Superior
Health Council

COVID-19 VACCINATION: AUTUMN / WINTER SEASON 2022 – 2023 INTERIM RECOMMENDATIONS

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Federal Public Service Health, Food Chain Safety and Environment

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Superior Health Council

ADVISORY REPORT OF THE SUPERIOR HEALTH COUNCIL no. 9721

COVID-19 vaccination: Autumn / Winter season 2022 – 2023
Interim recommendations

In this scientific advisory report, which offers guidance to public health policy-makers, the Superior Health Council of Belgium provides recommendations on COVID-19 vaccination during Autumn / Winter season 2022-2023 for the Belgian population.

Conclusions and recommendations approved by the members of the NITAG on 16 June 2022.
Approval of this full version of the advisory report by the NITAG on 30 June 2022.
Advisory report validated by the Council on 06 July 2022[1].

I INTRODUCTION

The Superior Health Council (SHC) received a request for advice from the Task Force Vaccination against COVID-19 on Coronavirus disease 2019 (COVID-19) vaccination during fall 2022 for the Belgian population. More specific questions were referred to the Council by the Interministerial Public Health Conference on 13 June 2022. The advice was requested by end of June 2022.

On 05 May 2022, the Council published the following recommendations:
https://www.health.belgium.be/en/report-9706-second-booster-vaccination-against-covid-19

SHC 9706 – 05/05/2022 ***"Primary plus first booster dose scheme remains priority in the fight against severe forms of COVID-19 and must be continued to be strongly promoted****. The SHC reiterates the importance of the rapid administration of a first booster dose for all those for whom it is recommended and especially for persons aged 65 years or over and for all previously determined comorbidities. At this time, the SHC did not recommend a second booster dose for the general population. At this time, the SHC also did not recommend a systematic second booster dose for people over 80 years of age and residents of nursing homes and care communities (regardless of their age).*

Timing *of administering additional booster doses* ***is crucial*** *and needs to be based on the most recent epidemiological data from Sciensano, Belgian reference mathematical models* and on international literature"*.*

In Europe, the administration of a second booster is currently **an off label use** of the vaccines but it is supported by a joint statement of European Centre for Disease Prevention and Control (ECDC) and European Medicines Agency (EMA) **for some groups** (06/04/2022).
https://www.ema.europa.eu/en/news/ecdc-ema-issue-advice-fourth-doses-mrna-covid-19-vaccines

[1] The Council reserves the right to make minor typographical amendments to this document at any time. On the other hand, amendments that alter its content are automatically included in an erratum. In this case, a new version of the advisory report is issued.

In US, the Food and Drug Administration (FDA) has already given a positive advice for the use of the mRNA vaccines as second booster dose.

- Comirnaty®:

"Second booster dose for individuals 50 years of age and older at least four months after receipt of a first booster dose of any authorized or approved COVID-19 vaccine.

Second booster dose for individuals 12 years of age and older with certain kinds of immunocompromise at least four months after receipt of a first booster dose of any authorized or approved COVID-19 vaccine".

- Spikevax®:

"Second booster dose for individuals 50 years of age and older at least four months after receipt of a first booster dose of any authorized or approved COVID-19 vaccine.

Second booster dose for individuals 18 years of age and older with certain kinds of immunocompromise at least four months after receipt of a first booster dose of any authorized or approved COVID-19 vaccine".

The scope of this report is to answer questions about the timing, the groups to be recommended for vaccination (and their level of priority), the minimum interval between two booster doses and the usefulness of using mRNA vaccines adapted to Omicron strains.

In Belgium (and more broadly in Europe), the mRNA vaccines Comirnaty® and Spikevax® (adapted with Omicron strains or not) are the main vaccines to be used for COVID-19 vaccination campaign during the Autumn / Winter season 2022 - 2023. Depending on the market launch after European Medicines Agency (EMA) recommendation and European Commission (EC) authorization of other vaccines as potential boosters, the SHC may update its recommendations in the future.

In order to best anticipate the COVID-19 vaccination campaign for Autumn / Winter season 2022 - 2023, the SHC entrusted the National Immunization Technical Advisory Group (NITAG) with the revision of these **interim recommendations** on COVID-19 vaccination.

II METHODOLOGY

The request was treated by the NITAG including experts in vaccinology, geriatrics, general medicine, paediatrics, microbiology, infectiology and epidemiology, etc. The experts of this working group provided a general and an *ad hoc* declaration of interests and the Committee on Deontology assessed the potential risk of conflicts of interest.

This advisory report is based on a review of the scientific literature published in both scientific peer-reviewed journals, preprint articles and reports from national and international organisations (FDA, CDC, EMA, ECDC, UKHSA, HAS, JCVI, etc.) competent in this field, as well as on the opinion of the experts.

Sciensano provided a report on the Belgian epidemiological data and the Simulation Models of Infectious Diseases consortium (SIMID) consortium on the Belgian mathematical modelling data. Both presented their reports at the NITAG meeting of April 16 2022 and Sciensano presented an update at June 16 2022. At this stage there is no updated mathematical modelling for BA.4 and BA.5 and a possible effect of a second booster dose in Belgium.

Once the advisory report was endorsed by the NITAG, it was ultimately validated by the members of the Board of the SHC.

Keywords

Keywords	**Sleutelwoorden**	**Mots clés**	**Schlüsselwörter**
Prevention	Preventie	Prévention	Verhütung
Booster	Booster	Rappel (dose)	Auffrischimpfung
COVID-19	COVID-19	COVID-19	COVID-19
Vaccination	Vaccinatie	Vaccination	Impfung

List of abbreviations used

BelSACI	Belgian Society for Allergy and Clinical Immunology
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
EC	European Commission
ECDC	European Centre for Disease Prevention and Control - EU
EMA	European Medicines Agency
FDA	Food and Drug Administration - US
HAS	*Haute Autorité de Santé* - FR
HR	Hazard Ratio
ICU	Intensive Care Unit
JCVI	Joint Committee on Vaccination and Immunisation - UK
LTCF	Long-Term Care Facilities
MIS-C	Multisystem inflammatory syndrome in children
mRNA	Messenger ribonucleic acid
NITAG	National Immunization Technical Advisory Group
NPI	Non-Pharmaceutical Intervention
OR	Odd Ratio
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SHC	Superior Health Council
SIMID	Simulation Models of Infectious Diseases consortium
UKHSA	UK Health Security Agency - UK
VE	Vaccine Effectiveness
VOC	Variants Of Concern

III CONCLUSIONS AND RECOMMENDATIONS

1 CONCLUSIONS

The BA.2 is now less than 30% of the new cases. Currently in Belgium (17/06/2022), there is a growing proportion of Omicron BA.5 (58%) and to a lesser extent BA.4 (9%) strains, **which are expected to rapidly become dominant in Belgium and Europe**. Some new Omicron variants could also emerge like for example the BA.2.75 sub-variant also seen in seven other countries like: Australia, New Zealand, and Japan in Asia and the Pacific region; UK and Germany in Europe; and USA, Canada in North America.

These different Omicron-related strains **partly escape the immunity and protection conferred by current vaccines and exposure to previous variants**. This is currently most evident for a shorter duration of protection and for the Vaccine Effectiveness (VE) against infections and mild forms of COVID-19.

Timing of administering additional booster doses **is still crucial** and needs to be based on the most recent epidemiological data from Sciensano and Belgian reference models (when feasible) and on international literature.
https://covid-19.sciensano.be/fr/covid-19-situation-epidemiologique
https://www.simid.be/

The Omicron BA.2 variant shows **a higher transmissibility** compared to the Delta variant, and is also characterized **by a lower severity**, attenuated by a factor of about 2 on intensive care unit (ICU) hospitalizations (risk reduction of 48-59% depending on the study) and by a factor of 4-9 on death (HAS, 25/05/2022). This is observed in high incomes countries with a high level of immunity and vaccination coverage.

The BA.4 and BA.5 sublineages of the Omicron variant **also show high transmissibility** (Tegally et al., 2022 preprint) **and partially escape natural and vaccine induced immunity** (Hachmann et al., 2022 ; Cao et al., 2022[a-b]).

Based on limited data in humans, **there is no evidence of BA.4 and BA.5 being associated with increased infection severity** compared to the circulating variants BA.1 and BA.2. Nevertheless in pre Omicron period, Ziyad and collaborators (2022 – pre-Omicron period – preprint) show that reinfection adds non-trivial risks of all-cause mortality, hospitalization, and adverse health outcomes in the acute and post-acute phase of the reinfection.

At present, **there are insufficient data for a robust assessment of the VE of COVID-19 vaccines against mild or severe disease with BA.4 and BA.5**. However, preliminary analyses indicate that the vaccination status of cases infected with BA.4 and BA.5 is not significantly different to that of cases infected with BA.2, suggesting that protection conferred by the vaccines likely remains comparable to that observed previously (UKHSA, 24/06/2022).

In the context of Omicron BA.1 et BA.2 (probably similar but with no data for BA.4 and BA.5)

- A separate analysis of three countries with complete data on severe outcomes and vaccination status demonstrates that **the highest burden of severe outcomes has been among unvaccinated people in all adult age groups** and this continues to be the case (ECDC, 28/04/2022).

- Published literature indicates VE against severe outcomes caused by Omicron **remains high, with continued strong protection in the range of 80−90% after receiving the first booster**. However, there is growing evidence of waning **around 3-6 months** (Adams et al., 2022 ; Tartof et al., 22/04/2022 ; CDC/VRBPAC, meeting 06/04/2022 ; Stowe et al., preprint 01/04/2022 ; Sciensano, 11/04/2022). In UK, we observed a further decrease in VE for severe outcome over time (for BA.1 / BA.2 to less than 75% after more than 70 days – UKHSA, 16/06/2022). Mathematical modelling suggests that increasing the proportion of the population who have been provided with immunity through a primary course and first booster has a substantial potential to reduce COVID-19 death burden by the end of October 2022.

  For Belgium, Sciensano provides more specific data in the line of international published studies for the period of January-June 2022, during which Omicron was dominant:

  - For 18+ (all adults, elderly included): VE against ICU after the booster wanes **very slowly** from 93% (CI 89-98) after 0-50 days to 89% (CI 83-95) after 150-200 days.

  - For 80+: VE against hospitalizations after the booster wanes approximatively from 86% (CI 80-90) after 0-50 days to 72% (CI 68-77) after 150-200 days.

  - For 65 to 79 y.o.: VE against hospitalizations after the booster wanes approximatively from 91% (CI 89-93) after 0-50 days to 78% (CI 74-82) after 150-200 days.

  - For 18 to 64 y.o.: VE against hospitalizations after the booster wanes approximatively from 87% (CI 85-90) after 0-50 days to 60% (CI 44-77) after 150-200 days (more uncertainty due to fewer cases).

In Belgium too, VE against severe outcomes caused by Omicron **remains high, with continued strong protection against ICU and hospitalisations 3 to 6 months after receiving the first booster, despite limited waning**.

In all groups, VE against symptomatic infection starts lower, wanes more rapidly and to a much larger extend (cf. point 5 for more data).

- Early data from Israel indicate that the risk of severe disease and/or death due to COVID-19 **is reduced for up to 10 weeks after the administration of a second booster dose**, compared to those receiving only the first booster dose. However, this is in populations already experiencing low levels of severe outcomes, thus providing small absolute reductions (Gazit et al., 2022). With regard to the second booster, modelling shows that its roll-out in some vulnerable groups could avert a substantial proportion of COVID-19 deaths between now and mid-autumn 2022 (ECDC, 28/04/2022). In the context of Omicron, 2 months after a second booster, there is no more additional effect on confirmed infection (rapid waning). A positive effect of the second booster on severe disease is observed up to at least 6 weeks (short evaluation period) with a wide confidence interval and therefore a large uncertainty (Bar-On et al., 2022). More recently, Muhsen and collaborators (2022) suggest that a fourth Comirnaty® dose was associated with high protection against COVID-19 hospitalizations and deaths among residents of long-term care facilities (LTCF) during a surge associated with the Omicron variant.

A second mRNA booster dose has a positive global clinical effect but, the maximum duration of this protection is not yet known due to the short follow-up periods after the second booster in the studies available and the change of Omicron subvariants.

At this stage of post-vaccination side effect surveillance, **there are no additional safety issues** related to the administration of a second booster.

EMA is working closely with international partners to facilitate the availability of adapted COVID-19 vaccines that provide improved protection against virus variants through non-inferiority studies, looking at protection against BA.1 and BA.2. EMA will assess all data on the immune response to the adapted vaccines as well as data on its efficacy against Omicron subvariants and provide adequate recommendation. **As with the annual influenza vaccination with vaccines adapted to circulating strains, it is not anticipated that a large amount of clinical efficacy data of mRNA vaccines adapted to current and future strains will be available at the time of recommendation of use by the EMA.**

2 RECOMMENDATIONS

1. Primary vaccination plus first booster dose remains priority for all adults and for children and adolescents at risk of severe outcomes

Primary plus first booster dose scheme remains priority in the fight against severe forms of COVID-19 and must be continued to be strongly promoted (ECDC, HAS, UKHSA, JCVI).

The SHC reiterates the importance of the timely administration of a first booster dose for all adults and for children and adolescents **at risk of severe outcomes** and especially for persons aged **65 years or over and for all previously determined comorbidities** (SHC 9618, 05/02/2021: level 1, 2 and 3 priority and SHC 9641, April 2021), **immunocompromised** (SHC 9691, March 2022) **and pregnant women** (SHC 9622, 22/04/2021).

2. Timing of Autumn / Winter season 2022 – 2023 COVID-19 vaccination

Based on current data and European prediction models, **the SHC recommends that all risk groups as defined in this opinion be vaccinated with an additional booster by the end of September 2022 at the latest**. Based on the experience of previous years, it is up to the TF Vaccination to determine the start of the campaign to achieve this goal, keeping in mind that the further away the vaccination is from the onset of the wave of infections, the more likely it is that the protection provided by the vaccines will be diminished, especially with regard to symptomatic infections and transmission risks. The longer the interval towards the booster, the more the waning is pronounced. **The campaign should therefore be "as compact as possible" to maximize de benefits of vaccination against COVID-19.**

3. Minimum interval between mRNA booster doses

As recommended for the first booster (SHC 9683, 2021), the SHC recommends an interval of at least 3 months but **preferably 6 months** for the administration of an additional mRNA booster dose. Taken into account the local epidemiology (ECDC, 14/06/2022) timing can be adapted to maximize the benefit for the general public health.

Note: It is up to the Taskforce vaccination and the Interministerial Public Health Conference to adapt this preferential timing of minimum 6 months between two booster doses for people who would have already recently (spring - summer 2022) received a booster dose so that these people can still be vaccinated before the onset of the Fall / Winter 2022 - 2023 wave. This includes some immunocompromised individuals who would have delayed taking their first booster recommended by the Council in March 2022 (SHC 9691, March 2022 - 2+1 + 1st booster) and some elderly who had already taken a second booster in the spring of 2021 when it was not recommended at that time for that group by the Council (SHC 9706, May 2022 - 2 + 1st booster). To help the decision in Belgium by the Taskforce and the Belgian Authorities, it's important to note that:

- ***EMA** proposed an minimum interval of **3 months** for the **first booster** administration;*
- ***ECDC** proposed **3 months (for public health reasons)** to **preferably 6 months** for the **first booster** administration (ECDC, 07/12/2021);*
- ***Israel** has started his **second booster** campaign with an interval of **4 months** without particularly safety issue and that for both vaccines;*
- ***FDA** recommends at least **4 months** between 1st and 2° booster, for Moderna as well as Pfizer vaccines (FDA briefing doc June 28, 2022).*

4. Hybrid immunity

An infection before or after completion of COVID-19 vaccination has a booster effect and the greatest levels of protection against both variants were provided by hybrid immunity (Pilz et al., 2022 ; Goldberg et al., 2022 ; Suarez et al., 2022). This has led some countries to postpone the administration of a booster dose in function of a previous infection (HAS, 25/05/2022).

However, on the data available, the SHC **cannot conclude yet on the duration and impact of a COVID-19 infection (naturally-acquired, vaccine-induced and hybrid immunity) as a clinical protection effect against severe outcomes**.

The relationship between levels of antibody titers and the necessity of a booster dose is not yet clear and no (immune) correlate of protection has been defined so far. Furthermore, for practical reasons, it is unfeasible to study antibody titers to decide on the necessity of a booster at an individual level.

To simplify the system, to obtain the highest possible level of protection and to ensure consistency with previous recommendations, the SHC recommends **a booster vaccination be given regardless of history of COVID-19 infection**, and at least 14 days after recovery of symptomatic COVID-19, or at least 14 days after a positive Polymerase Chain Reaction (PCR) test for asymptomatic COVID-19.

5. Risk groups for Autumn / Winter season 2022 – 2023 COVID-19 vaccination

In order to best anticipate the COVID-19 vaccination campaign for Autumn / Winter 2022 - 2023, the SHC recommends the administration of an additional mRNA vaccine for:

Category A: COVID-19 proactive mass vaccination campaign recommended by the SHC

Group 1: people with increased risk of death or severe forms of the disease (hospitalization, ICU, death)

- Any person aged **65 years and over or living in LTCF**;

- Any patient **with immunosuppression** due to disease or treatment (SHC 9691, 03/03/2022);

- Any patient **with at least one comorbidity** as defined above (all levels of priority 1, 2, and 3 - SHC 9618, 05/02/2021);

For children and adolescents, a specific attention should be made on patients with:

- Chronic kidney disease for at least 3 months
- Chronic liver disease for at least 6 months
- Hematological cancers (e.g. leukemia)
- Down syndrome
- Transplant patients (including those on the waiting list)
- Immune system disorders or use of immunosuppressants that increase the risk of infectious diseases
- Active HIV/AIDS
- Certain rare conditions. We would like to emphasize that the group for which the rare disease has an impact on cardiovascular, respiratory or neurological health is given special attention. In order to know the rare diseases mainly considered, please refer to the Orphanet list. https://www.orpha.net/consor/cgi-bin/Disease_Search_List.php?lng=EN

- **All pregnant women** regardless of the stage of pregnancy (SHC 9622, 22/04/2021);

- As mentioned at the beginning of the advisory report, primary vaccination plus 1st booster is key for all those eligible, in particular those at higher risk of severe disease. As pregnancy is a known risk factor for severe disease and vaccination has been proven to be safe in pregnancy and protect the infant, any pregnant woman who has not yet been vaccinated, should be vaccinated **with a complete primary vaccination and 1st booster dose 6 months after the primary vaccination**;

- All pregnant women who have already received a booster should receive their additional booster dose in Autumn / Winter season 2022 – 2023, with a minimum interval of **at least 3 months, but preferably 6 months** between the booster doses.

Group 2: all "persons active in the care sector", in and outside care institutions

In order to:

- Enable "care workers" to be protected as much as possible from the risk of severe forms of the disease on an individual basis;
- Minimize the risk of transmission to the most vulnerable patients (even though protection against infection with Omicron quickly wanes, data show reduced infectiousness or viral load after vaccination, e.g. Accorsi et al., 2022);
- Ensure maximum functioning of the overall health care sector for all patients during the critical winter period (Reichert et al., 2022).

The SHC recommends that these groups be vaccinated with an additional booster for the Autumn / Winter season 2022 - 2023. However, the SHC reiterates that the duration of protection against infections and transmission, in the context of Omicron, declines very rapidly over time. **This vaccination strategy complements but does not replace non-pharmaceutical interventions (NPIs)** for people at risk of severe disease in contact with these “persons active in the care sector”.

The term "persons active in the care sector" covers all the socio-professional categories listed in the SHC 9597 and 9611 of September 2020.
https://www.health.belgium.be/fr/avis-9597-strategie-de-vaccination-covid-19

This group "people active in the care sector" includes all people involved and active (including volunteers and trainees):

- In an acute and chronic care institution (with or without direct contact with the patient). For example: nursing staff, medical staff, technicians, maintenance, catering, administrative staff, etc;
- In preventive health services (e.g. ONE, Kind & Gezin, etc.);
- As well as all health professionals and their staff working outside the institution at the practice, in a pharmacy or in the home. For example: pharmacist, GP, nurse, physiotherapist, occupational therapist, speech therapist, psychologist, dentist, etc.

Group 3: People living in the same household as people at high risk of severe disease

- All household members of people belonging to group 1 (“cocoon vaccination”)

It is recommended to minimize the risk of transmission to the most vulnerable patients (even though protection against infection with Omicron quickly wanes less, data show reduced infectiousness or viral load after vaccination, e.g. Accorsi et al., 2022). The SHC reiterates that, in this specific case of Omicron, **cocoon vaccination strategy complements but does not replace non-pharmaceutical interventions (NPIs)** for people at risk of severe disease.

Category B: The SHC recommends an additional COVID-19 booster dose for people aged between 50 and 64 with some risk factors like obesity (BMI ≥ 30 kg/m2), **smoking or excessive alcohol consumption** (SHC 9438, 2018).

Obesity is a well-known risk factor for COVID-19 severe outcomes (Body Mass Index (BMI) ≥ 30 kg/m2 - Mahamat-Saleh et al., 2021 - SR and M-A ; Pranata et al., 2021 - SR and M-A ; Ho et al., 2020 - SR and M-A) but is less easily identifiable by the Authorities with codes and systematic invitation to vaccination.

This is also the case for people **who smoke** (Reddy et al., 2021 – SR and M-A ; Vardavas et al., 2020 – SR ; Zhao et al., 2020 - SR and M-A ; Zhang et al., 2022) or **drink alcohol excessively** (Pavarin et al., 2022 ; Ostinelli et al., 2022 ; Webb et al. 2020 ; Tsai et al., 2020 ; SHC 9438, 2018).

Category C: COVID-19 additional booster possible on safety profile data (but not recommended yet by the SHC) **for children, adolescents and adults until 64 y.o. in good health**

Pending marketing authorization by the EC of the different vaccines, covid-19 vaccination could be offered on an individual and voluntary base.

For people between 18 and 64 years old **in good health and not included in categories A and B**

- Without immunosuppression;
- Without comorbidities;
- Not pregnant;
- Without risk factors like obesity, smoking or excessive alcohol consumption;
- Who do not work in the care sector;
- Who are not living in the same household as an at-risk person.

1) COVID-19 additional booster is possible on safety profile data (but not recommended yet by the SHC) for adults until 64 y.o. in good health. **Pending marketing authorization by the EC of the different vaccines**: primary vaccination and boosters doses could be offered on an individual and voluntary base.

The SHC has revised the data for children and adolescents regarding Omicron:

- **VE against infection, transmission, hospitalization**: moderate to low effect on a shorter period of time but a positive effect of a first booster dose in children and adolescents (Fleming-Dutra et al., 2022 ; Katz and Edwards, 2022 ; Dorabawila at al., 2022);

- **Data on hospitalizations in Belgium**: very low numbers of hospitalizations and deaths for this age group in Belgium – differences with US data? (Sciensano cf. point 5.2);

- **Multisystem inflammatory syndrome in children (MIS-C)**: less important and less severe with Omicron (Holm et al., 2022 ; Levy et al., 2022 ; Wang et al., 2022);

- **Long Covid**: less frequent with Omicron in the adult population (Antonelli et al., 2022).

Considering these new data, the SHC maintains for now its previous recommendations (SHC 9680, 17/12/2021; SHC 9693, 03/16/2022) for the Autumn / Winter season 2022 - 2023:

2) COVID-19 additional booster is possible on safety profile data (but not recommended yet by the SHC) for all healthy children and adolescents of 12-17 y.o. (except those included in category A). **Pending marketing authorization by the EC of the different vaccines**: primary vaccination and booster doses could be offered on an individual and voluntary base.

3) COVID-19 additional booster is possible on safety profile data (but not recommended yet by the SHC) for all healthy children of 5-11 y.o. (except those included in category A). **Pending marketing authorization by the EC of the different vaccines**: primary vaccination and booster doses could be offered on an individual and voluntary base.

*4) Remarks : primary COVID-19 vaccination for **healthy children of 6 months to 4 years old**. (except those included in category A), will be addressed in an separate advisory report when more data will be available and after the safety advice of EMA on this subject. Food and Drug Administration (FDA) Infant Formula Update: June 17, 2022. https://www.fda.gov/news-events/press-announcements/fda-infant-formula-update-june-17-2022*

6. Omicron adapted versions of mRNA vaccines

On 17 June 2022, the WHO published an Interim statement on the composition of current COVID-19 vaccines. Interim statement on the composition of current COVID-19 vaccines (who.int)

"The use of currently licensed vaccines based on the index virus confers high levels of protection against severe disease outcomes for all variants, including Omicron with a booster dose. As such, the continued use of currently licensed vaccines for primary vaccination AND as a booster dose is appropriate to achieve the primary goals of COVID-19 vaccination".

On 28 June 2022, the FDA-VRBPAC published an Interim statement on the composition of current COVID-19 vaccines with **some important arguments for discussion**.
https://www.fda.gov/media/159452/download

On 30 June 2022, FDA: "*Following the vote, and striving to use the best available scientific evidence, we have advised manufacturers seeking* ***to update their COVID-19 vaccines that they should develop modified vaccines that add an omicron BA.4/5 spike protein component to the current vaccine composition to create a two component (bivalent) booster vaccine****, so that the modified vaccines can potentially be used starting in early to mid-fall 2022*".
https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-recommends-inclusion-omicron-ba45-component-covid-19-vaccine-booster

At this stage, EMA has started a rolling review for a version of both Comirnaty (15/06/2022) and Spikevax (17/06/2022) adapted to provide better protection against a specific variant or variants of SARS-CoV-2, the virus that causes COVID-19. The review will initially focus on data from laboratory studies (non-clinical data) and data on chemistry, manufacturing and controls, which relate to the manufacturing of the vaccine. As the companies makes progress in the development of the both vaccines, EMA will receive more data, including data on the immune response against the original strain and the Omicron variant of concern. As long as these adapted vaccines are not recommended by the EMA and authorized by the EC, **it is important to consider the available clinical evidence of the currently authorized vaccines (non-adapted versions of mRNA vaccines) to recommend their use as the best option available**. Clear and transparent communication to the general public on this sensitive issue is essential to maintain public confidence in vaccination.

Remarks: if only limited stocks of adapted mRNA vaccine are available at the time of the 2022 – 2023 booster campaign, it is reasonable to prioritized these adapted versions to the groups most at risk of severe forms (group 1 of category A).

7. Simultaneous vaccination

Some studies show that simultaneous vaccination is **safe and effective.** Therefore, simultaneous vaccination against COVID-19 and seasonal influenza is possible (SHC 9675, 07/10/2021). However, under no circumstances should any vaccination be delayed for this reason alone, but only on the basis of the most reliable epidemiological forecasts and the expected duration of vaccine efficacy of the various vaccines.

- For COVID-19 : the SHC recommends that all risk groups as defined in this opinion be vaccinated **by the end of September 2022 at the latest**.

- For Influenza : the SHC recommends 2022 - 2023 seasonal influenza vaccination starting **in mid-October 2022** (SHC 9699, 06/04/2022).

IV ELABORATION

1 Omicron

Genetically distinct viral variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been recorded. In late 2021, the Omicron virus variant emerged, with significant genetic differences and clinical effects from other variants of concern (VOC). This variant demonstrated higher numbers of polymorphisms in the gene encoding the Spike (S) protein, and there has been displacement of the dominant Delta variant.

The BA.2 is now less than 30% of the new cases. Currently in Belgium (17/06/2022), there is a growing proportion of Omicron BA.5 (58%) and to a lesser extent BA.4 (9%) strains, **which are expected to rapidly become dominant in Belgium and Europe**.. It is likely that these BA.5 and BA.4 strains will be the most circulating during the Autumn / Winter 2022 - 2023, but **the emergence of other VOCs or other Omicron lineages cannot be excluded**.

Some new BA.2 Omicron variants could also emerge like for example the BA.2.75 sub-variant also seen in seven other countries like: Australia, New Zealand, and Japan in Asia and the Pacific region; UK and Germany in Europe; and USA, Canada in North America.

These different Omicron-related strains **partly escape the immunity and protection conferred by current vaccines and exposure to previous variants**. This is currently most evident for a shorter duration of protection and for the Vaccine Effectiveness (VE) against infections and mild forms of COVID-19.

The Omicron BA.2 variant shows **a higher transmissibility** compared to the Delta variant, and is also characterized **by a lower severity**, attenuated by a factor of about 2 on intensive care unit (ICU) hospitalizations (risk reduction of 48-59% depending on the study) and by a factor of 4-9 on death (HAS, 25/05/2022). This is observed in high incomes countries with a high level of immunity and vaccination coverage.

The BA.4 and BA.5 sublineages of the Omicron variant **also show high transmissibility** (Tegally et al., 2022 preprint) **and partially escape natural and vaccine induced immunity** (Hachmann et al., 2022).

The two subvariants are more similar to BA.2 than to the BA.1 strain that kicked off most countries' Omicron waves late last year. But BA.4 and BA.5 carry their own unique mutations, including changes called L452R and F486V in the viral spike protein that might tweak its ability to latch onto host cells and skirt some immune responses (Callaway, 2022).

Cao and collaborators (2022a-b) indicate that Omicron may evolve mutations to evade the humoral immunity elicited by BA.1 infection, suggesting that BA.1-derived vaccine boosters may not achieve broad-spectrum protection against new Omicron variants.

Kimura and collaborators show in a statistical analysis that the effective reproduction numbers of these L452R/M/Q-bearing BA.2-related Omicron variants are greater than that of the original BA.2. Neutralization experiments revealed that the immunity induced by BA.1 and BA.2 infections is less effective against BA.4/5. Cell culture experiments showed that BA.2.12.1 and BA.4/5 replicate more efficiently in human alveolar epithelial cells than BA.2, and particularly, BA.4/5 is more fusogenic than BA.2. Furthermore, infection experiments using hamsters indicated that BA.4/5 is more pathogenic than BA.2. Altogether, our multiscale investigations suggest that the risk of L452R/M/Q-bearing BA.2-related Omicron variants, particularly BA.4 and BA.5, **to global health is potentially greater than that of original BA.2**.

Based on limited data in humans, **there is no evidence of BA.4 and BA.5 being associated with increased infection severity** compared to the circulating variants BA.1 and BA.2. Nevertheless in pre Omicron period, Ziyad and collaborators (2022 – pre-Omicron period – preprint) show that reinfection adds non-trivial risks of all-cause mortality, hospitalization, and adverse health outcomes in the acute and post-acute phase of the reinfection. As in previous waves, an increase in COVID-19 cases overall can result in an increase in hospitalisations, ICU admissions and deaths (HAS, 25/05/2022 ; ECDC, 14/06/2022).

At present, **there are insufficient data for a robust assessment of the VE of COVID-19 vaccines against mild or severe disease with BA.4 and BA.5**. However, preliminary analyses indicate that the vaccination status of cases infected with BA.4 and BA.5 is not significantly different to that of cases infected with BA.2, suggesting that protection conferred by the vaccines likely remains comparable to that observed previously (UKHSA, 24/06/2022).

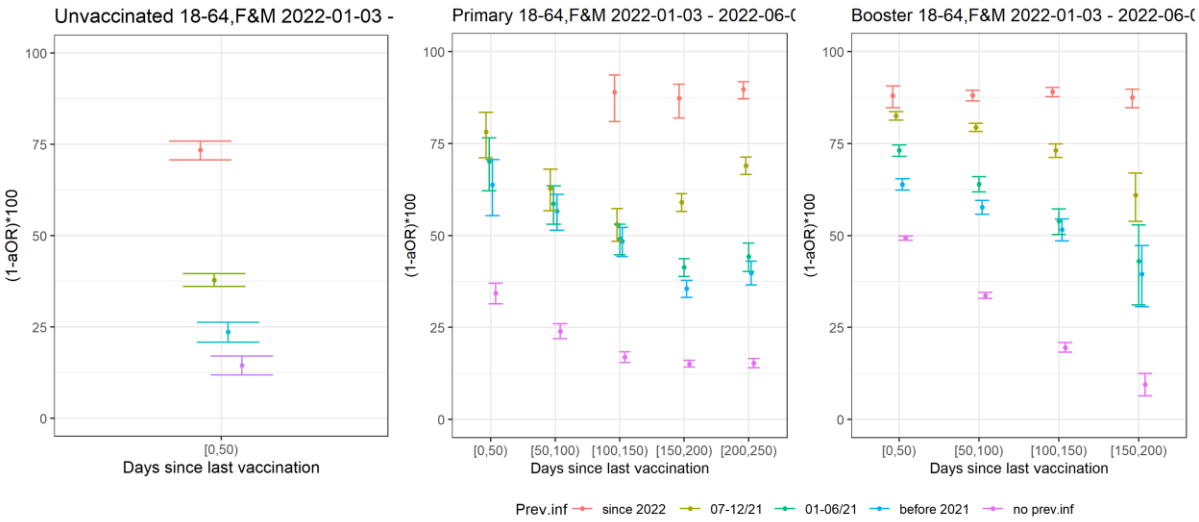
2 Naturally-acquired, vaccine-induced and hybrid immunity

Pilz and collaborators (2022) say that: “National surveys covering 2020-2021 documented that a previous SARS-CoV-2 infection is associated with a significantly **reduced risk of reinfections with efficacy lasting for at least one year and only relatively moderate waning immunity**. Importantly, **natural immunity showed roughly similar effect sizes regarding protection against reinfection across different SARS-CoV-2 variants, with the exception of the Omicron** variant for which data are just emerging before final conclusions can be drawn. **Risk of hospitalizations and deaths was also reduced in SARS-CoV-2 reinfections versus primary infections**. **The combination of a previous SARS-CoV-2 infection and a respective vaccination, termed hybrid immunity, seems to confer the greatest protection against SARS-CoV-2 infections**, but several knowledge gaps remain regarding this issue. Natural immunity should be considered for public health policy regarding SARS-CoV-2”.

Goldberg and collaborators (2022) say that: “Among persons who had been previously infected with SARS-CoV-2 (regardless of whether they had received any dose of vaccine or whether they had received one dose before or after infection), protection against reinfection decreased as the time increased since the last immunity-conferring event; **however, this protection was higher than that conferred after the same time had elapsed since receipt of a second dose of vaccine among previously uninfected persons**. A single dose of vaccine after infection reinforced protection against reinfection”.

Suarez and collaborators (2022) “assessed the protection conferred by naturally-acquired, vaccine-induced and hybrid immunity during the concomitant Omicron and Delta epidemic waves in France on symptomatic infection and severe COVID-19. **The greatest levels of protection against both variants were provided by hybrid immunity**. Protection against Omicron symptomatic infections was systematically lower and waned at higher speed than against Delta in those vaccinated. **In contrast, there were little differences in variant-specific protection against severe inpatient outcomes in symptomatic individuals**”.

In conclusion, as shown in Belgium too (graph below), a natural infection before or after completion of COVID-19 vaccination has a booster effect and the greatest levels of protection against both variants were provided by hybrid immunity (Pilz et al., 2022 ; Goldberg et al., 2022 ; Suarez et al., 2022).



This has led some countries to postpone the administration of a booster dose in function of a previous infection (HAS, 25/05/2022).

However, on the data available, the SHC **cannot conclude yet on the duration and impact of a COVID-19 infection (naturally-acquired, vaccine-induced and hybrid immunity) as a clinical protection effect against severe outcomes**.

The relationship between levels of antibody titers and the necessity of a booster dose is not yet clear and **no (immune) correlate of protection has been defined so far**. Furthermore, for practical reasons, it is unfeasible to study antibody titers to decide on the necessity of a booster at an individual level.

To simplify the system, to obtain the highest possible level of protection and to ensure consistency with previous recommendations, the SHC recommends a booster vaccination be given regardless of history of COVID-19 infection, and at least 14 days after recovery of symptomatic COVID-19, or at least 14 days after a positive Polymerase Chain Reaction (PCR) test for asymptomatic COVID-19.

3 VE against infection and transmission in general

Several studies have provided evidence that vaccines are effective at preventing infection. Uninfected individuals cannot transmit. Therefore, the vaccines also provide some protection against transmission. There may be additional benefit, beyond that due to prevention of infection, if some of those individuals who become infected despite vaccination are also at a reduced risk of transmitting (**for example, because of reduced duration or level of viral shedding – Accorsi et al., 2022**). Several studies have provided evidence of reduced risk of household transmission from vaccinated cases compared to unvaccinated cases (see references 19 to 22 of UKHSA, 16/06/2022). Among individuals seeking testing for COVID-like illness in the US in December 2021, receipt of 3 doses of mRNA COVID-19 vaccine (compared with unvaccinated and with receipt of 2 doses) was less likely among cases with symptomatic SARS-CoV-2 infection compared with test-negative controls. These findings suggest that receipt of 3 doses of mRNA vaccine, relative to being unvaccinated and to receipt of 2 doses, was associated with protection against both the Omicron and Delta variants, although **the higher odds ratios for Omicron suggest less protection for Omicron than for Delta** (Accorsi et al., 2022).

Colosi and collaborators (2022) developed an agent-based model of SARS-CoV-2 transmission in schools. They used empirical contact data in a primary and a secondary school and data from pilot screenings in 683 schools during the alpha variant (B.1.1.7) wave in March-June, 2021, in France. They fitted the model to observed school prevalence to estimate the school-specific effective reproductive number for the alpha (Ralpha) and delta (B.1.617.2; Rdelta) variants and performed a cost-benefit analysis examining different intervention protocols. They conclude that: “the COVID-19 pandemic will probably continue to pose a risk to the safe and normal functioning of schools. Extending vaccination coverage in students, complemented by regular testing with good adherence, are essential steps to keep schools open when highly transmissible variants are circulating”.

4 VE data of the first and second booster dose against Omicron

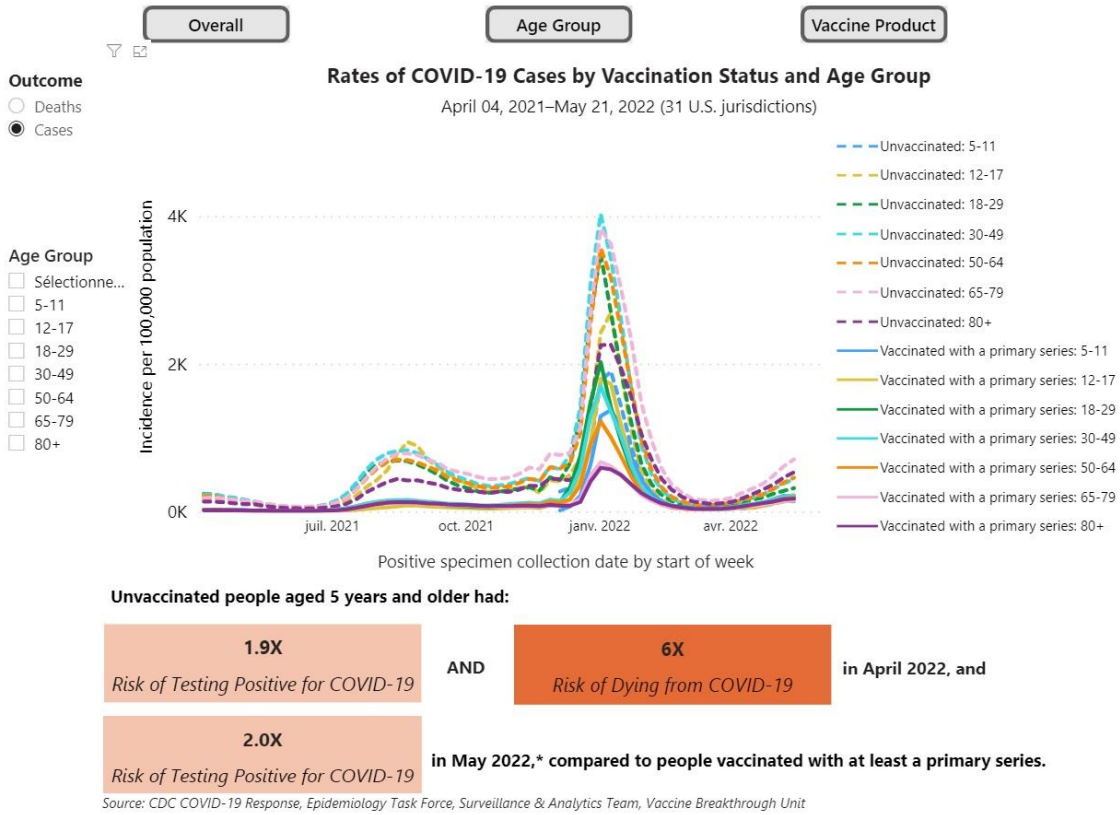
4.1 CDC - 04/07/2022

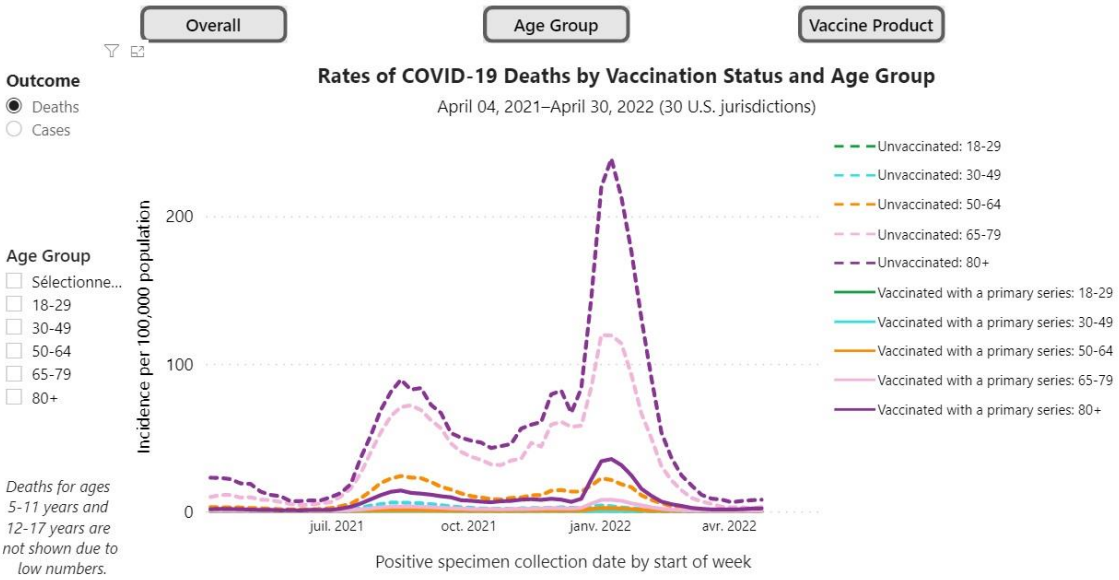
https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status

Several factors likely affect crude case rates by vaccination and booster dose status, making interpretation of recent trends difficult. Limitations include higher prevalence of previous infection among the unvaccinated and un-boosted groups; difficulty in accounting for time since vaccination and waning protection; and possible differences in testing practices (such as at-home tests) and prevention behaviors by age and vaccination status. These limitations appear to have less impact on the death rates presented here. CDC is assessing whether to continue using these case rate data to provide preliminary information on vaccine impact.

- **People who were unvaccinated** had a greater risk of testing positive for COVID-19 and a greater risk of dying from COVID-19 than people who were vaccinated overall (see below for the most recent rates).

- **People who were vaccinated with a primary series and two additional or booster doses** had lower death rates, followed by people who received one additional or booster dose, compared with those without an additional or booster dose. All vaccinated groups had lower risk of dying from COVID-19 compared with people who were unvaccinated.



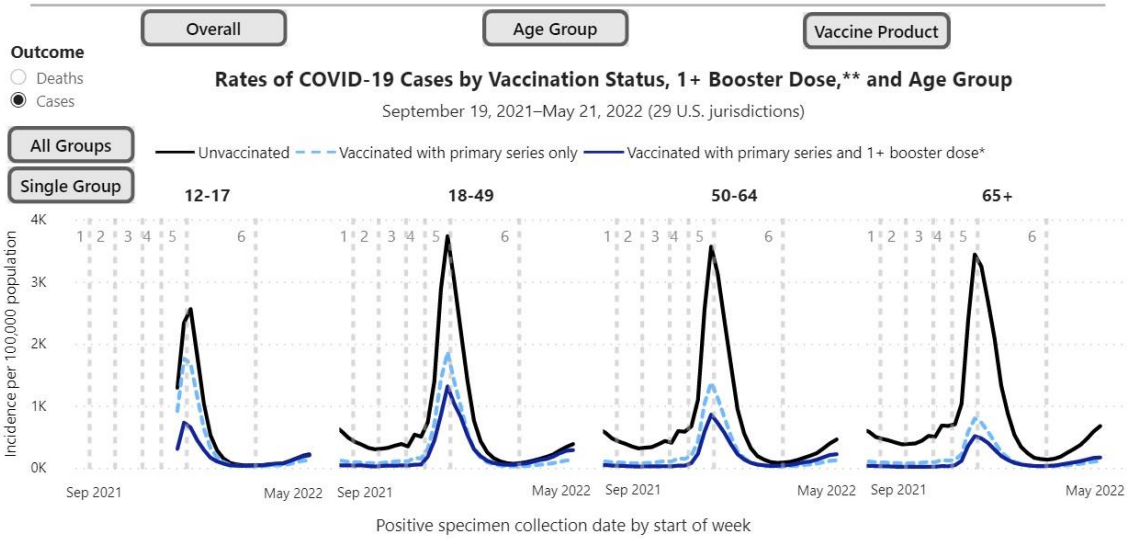


Unvaccinated people aged 5 years and older had:

1.9X *Risk of Testing Positive for COVID-19* **AND** **6X** *Risk of Dying from COVID-19* **in April 2022, and**

2.0X *Risk of Testing Positive for COVID-19* **in May 2022,* compared to people vaccinated with at least a primary series.**

Source: CDC COVID-19 Response, Epidemiology Task Force, Surveillance & Analytics Team, Vaccine Breakthrough Unit

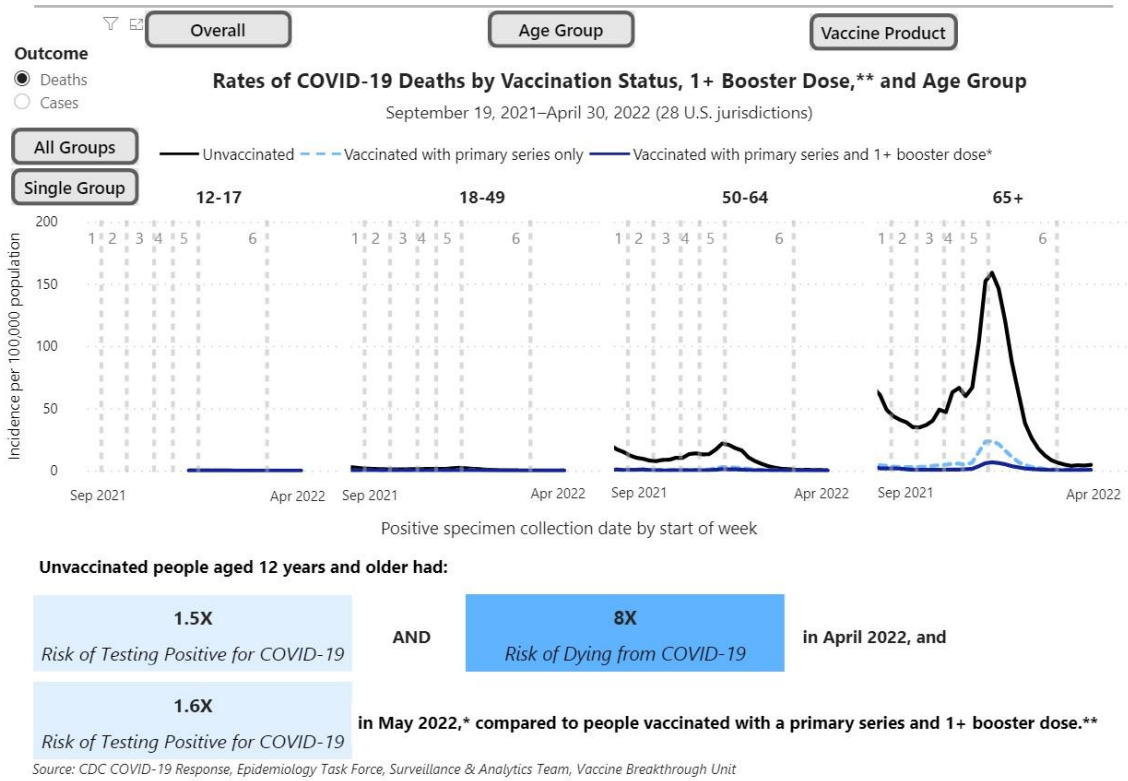


Unvaccinated people aged 12 years and older had:

1.5X *Risk of Testing Positive for COVID-19* **AND** **8X** *Risk of Dying from COVID-19* **in April 2022, and**

1.6X *Risk of Testing Positive for COVID-19* **in May 2022,* compared to people vaccinated with a primary series and 1+ booster dose.****

Source: CDC COVID-19 Response, Epidemiology Task Force, Surveillance & Analytics Team, Vaccine Breakthrough Unit



4.2 UKHSA - 16/06/2022

These CDC data are confirmed by UK Health Security Agency (UKHSA, 16/06/2022) in UK for different outcomes and vaccines.

Consensus vaccine effectiveness estimates

Table 3 summarises consensus estimates of vaccine effectiveness against different outcomes that have been reached by the UK Vaccine Effectiveness Expert Panel. These take into account estimates from UK studies by public health agencies and academic groups as well as international data.

Table 3. Consensus estimates of vaccine effectiveness against the Omicron variant

Vaccine product for primary course	Outcome	Second dose: 0 to 3 months	Second dose: 4 to 6 months	Second dose: 6+ months	Booster dose: All Periods	Booster dose: 0 to 3 months	Booster dose: 4 to 6 months	Booster dose: 6+ months
AstraZeneca	All Infection	30% (20 to 40%)	0 to 30% (range only)	0% (0 to 10%)	See Individual Periods	45% (35 to 55%)	15% (0 to 30%)	0% (0 to 10%)
	Symptomatic	40% (30 to 50%)	20% (5 to 30%)	5% (0 to 5%)	See Individual Periods	60% (50 to 70%)	40% (30 to 50%)	10% (0 to 20%)
	Hospitalisation	85% (60 to 90%)	70% (50 to 75%)	65% (45 to 85%)	See Individual Periods	90% (85 to 95%)	85% (85 to 95%)	70% (50 to 85%)
	Mortality	Insufficient Data	Insufficient Data	Insufficient Data	See Individual Periods	90% (85 to 98%)	Insufficient Data	Insufficient Data
	Transmission	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data
Moderna	All Infection	30% (20 to 40%)	0 to 30% (range only)	30% (10 to 50%)	See Individual Periods	45% (35 to 55%)	15% (0 to 30%)	0% (0 to 10%)
	Symptomatic	55% (35 to 75%)	30% (15 to 35%)	15% (10 to 20%)	See Individual Periods	65% (55 to 75%)	40% (30 to 50%)	10% (0 to 20%)
	Hospitalisation	85 to 95% (range only)	75 to 85% (range only)	55 to 90% (range only)	See Individual Periods	85 to 95% (range only)	Insufficient Data	Insufficient Data
	Mortality	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data
	Transmission	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data	Insufficient Data
Pfizer	All Infection	30% (20 to 40%)	0 to 30% (range only)	20% (10 to 30%)	See Individual Periods	45% (35 to 55%)	15% (0 to 30%)	0% (0 to 10%)
	Symptomatic	50% (30 to 65%)	20% (15 to 30%)	15% (10 to 15%)	See Individual Periods	65% (55 to 75%)	45% (35 to 55%)	10% (0 to 20%)
	Hospitalisation	90% (85 to 95%)	80% (75 to 85%)	70% (55 to 90%)	See Individual Periods	90% (85 to 95%)	85% (85 to 95%)	70% (50 to 85%)
	Mortality	Insufficient Data	Insufficient Data	Insufficient Data	See Individual Periods	90% (85 to 98%)	Insufficient Data	Insufficient Data
	Transmission	Insufficient Data	Insufficient Data	Insufficient Data	0 to 25% (range only)	Insufficient Data	Insufficient Data	Insufficient Data

Booster data is based on use of the Moderna or Pfizer vaccines as a booster.
This table provides overall estimates but there may be variation by age group or other clinical or demographic factors.

High Confidence	Evidence from multiple studies which is consistent and comprehensive
Medium Confidence	Evidence is emerging from a limited number of studies or with a moderately level of uncertainty
Low Confidence	Little evidence is available at present and results are inconclusive

They also investigated the impact of using more specific and more severe hospitalisation indicators on VE. With generally milder disease seen with Omicron, in particular in younger adults, “contamination” of hospitalisations with incidental cases is likely to reduce VE estimates against hospitalisation. VE estimates improve and waning is more limited **when definitions of hospitalisation that are more specific to severe respiratory disease are used**.

Among 18 to 64 year olds using all COVID-19 cases admitted via emergency care VE after a booster peaked at 82.4% and dropped to 53.6% by 15+ weeks after the booster; using all admissions for >= 2 days with a respiratory code in the primary diagnostic field VE ranged from 90.9% down to 67.4%; further restricting to those on oxygen/ventilated/on intensive care VE ranged from 97.1% down to 75.9%. Among 65+ year olds the equivalent VE estimates were 92.4% down to 76.9%; 91.3% down to 85.3% and 95.8% down to 86.8%. Given that Omicron generally causes milder disease than previous variants, in particular among younger individuals, and that all individuals who are hospitalised for any reason in the UK are tested for COVID-19, an increasing proportion of individuals hospitalised with a positive COVID-19 test are likely to have COVID-19 as an incidental finding rather than the primary reason for admission. This can be seen in the vaccine effectiveness estimates against hospitalisation, whereby outcomes using broad definitions for hospitalisation give lower estimates that are likely more reflective of vaccine effectiveness against infection. Whereas definitions of hospitalisation that are more specific to severe respiratory disease give higher vaccine effectiveness estimates with less evidence of waning. This is also likely to explain the higher vaccine effectiveness against hospitalisation in 65+ year olds compared to 18 to 64 year olds. There appears to be little variation in vaccine effectiveness against hospitalisation after a booster dose according to the type of vaccine used for priming or boost.

Table 1. vaccine effectiveness against hospitalisation using different definitions of hospitalisations in a) 18 to 64 year olds and b) 65 year olds and over

		ECDS symptomatic with onset date	SUS at least 2 days with ARI code in primary field	SUS at least 2 days and either oxygen, ventilation or ICU with ARI code in primary field
18 to 64				
	Interval	VE	VE	VE
Dose 1	0 to 27	48.5 (12.3 to 69.7)	36.2 (-33.9 to 69.6)	
	28+	48.7 (32.8 to 60.8)	44.1 (25.6 to 58)	75 (42.4 to 89.1)
Dose 2	0 to 13	39.6 (-31.5 to 72.2)	88.9 (58.4 to 97)	
	14 to 174	54.7 (45.3 to 62.4)	69 (58.1 to 77)	86.7 (63.6 to 95.1)
	175+	34.6 (21.7 to 45.4)	56.1 (46.4 to 64)	82.3 (67.7 to 90.3)
Booster	0 to 6	63.9 (52.2 to 72.8)	74.3 (55.9 to 85)	90.7 (56 to 98.1)
	7 to 13	80.1 (73.5 to 85.1)	90.9 (83.2 to 95.1)	
	14 to 34	82.4 (78.6 to 85.6)	88.6 (84.9 to 91.5)	97.1 (92.2 to 98.9)
	35 to 69	72.7 (67.2 to 77.2)	85.8 (82.4 to 88.5)	94.3 (88.9 to 97.1)
	70 to 104	66.9 (59.1 to 73.3)	80.2 (74.9 to 84.4)	89.9 (78.3 to 95.3)
	105+	53.6 (36.9 to 65.9)	67.4 (53.1 to 77.4)	75.9 (15.8 to 93.1)
65+				
	Interval	VE	VE	VE
Dose 1	0 to 27		43.9 (-41 to 77.7)	
	28+		53.4 (36.3 to 65.9)	78.3 (43.7 to 91.7)
Dose 2	0 to 13			
	14 to 174	77.8 (45 to 91)	82.3 (74.3 to 87.8)	90.9 (72.6 to 97)
	175+	66.7 (43.4 to 80.4)	57.7 (49.6 to 64.4)	73.4 (55.1 to 84.3)
Booster	0 to 6	85.8 (61.5 to 94.7)	77.9 (65.3 to 85.9)	89.2 (63.1 to 96.8)
	7 to 13	92.3 (76.3 to 97.5)	84.7 (76 to 90.2)	94.7 (71.6 to 99)
	14 to 34	92.4 (86 to 95.8)	91.3 (89.1 to 93.1)	95.8 (91.3 to 97.9)
	35 to 69	87 (79.2 to 91.8)	89.3 (87.3 to 90.9)	92.8 (88.4 to 95.6)
	70 to 104	84 (74.6 to 89.9)	88.1 (86.1 to 89.9)	92.5 (88.1 to 95.2)
	105+	76.9 (60.6 to 86.4)	85.3 (82.4 to 87.6)	86.8 (77.1 to 92.3)

ECDS = Emergency Care Dataset (this analysis includes all admissions with a positive COVID-19 test via emergency care except for those coded as injuries). SUS = Secondary Users Service (this analysis includes all admissions to secondary care for >=2 days with a respiratory code in the first diagnostic field) (11).

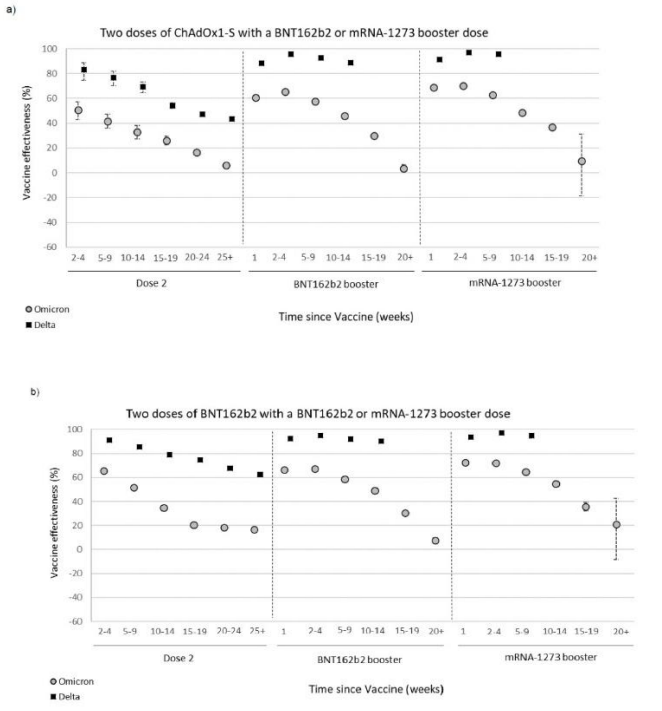
Vaccine effectiveness against mortality with the Omicron variant has been estimated for those aged 50 years and older using a test-negative case control study design (all vaccines combined) (Table 2). At 25-plus weeks following the second dose, vaccine effectiveness was around 50%. At 2 or more weeks following booster vaccination, effectiveness was 93.6% against mortality while at 10 or more weeks VE was 87.6%. This analysis is also likely to include some incidental deaths of individuals who died with COVID-19 as opposed to from COVID-19, and we suspect the true VE against mortality is likely higher than the estimates presented here.

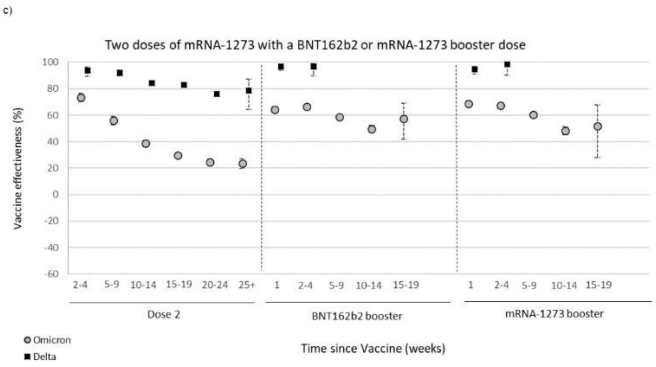
Table 2. Vaccine effectiveness against mortality in those aged 50 years and older (all vaccine brands combined). VE = vaccine effectiveness, CI = confidence intervals.

Dose	Interval after dose	Odds Ratio	VE (95% CI)
2	25+ weeks	0.52 (0.34-0.81)	47.9 (19.3 to 66.4)
3	2-4 weeks	0.06 (0.03-0.12)	93.6 (88 to 96.6)
3	5-9 weeks	0.11 (0.07-0.17)	88.9 (83.4 to 92.6)
3	10+ weeks	0.12 (0.09-0.18)	87.6 (81.9 to 91.5)

The VE against symptomatic infections for different vaccines is estimated as:

Figure 1. Vaccine effectiveness against symptomatic disease by period after the second and booster doses for Delta (black squares) and Omicron (grey circles) for a) recipients of 2 doses of AstraZeneca (ChAdOx1-S) vaccine as the primary course and Pfizer (BNT162b2) or Moderna (mRNA-1273) as a booster; b) recipients of 2 doses of Pfizer vaccine as the primary course and Pfizer or Moderna as a booster, and c) 2 doses of Moderna as a primary course and Pfizer or Moderna as a booster





After 2 doses of the AstraZeneca vaccine, vaccine effectiveness against the Omicron variant starts at 45 to 50% then drops to almost no effect from 25 weeks after the second dose. With 2 doses of Pfizer or Moderna effectiveness dropped from around 65 to 70% down to around 15% by 25 weeks after the second dose. Two to 4 weeks after a booster dose of either the Pfizer or Moderna vaccine following an AstraZeneca or Pfizer primary course, effectiveness ranges from around 60 to 75%, dropping to almost no effect from 20+ weeks after the booster. Vaccine effectiveness estimates for the booster dose are very similar, irrespective of the primary course received. Vaccine effectiveness is generally slightly higher in younger compared to older age groups.

At present, **there are insufficient data for a robust assessment of the VE of COVID-19 vaccines against mild or severe disease with BA.4 and BA.5**. However, preliminary analyses indicate that the vaccination status of cases infected with BA.4 and BA.5 is not significantly different to that of cases infected with BA.2, suggesting that protection conferred by the vaccines likely remains comparable to that observed previously. In UK, cases were identified from hospital (pillar 1) and community (pillar 2) testing data from the period from 18 April to 29 May 2022 and classified as BA.2, BA.4 and BA.5 based on sequencing information. Logistic regression was used to estimate the vaccination status of BA.4 or BA.5 cases as compared to BA.2 control cases. Previous positivity, testing pillar, health and social care worker status, clinical risk status, age, gender, and week of test were adjusted for. The vaccination status of those recently vaccinated (within the last 25 weeks) with either a second, third or fourth dose was compared to a baseline group of those with a 'waned' (>25 weeks since vaccination) second or third dose. Vaccine types were combined. The vaccination status of BA.4 and BA.5 cases did not differ significantly from that of BA.2 cases; (adjusted odd ratio-aOR 1.13; 95% CI 0.88-1.44 and aOR 0.83; 95% CI 0.88-1.44, respectively - Table 4). These early data do not indicate a difference in VE against BA.4 or BA.5 as compared to BA.2; however, a formal analysis using a test-negative case control design will be conducted as the data become available (UKHSA, 24/06/2022).

Table 4. Adjusted odds ratios of BA.4 and BA.5 cases as compared to BA.2 controls by vaccination status

Doses	Interval	Controls	Cases	Adjusted odds ratio	95% Confidence interval
		BA.2	BA.4		
Dose 2/3/4	< 25 weeks	8,663	123	1.13	(0.88-1.44)
Dose 2/3	>= 25 weeks	10,896	214	Baseline	
		BA.2	BA.5		
Dose 2/3/4	< 25 weeks	8,663	103	0.83	(0.64-1.08)
Dose 2/3	>= 25 weeks	10,896	232	Baseline	

4.3 Other publications on VE – **for additional information only**

Evolving evidence based on early VE data and analysis of antibody levels after the first booster dose suggest there is gradual waning of immunity against the Omicron variant. This is most prominent for VE against symptomatic infection, which declines from 60–75% at 2-4 weeks after a booster dose of either the Pfizer or Moderna vaccine to 25–40% from 15 or more weeks after the booster. VE against COVID-19 hospitalisation after the first booster dose is high at 88–95% after an mRNA booster, and appears to wane more slowly than VE against symptomatic infection. VE against hospitalisation was 75% by 10–14 weeks for Pfizer vaccine and 78% ≥4 months after mRNA vaccine (Chemaitelly et al., 2022; Ferdinands et al., 2022, Tseng et al., 2022).

Chemaitelly et al. (Qatar) show that BNT162b2 effectiveness against severe, critical, or fatal COVID-19 (Omicron) was maintained at >70% after the second dose and at >90% after the first booster (after 7 weeks) with no evidence for declining effectiveness over time. A limitation of this study is that only a small proportion of Qatar's population is ≥50 years.

Tartof et al. (22/04/2022 – USA) analyse 11 123 hospital or emergency department admissions. In adjusted analyses, effectiveness of two doses of the BNT162b2 vaccine against the omicron variant was 41% (95% CI 21−55) against hospital admission and 31% (16−43) against emergency department admission at 9 months or longer after the second dose. **After three doses, effectiveness of BNT162b2 against hospital admission due to the omicron variant was 85% (95% CI 80−89) at less than 3 months but fell to 55% (28−71) at 3 months or longer, although confidence intervals were wide for the latter estimate**. **Against emergency department admission, the effectiveness of three doses of BNT162b2 against the omicron variant was 77% (72−81) at less than 3 months but fell to 53% (36−66) at 3 months or longer**. Trends in waning against SARS-CoV-2 outcomes due to the delta variant were generally similar, but with higher effectiveness estimates at each timepoint than those seen for the omicron variant. Three doses of BNT162b2 conferred high protection against hospital and emergency department admission due to both the delta and omicron variants in the first 3 months after vaccination. However, 3 months after receipt of a third dose, waning was apparent against SARS-CoV-2 outcomes due to the omicron variant, including hospital admission. Additional doses of current, adapted, or novel COVD-19 vaccines might be needed to maintain high levels of protection against subsequent waves of SARS-CoV-2 caused by the omicron variant or future variants with similar escape potential.

Adams and collaborators (2022) compare the effectiveness of a primary COVID-19 vaccine series plus a booster dose with a primary series alone for the prevention of Omicron variant COVID-19 hospitalization in a multicenter observational case-control study using the test-negative design to evaluate VE in the United States during the Omicron period. VE against COVID-19 hospitalization was calculated for a primary series plus a booster and a primary series alone by comparing the odds of being vaccinated with each of these regimens versus being unvaccinated among cases versus controls. VE analyses were stratified by immune status (immunocompetent; immunocompromised) because the recommended vaccine schedules are different for these groups. The primary analysis evaluated all COVID-19 vaccine types combined and secondary analyses evaluated specific vaccine products. Among immunocompetent patients, VE against Omicron COVID-19 hospitalization for a primary series plus one booster of any vaccine product dose was 77% (95% CI: 71–82%), and for a primary series alone was 44% (95% CI: 31–54% - p<0.001). VE was higher for a boosted regimen than a primary series alone for both mRNA vaccines used in the US (BNT162b2: primary series plus booster VE 80% (95% CI: 73-85%), primary series alone VE 46% (95% CI: 30-58%) [p<0.001]; mRNA-

1273: primary series plus booster VE 77% (95% CI: 67-83%), primary series alone VE 47% (95% CI: 30-60%) [p<0.001]). Among immunocompromised patients, VE for a primary series of any vaccine product against Omicron COVID-19 hospitalization was 60% (95% CI: 41-73%). Insufficient sample size has accumulated to calculate effectiveness of boosted regimens for immunocompromised patients. Conclusions: **Among immunocompetent people, a booster dose of COVID-19 vaccine provided additional benefit beyond a primary vaccine series alone for preventing COVID-19 hospitalization due to the Omicron variant**.

5 Belgian epidemiological situation (Sciensano, presentation NITAG 16/06/2022)

5.1 VE by age group – Data from 3th of January until 7th of June 2022 – Omicron dominance

Data on hospitalisations and ICU admissions are derived from the Clinical Hospital Surveillance (non-exhaustive); only those admitted **FOR COVID** are included in the analyses;

- Immunity status was defined by:
* (1) the vaccination status: unvaccinated, primary or booster-vaccination;
* (2) time since vaccination in 50-day blocks (from the date on which the last administered vaccine was considered effective).

- Test negative design to estimate VE against symptomatic infection (VEi):
* persons testing positive were matched to persons testing negative. Persons were matched on age group (5 years), sex, province of residence and calendar week of sampling;
* unvaccinated persons without a prior infection were set as reference category;
* using conditional logistic regression to obtain adjusted odds ratios (aOR). VEi was estimated as 1-aOR.

- Proportional hazard analysis to estimate VE against hospitalization (VEh):
* symptomatic persons with a positive PCR-test had a follow-up of four weeks to see if hospitalization occurred. Persons were censored from follow-up if they died or received a vaccine during follow-up;
* estimation of additional VE against hospitalization given symptomatic infection (VEh|i);
* using Cox-regression, hazard ratio (HR) was estimated for hospital intake FOR COVID-19 by immunity status while adjusting for age group (5 years), sex and province of residence. VEh|i is estimated as 1-HR. Then VEh is obtained by combining VEi and VEh|i.

For Belgium, Sciensano provides more specific data in the line of published studies for the period of January-June 2022, during which Omicron was dominant:

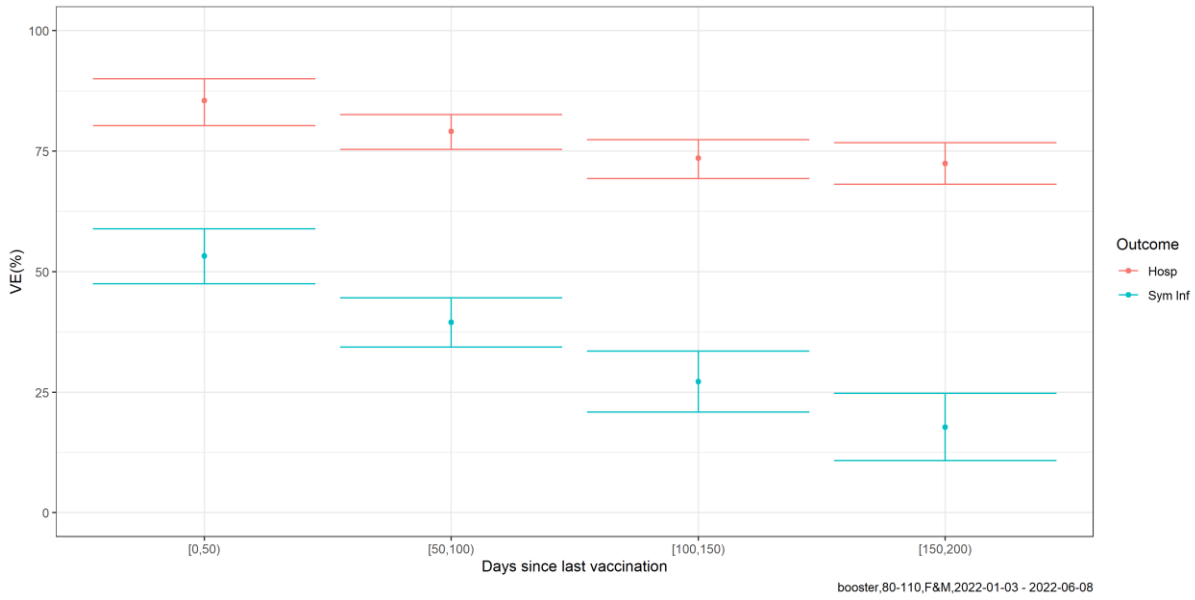
- For 18+ (all adults, elderly included): VE against ICU after the booster wanes **very slowly** from 93% (CI 89-98) after 0-50 days to 89% (CI 83-95) after 150-200 days;

- For 80+: VE against hospitalizations after the booster wanes approximatively from 86% (CI 80-90) after 0-50 days to 72% (CI 68-77) after 150-200 days;

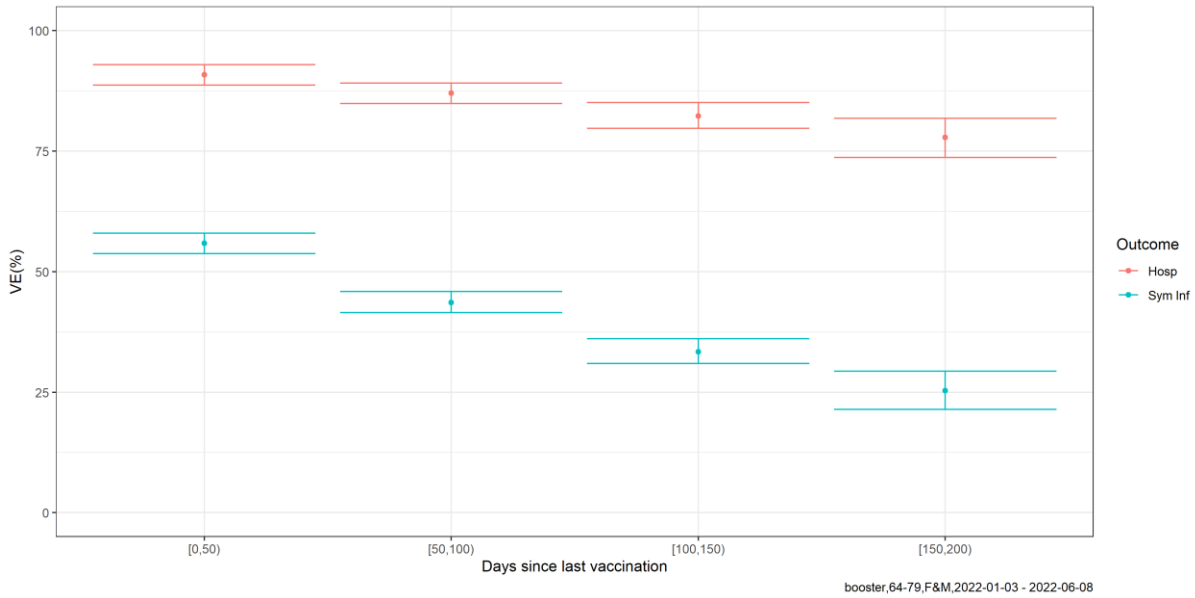
- For 65 to 79 y.o.: VE against hospitalizations after the booster wanes approximatively from 91% (CI 89-93) after 0-50 days to 78% (CI 74-82) after 150-200 days;

- For 18 to 64 y.o.: VE against hospitalizations after the booster wanes approximatively from 87% (CI 85-90) after 0-50 days to 60% (CI 44-77) after 150-200 days (more uncertainty due to fewer cases).

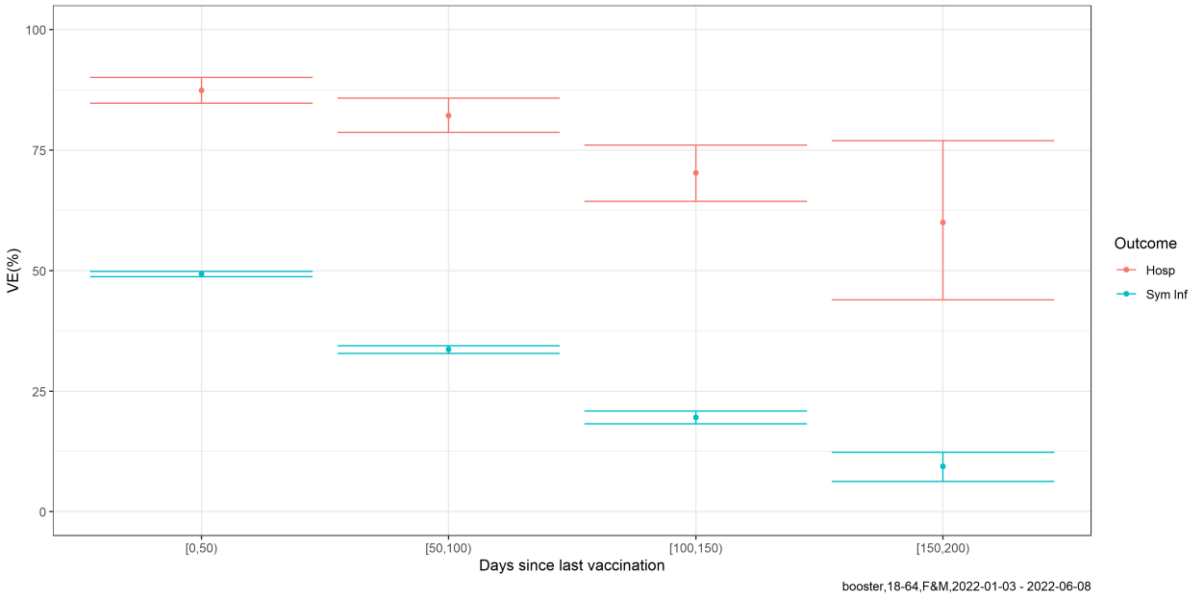
Booster-vaccination VEi and VEh **for 80+ year olds**, 03/01/2022-07/06/2022, Belgium



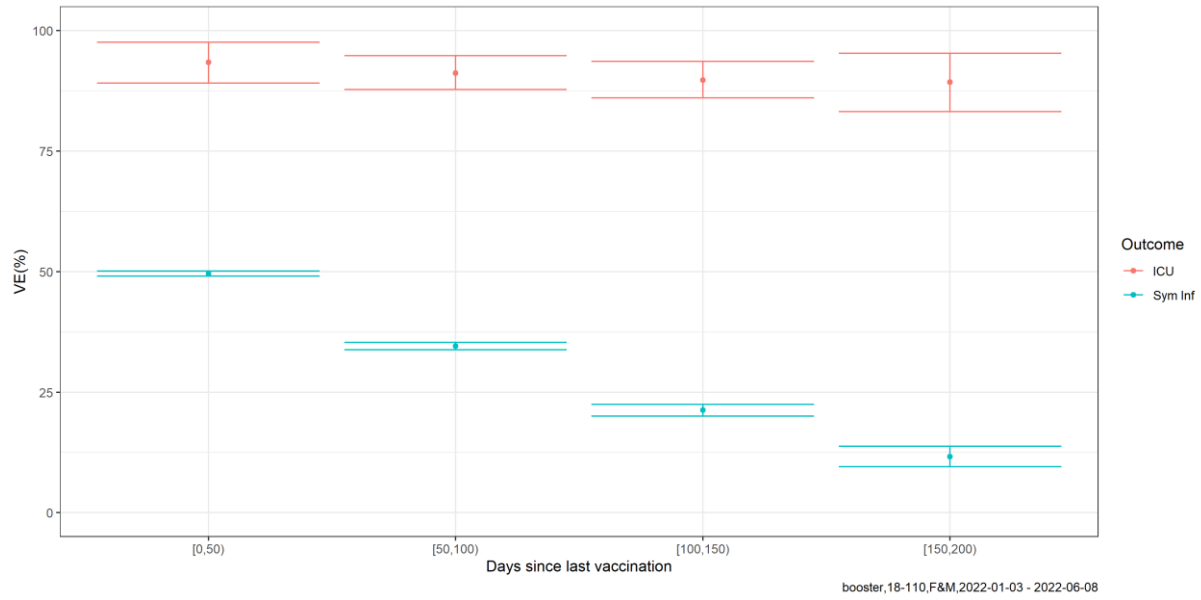
Booster-vaccination VEi and VEh **for 65-79 year olds**, 03/01/2022-07/06/2022, Belgium



Booster-vaccination VEi and VEh **for 18-64 year olds**, 03/01/2022-07/06/2022, Belgium



VE against ICU-admission (red) and symptomatic infection (blue), booster, for 18+ year olds, 03/01/2022-07/06/2022, Belgium



In Conclusion, in Belgium too, VE against severe outcomes caused by Omicron **remains high, with continued strong protection against ICU and hospitalisations after 3 to 6 months after receiving the first booster.**

In all groups, VE against symptomatic infection wanes more rapidly and in a much larger extend.

5.2 Profile of hospitalizations among adults, adolescents and children in Belgium

The overall number of hospitalizations among adolescents over this time period (n=340) **remains very low**.

The large majority of admissions among children in the period March-May 2022 are among the very young (median age 0), and that the median duration of admission was low and in the large majority for surveillance of fever (2 days, versus 8 days in adults). The data are not exhaustive for Belgium, but we expect them to be representative for hospitalised patients.

	18-			18+		
	03-22 (N=290)	04-22 (N=227)	05-22 (N=127)	03-22 (N=1653)	04-22 (N=1439)	05-22 (N=574)
Age						
Median [Q1, Q3]	0 [0, 2.00]	0 [0, 1.50]	0 [0, 2.00]	80.0 [71.0, 87.0]	81.0 [71.0, 87.0]	78.0 [69.0, 86.0]
Gender						
Femme	142 (49.0%)	108 (47.6%)	63.0 (49.6%)	767 (46.4%)	696 (48.4%)	286 (49.8%)
Homme	146 (50.3%)	117 (51.5%)	64.0 (50.4%)	884 (53.5%)	743 (51.6%)	288 (50.2%)
Vaccination status						
Not vaccinated	263 (90.7%)	206 (90.7%)	116 (91.3%)	173 (10.5%)	150 (10.4%)	63.0 (11.0%)
Partially vaccinated	0 (0%)	1.00 (0.4%)	1.00 (0.8%)	16.0 (1.0%)	10.0 (0.7%)	2.00 (0.3%)
Fully vaccinated	8.00 (2.8%)	6.00 (2.6%)	4.00 (3.1%)	146 (8.8%)	106 (7.4%)	47.0 (8.2%)
Fully vaccinated + booster	1.00 (0.3%)	1.00 (0.4%)	0 (0%)	1278 (77.3%)	1160 (80.6%)	455 (79.3%)
Unknown	18.0 (6.2%)	13.0 (5.7%)	6.00 (4.7%)	40.0 (2.4%)	13.0 (0.9%)	7.00 (1.2%)
Number of comorbidities						
0	283 (97.6%)	222 (97.8%)	123 (96.9%)	189 (11.4%)	154 (10.7%)	77.0 (13.4%)
1	5.00 (1.7%)	4.00 (1.8%)	3.00 (2.4%)	378 (22.9%)	349 (24.3%)	129 (22.5%)
2	2.00 (0.7%)	1.00 (0.4%)	0 (0%)	432 (26.1%)	389 (27.0%)	149 (26.0%)
3	0 (0%)	0 (0%)	0 (0%)	345 (20.9%)	312 (21.7%)	125 (21.8%)
4+	0 (0%)	0 (0%)	1.00 (0.8%)	308 (18.6%)	234 (16.3%)	94.0 (16.4%)
Length of hospital stay (days)						
Median [Q1, Q3]	2.00 [1.00, 3.00]	2.00 [1.50, 3.00]	2.00 [1.75, 3.00]	8.00 [4.00, 14.0]	8.00 [4.00, 13.0]	7.00 [4.00, 11.0]

Source: Clinical Hospital Surveillance

	12-17 (N=71)	18+ (N=8034)
Age		
Median [Q1, Q3]	14.0 [13.0, 16.0]	78.0 [65.0, 86.0]
Gender		
Femme	40.0 (56.3%)	3692 (46.0%)
Homme	31.0 (43.7%)	4340 (54.0%)
Vaccination status		
Not vaccinated	23.0 (32.4%)	1458 (18.1%)
Partially vaccinated	1.00 (1.4%)	91.0 (1.1%)
Fully vaccinated	42.0 (59.2%)	1261 (15.7%)
Fully vaccinated + booster	0 (0%)	4985 (62.0%)
Unknown	5.00 (7.0%)	239 (3.0%)
Number of comorbidities		
0	53.0 (74.6%)	1149 (14.3%)
1	13.0 (18.3%)	1792 (22.3%)
2	4.00 (5.6%)	1974 (24.6%)
3	1.00 (1.4%)	1617 (20.1%)
4+	0 (0%)	1495 (18.6%)
Length of hospital stay (days)		
Median [Q1, Q3]	2.00 [1.00, 3.00]	8.00 [4.00, 14.0]

Source: Clinical Hospital Surveillance, 27th of December 2021 until 31st of May 2022

6 Belgian mathematical modelling data from SIMID consortium

Presentation NITAG 11/04/2022 – not adapted for BA.4 et BA.5

https://covid-en-wetenschap.github.io/2022/04/technical-note-simid-april

Conclusions NITAG 11/04/2022 – not adapted for BA.4 et BA.5

At least up until mid-July, the model doesn't show a capacity problem if our set of assumptions hold regarding:

- schedule specific waning of vaccines already administered
- overall age specific contact frequencies for frail elderly in collectivities

What happens until November-December, or when a new VOC arises, will have to be estimated closer to date.

7 FDA Authorizes Second Booster Dose for Older and Immunocompromised Individuals (March 29, 2022)

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-second-booster-dose-two-covid-19-vaccines-older-and

FDA authorized a second booster for people 50 years of age and older. The second booster may be administered to these individuals. Conclusion were taken mainly based on Israelian data[2].

8 Joint EMA and ECDC statement (April 6, 2022)

COVID-19: Joint statement from ECDC and EMA on the administration of a fourth dose of mRNA vaccines (europa.eu)

"This statement is based on the currently available scientific evidence and, as such, is preliminary and may be subject to change as more data become available. This statement should not be interpreted as a regulatory decision in terms of changes to the product information. National recommendations regarding COVID-19 vaccines policies are made by National Immunisation Technical Advisory Groups".

This position is actually challenged by ACIP
https://www.cnbc.com/2022/04/21/cdc-panel-skeptical-of-fourth-covid-shots-for-broader-population-says-us-needs-clear-vaccine-strategy.html
" Long criticized the CDC for clearing fourth shots for older adults without consulting the committee, saying the decision has created public confusion and could lead to booster fatigue. She said having a full public discussion in the committee about vaccine recommendations would help restore public trust. "

9 Immunogenicity, efficacy and safety of the second booster (international publications and preprints)

Preliminary finding show that a fourth dose of mRNA vaccine is immunogenic, safe, and somewhat efficacious (primarily against symptomatic disease). A comparison of the initial response to the fourth dose with the peak response to a third dose did not show substantial differences in humoral response or in levels of omicron-specific neutralizing antibodies. Along with previous data showing the superiority of a third dose to a second dose, these results suggest that maximal immunogenicity of mRNA vaccines is achieved after three doses and that antibody levels can be restored by a fourth dose (Regev-Yochay et al, 2022).

A study from Israel by Bar-on et al., published on 5 April 2022, used the Israeli Ministry of Health database and extracted data on 1,252,331 persons who were 60 years of age or older and eligible for the fourth dose during a period in which the B.1.1.529 (omicron) variant of SARS-CoV-2 was predominant (January 10 through March 2, 2022). For persons in the fourth week after receipt of the fourth dose, the adjusted rate of severe illness was lower by a factor of 3.5 (95% CI, 2.7 to 4.6) than that in the three-dose group and was lower by a factor of 2.3 (95% CI, 1.7 to 3.3) than that in the internal control group. Severe illness continued to occur at lower rates in the four-dose groups than in the control groups in later weeks after receipt of the fourth dose, and no signs of waning were evident by the sixth week after receipt of the fourth dose. (Bar-On et al., 2022). However, the SHC notes large confidence intervals for severe illness and a very short time of evaluation. After 6 weeks the adjusted rate difference compared with the three dose group was 4.9 (CI, 2.6-7.1).

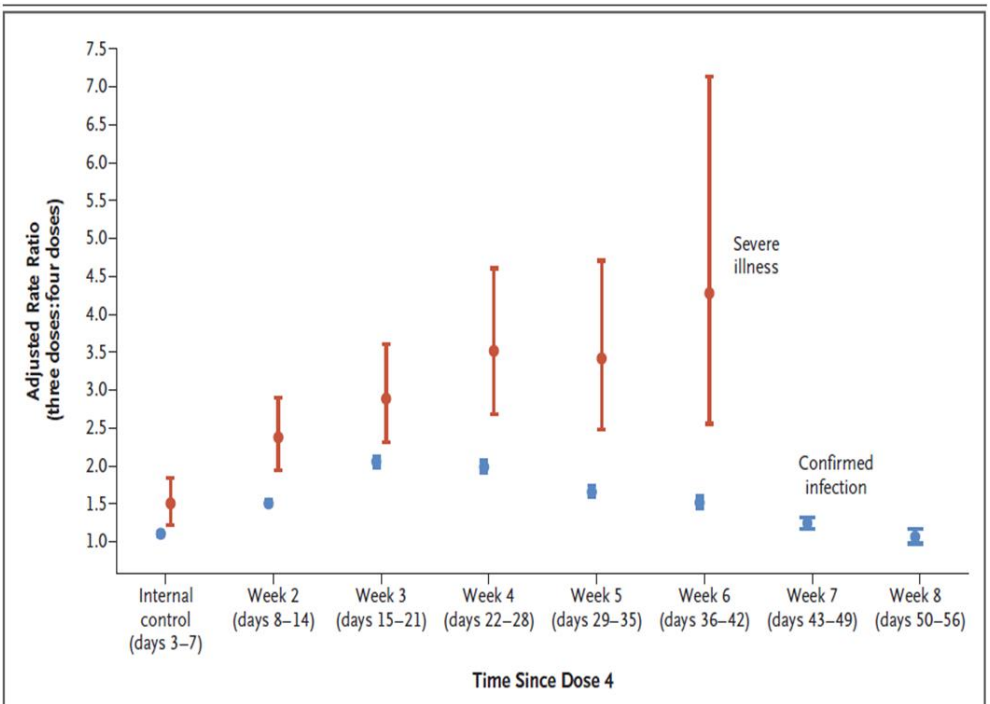


Figure 2. Adjusted Rate Ratios for Confirmed Infection and Severe Illness.

Shown are adjusted rate ratios for confirmed SARS-CoV-2 infection and severe Covid-19 in the group of persons eligible for a fourth dose who had not yet received it (three-dose group) as compared with those who had received a fourth dose, as a function of time since the fourth dose (the higher the rate ratio, the greater the protection conferred by the fourth dose of vaccine). Persons in the internal control group had received a fourth dose 3 to 7 days earlier (a period in which the fourth dose was not expected to affect the rate of confirmed infection or severe illness). Because of the 14-day follow-up period for severe Covid-19, the study period for this outcome was 2 weeks shorter than that for confirmed infection, and therefore the estimates of the adjusted rate ratio for severe illness end at week 6 instead of week 8.

A retrospective study by Arbel et al. investigated the second Booster vaccine and Covid-19 mortality in 563,465 adults 60 to 100 years old (Israel). During the study, death due to Covid-19 occurred in 92 of the second-booster recipients and 232 participants in the first-booster group. The adjusted hazard ratio for death due to Covid-19 in the second booster group compared with the first-booster group was 0.22 (95% CI: 0.17-0.28). In the Cox regression model, higher age group, male sex, ultra-orthodox Jewish, chronic heart failure, chronic obstructive pulmonary disease, and diabetes were confounding variables that had a significant association with death due to Covid-19:

Variable	Hazard Ratio for Death Due to Covid-19 (95% CI)
Second booster received	0.22 (0.17-0.28)
Age group	
60-69	Reference
70-79	2.24 (1.51-3.34)
≥ 80	9.95 (6.93-14.28)
Male sex	1.59 (1.26-1.99)
Population sector	
General Jewish	Reference
Ultra-Orthodox Jewish	1.61 (1.00-2.59)
BMI	0.96 (0.94-0.98)
Chronic Heart Failure	4.11 (3.22-5.25)
Chronic obstructive pulmonary disease	1.82 (1.35-2.43)
Diabetes	2.06 (1.64-2.58)
History of stroke	1.84 (1.44-2.37)

More recently, Muhsen and collaborators (2022) suggest that a fourth BNT162b2 dose was associated with high protection against COVID-19 hospitalizations and deaths among residents of long-term care facilities (LTCF) during a surge associated with the Omicron variant.

A second mRNA booster dose has a positive global clinical effect but, the maximum duration of this protection is not yet known due to the short follow-up periods after the second booster in the studies available and the change of Omicron subvariants.

At this stage of post-vaccination side effect surveillance, **there are no additional safety issues** related to the administration of a second booster.

10 Safety of the second booster and repeated doses (EMA/ECDC, 06/04/2022)

At this stage of post-vaccination side effect surveillance, **there are no additional safety issues related to the administration of a second booster**.

- As with any allergen, repeated injection involves a risk (small) of inducing an allergy. This is true for all allergens (drugs, venoms, etc.).
- At this stage of our knowledge, there are no examples of the immune system being "overloaded" by too many repeated doses of vaccines.

These two statements (Personal communication of Prof. Antoine Froidure - BelSACI - 55024973C) are possible theoretical risks but there is no scientific evidence for it in the real life context concerning COVID-19 vaccination and other vaccination campaigns.

11 Safety and efficacy of adapted Omicron mRNA vaccines

In Belgium (and more broadly in Europe), the mRNA vaccines Comirnaty® and Spikevax® (adapted with Omicron strains or not) are the main vaccines to be used for COVID-19 vaccination campaign during the Autumn / Winter season 2022 - 2023. Depending on the market launch after EMA recommendation and EC authorization of other vaccines as potential boosters, the SHC may update its recommendations in the future.

At this stage, EMA has started a rolling review for a version of both Comirnaty (15/06/2022) and Spikevax (17/06/2022) adapted to provide better protection against a specific variant or variants of SARS-CoV-2, the virus that causes COVID-19. The review will initially focus on data from laboratory studies (non-clinical data) and data on chemistry, manufacturing and controls, which relate to the manufacturing of the vaccine. As the companies makes progress in the development of the both vaccines, EMA will receive more data, including data on the immune response against the original strain and the Omicron variant of concern. As long as these adapted vaccines are not recommended by the EMA and authorized by the EC, **it is important to consider the available clinical evidence of the currently authorized vaccines (non-adapted versions of mRNA vaccines) to recommend their use as the best option available**. Clear and transparent communication to the general public on this sensitive issue is essential to maintain public confidence in vaccination.

Remarks: if only limited stocks of adapted mRNA vaccine are available at the time of the 2022 – 2023 booster campaign, it is reasonable to prioritized these adapted versions to the groups most at risk of severe forms (group 1 of category A).

As with the annual influenza vaccination with vaccines adapted to circulating strains, it is not anticipated that a large amount of clinical efficacy data of mRNA vaccines adapted to current and future strains will be available at the time of recommendation of use by the EMA.

EMA statement on this topic is expected for September 2022.

*****

On 17 June 2022, the WHO published an Interim statement on the composition of current COVID-19 vaccines.
Interim statement on the composition of current COVID-19 vaccines (who.int)

"In this context (Omicron), the primary goals of COVID-19 vaccination using currently licensed vaccines continue to be to ***reduce hospitalization, severe disease and death, and to protect health systems****. A primary series of currently licensed vaccines based on the virus that was identified from the first cases of COVID-19 in December 2019 (termed the index virus e.g. GISAID: hCoV-19/Wuhan/WIV04/2019) confers lower levels of protection against severe disease outcomes for Omicron, compared to prior VOCs. However, a booster dose of the currently licensed COVID-19 vaccines based on the index virus appears to restore protection against severe disease and death against currently circulating variants at levels that remain acceptable".*

- ➔ *"**The use of currently licensed vaccines based on the index virus confers high levels of protection against severe disease outcomes for all variants, including Omicron with a booster dose. As such, the continued use of currently licensed vaccines for primary vaccination AND as a booster dose is appropriate to achieve the primary goals of COVID-19 vaccination**".*

" Available data (see Annex) indicate that ***the inclusion of Omicron****, as the most antigenically distinct SARS-CoV-2 Variant of Concern, in an updated vaccine composition may be beneficial if administered as a booster dose to those who have already received a COVID-19 vaccination primary series".*

"For an ***Omicron-specific vaccine product****, the TAG-CO-VAC recognizes that viruses or viral genetic sequences very closely related to hCoV/South Africa/NICD-N21668/2021 or hCoV/USA/CA-CDC-4358237-001/2021 are some of the most antigenically distant from the index virus to date and are likely to enhance the magnitude and breadth of the antibody response".*

"Importantly, the TAG-CO-VAC considers that the protection offered by an Omicron-specific vaccine product is likely to differ in those who have already received a COVID-19 vaccine primary series (primed), as compared to those who have not (unprimed). Based on the data to date, it is inferred that ***an Omicron-specific monovalent vaccine product administered as a booster dose for those who have already received a primary vaccine series may elicit greater breadth in the immune response****. In contrast,* ***an Omicron-specific monovalent vaccine product as a standalone formulation for the primary series is not advised*** *as it is not yet known whether Omicron-specific vaccines will offer similar cross-reactive immunity and cross-protection from severe illness caused by other VOCs in unprimed individuals as the index virus-based vaccines have done.*

Although ***bi- or multivalent products have yet to be approved by regulatory authorities****, vaccines containing index virus and Omicron in a single product may be able to achieve similar outcomes as the proposed sequential approach. However, at this time, only limited data are available to assess whether the cross-reactive immune responses in humans using an Omicron-containing bi/multivalent product will be equivalent to those elicited with a sequential vaccine approach.*

On 28 June 2022, the FDA-VRBPAC published an Interim statement on the composition of current COVID-19 vaccines with **some important arguments for discussion**.
https://www.fda.gov/media/159452/download

On 30 June 2022, FDA: "*Following the vote, and striving to use the best available scientific evidence, we have advised manufacturers seeking* ***to update their COVID-19 vaccines that they should develop modified vaccines that add an omicron BA.4/5 spike protein component to the current vaccine composition to create a two component (bivalent) booster vaccine****, so that the modified vaccines can potentially be used starting in early to mid-fall 2022*".
https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-recommends-inclusion-omicron-ba45-component-covid-19-vaccine-booster

12 Some others NITAGs recommendations (05/07/2022)

12.1 STIKO - Germany (17/02/2022)

https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2022/07/Art_03.html

«Wie das Epidemiologische Bulletin 7/2022 ausführt, empfiehlt die STIKO nach abgeschlossener COVID-19-Grundimmunisierung und erfolgter 1. Auffrischimpfung eine 2. Auffrischimpfung (frühestens 3 Monate nach der 1. Auffrischimpfung) mit einem mRNA-Impfstoff für ≥ 70-Jährige, BewohnerInnen und Betreute in Einrichtungen der Pflege und für Personen mit Immundefizienz. Ebenfalls empfohlen wird die 2. Auffrischimpfung Tätigen in medizinischen Einrichtungen und Pflegeeinrichtungen, hier jedoch frühestens 6 Monate nach der 1. Auffrischimpfung. In begründeten Einzelfällen kann bei Letztgenannten die 2. Auffrischimpfung auch bereits nach frühestens 3 Monaten erwogen werden».

12.2 GR - Netherlands (25/03/2022)

https://www.gezondheidsraad.nl/over-ons/documenten/adviezen/2022/03/25/vervolgadvies-tweede-boostervaccinatie-tegen-covid-19

"De bescherming die COVID-19-vaccinatie biedt tegen ernstige ziekte en sterfte neemt af na verloop van tijd. Een extra vaccinatie zorgt ervoor dat de bescherming weer toeneemt, maar dat effect is tijdelijk. Door vaccinatie nog een keer te herhalen (revaccinatie) neemt de bescherming weer toe. Eerder adviseerde de Gezondheidsraad om zo'n revaccinatie aan te bieden aan 70-plussers en de meest kwetsbare groepen, omdat zij een hoger risico lopen op ernstige ziekte en sterfte door COVID-19 en doordat het aantal besmettingen waarschijnlijk nog hoog zou zijn op het moment dat de bescherming van de booster bij hen afneemt.

Doordat de besmettingsgolf door de omikronvariant langer aanhoudt dan verwacht, speelt dit scenario nu ook voor mensen van 60 tot en met 69 jaar. Bij hen zal de bescherming door de booster zijn afgenomen op het moment dat het aantal besmettingen waarschijnlijk nog hoog is. Dat kan in deze groep, die een hoger risico loopt op een ernstig beloop van COVID-19 dan mensen onder de 60, leiden tot een toename van het aantal ziekenhuisopnames. De Gezondheidsraad adviseert daarom om een tweede booster (revaccinatie) beschikbaar te stellen voor mensen van 60 tot en met 69 jaar die dat willen en die langer dan 3 maanden geleden een vaccinatie hebben gehad of COVID-19 hebben doorgemaakt".

12.3 JCVI – United Kingdom (19/05/2022)

https://www.gov.uk/government/publications/jcvi-interim-statement-on-covid-19-autumn-2022-vaccination-programme/joint-committee-on-vaccination-and-immunisation-jcvi-interim-statement-on-the-covid-19-vaccination-programme-for-autumn-2022

"The following advice should be considered as interim and for the purposes of operational planning for autumn 2022. The JCVI's current view is that in autumn 2022, a COVID-19 vaccine should be offered to:

- *residents in a care home for older adults and staff working in care homes for older adults;*
- *frontline health and social care workers;*
- *all those 65 years of age and over;*
- *adults aged 16 to 64 years in a clinical risk group;*
- *Vaccination of other groups of people remains under consideration within JCVI's ongoing review".*

12.4 HAS - France (25/05/2022)

https://www.has-sante.fr/jcms/p_3340479/fr/strategie-de-vaccination-contre-la-covid-19-anticipation-des-scenarios-possibles-a-l-automne-2022

« Afin d'anticiper la préparation d'une campagne vaccinale à l'automne prochain, la HAS recommande de considérer le scénario 2 caractérisé par la survenue de reprises épidémiques périodiques, comme le plus probable.

Tenant compte de la situation épidémiologiques actuelle marquée par la circulation du sous variant B-A.2 plus transmissible mais moins sévère que le variant Delta, du profil des patients actuellement hospitalisés et en réanimation (patients immunodéprimés majoritairement et patients à risque de forme sévère), de la couverture vaccinale (primovaccination et rappel) et du nombre particulièrement élevé de contaminations durant la vague Omicron, la HAS préconise ainsi de prévoir la vaccination des populations les plus à risque de forme grave de la maladie (en particulier, les personnes immunodéprimées et leur entourage, les personnes de 65 ans et plus et/ou présentant des comorbidités identifiées comme étant à risque de forme grave) et d'envisager la vaccination des professionnels de santé (au regard notamment des données d'efficacité vaccinale contre les contre les formes asymptomatiques de la maladie).

Pour des raisons de mobilisation et de logistique, la HAS recommande de coupler la campagne de vaccination à celle de la grippe, et de considérer qu'en l'absence de vague épidémique liée à la Covid-19 d'ici l'automne prochain, la date de début de la campagne contre la Covid-19 soit déterminée par la date de début de la vaccination contre la grippe saisonnière.

Compte tenu du caractère imprévisible de l'apparition de nouveaux variants plus sévères, la HAS recommande néanmoins de ne pas exclure la possibilité d'un scénario plus pessimiste, bien que moins probable, et, d'anticiper la nécessité d'une campagne de vaccination à plus large échelle, en population générale, en capitalisant sur les expériences acquises lors de la campagne de primovaccination contre la Covid-19. Les moyens mis en œuvre pour mobiliser les professionnels de santé de ville ou l'ouverture des centres de vaccination devraient ainsi être envisagés. De même, dans le cas où la prochaine vague de Covid-19 apparaîtrait de façon prématurée (par rapport au début de la vaccination contre la grippe), des campagnes vaccinales indépendantes contre la Covid-19 et contre la grippe devraient être mises en place ».

12.5 SPAIN – Government communication (16/06/2022)

"The government will approve a fourth COVID-19 dose in the autumn, prioritising the most vulnerable groups, Spanish health minister Carolina Darias confirmed on Thursday. There will be a fourth dose for the entire population. This has been decided by the Public Health Commission (…) Probably, a date that can be considered is around autumn, because we are waiting for (…) the arrival of new vaccines adapted to variants, as it is in the contracts that we have signed (…) through the European Union with pharmaceutical companies," Darias told private TV station La Sexta. The new vaccination will start with the elderly and people living in retirement homes before progressing to lower age groups, health sources told EURACTIV's partner EFE".

12.6 DHA - Denmark (23/06/2022)

Vaccination fall/winter 2022-2023 - Sundhedsstyrelsen

"We expect to offer covid-19 vaccination to anyone 50 years of age or older.

People younger than 50 years with a higher risk of serious courses of illness due to covid-19, for example people with weakened immune systems, may be offered booster vaccination against covid-19 after a specific assessment by a general practitioner or hospital doctor. The Danish Health Authority will later assess whether all pregnant women, or only selected pregnant women, should be offered vaccination after a specific medical assessment".

12.7 CDC – USA (24/06/2022)

COVID-19 Vaccine Boosters | CDC

"2 Boosters recommended for:

- *Adults ages 50 years and older;*
- *Some people ages 12 years and older who are moderately or severely immunocompromised".*

12.8 NACI - Canada (29/06/2022)

https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/naci-summary-june-29-2022.pdf

*"1. Individuals who are at increased risk of severe illness from COVID-**19 should be offered** a fall COVID-19 vaccine booster dose* regardless of the number of booster doses previously received, including:*

- *Older adults (≥65 years of age);*
- *Residents of long-term care facilities or congregate living settings for seniors;*
- *Individuals 12 years of age and older with an underlying medical condition that places them at high risk of severe COVID-19;*
- *Adults in or from First Nations, Métis, or Inuit communities, where infection can have disproportionate consequences;*
- *Adults in racialized communities and marginalized communities (e.g., people living with disabilities) disproportionately affected by COVID-19;*
- *Residents of other congregate living settings (e.g., quarters for migrant workers, shelter);*

*2. All other individuals **12 to 64 years of age maybe offered** a COVID-19 booster dose* in the fall of 2022, regardless of the number of booster doses they have previously received (Discretionary NACI Recommendation);*

*3. COVID-19 booster doses may be offered at an **interval of 6 months** since a previous COVID-19 vaccine dose or SARS-CoV-2 infection. Ashorter interval of at least 3 months may be warranted in the context of heightened epidemiologic risk, as well as operational considerations for the efficient deployment of vaccine programs (Discretionary NACI Recommendation)".*

12.9 ATAGI - Austria (05/07/2022)

https://www.health.gov.au/news/atagi-update-following-weekly-covid-19-meeting-29-june-2022

"As outlined in ATAGI statements on winter booster doses (25 March 2022 and 25 May 2022), ATAGI continue to review evidence on the need for winter booster doses for people outside of the currently identified high-risk groups. The primary goal of the Australian COVID-19 vaccine program is to minimise the risk of severe disease, including hospitalisation and death, from COVID-19.

This week ATAGI reviewed epidemiology, vaccine protection, and disease severity in healthy people aged 16 to 64 years (not currently recommended to receive an additional booster dose). In the coming weeks ATAGI will review information including epidemiology, and variant-specific vaccines for COVID-19. Recommendations may be updated as required.

ATAGI continue to emphasise the importance of remaining up to date with COVID-19 vaccinations by receiving the primary course and one or two booster doses according to eligibility. The booster doses provide additional protection against severe disease, hospitalisation and death as compared with the primary course.

ATAGI also recommends everyone in Australia over the age of 6 months should receive an influenza vaccination. Influenza vaccinations can be given at the same time as COVID-19 vaccines and should not be delayed".

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VI COMPOSITION OF THE WORKING GROUP

The composition of the Committee and that of the Board as well as the list of experts appointed by Royal Decree are available on the following website: About us.

All experts joined the working group ***in a private capacity***. Their general declarations of interests as well as those of the members of the Committee and the Board can be viewed on the SHC website (site: conflicts of interest).

Based on the discussions and conclusions of the NITAG meeting on April 16 2022, June 16 and June 30 2022, this advisory report was drafted. The following experts participated at the NITAG meeting and approved the conclusions or send their approval by mail on 27 and 30 June 2022. The NITAG meeting was chaired by **Yves VAN LAETHEM**; the scientific secretariat were Veerle MERTENS and Fabrice PETERS.

BEUTELS Philippe	Health Economics	UAntwerpen
BLUMENTAL Sophie	Pediatric Infectious Disease	HUDERF
BOIY Tine	Pediatrics	UZA
BRASSEUR Daniel	Pediatrics	CEPI
CARILLO Paloma	General medicine, vaccination	ONE
CHATZIS Olga	Pediatrics, Vaccinology	UCL
CORNELISSEN Laura	Epidemiology, Obstetrics, Gynaecology	Sciensano
DE LOOF Geert	General medicine	BCFI
DE SCHEERDER Marie-Angélique	Internal medicine, Infectiology, Travel clinic, HIV	UZ Gent
DE SCHRYVER Antoon	Family Medicine and Population Health	UZA
DESMET Stefanie	Microbiology, Bacteriology	UZ Leuven
DOGNE Jean- Michel	Pharmacovigilance	UNamur, EMA
FLAMAING Johan	Geriatry	UZ Leuven
FRERE Julie	Pediatrics, Infectiology	CHU Liège
HULSTAERT Frank	Epidemiology, Health Economics	KCE
LEROUX-ROELS Isabel	Vaccinology, Infection prevention, Microbiology	UZ Gent
MAERTENS Kristen	Vaccinology	UAntwerpen
MALFROOT Anne	Pediatrics, Infectiology	UZ Brussel
MICHIELS Barbara	General medicine	UAntwerpen
PELEMAN Renaat	Infectiology, Vaccinology	UZ Gent
ROBERFROID Dominique	Epidemiology, Anthropology, Health sciences	KCE
ROSSI Camelia	Infectiology, internal medicine	CHU Ambroise Paré
SCHELSTRAETE Petra	Infectiology, pediatrics	UZ Gent
SOENTJENS Patrick	Infectiology, Tropical diseases, Vaccinology	ITG Defence
SPODEN Julie	General medicine	SSMG
SWENNEN Béatrice	Epidemiology, Vaccinology	ULB
TILMANNE Anne	Pediatrics, Infectiology	CHU TIVOLI

TUERLINCKX David	Pediatrics, Vaccinology	CHU UCL Namur
VAN DAMME Pierre	Epidemiology, Vaccinology	UAntwerpen
VAN DER LINDEN Dimitri	Infectiology, pediatrics	UCL
VAN LAETHEM Yves	Infectiology, Vaccinology, Travel medicine, HIV	CHU Saint-Pierre, ULB
VAN LOENHOUT Joris	Epidemiology, Post-authorization surveillance of COVID-19 vaccines	Sciensano
VEKEMAN Veerle	General medicine	Kind en Gezin
VERHAEGEN Jan	Microbiology, Bacteriology	UZ Leuven
WAETERLOOS Geneviève	Quality of vaccines and blood products	Sciensano

The following experts or administrations were heard but did not take part in endorsing the advisory report.

DAEMS Joël	Directorate Drugs	RIZIV-INAMI
MALI Stéphanie	Coordinator, center of excellence for vaccines	FAMHP
THEETEN Heidi	Vaccinology	VAZG
TOP Geert	Manager vaccination program	VAZG
WILLEM Lander	Epidemiology, Health economics, Transmission dynamics	SIMID Consortium
VANDEN DRIESSCHE Koen	Pediatric infectious diseases	UZA
WUILLAUME Françoise	Vaccine vigilance	AFMPS-FAGG

About the Superior Health Council (SHC)

The Superior Health Council is a federal advisory body. Its secretariat is provided by the Federal Public Service Health, Food Chain Safety and Environment. It was founded in 1849 and provides scientific advisory reports on public health issues to the Ministers of Public Health and the Environment, their administration, and a few agencies. These advisory reports are drawn up on request or on the SHC's own initiative. The SHC aims at giving guidance to political decision-makers on public health matters. It does this on the basis of the most recent scientific knowledge.

Apart from its 25-member internal secretariat, the Council draws upon a vast network of over 500 experts (university professors, staff members of scientific institutions, stakeholders in the field, etc.), 300 of whom are appointed experts of the Council by Royal Decree. These experts meet in multidisciplinary working groups in order to write the advisory reports.

As an official body, the Superior Health Council takes the view that it is of key importance to guarantee that the scientific advisory reports it issues are neutral and impartial. In order to do so, it has provided itself with a structure, rules and procedures with which these requirements can be met efficiently at each stage of the coming into being of the advisory reports. The key stages in the latter process are: 1) the preliminary analysis of the request, 2) the appointing of the experts within the working groups, 3) the implementation of the procedures for managing potential conflicts of interest (based on the declaration of interest, the analysis of possible conflicts of interest, and a Committee on Professional Conduct) as well as the final endorsement of the advisory reports by the Board (ultimate decision-making body of the SHC, which consists of 30 members from the pool of appointed experts). This coherent set of procedures aims at allowing the SHC to issue advisory reports that are based on the highest level of scientific expertise available whilst maintaining all possible impartiality.

Once they have been endorsed by the Board, the advisory reports are sent to those who requested them as well as to the Minister of Public Health and are subsequently published on the SHC website (www.hgr-css.be). Some of them are also communicated to the press and to specific target groups (healthcare professionals, universities, politicians, consumer organisations, etc.).

In order to receive notification about the activities and publications of the SHC, please contact: info.hgr-css@health.belgium.be.

www.css-hgr.be

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