Superior
Health Council

BOOSTER DOSE OF AN mRNA VACCINE FOR INDIVIDUALS VACCINATED AGAINST COVID-19 WITH THE JANSSEN VACCINE

DECEMBER 2021
SHC № 9677

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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. 9677

Booster dose of an mRNA vaccine for individuals vaccinated against SARS-CoV-2 with the COVID-19 Vaccine Janssen®

In this scientific advisory report, which offers guidance to public health policy-makers, the Superior Health Council of Belgium provides recommendations of the need of a booster dose of mRNA COVID-19 vaccine for individuals primary vaccinated with the COVID-19 Vaccine Janssen® (1 dose).

This version was validated by the Board on December 1, 2021[1]

I INTRODUCTION AND ISSUE

On September 30 2021, the Superior Health Council (SHC) received a request for advice from the Task Force Operationalisation Vaccination Strategy Coronavirus disease 2019 (COVID-19) on the need of a booster dose of mRNA COVID-19 vaccine for individuals vaccinated with the COVID-19 Vaccine Janssen® (1 dose).

A difference must be made between booster doses and additional doses. The World Health Organization (WHO) defined both as in the interim statement published on October 4 2021:

- **Booster doses** are administered to a vaccinated population that has completed a primary vaccination series (currently one or two doses of COVID-19 vaccine depending on the product) when, with time, the immunity and clinical protection has fallen below a rate deemed sufficient in that population. The objective of a booster dose is to restore vaccine effectiveness from that deemed no longer sufficient.

- **Additional doses** of a vaccine may be needed as part of an extended primary series for target populations where the immune response rate following the standard primary series is deemed insufficient. The objective of an additional dose in the primary series is to optimize or enhance the immune response to establish a sufficient level of effectiveness against disease. In particular, immunocompromised individuals often fail to mount a protective immune response after a standard primary series, but also older adults may respond poorly to a standard primary series.

In Belgium, **an additional dose** is already implemented for immunocompromised patients (KCE, 2021). **Booster doses** are implemented for individuals who received one dose of the COVID-19 Vaccine Janssen® (SHC 9677, 2021), elderly (> 65 years), individuals living in care facilities such as nursing homes (SHC 9650, 2021) and healthcare workers (SHC 9679, 2021).

[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.

II RECOMMENDATION

At this moment, the effectiveness of the COVID-19 vaccines available in Belgium against severe forms of the disease remains proven for the general population under 65 years of age.

The SHC reiterates the importance of the rapid implementation of a booster dose for the groups determined previously.

The SHC recommends that individuals vaccinated with the COVID-19 Vaccine Janssen® should receive a booster dose with an mRNA vaccine (full dose for Comirnaty® - ½ dose for Spikevax®[2]) at least two months after their primary vaccination.

- ➔ In addition, **the SHC recommends the administration of the Comirnaty® vaccine as primovaccination for persons under 30 years of age** (based on preliminary findings of Nordic countries (GACVS, 2021) and a French study (EPI-PHARE, 2021) showing an increased risk of myocarditis and pericarditis after the Spikevax® vaccine - observed in young men under 30 years old after primary vaccination - in comparison with the Comirnaty® vaccine).

- ➔ **As a precaution, the SHC prefers the administration of the Comirnaty® vaccine as a booster dose for persons under 30 years of age**. However, at present, we do not have any evidence of the effect of the ½-dose booster Spikevax® on the incidence of myocarditis and pericarditis (dose-related effect?). Therefore, it is possible for TF Vaccination to temporarily not take into account this precautionary recommendation, waiting for more data.

- ➔ The priority for vaccination in this case is age.

This recommendation is based on immunological data and trends from different countries for breakthrough infections resulting in more severe outcomes such as Intensive Care Unit (ICU) admission or death.

Keywords

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

[2] whatever the age or the primary schedule received

III METHODOLOGY

After analysing the request, the Board and Chair of the National Immunization Technical Advisory Group (NITAG) identified the necessary fields of expertise. An *ad hoc* working group was then set up which included experts in microbiology, infectiology, epidemiology, vaccinology and general medicine. 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 journals and reports from national and international organisations competent in this field (peer-reviewed and preprint), as well as on the opinion of the experts.

Once the conclusions of the advisory report were endorsed by the *ad hoc* working group, it was ultimately validated by the members of the Board of the SHC.

IV ELABORATION AND ARGUMENTATION

List of abbreviations used

ASNM	*Agence Nationale de Sécurité du Médicament et des Produits de santé*
ECDC	European Center for Disease Prevention and Control
CHS	Clinical Hospital Surveillance
COVID-19	Coronavirus disease 2019
EMA	European Medicines Agency
FDA	Food and Drug Administration
HAS	*Haute Autorité de santé* - France
ICU	Intensive care unit
IMC	Interministerial Conference on Public Health
NITAG	National Immunization Technical Advisory Group
PCR	Polymerase Chain Reaction
SHC	Superior Health Council
VE-D	Vaccine effectiveness against death
WHO	World Health Organization

1 COVID-19 Vaccine Janssen® (Johnson & Johnson)

1.1 Belgium (Sciensano, van Loenhout et al., 2021)

On October 22 2021 and November 9 2021, an *ad hoc* meeting was organised to discuss the need of a booster dose of COVID-19 vaccine for individuals vaccinated with the COVID-19 Vaccine Janssen® (Johnson & Johnson).

At this first meeting, Sciensano presented their preliminary data on the level of protection offered by different vaccine brands in Belgium (Sciensano, van Loenhout et al., 2021).

The COVID-19 Vaccine Janssen® (Johnson & Johnson) became available in Belgium on the April 28 2021.

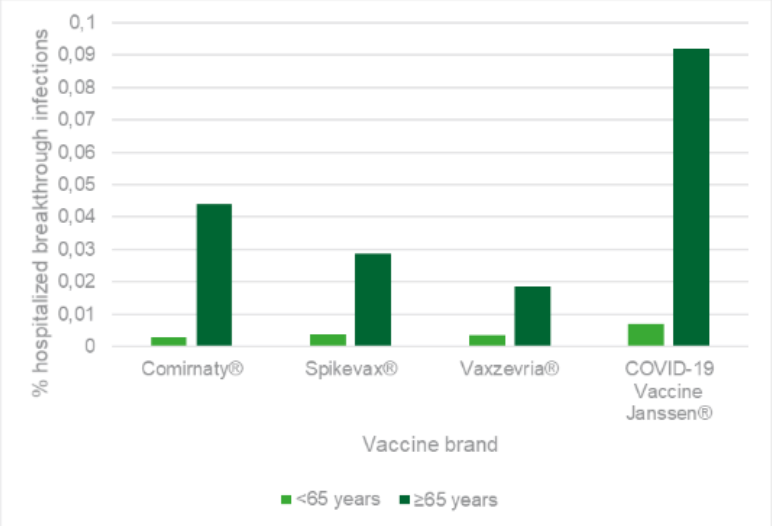
The COVID-19 Vaccine Janssen® was initially available for all age groups. However, as of May 26 2021, the Interministerial Conference on Public Health (IMC) decided to adopt a precautionary principle and temporarily limit this vaccine to people aged 41 and older. On June 9, the IMC decided that people between 18 and 40 years of age could voluntarily choose the

COVID-19 Vaccine Janssen®. Note that, as only one dose of the vaccine is needed to achieve full immunization, it was also used among difficult-to-reach groups (e.g. the homeless, sex workers, foreign students).

1.2 Belgian data on breakthrough infections for the COVID-19 Vaccine Janssen® (Sciensano, van Loenhout et al., 2021, 13 Oct 2021)

A breakthrough infection is defined as a new laboratory confirmed COVID-19 infection (positive RT-PCR or Rapid Antigen test; no positive test in prior 90 days) occurring in a fully immunized person. Fully immunized persons are those fully vaccinated for at least 14 days.

For the age group < 65 years, the lowest proportion of **hospitalized breakthrough infections** is for Comirnaty® (0.003%) and the **highest for the COVID-19 Vaccine Janssen® (0.007%).** However, there are some important limitations to consider when interpreting these analyses. Due to the aforementioned non-exhaustiveness of hospitals in the Clinical Hospital Surveillance (CHS), the proportions presented are an underestimation of the actual impact.



When comparing only vaccine brands, no statistically significant differences in the severity indicators are found after performing univariate analysis, except for a difference between Comirnaty® and Vaxzevria® for ICU transfer (p = 0.029 - table below).

***Table 1**. Indicators of severe disease by vaccine brand, for hospitalized patients for whom a discharge record was available. Since beginning of vaccination campaign to 7th of October 2021; Belgium. N.B. the data underlying this table are not exhaustive.*

	Comirnaty®[1]	Spikevax®[1]	Vaxzevria®[1]	COVID-19 Vaccine Janssen®[1]	Non-vaccinated[2]
	N = 598	N = 47	N = 103	N = 50	N = 15 974
Acute respiratory distress syndrome	24 (4.0%)	4 (8.5%)	7 (6.8%)	3 (6.0%)	1 711 (10.7%)
ICU transfer	50 (8.4%)	8 (17.0%)	14 (13.6%)	5 (10.0%)	3 048 (19.1%)
Length of hospital stay (Median [Q1-Q3] days)	8 [4-16]	6 [3-11]	7 [4-14]	10 [4-13]	8 [4-16]
Discharge status					
Recovered	484 (80.9%)	38 (80.9%)	85 (82.5%)	40 (80.0%)	13 188 (82.6%)
Deceased	95 (15.9%)	9 (19.1%)	13 (12.6%)	10 (20.0%)	2 191 (13.7%)
Unknown	19 (3.2%)	0 (0%)	5 (4.9%)	0 (0%)	595 (3.7%)

1) Data available until the 7th of October 2021
2) Data available until the 20th of September 2021

Source: Clinical Hospital Surveillance & Vaccinnet+ (LINK-VACC), accessed 7th of October 2021.

Based on the available data from Sciensano, there are minor differences between vaccine brands in the development of severe infection among fully immunized individuals who are hospitalized, however conclusions cannot be drawn due to too few cases.

1.3 International publications

In France, vaccine failure was reported by ANSM (*Agence Nationale de Sécurité du Médicament et des Produits de santé)* on October 15 2021 (HAS, 5 Nov 2021). These data are not exhaustive and are affected by underreporting. They should therefore not be interpreted as incidence data but as a sample to understand the characteristics of vaccine failures.

Vaccine	% vaccine failure ≥ 85 Y	% vaccine failure ≥ 65 Y	Hospitalization	Intensive care	Death	Median age of vaccine failures admitted to the ICU
Comirnaty® (n = 1193)	38.6% (461/1 193)	76.6% (914/1 193)	49.9% (595/1 193)	11.5%	19.5%	75 Y
Spikevax® (n=49)	20.4% (10/49)	57.1% (28/49)	61.2% (30/49)	10.2%	4.1%	76 Y
Vaxzevria® (n = 120)	9.2% (11/120)	63.6% (7/11)	79.2% (95/120)	30.0%	8.0%	70 Y
Janssen® (n= 85)	% vaccine failure : **50 to 84 Y** (min 36 Y; max 90 Y; IQ 58-75 Y)		Hospitalization	Intensive care	Death	Median age of vaccine failures admitted to the ICU
	83.3% (4/6)		78.8% (67/85)	43.5%	16.4%	**65 Y**

For the COVID-19 Vaccine Janssen®, the majority of vaccine failures occurred in the 50-84 year age group (87.1%, 74/85). Among those aged 85 and over, 83.3% (4/6) of those with vaccine failure were hospitalized, 33.3% were admitted to intensive care and 66.7% died. Across all age groups, 78.8% (67/85) of vaccine failures led to hospitalization, 43.5% to admission to intensive care and 16.4% to death. The median age of vaccine failures admitted to the ICU was 65 years.

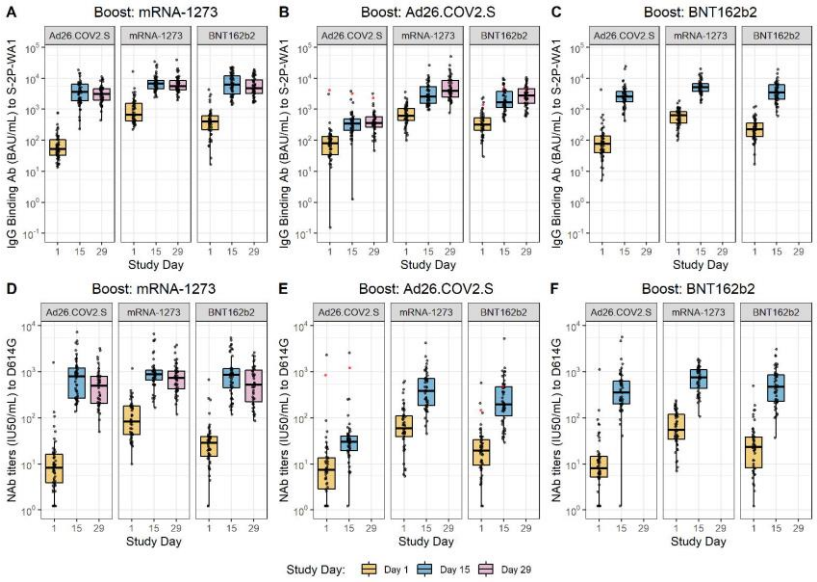
A recent study by Cohn et al. investigated breakthrough infections in the US. For age < 65 years, **vaccine effectiveness against death (VE-D)** was 81.7% (95% CI: 75.7% to 86.2%) for any vaccine; **73.0% (95% CI: 52.0% to 84.8%) for Janssen**; 81.5% (95% CI: 70.7% to 88.4%) for Moderna; and 84.3% (95% CI: 76.3% to 89.7%) for Pfizer-BioNTech. Vaccination still provide protection against death in infected persons and this benefit was observed for the Moderna, Pfizer-BioNtech and Janssen vaccines during the Delta period, although the benefit was greater for Moderna and Pfizer-BioNtech compared to COVID-19 Vaccine Janssen®.

1.4 Booster vaccination

The Food and Drug Administration (FDA) decided on October 20 2021 that a single booster dose of the COVID-19 Vaccine Janssen® (Johnson and Johnson) may be administered at least 2 months after completion of the single-dose primary regimen to individuals 18 years of age and older.

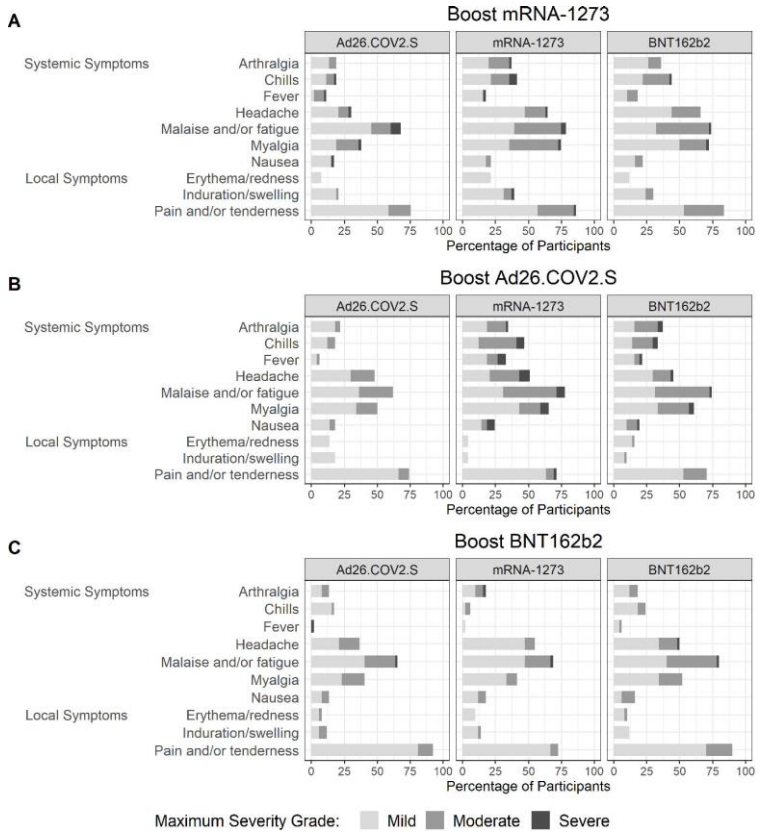
The decision of the European Medicines Agency (EMA) on booster doses is still pending.

A preprint study by Atmar et al. showed that the increases from baseline in both binding and neutralizing antibody titers were similar or greater after heterologous boosts compared to homologous boosts (figure below - Atmar et al., 2021).



1.5 Safety and reactogenicity of a heterologous booster

Reactogenicity of a heterologous booster was similar to that described in prior evaluations of COVID-19 Vaccine Janssen®, Spikevax® and Comirnaty® vaccines (figure below - Atmar et al., 2021).



In contrast, Shaw et al. found an increase in systemic reactogenicity after the boost dose reported by participants in heterologous vaccine schedules in comparison to homologous vaccine schedules. Compared with homologous vaccination, heterologous boost induced higher rates of fever (Shaw et al., 2021).

2 Summary table country recommendations (last update based on ECDC technical report 11 Nov 2021)

Countries	Booster dose?	Who?	When?	With?
Austria	Yes	J&J vaccinated > 18Y	>28 days	mRNA vaccine or COVID-19 Janssen
Croatia	Yes	J&J vaccinated	≥ 6 months	mRNA vaccine (Comirnaty)
Denmark	Yes	J&J vaccinated	≥ 1-8 months	mRNA vaccine
France	Yes	J&J vaccinated	≥ 6 months	mRNA vaccine
Germany	Yes	J&J vaccinated	4 weeks	mRNA vaccine
Iceland	Yes	J&J vaccinated BUT without history or COVID 19 antibodies	≥ 1 month	mRNA vaccine
Italy	Yes	J&J vaccinated	> 6 months	mRNA vaccine
Latvia	Yes	J&J vaccinated	≥ 2 months	Not specified
Luxembourg	Yes	J&J vaccinated	≥ 2 months	mRNA vaccine
Netherlands	Waiting EMA			
Norway	Yes	J&J vaccinated	At least 8-12 weeks	mRNA vaccine
Slovenia	Yes	J&J vaccinated	≥ 2 months	mRNA vaccine
Spain	Yes	J&J vaccinated	≥ 3 months	mRNA vaccine
Canada	Yes	AZ or J&J vaccinated at risk	≥ 6 months	mRNA vaccine
USA	Yes	J&J vaccinated > 18 Y	At least 2 months	J&J vaccine - mix-and-match vaccinations under discussion

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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).

An ad hoc meeting was organised on Friday October 22 2021 and Tuesday November 9 2021. Based on the discussions and conclusions at the meeting of November 9 2021 this advisory report was drafted. The following experts participated at the last ad hoc meeting and approval of the conclusions of the report. The ad hoc working group was chaired by **Yves VAN LAETHEM**; the scientific secretariat were Veerle MERTENS, Fabrice PETERS, Muriel BALTES and Jean-Jacques DUBOIS.

BEUTELS Philippe	Health Economics	UAntwerpen
CALLENS Steven	Infectiology, Internal medicine	UZ Gent
CHATZIS Olga	Pediatrics, Vaccinology	UCL
DE LOOF Geert	General medicine	BCFI
DE SCHEERDER Marie-Angélique	Internal medicine, Infectiology, Travel clinic, HIV	UZ Gent
DOGNE Jean- Michel	Pharmacovigilance	UNamur, EMA
FRERE Julie	Pediatrics, Infectiology	CHU Liège
GOVAERTS Frans	General medicine, Prevention and health promotion	Domus Medica
LEROUX-ROELS Isabel	Vaccinology, Infection prevention, Microbiology	UZ Gent
MANIEWSKI Ula	Infectiology, Tropical infectious diseases, Vaccinology	ITG-IMT
PELEMAN Renaat	Infectiology, Vaccinology	UZ Gent
ROBERFROID Dominique	Epidemiology	KCE, UNamur
SOENTJENS Patrick	Internal medicine, Tropical infectious diseases	ITG - Defensie
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 LAETHEM Yves	Infectiology, Vaccinology, Travel medicine, HIV	CHU Saint-Pierre, ULB
VANDEN DRIESSCHE Koen	Pediatrics, Immunology, Pneumology	UZA
WYNDHAM-THOMAS Chloé	Epidemiology, Infectiology	Sciensano

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

MAHIEU Romain	General medicine	CCC-GGC, Directorate for Health
MALI Stéphanie	Pharmacology, clinical survey	AFMPS-FAGG
TOP Geert	Manager vaccination program	VAZG
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.

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