Superior
Health Council

BOOSTER VACCINATION AGAINST COVID-19 FOR CHILDREN AND ADOLESCENTS AGED 12-17 YEARS

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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. 9693

Booster vaccination against COVID-19 for children and adolescents aged 12-17 years in Belgium

In this scientific advisory report, which offers guidance to public health policy-makers, the Belgian Superior Health Council provides recommendations on the need for a booster vaccination against COVID-19 for children and adolescents aged 12-17 years in Belgium.

This report aims at providing the Belgian Immunization Strategy and Operationalization Taskforce and general practitioners with specific recommendations on strategic COVID-19 vaccination in Belgium.

This version was approved by the members of the NITAG (meeting of 17 February 2022 and mail).
This version was validated by the Council on 2 March 2022[1].

I INTRODUCTION

The Superior Health Council (SHC) received on Wednesday January 26 2022 an urgent request for advice from the Belgian Interministerial Conference on Public Health on the need of a booster dose of COVID-19 (Coronavirus disease 2019) vaccination for children and adolescents aged 12-17 years.

In May 2021, the SHC published the recommendations on vaccination against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) for children aged 12 and over (SHC 9655, 09/07/2021).
https://www.health.belgium.be/fr/avis-9655-vaccination-contre-le-sars-cov-2-partir-de-12-ans

In Belgium, booster doses have been recommended for the general Belgian population since December 2021 for all persons over 18 years of age (SHC 9683, 16/12/2021) and recently also for all immunocompromised patients over 12 years of age (SHC 9691, 2022).
https://www.health.belgium.be/fr/avis-9683-vaccination-de-rappel-contre-la-covid-19
https://www.health.belgium.be/en/report-9691-booster-vaccination-immunocompromised-patients

On January 28 2022, the Board of the SHC answered to the Belgian Interministerial Conference on Public Health with an emergency letter (annex 1) saying that at that time and stage of knowledge, the scientific evidence supporting the administration of a booster dose of COVID-19 vaccination for children and adolescents aged 12-17 years, especially in the context of Omicron, is insufficient for the SHC to support it with a sufficient level of evidence for the usefulness, effectiveness, need and safety in terms of public health. As already discussed at the National Immunization Technical Advisory Group (NITAG) meeting of

[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.

January 20 2022 and confirmed by the Board of the SHC on January 27 2022, the SHC decided to wait for the European Medicines Agency (EMA) recommendation and for more scientific evidence before giving an opinion. More information would be collected on COVID-19 booster vaccination of adolescents from 12 years of age at the international NITAG webinar on the subject which took place on February, 4. The SHC also recommended that the Belgian Authorities strongly advocate for standardization of the rules relating to Covid Safe Ticket (CST) and the obligation to vaccinate against COVID-19 at European Union and global level. Pending this hypothetical standardization of the rules, the SHC proposed that the Federal Agency for Medicines and Health Products (FAMHP), EMA and the Belgian Vaccination Task Force take responsibility (at the safety level) for making the booster doses available (or not). This, for all people (children - teenagers - adults) who must or wish to travel in Europe and around the world for family, friendship, leisure and/or professional reasons. The latter must be duly informed that there is no EMA approval yet.

On January 5, 2022, the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) recommended a COVID-19 vaccine booster for everyone aged 12 years and older.
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html

On February 8 2022, the European Centre for Disease Prevention and Control (ECDC) published the technical report: “COVID-19 vaccine effectiveness in adolescents aged 12–17 years and interim public health considerations for administration of a booster dose.”
https://www.ecdc.europa.eu/en/news-events/covid-19-vaccines-adolescents-offer-very-high-level-protection-against-infection

On February 24 2022, the EMA recommended authorization of booster doses of Comirnaty® from 12 years of age.
https://www.ema.europa.eu/en/news/ema-recommends-authorisation-booster-doses-comirnaty-12-years-age

“EMA’s human medicines committee (CHMP - Committee for Medicinal Products for Human Use) has recommended that a booster dose of the COVID-19 vaccine Comirnaty® **may be given where appropriate to adolescents from 12 years of age**. Comirnaty® is already authorised in the EU as a 2-dose primary course in adolescents (as well as adults and children from 5 years of age) and a booster dose is currently authorised from 18 years of age.

The CHMP opinion follows an evaluation of interim safety and efficacy data from a clinical trial of a booster dose of the vaccine in those aged 16 and over, together with published literature and post authorisation data plus real-world evidence from the use of booster doses in young recipients in Israel. Booster doses are given to vaccinated people (i.e. people who have completed their primary vaccination course) to restore protection after it has waned. **The CHMP considered that the available evidence was sufficient to conclude that the immune response to a booster dose in adolescents would be at least equal to that in adults**. **No new safety concerns were identified from the data available**.

The EMA’s decision will support the national vaccination campaigns in those Member States that decide to offer booster vaccinations to adolescents. However, the decision on whether and when to offer boosters in this age group will need to take into account such factors as the spread and likely severity of the disease (especially with the Omicron variant) in younger persons, the known risk of side effects (particularly the very rare but serious complication of myocarditis) and the existence of other protective measures and restrictions. Just as with previous decisions on vaccination, **it will thus be for the experts guiding the vaccination campaign in each Member State to advise on the optimum decision and timing for their country.**”

II CONCLUSION AND RECOMMENDATIONS

1) EMA-approved vaccines are safe and effective and have saved, are saving and will save lives.

2) The mass vaccination campaign against COVID-19 in Belgium was an absolute necessity. It is/was based on the best available scientific evidence and the consensus of multidisciplinary experts. It is/was very effective, it saved many lives and to a large extent limited serious forms and hospitalizations in Belgium.

3) In the current epidemiologic context of COVID-19 in Belgium and the Variant of concern (VOC) Omicron, the Council recommends in the course of 2022 a gradual transition from a mass vaccination campaign to an increasingly targeted and individualized one for at risk people. In case of a deterioration of the global or Belgian epidemiological situation or in case of the appearance of new VOCs more critical than Omicron, Belgium must also be ready to quickly relaunch a mass vaccination campaign.

4) Optimal protection of people at risk of severe disease remains the first priority. It has been shown that a booster dose is required to maintain this optimal protection. Vaccine effectiveness (VE) against severe outcomes (hospitalizations, admissions to intensive care units (ICU) or death) continues to be very high in the context of Omicron. Risk communication activities to people at risk, emphasizing the importance of being fully vaccinated (including recommended additional or booster doses), remain of great importance.

Remarks : Two doses of BNT162b2 vaccine were associated with high short-term protection against SARS-CoV-2 infection; this protection waned considerably after 6 months. Infection-acquired immunity boosted with vaccination remained high more than1 year after infection for healthy adults in the Delta period (Hall et al., 2022).

5) The protection offered by vaccination against infection and onwards transmission is lower for the Omicron than for the Delta SARS-CoV-2-variant and decreases more rapidly with time.

6) **Concerning the booster dose for 12- to 17-year-olds, the SHC recommends the systematic administration of a booster dose for:**

   - All children and adolescents who are immunocompromised patients (SHC 9691, February 2022);

   - All children and adolescents with level 1, 2 and 3 priority comorbidities (SHC 9618, February 2021 and SHC 9641, April 2021).

   - All children and adolescents living under the same roof as people who remain at risk of severe disease despite full vaccination (e.g. frail grandparents, immunocompromised brother or sister, etc.). The aim of this vaccination is to indirectly help protect those risk groups (SHC 9618, February 2021). However, the SHC again indicates that the duration of protection in the context of Omicron is lower and decreases more rapidly with time and that cocoon vaccination complements but does not replace non-pharmaceutical interventions (NPIs) for those at risk of severe disease.

The use of the Pfizer-BioNTech mRNA booster dose (30 µg) is recommended in adolescents to further minimize the rare risk of myocarditis and/or pericarditis following vaccination in this age group.

7) **In the current epidemiologic context related to Omicron (clear decrease of virus circulation in the population) and the administration of a booster dose for healthy 12-17 year olds, the SHC considers that:**

Based on the current knowledge and without knowing the mid-term or long-term consequences of COVID-19 infections in this age group, we assume that the direct health benefit of booster vaccination in 12-17 year olds is limited.

Breakthrough infections with the Omicron variant are generally mild and the risk of hospitalization is minimal for vaccinated (primary vaccination) adolescents who already received two vaccine doses.

The risk of Multisystem Inflammatory Syndrome in Children (MIS-C) and long-COVID after a breakthrough infection with Omicron and the effect of a booster dose in this age group are not currently adequately documented. Some Belgian experts and the Dutch NITAG (GR, 04/02/2022) consider that the risk of developing MIS-C or long-COVID is probably lower in vaccinated adolescents (primary vaccination).

The direct health benefits need to be compared to the risks of adverse events, even if serious adverse events have been shown to be very rare. For adolescents, particular attention should be given to the risk of post-vaccination myocarditis. Current evidence on safety of a booster dose in adolescents is limited. **The EMA-CHMP considered that the available evidence was sufficient to conclude that the immune response to a booster dose in adolescents would be at least equal to that in adults. Booster doses are given to vaccinated people (i.e. people who have completed their primary vaccination course) to restore protection after it has waned. The Committee considered that the available evidence was sufficient to conclude that the immune response to a booster dose in adolescents would be at least equal to that in adults. No new safety concerns were identified from the data available. The CHMP opinion follows an evaluation of interim safety and efficacy data from a clinical trial of a booster dose of the vaccine in those aged 16 and over, together with published literature and post authorisation data plus real-world evidence from the use of booster doses in young recipients in Israel.** (EMA, 24/02/2022).

The protection offered by vaccination against infection and onwards transmission is lower for the Omicron than for the Delta SARS-CoV-2-variant and decreases more rapidly with time. Moreover, Belgium is currently on a downward trend after an Omicron wave that caused very high numbers of infections in all age groups. Furthermore, modelling by ECDC estimated that booster vaccination for adolescents would only have a very limited impact on spread of the virus in the population. In Belgium, the latest update from the Simulation Models of Infectious Diseases (SIMID) is available at: https://covid-en-wetenschap.github.io/assets/20220208_technical_note_SIMID.pdf. In this model, the authors conservatively assumed that no more boosters would be given to teenagers than were already given at that time. According to this modelling, additional boosters would have a positive effect in reducing the burden of disease in the population and a faster relief of care and school populations. However, the simulations do not predict that, with the current variant, the boosters of teenagers make a difference to a possible new disruption of the healthcare system. **Therefore, the SHC concludes that booster vaccination of healthy adolescents in the context of Omicron does not provide, at this time, any significant indirect health gains for the society.**

Since EMA approval, all children and adolescents who wish to receive this booster, for whatever reason, can have access to it. A primary vaccination schedule against COVID-19 can be completed by a booster immunization, in order to trigger immune memory and broader immune response, as observed in the 18-plus population. But, there is uncertainty about the magnitude of the impact of this booster on this age group in the current (postomicron wave) context.

Based on this, the SHC recommends that a booster dose for healthy vaccinated adolescents 12 to 17 years of age **would be given in Belgium when appropriate**. Taking into account the current spread of COVID-19, the severity of the disease in younger persons, and the known risk of side effects (particularly the very rare complications of myocarditis), the SHC **is not in favor of the systematic administration** of a booster dose for healthy vaccinated adolescents 12 to 17 years of age at this very moment.

Finally, the SHC again recommends the Belgian Authorities to strongly advocate for standardization of the rules relating to Digital COVID Certificates (at least EU level). As a minimum, the requirements should at least take into account the availability of EMA-approved vaccines for the different age groups. In general, access to areas of public life should not be restricted for children and adolescents depending on their vaccination status.

III METHODOLOGY

After analysing the request, the Board and Chair of the NITAG identified the necessary fields of expertise, such as experts in paediatrics, infectiology, epidemiology, vaccinology, biostatistics and general medicine. The experts 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 preprint studies, the scientific literature published in both scientific journals and reports from national and international organizations competent in this field (peer-reviewed), as well as on the opinion of the experts.

The main sources of information of this report are the technical report of the ECDC (ECDC, 08/02/2022) and the EMA's recommendation for authorization of booster doses of Comirnaty® from 12 years of age (EMA, 24/02/2022).

Once the advisory report was endorsed by the NITAG, the members of the Board and the Committee of the SHC ultimately validate the report.

Keywords

Keywords	**Sleutelwoorden**	**Mots clés**	**Schlüsselwörter**
COVID-19	COVID-19	COVID-19	COVID-19
Vaccination	Vaccinatie	Vaccination	Impfung
Booster Immunization	Booster-immunisatie	Immunisation de rappel	Booster-Immunisierung
Adolescent	Adolescent	Adolescent	Jugendlicher

List of abbreviations used

ACIP	Advisory Committee on Immunization Practices
CDC	Centers for Disease Control and Prevention
CHMP	Committee for Medicinal Products for Human Use
COVID-19	Coronavirus disease 2019
CST	Covid Safe Ticket
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
FAMHP	Federal Agency for Medicines and Health Products - Belgium
FDA	Food and Drug Administration - USA
ICU	Intensive Care Units
MIS-C	Multisystem inflammatory syndrome in children
NITAG	National Immunization Technical Advisory Group
NPI	Non-Pharmaceutical Interventions
SAGE	Strategic Advisory Group of Experts on Immunization
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SHC	Superior Health Council - Belgium
SIMID	Simulation Models of Infectious Diseases
VE	Vaccine effectiveness
VOC	Variant of concern
WHO	World Health Organization

IV ELABORATION AND ARGUMENTATION

1 Belgian data (Sciensano, 25/02/2022)

1.1 Vaccination coverage of 12-17 year-olds

As of week 4 (30 January 2022), the median uptake of the primary course of COVID-19-vaccines among adolescents aged 15-17 years old was 70.9% (range: 17.9-92.6%). Among 10-14-year-olds, it was 34.8% (range: 3-63.8%) with broad heterogeneity across EU/EEA countries. More than half of adolescents aged 10 to 17 in the EU/EEA have not yet completed a primary course (ECDC, 08/02/2022).

The table below shows the vaccination coverage rate in Belgium on 22 February 2022 in Belgium. 17.6% of adolescents aged 12 to 17 received their booster, 78.6% received the primary vaccination and 79.8% received at least one dose.

		Population totale [1]	Population âgée de 5-11 ans [1,2]	Population âgée de 12-17 ans [1,2]	Population âgée de 18 ans et plus [1,2]	Population âgée de 65 ans et plus [1,2]
Couverture vaccinale au moins 1 dose	Belgique	79,9%	32,1%	79,8%	89,7%	94,1%
	Bruxelles [3]	62,4%	10,1%	49,7%	74,9%	85,1%
	Flandre [3]	85,0%	45,3%	88,6%	93,5%	96,4%
	Wallonie [3,4]	74,3%	17,0%	73,6%	85,0%	90,7%
	Communauté germanophone [3]	71,6%	20,7%	70,4%	81,1%	89,6%
Couverture vaccinale entièrement vacciné	Belgique	78,5%	25,0%	78,6%	88,9%	93,4%
	Bruxelles [3]	60,8%	7,0%	47,8%	73,4%	84,1%
	Flandre [3]	83,7%	35,6%	87,8%	92,9%	95,8%
	Wallonie [3,4]	73,2%	13,1%	72,1%	84,1%	89,8%
	Communauté germanophone [3]	70,3%	15,6%	68,7%	80,2%	88,6%
Couverture vaccinale entièrement vacciné + dose de rappel	Belgique	60,3%	0,7%	17,6%	73,8%	87,3%
	Bruxelles [3]	35,3%	0,0%	4,2%	45,2%	70,9%
	Flandre [3]	68,8%	1,1%	25,6%	83,2%	91,6%
	Wallonie [3,4]	52,3%	0,1%	8,6%	65,0%	82,0%
	Communauté germanophone [3]	51,8%	0,2%	9,8%	63,3%	80,2%

Source de données: registre Vaccinnet+. Un délai entre le moment de la vaccination et celui de l'enregistrement dans la base de données est possible, et doit être pris en compte lors de l'interprétation des résultats.
[1] Les dénominateurs utilisés pour ces calculs sont les chiffres de la population belge au 01/01/2021 publiés par STATBEL.
[2] Les personnes dont l'âge n'était pas connu ne sont pas incluses dans ces calculs.
[3] La répartition géographique est basée sur le code postal du lieu de résidence de la personne vaccinée. Les personnes dont le code postal était inconnu ne sont pas incluses dans la répartition géographique.
[4] A l'exclusion de la Communauté germanophone.

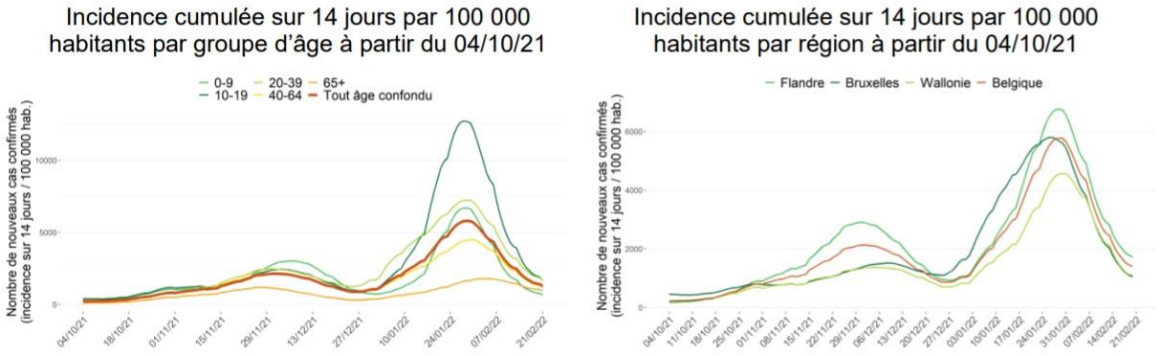
More information is available and continuously updated via the Sciensano website: https://datastudio.google.com/u/0/reporting/c14a5cfc-cab7-4812-848c-0369173148ab/page/p_j1f02pfnpc

Primary vaccination against COVID-19 for children and adolescents is not evenly distributed between Belgian regions. Primary vaccination should remain the first priority.
During the Omicron wave, the proportion of adolescents who received the booster before EMA approval was 17.6%.

1.2 Monitoring of confirmed COVID-19 disease cases

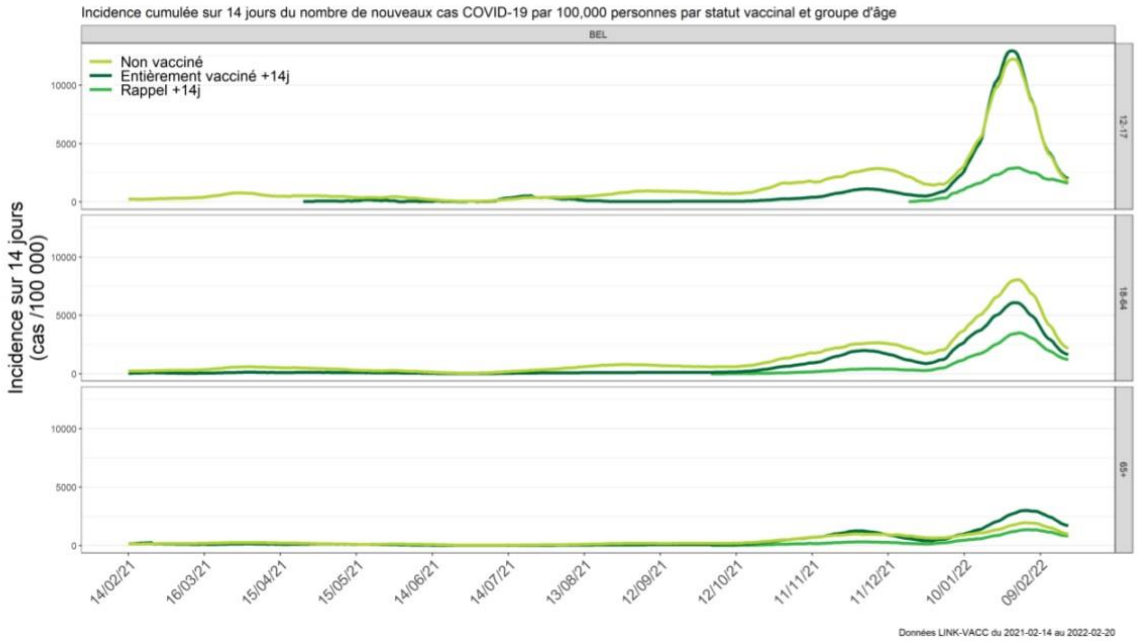
SARS-CoV-2 notification rates of symptomatic disease in 12-17-year-olds have increased steadily since July 2021, largely mirroring the increased reporting rate observed in all age groups during the Delta- and Omicron-waves. However, a decrease in notification rates has been recently observed (ECDC, 08/02/2022).

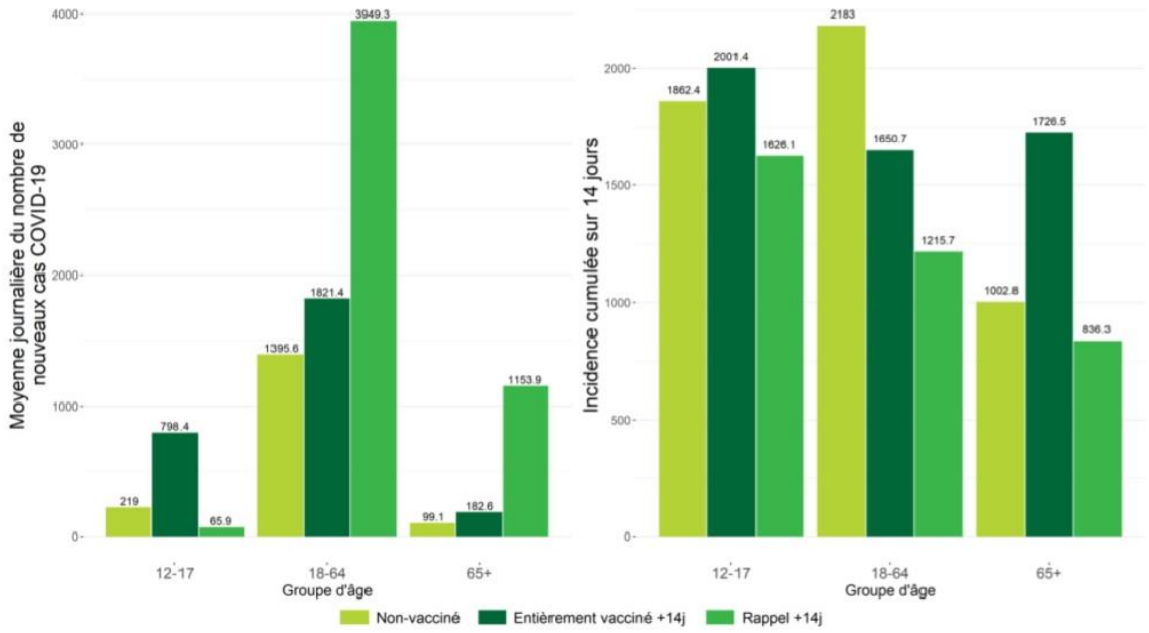
The evolution of the epidemic in Belgium by age group is visualized below:



Les dénominateurs utilisés pour calculer l'incidence sont les chiffres de la population belge au 01/01/2021 publiés par STATBEL.

The graphs below show the daily average and the cumulative 14-day incidence for the number of cases, by vaccination status and age group, for the period from 14 February to 25 February 2022.



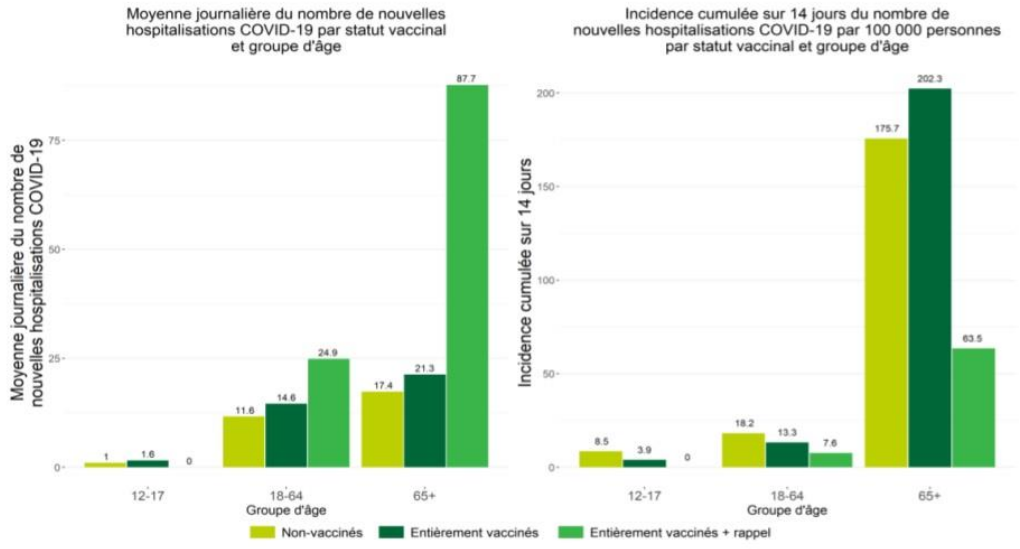


The incidence rate is rising in 12-17 years for vaccinated and un-vaccinated children and adolescents. Shortly after booster vaccination, a reduction in COVID-19 cases is observed.

1.3 Hospitalization

The crude risk of hospitalization, ICU admission and death remains very low for 12-17-year-olds (ECDC, 08/02/2022).

The graphs below show the average number of hospital admissions per day and the cumulative incidence over 14 days, by vaccination status and age group, for the period from 7 to 20 February 2022 in Belgium.



The table below shows the unadjusted estimate of the risk reduction of COVID-19 hospitalization and ICU between unvaccinated, fully vaccinated and people who received a booster dose.

Catégorie d'âge	Réduction relative du risque d'admission en USI (non ajustée)		
	Entièrement vacciné (+14 jours) vs. non vacciné	Dose de rappel (+14 jours) vs. Non vacciné	Dose de rappel (+14 jours) vs. entièrement vacciné (+14 jours)
12-17	25 %	Non détectable	Non détectable
18-64	45 %	68 %	43 %
65+	8 %	74 %	71 %

Catégorie d'âge	Réduction relative du risque d'hospitalisation (non ajustée)		
	Entièrement vacciné (+14 jours) vs. non vacciné	Dose de rappel (+14 jours) vs. Non vacciné	Dose de rappel (+14 jours) vs. entièrement vacciné (+14 jours)
12-17	54 %	Non détectable	Non détectable
18-64	27 %	58 %	42 %
65+	Non détectable	64 %	69 %

The hospitalization admission cumulative incidence remains low for children and adolescents between 12-17 years (not enough data to draw conclusions at this moment).

The table below shows an overview of hospitalized patients in the age group 12-17 years since 1 January 2021, by vaccination status, including the number and type of comorbidities. It is important to note that this information was collected through a non-exhaustive survey among hospitals, and therefore does not provide a complete overview.

Included data:	Clinical Hospital Surveillance (not exhaustive): all patients aged 11-17 years old at admission, admitted since 01-01-2021				
	Fully vaccinated + booster	**Fully vaccinated**	**Partially vaccinated**	**Not vaccinated**	**Unknown**
Total number of patients	1	102	8	217	18
Comorbidities	**Fully vaccinated + booster**	**Fully vaccinated**	**Partially vaccinated**	**Not vaccinated**	**Unknown**
Cognitive	0 (0%)	1 (1%)	1 (12%)	3 (1%)	0 (0%)
Cardiovascular disease	0 (0%)	0 (0%)	1 (12%)	4 (2%)	0 (0%)
Diabetes	0 (0%)	1 (1%)	0 (0%)	7 (3%)	0 (0%)
High blood pressure	0 (0%)	0 (0%)	0 (0%)	2 (1%)	0 (0%)
Hematological cancer	0 (0%)	2 (2%	0 (0%)	3 (1%	0 (0%)
Immunodepressed	0 (0%)	3 (3%)	1 (12%)	7 (3%)	1 (6%)
Chronical liver disease	0 (0%)	2 (2%	1 (12%)	2 (1%	0 (0%)
Chronical lung disease	0 (0%)	0 (0%)	0 (0%)	10 (5%)	1 (6%)
Chronical neurological disease	0 (0%)	3 (3%	1 (12%)	8 (4%	1 (6%)
Chronical renal disease	0 (0%)	2 (2%)	1 (12%)	14 (6%)	2 (11%)
Obesity	0 (0%)	1 (1%)	0 (0%)	6 (3%)	0 (0%)
Pregnancy	0 (0%)	1 (1%)	0 (0%)	1 (0%)	3 (17%)
Solid cancer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Transplant	0 (0%)	1 (1%)	0 (0%)	2 (1%)	1 (6%)
(Number and percentage of patients in each vaccination group)					
Number of comorbidities	**Fully vaccinated + booster**	**Fully vaccinated**	**Partially vaccinated**	**Not vaccinated**	**Unknown**
0	1 (100%)	89 (87%)	6 (75%)	165 (76%)	14 (78%)
1	0 (0%)	12 (12%)	0 (0%)	42 (19%)	3 (17%)
2	0 (0%)	1 (1%)	1 (12%)	1 (0%)	1 (6%)
3	0 (0%)	0 (0%)	0 (0%)	8 (4%)	0 (0%)
4	0 (0%)	0 (0%)	1 (12%)	0 (0%)	0 (0%)
(Number and percentage of patients in each vaccination group)					

2 Country recommendations regarding the booster dose of COVID-19 vaccination for children and adolescents aged 12-17 years (ECDC 08/02/2022)

All 30 EU/EEA countries are recommending primary vaccination against COVID-19 for 12-17-year-olds. Regarding the administration of a booster dose, most EU/EEA countries (19/30) are recommending booster doses to all adults of 18 years and over and one country recommends them only to priority groups including those aged 40 years and over. Ten countries are recommending boosters doses for adolescents below 18 years of age. Two countries are recommending booster doses to all of those who are 16 years of age and over (Iceland and Ireland) and eight countries to all of those who are 12 years and over (Austria, France, Germany, Hungary, Italy, Liechtenstein, Luxembourg and Romania).

On February 24 2022, the EMA recommended authorisation of booster doses of Comirnaty® from 12 years of age. https://www.ema.europa.eu/en/news/ema-recommends-authorisation-booster-doses-comirnaty-12-years-age

In the US, on 5 January 2022, the CDC endorsed the Advisory Committee on Immunization Practices' (ACIP) recommendations to also offer booster doses to those who are 12-15 years old, following the previous recommendation to offer them to those of 16 years and older. The CDC recommends that adolescents aged 12-17 years old should receive a booster dose five months after the completion of the primary vaccination series with Comirnaty® and 2 months after completion of a Janssen COVID-19 Vaccine® primary dose. This decision was based on safety data following the administration of over 25 million vaccine doses in adolescents and data showing that booster doses strengthen the protection against the Omicron and other variants. Currently, Comirnaty® is the only COVID-19-vaccine authorized and recommended for adolescents in the US. This decision was based on individual benefit-risk considerations acknowledging that there is limited data directly on the impact of boosters in adolescent population.

Israel has recommended booster doses for everyone aged 16 years and older since late August. In November, this was extended to also include those aged 12 to 15 years. Due to the spread of the Omicron variant, the Ministry of Health's Director General has issued a directive for the administration of a booster to be given within three months of the second dose, rather than five months afterwards, as was the protocol before.

In the UK, the National Health Service: "A booster dose of the coronavirus (COVID-19) vaccine is available for everyone aged 16 and over, and some children aged 12 to 15, who have had 2 doses of the vaccine at least 3 months ago. People aged 18 and over, and eligible children aged 12 to 15, need to wait 4 weeks. Young people aged 16 and 17 need to wait 12 weeks.

Some children aged 12 to 15 can get a booster dose if either:

- they have a condition that means they're at high risk of getting seriously ill from COVID-19.
- they live with someone who has a weakened immune system.

People with a severely weakened immune system: If you have or had a severely weakened immune system when you had your first 2 doses of the COVID-19 vaccine, you may have been offered a 3rd dose of the vaccine. You can get a booster dose (4th dose) from 3 months after you had your 3rd dose".

https://www.nhs.uk/conditions/coronavirus-covid-19/coronavirus-vaccination/how-to-get-a-coronavirus-vaccine/how-to-get-a-booster-dose/

Switzerland also recommends booster doses to all adolescents 12-17 years of age 4 months after full vaccination (initial immunization) for everyone aged 12 or over.

In addition, on 21 January 2022, **the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE)** on Immunization issued an update of the roadmap for prioritizing the use of COVID-19-vaccines, in which children and adolescents with comorbidities are identified as a medium priority-use population group for the administration of primary series and booster doses, while healthy children and adolescents are the lowest priority-use group because of their relatively low risk of severe disease, hospitalization, and death. The decision to expand the administration of booster doses to lower priority-use groups should also consider the evidence of waning immunity and the vaccine coverage of higher priority-use groups first to optimize vaccination impact. For instance, countries with moderate-to-high rates of primary series coverage in higher priority-use groups should prioritize available resources to first achieve high booster dose coverage rates in higher priority-use groups before offering booster doses to lower priority-use groups.

3 Clinical evidence for boosting 12-17-year-olds, real-world data (ECDC 08/02/2022)

Pfizer is conducting a study for the age group of 12-17 years old, however results are not available yet (expected in at least 2 months).

A cohort study from Israel (not yet peer-reviewed) investigated the effect of an additional (third) dose of Comirnaty® in 16-18-year-olds compared to individuals aged 12-14 who had recently completed their primary vaccination course with two doses of the same vaccine. The data were collected **during the Delta-dominant period**. The analysis showed that the additional dose provided a 3.7- fold (95% Confidence Interval (CI): 2.7-5.2) increase in protection against documented infection compared to the primary vaccination course only. The VE of the primary vaccination course calculated from the data in this study was estimated to be around 90% in both age groups, at 14-60 days after the second dose. The VE of an additional dose was estimated at 92% (95% CI: 91-93%) when compared to unvaccinated and 73% (95% CI: 67-79%) when compared to individuals who completed the primary course.

In New York City (NYC Health, 13/01/2022), total pediatric hospital census was stable to slightly lower during the Omicron wave, although pediatric hospitalizations due to or with COVID-19 increased significantly. **Children who were not vaccinated were significantly more likely to be hospitalized with COVID-19 compared to all children** (data on vaccination status is lagged and may be incomplete; there is no information about boosted children).

There are currently limited data available on benefits and risks of a booster dose administered to adolescents who completed their primary vaccination course against COVID-19.

Preliminary findings suggest an increase of vaccine effectiveness against documented SARS-CoV-2 infection in adolescents who received a booster compared to adolescents who have recently completed the primary vaccination course.

However, few data are available yet on the duration of protection from a booster dose and on the additional effectiveness against severe disease of a booster dose in adolescents.

EMA considered that the available evidence was sufficient to conclude that the immune response to a booster dose in adolescents would be at least equal to that in adults.

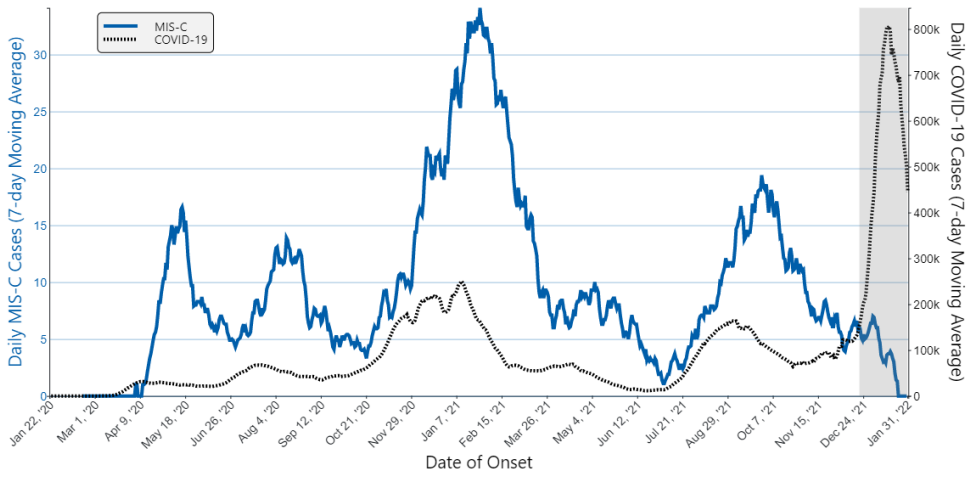
MIS-C data

No data are currently available about the effectiveness of booster doses to prevent severe COVID-19, MIS-C or post-COVID-19 conditions in adolescents 12-17 years old.

In the USA:

- The median age of patients with MIS-C **was 9 years**. Half of children with MIS-C were between the ages of 5 and 13 years.
- 59% of the reported patients with race/ethnicity information available occurred in children who are Hispanic/Latino (1,746 patients) or Black, Non-Hispanic (2,050 patients).
- 98% of patients had a positive test result for SARS CoV-2, the virus that causes COVID-19. The remaining 2% of patients had contact with someone with COVID-19.
- 60% of reported patients were male.

Daily MIS-C Cases and COVID-19 Cases Reported to CDC (7-Day Moving Average)



https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance

The risk of Multisystem inflammatory syndrome in children (MIS-C) and long-COVID after a breakthrough infection with Omicron and the effect of a booster dose in this age group are not currently adequately documented. Some Belgian experts and the Dutch NITAG (GR, 04/02/2022) believe that the risk of developing MIS-C or long-COVID is probably lower in vaccinated adolescents (primary vaccination).

4 Safety of vaccination against COVID-19 of children and adolescents aged 12-17 years (EMA, 24/02/2022)

"EMA recommends authorisation of booster doses of Comirnaty from 12 years of age.

EMA's human medicines committee (CHMP) has recommended that a booster dose of the COVID-19 vaccine Comirnaty may be given where appropriate to adolescents from 12 years of age. Comirnaty is already authorised in the EU as a 2-dose primary course in adolescents (as well as adults and children from 5 years of age) and a booster dose is currently authorised from 18 years of age.

The CHMP opinion follows an evaluation of interim safety and efficacy data from a clinical trial of a booster dose of the vaccine in those aged 16 and over, together with published literature and post authorisation data plus real-world evidence from the use of booster doses in young recipients in Israel.

Booster doses are given to vaccinated people (i.e. people who have completed their primary vaccination course) to restore protection after it has waned. The Committee considered that the available evidence was sufficient to conclude that the immune response to a booster dose in adolescents would be at least equal to that in adults. No new safety concerns were identified from the data available.

Further data are expected from studies and analyses in adolescents in the coming months. EMA will continue to monitor and evaluate the evidence and to update the product information or take other appropriate regulatory action as required.

The Agency's decision will support the national vaccination campaigns in those Member States that decide to offer booster vaccinations to adolescents. However, the decision on whether and when to offer boosters in this age group will need to take into account such factors as the spread and likely severity of the disease (especially with the Omicron variant) in younger persons, the known risk of side effects (particularly the very rare but serious complication of myocarditis) and the existence of other protective measures and restrictions. Just as with previous decisions on vaccination, it will thus be for the experts guiding the vaccination campaign in each Member State to advise on the optimum decision and timing for their country.

The CHMP opinion will now be forwarded to the European Commission, which will issue a final decision shortly.

Comirnaty is a vaccine for preventing COVID-19. It contains a molecule called messenger RNA (mRNA) with instructions for producing a protein, known as the spike protein, naturally present in SARS-CoV-2, the virus that causes COVID-19. The vaccine works by preparing the body to defend itself against SARS-CoV-2".

*****

A recent published letter to the editor in the New England Journal of Medicine described myocarditis incidence in Israelian adolescents. The risk estimates of myocarditis among male recipients in the 21 days after the first and second doses were 0.56 cases per 100,000 after the first dose and 8.09 cases per 100,000 after the second dose. The risk estimates among female recipients were 0 cases per 100,000 after the first dose and 0.69 cases per 100,000 after the second dose. The risk of myocarditis after receipt of the second vaccine dose among male adolescents 12 to 15 years of age was estimated to be 1 case per 12,361; the corresponding risk among female adolescents was estimated to be 1 case per 144,439 (Mevorach et al., 2022).

In a presentation by S Oliver (CDC) based on Israelian data, it is **suggested that rates of myocarditis after a third dose <u>are likely lower</u> than what is seen after the second dose** (slide 28, Oliver S., CDC). https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-01-05/06_covid_oliver_2022-01-05.pdf

Preliminary evidence from CDC of safety of an additional dose of Comirnaty® in adolescents of 16-17 years shows that most reported adverse events were not serious. Very rare cases of mild myocarditis were reported in lower rates than what was observed after dose 2 (ECDC, 08/02/2022). However, the risk of myocarditis in adolescents after a third dose still needs to be fully characterized.

EMA-approved vaccines are safe and effective and have saved, are saving and will save lives.

Data on the safety of booster vaccinations for children are limited at this time but, according to the EMA “no new safety concerns were identified from the data available for a booster in this age group” (EMA, 24/02/2022).

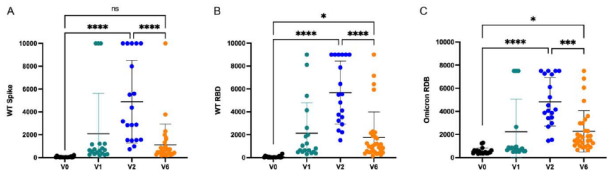
The risk of myocarditis in adolescents after a third dose still needs to be fully characterized.

5 Waning effectiveness of vaccination against COVID-19 for children and adolescents aged 12-17 years

A recent preprint study suggests that, compared to those who are unvaccinated, adolescents aged 12 to 16 who received two doses of Comirnaty® vaccine have a lower risk of contracting SARS-CoV-2 infection, as detected by PCR, and a lower risk of symptomatic infection. However, like adults, vaccine-induced protection against both SARS-CoV-2 infection and symptomatic infection wanes with time, starting three months after inoculation and continuing for more than five months (Prunas et al., 2022).

Burns et al. show that as seen in adult populations, mRNA vaccine-induced immunity wanes over a 6-month time period in adolescent children to near pre-vaccination levels. This finding demonstrates a vulnerability for infection in adolescent children ages 12-15 years, many of whom have now received their vaccine series over six months ago (Burns et al., 2022, figure below).

Figure 1: Adolescent anti-SARS-CoV-2 antibody responses over time. Humoral responses to a) Wildtype (WT) Spike b) WT Receptor Binding Domain (RBD), and c) Omicron RBD are quantified prior to vaccination, 2-3 weeks following the first vaccine dose, 2-4 weeks following the second mRNA vaccine dose, and 6 months following the second mRNA vaccine dose. Displayed as international units. Analysis by ANOVA. ns = not significant, * P < 0.05, *** P < 0.001, **** P < 0.0001

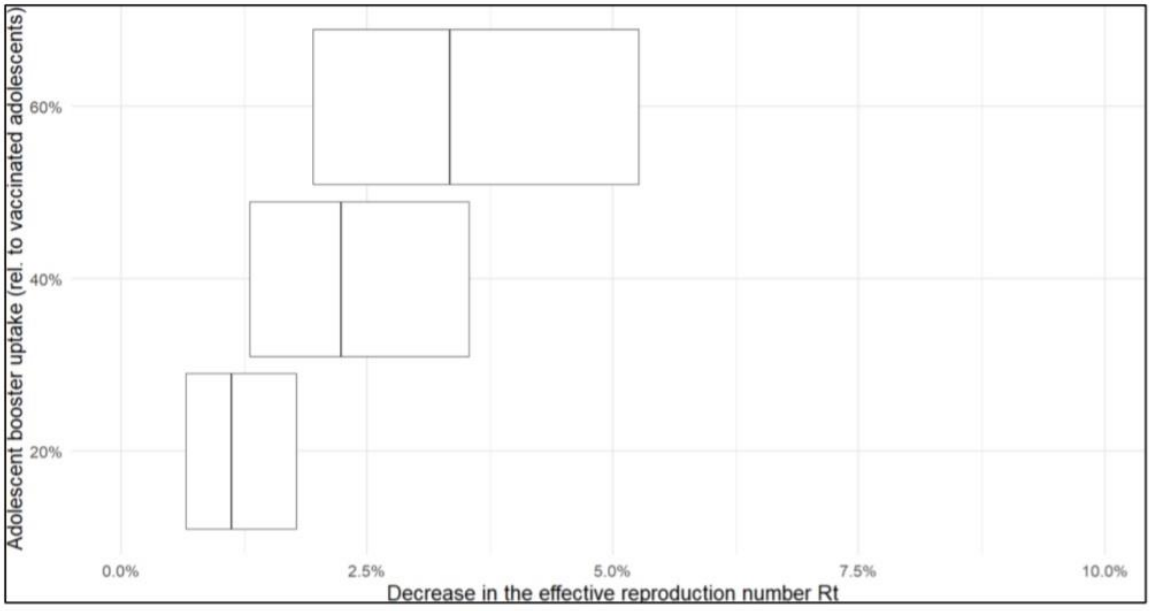


Preliminary studies show waning of effectiveness of COVID-19 vaccination after the second dose as previously also observed in the adult population.

6 EU/Belgian statistical models (ECDC, 08/02/2022; SIMID, 08/02/2022)

Mathematical modelling suggests that the administration of a booster dose against COVID-19 to adolescents aged 12-17 years results in a small reduction (1-3%) of the effective reproduction number (R(t)) in the whole population, varying according to the level of uptake of booster doses among adolescents. When considering the possibility of administering a booster dose to adolescents who completed the primary course, data on the benefit-risk of a booster dose in this age group should be carefully reviewed as they become available. Additionally, consideration should be given to the epidemiological situation, the national priorities and objectives of the COVID-19 vaccination campaign, the status of the rollout of the COVID-19 vaccine and of additional doses in priority groups and in the general population, as well as vaccine equity and supply (ECDC, 08/02/2022).

Figure 3. The expected impact of providing booster doses to adolescents on the SARS-CoV-2 transmission at population level, quantified by the relative decrease of the effective reproduction number R_t, for a high, medium, and low uptake of booster doses in the group of adolescents



The vertical bars correspond to the respective median estimate, and the boxes cover the 95% Confidence Interval (CI).

In Belgium, the latest update from the Simulation Models of Infectious Diseases (SIMID) is available at:
https://covid-en-wetenschap.github.io/assets/20220208_technical_note_SIMID.pdf.

In this model, the authors conservatively assumed that no more boosters would be given to teenagers than were already given at that time. According to this modelling, additional boosters would have a positive effect in reducing the burden of disease in the population and a faster relief of care and school populations. However, the simulations do not predict that, with the current variant, the boosters of teenagers make a difference to a possible new disruption of the healthcare system.

The SHC concludes that booster vaccination of healthy adolescents in the current context of Omicron does not provide, at this time, any significant indirect health gains for the society.

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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 February 17 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 March 01 2022. The NITAG meeting was chaired by **Yves VAN LAETHEM** and co-chaired by **Anne TILMANNE and Petra SCHELSTRAETE** for the topic booster dose for adolescents; the scientific secretariat were Fabrice PETERS, Veerle MERTENS, Muriel BALTES and Jean-Jacques DUBOIS.

BLUMENTAL Sophie	Pediatric Infectious Disease	HUDERF
BOIY Tine	Pediatrics, Infectiology	UZA
BRASSEUR Daniel	Pediatrics	CEPI
CALLENS Steven	Infectiology, Internal medicine	UZ Gent
CARILLO SANTISTEVE Paloma	General medicine, vaccination	ONE
CHATZIS Olga	Pediatrics, Vaccinology	UCL
CORNELISSEN Laura	Epidemiology, Obstetrics, Gynaecology	Sciensano
DAELEMANS Siel	Paediatric Pulmonology and Infectious Diseases	UZ Brussel
DE LOOF Geert	General medicine	BCFI
DOGNE Jean- Michel	Pharmacovigilance	UNamur, EMA
FRERE Julie	Pediatrics, Infectiology	Citadelle Liège
LEROUX-ROELS Isabelle	Vaccinology	UGent
MALFROOT Anne	Pediatrics, Infectiology	UZ Brussel
MICHIELS Barbara	General medicine	UAntwerpen
PELEMAN Renaat	Infectiology, Vaccinology	UZ Gent
ROBERFROID Dominique	Epidemiology	KCE, UNamur
ROSSI Camelia	Infectiology, Internal medicine	CHU Ambroise Paré
SCHELSTRAETE Petra	Pediatrics, Pneumology, Vaccinology	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 DER LINDEN Dimitri	Pediatrics, Infectiology	UCLouvain
VAN DAMME Pierre	Epidemiology, Vaccinology	UAntwerpen

VAN LAETHEM Yves	Infectiology, Vaccinology, Travel medicine, HIV	CHU Saint-Pierre, ULB
VERHAEGEN JAN	Microbiology, Bacteriology	UZLeuven

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

MALI Stéphanie	AFMPS-FAGG
DAEMS Joël	INAMI-RIZIV
MENDEZ Murielle	Kaleido
THEETEN Heidi	Agentschap Zorg en Gezondheid
TOP Geert	Agentschap Zorg en Gezondheid
VANDEN DRIESSCHE Koen	UZA
WUILLAUME Françoise	AFMPS-FAGG

VII APPENDIXES

Appendix 1: emergency letter - Booster vaccination against COVID-19 for children and adolescents aged 12-17 years. DEADLINE: 28 January 2022

Superior Health Council

YOUR LETTER DATED Mail January 26, 2022 (evening)
YOUR REF.

OUR REF. SHC 9693
DATE 28/01/2022

ENCLOSURE(S) -

Ter attentie van de Ministers van de IMC Volksgezondheid

A l'attention des Ministres de la CIM Santé Publique

SUBJECT : URGENT REQUEST - Booster vaccination against COVID-19 for children and adolescents aged 12-17 years
DEADLINE: 28 January 2022

The Superior Health Council (SHC) received on Wednesday January 26 (evening) an urgent request for advice from the Belgian Interministerial Conference on Public Health on the need of a booster dose of COVID-19 vaccination for children and adolescents aged 12-17 years.
In Belgium, booster doses are already recommended for the general Belgian population since December 2021 for all persons over 18 years of age (SHC 9683, 2021) and recently also for all immunocompromised patients over 12 years of age (SHC 9691, 2022).

CURRENT POSITION OF THE SHC

At this time and stage of knowledge, the scientific evidences supporting the administration of a booster dose of COVID-19 vaccination for children and adolescents aged 12-17 years, especially in the context of Omicron, are insufficient for the SHC to support it with a sufficient level of evidence for the usefulness, effectiveness, need and safety in terms of public health.
As already discussed at the NITAG meeting of January 20 2022 and confirmed by the Board of the SHC on January 27 2022, the SHC decided to wait for the EMA recommendation and for more scientific evidence before giving an opinion. More information could be collected on COVID-19 booster vaccination of adolescents from 12 years of age at the international NITAG webinar on the subject which will take place on February, 4.
The SHC recommends that the Belgian Authorities strongly advocate for standardization of the rules relating to CSTs and the obligation to vaccinate against COVID-19 at European Union and global level. Pending this hypothetical standardization of the rules, the SHC proposes that the FAMHP-EMA and the Belgian Vaccination Task Force take responsibility (at the safety level) for making the booster doses available (or not). And this, for all people (children - teenagers - adults) who must or wish to travel in Europe and around the world for family, friendship, leisure and/or professional reasons. The latter must be duly informed that there is no EMA approval yet.

Prof. Jean Nève.
President of the Superior Health Council

Dr. Yves Van Laethem,
President of the NITAG.

Superior Health Council
Place Victor Horta 40/10 • 1060 Brussels • www.shc-belgium.be

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.fgov.be.

www.css-hgr.be

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