19 vaccine Janssen against infection declines more rapidly than vaccines with a two-dose schedule, offering an earlier booster vaccine may help to control the surge in case numbers in younger people whose lifestyle, work and living conditions may increase their social mixing.

Heterologous boosting following single dose COVID-19 vaccine Janssen is more immunogenic than homologous boosting and booster doses of mRNA vaccines have not shown any unexpected short term

safety concerns. The risk of myocarditis or other rare adverse reaction following an mRNA booster dose has yet to be characterised and will be closely monitored.

NIAC continues to examine new evidence regarding the vaccination of younger children and durability of protection of the primary vaccine series in other groups, e.g., the immunocompromised who received an additional dose and those aged 12 to 15 years.

10. Recommendations

1. All those who are unvaccinated or incompletely vaccinated are strongly recommended to complete a primary COVID-19 vaccination course. Booster doses are strongly recommended for those eligible. Seasonal influenza vaccine can be given at the same time to those for whom it is recommended.

2. All must continue to observe all recommended public health and social measures. The use of masks, physical distancing, hand hygiene, and ventilation of indoor spaces are key to reducing transmission of SARS-CoV-2. Booster vaccines will not immediately contribute to outbreak management and do not take the place of public health and social measures.

3. Priority for booster vaccines must be given to those at highest risk of severe COVID-19 breakthrough infection i.e., those in the older age cohorts and those with underlying conditions. Booster vaccines should be offered to those in previously recommended groups before progression to the younger age cohorts.

   In addition to prior recommendations, in next order of priority, a booster dose of an mRNA vaccine is recommended for
   - all pregnant women aged 16 years and older
   - all those aged 40 - 49 years who received any COVID-19 vaccine including COVID-19 vaccine Janssen
   - those aged 16 - 39 years, who received an mRNA vaccine in descending order by age cohort; 30 - 39 years, 20 - 29 years and 16 -19 years
   - those aged 16 - 29 years who received COVID-19 vaccine Janssen can be offered a booster vaccine in parallel with those aged 30 - 39 years.

4. For those aged 30 years and older, a full dose of Comirnaty (0.3ml/30 micrograms) or a half dose of Spikevax (0.25ml/50 micrograms) should be given six months (or at least five months for operational reasons) or longer following completion of a primary two dose course of any COVID-19 vaccine.

   For those aged 16 to 29 years, a full dose of Comirnaty (0.3ml/30 micrograms) should be given six months (or at least five months for operational reasons) or longer following completion of a primary two dose course of any COVID-19 vaccine.

   Recipients of COVID-19 vaccine Janssen should receive an mRNA booster dose after a minimum interval of three months.

5. Those who have a breakthrough infection following a primary vaccination course should defer booster vaccination for at least six months following infection onset.

6. If an mRNA vaccine is contraindicated, consideration can be given to boosting with an authorised non-mRNA vaccine following an individual benefit-risk assessment.

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

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