Superior
Health Council

VACCINATION AGAINST COVID-19 WITH MRNA VACCINES FOR CHILDREN FROM 6 MONTHS OF AGE IN BELGIUM

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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. 9722

Vaccination against COVID-19 with mRNA vaccines for children from 6 months of age in Belgium

In this scientific advisory report, which offers guidance to public health policy-makers, the Belgian Superior Health Council provides recommendations of mRNA COVID-19 vaccination for infants and children (preschool - 6 months to 5 years old) in Belgium.

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

Approval of this full version of the advisory report by the NITAG on 20/10/2022
This version was validated by the Board on 09/11/2022[1].

I INTRODUCTION AND SCOPE

On 17 June 2022, the Food and Drug Administration (FDA) announced the emergency use authorization of the Moderna and Pfizer-BioNTech's Coronavirus disease 2019 (COVID-19) vaccine for the prevention of COVID-19 to include use in children down to six months of age. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-and-pfizer-biontech-covid-19-vaccines-children

On 19 June 2022, the Centers for Disease Control and Prevention (CDC) recommend COVID-19 vaccines for everyone 6 months and older (*scope of this advisory report*) and boosters for everyone 5 years and older, if eligible.
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/children-teens.html

At this moment, boosters are not recommended in Belgium for children and adolescents in good health and ≥ 5 years (SHC 9721, July 2022 ; SHC 9680, December 2021).

On 19 October 2022 European Medicines Agency (EMA) recommends approval of Comirnaty and Spikevax COVID-19 vaccines (mRNA vaccines) for children from 6 months of age.
https://www.ema.europa.eu/en/news/ema-recommends-approval-comirnaty-spikevax-covid-19-vaccines-children-6-months-age

This advisory report of the Superior Health Council (SHC) will be transferred to the Task Force 'Operationalisation vaccination strategy COVID-19' and the Interministerial Public Health Conference (IMC) to take political decisions and operationalising in Belgium.

[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 METHODOLOGY

After analysing the request, the Board and the Chair of the National Immunization Technical Advisory Group (NITAG) identified the necessary fields of expertise. The request was treated by the NITAG which included experts in vaccinology, geriatrics, general medicine, pediatrics, microbiology, infectiology and epidemiology. 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) competent in this field, as well as on the opinion of the experts.

Sciensano provided a report on the Belgian epidemiological data for children.

Simulation Models of Infectious Diseases consortium (SIMID) provided regular updates on modelling data for 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**
Coronavirus	Coronavirus	Coronavirus	Coronavirus
COVID-19	COVID-19	COVID-19	COVID-19
Vaccination	Vaccinatie	Vaccination	Impfung
Comorbidity	Comorbiditeit	Comorbidité	Komorbidität
Prevention	Preventie	Prévention	Prävention
Infant	Zuigeling	Nourrisson	Kleinkind
Child	Kind	Enfant	Kind

List of abbreviations used

CDC	Centers for Disease Control and Prevention - USA
CGD	Chronic Granulomatous Disease
CHMP	Human medicines committee – EMA - EU
CI	Confidence Interval
CID	Combined immunodeficiency
COVID-19	Coronavirus disease 2019
ECDC	European Centre for Disease Prevention and Control - EU
EMA	European Medicines Agency - EU
FDA	Food and Drug Administration - US
FMF	Familial Mediterranean Fever
HLH	Hemophagocytic Lymphohistiocytosis
ICU	Intensive Care Unit
IMC	Interministerial Conference on Public Health - BE
IQR	Interquartile range
IR / IRR	incidence rate / incidence rate ratio (in epidemiology)
MIS-C	Multisystem inflammatory syndrome in children
mRNA	Messenger ribonucleic acid
NITAG	National Immunization Technical Advisory Group
NPI	Non-Pharmaceutical Interventions
ONS	Office for National Statistics - UK
PDCO	Paediatric Committee – EMA - EU
PID	Primary immune deficiency
PIP	Paediatric Investigation Plan
PR	Positivity Rate
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SHC	Superior Health Council
SIMID	Simulation Models of Infectious Diseases consortium
VE	Vaccine Effectiveness
VOC	Variants Of Concern

III SUMMARY AND RECOMMENDATIONS

1 SUMMARY

- In Belgium:
  - Children aged between 0-4 years represented a total of **max 3% of the total number of COVID-19 cases.** The highest proportion was found during the fourth, 'delta'-wave from 06/2021 to 01/2022.
  - During the 5th (start the 27th of December 2021, Omicron BA.1 dominant) and 6th waves (start the 28th February 2022, Omicron BA.2 dominant), a total of **1,631 children aged 0 to 4 years** old were hospitalized because of COVID-19. **Median length of stay was 2 days** (interquartile range of 1-3 days). The large majority does not present comorbidities (97.2%). For those who had **one or more comorbidities, the main comorbidity group was cardiovascular diseases, followed by immunodeficiency disorders and renal disease.** It is also important to note that a large proportion of these cases were very young infants (0 to 3-4 months) who are not currently eligible for COVID-19 vaccination and are out of scope of this scientific advisory report.
  - Since the beginning of the pandemic until now, mortality due to COVID-19 in children is very rare, although it does unfortunately occur. Overall <5 deaths[2] have occurred among children aged 6 months to 4 years old due to COVID-19. All deaths occurred between the 1st wave (1st of March 2020 – 21st of June 2020) and the 3rd one (15th of February 2021 – 27th of June 2021) and concerned children with severe comorbidities.

- There is an overall **decreased risk of hospitalisation during the Omicron-period** compared to Alpha in unvaccinated children < 18 years.

- The risk of multisystem inflammatory syndrome in children (MIS-C) is **higher in the older age group of 5-11 years old** than in the other age groups.

- According to international data vaccination has been shown to reduce the risk of MIS-C, especially in the Delta context but also during Omicron.

- International data show a drastic **reduction in MIS-C risk** and in clinical severity in case of MIS-C **during Omicron**.

- ECDC (14 June 2022):
  - For children, the risk of infection and severe disease from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) **is low**. There is, however, an increased risk of severe disease in children with comorbidities. Vaccination is of particular importance for children at higher risk of severe disease. The implementation of multi-layered mitigation measures in schools, particularly during periods of high community transmission, is important to ensure the safe operation of schools and limit transmission in children.
  - Most recent available data from peer-reviewed studies and systematic reviews are from before the widespread circulation of the Delta and Omicron variants of concern (VOCs). Therefore, there is uncertainty if the conclusions drawn from these data can be extrapolated to future waves/VOCs.

[2] In order to best protect the privacy of the relatives and families of these deceased children, the exact number is not given in this public report. All deaths in very young children have nevertheless received special attention from Sciensano's surveillance teams in order to establish the causal link with COVID-19 but also to best ensure anonymity.

- In the context of Omicron and currently circulating variants, scarce studies exist on the effect on transmission when vaccinating young children.

- Vaccine effectiveness (VE) estimates are consistent with VE estimates in adults during the time of the Omicron surge.

- The safety profile was consistent with the safety and reactogenicity profile of the formulations used in older age groups.

- For the wave expected in autumn 2022, results of a recently published stochastic dynamic transmission model by the Simulation Models of Infectious Diseases (SIMID) consortium, showed that a booster vaccine campaign with an Omicron dedicated booster and coverage of at least 50% of the oldest population (65 years and older) with already one booster shows a substantial impact on hospital admission with COVID-19. **The incremental impact of vaccinating younger age groups on hospital admissions in the general population seems limited.**

- Pediatric vaccines **are not yet adapted to Omicron**.

2 RECOMMENDATIONS

Based on the summary/conclusions mentioned before and the current circulation of the Omicron variant, the following recommendations are made by the SHC:

1. The SHC recommends primary vaccination of children aged 6 months to 5 years old in those at risk of developing severe COVID-19

- **The SHC emphasizes that priority always has to be given to vaccines from the basic vaccination schedule AND vaccination against seasonal influenza for children at risk.**

- COVID-19 vaccination may be carried out simultaneously (SHC 9675, 2021) or at any interval, but it is important to emphasize that, when vaccinating infants and children, priority is always given to vaccines from the basic vaccination schedule.

- The SHC has already recommended primary vaccination of children with comorbidities and immunosuppression (SHC 9618, 05/02/2021 ; SHC 9691, 03/03/2022) based on an "off label use" and after an individual evaluation of the benefit/risk balance.

Children at risk to be vaccinated against COVID-19

- **Immunocompromised patients**
  - Immunosuppressive treatment in transplant or auto-immune disease, haemato-oncological disease treatment;
  - Some primary immunodeficiencies (PID):
    - **PID with severe combined immune disorder** ((S)CID or severe lymphopenia (CD4 T cell count < 200));
    - **PID AND severe lung disease;**
    - **PID patients who will receive or have received stem cell transplant or gene therapy** < 1 year ago or longer if additional treatment is required;
    - **Other PID namely chronic granulomatous disease (CGD), familial haemophagocytic lymphohistiocytosis (HLH), congenital autoinflammatory diseases (except familial Mediterranean fever FMF), PID and active* immune dysregulation (LRBA, NFKB1, NFKB2, STAT3 GOF, IRAK4, MyD88, STAT2, etc.);**

***** autoimmune or autoinflammatory optic surge during the past year or recently started immunosuppressive medication

    - **Other serious PID conditions for which the patient himself was contacted by the treating physician for COVID vaccination.**

- **Severe chronic diseases** (including rare diseases) affecting renal, gastro intestinal, cardiovascular, respiratory or neurological health;

2. Based on the available scientific data and conclusions , primary vaccination against COVID-19 of children aged 6 months to 5 years in good health is not recommended by the SHC

- COVID-19 vaccination may be carried out simultaneously (SHC 9675, 2021) or at any interval, but it is important to emphasize that, when vaccinating infants and children, **priority is always given to vaccines from the basic vaccination schedule**.

- Access to areas of public life for children **should not be restricted** depending on their vaccination status.

- Primary vaccination against COVID-19 of children aged 6 months to 5 years in good health could be done on an individual basis with consent of the parents or legal representatives. Clear and adapted information on the expected personal and societal benefits of vaccinating young children should be offered to his/her parents or legal representative before accepting the vaccine.

- **Primary vaccination against COVID-19 children in good health should not be the subject of a pro-active mass vaccination campaign organized by the Belgian authorities**.

Remarks: The role that very young children play in transmission within households remains difficult to estimate because of their high prevalence of asymptomatic infection and the changing transmissibility of new variants (Cheng et al., 2022). In the context of Omicron and variants currently in circulation there are no studies on the effect of vaccination young children on transmission. Vaccination was associated with a smaller reduction in transmission of the Delta variant than of the Alpha variant, and the effects of vaccination decreased over time (Eyre et al., 2022). ***In the context of Omicron and variants currently in circulation, there are scarce studies on the effect of vaccinating young children on transmission****.*

As the vaccine-induced protection in some immunocompromised persons is low, cocoon vaccination of healthy children in close contact with the person at risk **could be an option on an individual level based and on a risk/benefit analysis by the treating physician**.

However, the SHC reiterates that whilst vaccination does protect against infection, in the context of Omicron this protection declines rapidly over time. The impact on transmission is low, therefore, cocoon vaccination strategy complements but does not replace non-pharmaceutical interventions (NPIs) for people at risk of severe disease.

At the public health point of view and in the general context of the COVID-19 pandemic, the SHC would like to remind that reinforcement of primary Covid-19 vaccination for the general healthy adult population (18+) is still important, **mostly above 50 years old**.

3. Vaccination schedule against COVID-19 with mRNA vaccines for children from 6 months of age in Belgium (EMA, 19/10/2022)

EMA's human medicines committee (CHMP) has recommended extending the use of Comirnaty and Spikevax targeting the original strain of SARS-CoV-2.

The Committee recommended including the use in children aged 6 months to 4 years for Comirnaty® and use in children aged 6 months to 5 years for Spikevax®. Comirnaty and Spikevax are already approved in both adults and children aged from 5 and 6 years, respectively. Compared to the doses for already authorized age groups, the doses of both vaccines in these new younger age groups will be lower.

In children from 6 months to 4 years of age, Comirnaty® can be given as primary vaccination consisting of three doses (of 3 micrograms each); the first two doses are given three weeks apart, followed by a third dose given at least 8 weeks after the second dose.

In children from 6 months to 5 years of age, Spikevax® can be given as primary vaccination consisting of two doses (of 25 micrograms each), four weeks apart.

For children within these age groups, both vaccines are given as injections in the muscles of the upper arm or the thigh.

Primary vaccination schedule against COVID-19 with mRNA vaccines (pediatrics formulations not yet adapted to Omicron) for infants and children from 6 months of age

mRNA vaccines	**doses**	**Intervals**
Spikevax® (25 µg/dose) 6 month to 5 years	2 Option : additional dose IC (FDA)*	1 month between 1 and 2 1 month between 2 and 3
Comirnaty® (3 µg/dose) 6 month to 4 years	3	3 weeks between 1 and 2 2 months between 2 and 3

* Option : additional dose of Spikevax® vaccine for IC patients (FDA)

At this time, EMA **does not recommend** an additional dose of Spikevax® vaccine (25 µg/dose) in **immunocompromised patients** from 6 month to 5 years old. But an additional dose of Spikevax® vaccine **may be given** to people aged 6 years and older with a severely weakened immune system, at least 28 days after their second dose. Since 12/10/2022, **FDA recommends a third primary series dose** of Spikevax® vaccine for individuals 6 months of age and older who have been determined to have certain kinds of immunocompromise.

Considering this difference of opinion between the FDA and the EMA and considering that we will not have more scientific evidence in the coming months, the Council considers that the administration of an additional dose of Spikevax® vaccine, 1 month after the second dose, to people aged 6 month to 5 years old with a severely weakened immune system **may be an option**.

As an off label use of the vaccine, this option **should be applied on an individual level based and on a risk/benefit analysis by the treating physician for some patients with a severely weakened immune system** as defined in section 1.

More information from FDA

The Moderna COVID-19 Vaccine is a suspension for intramuscular injection.
https://www.fda.gov/media/159307/download
https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccines

The Pfizer-BioNTech COVID-19 Vaccine is a suspension for intramuscular injection.
https://www.fda.gov/media/159312/download
https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccines

IV ELABORATION AND ARGUMENTATION

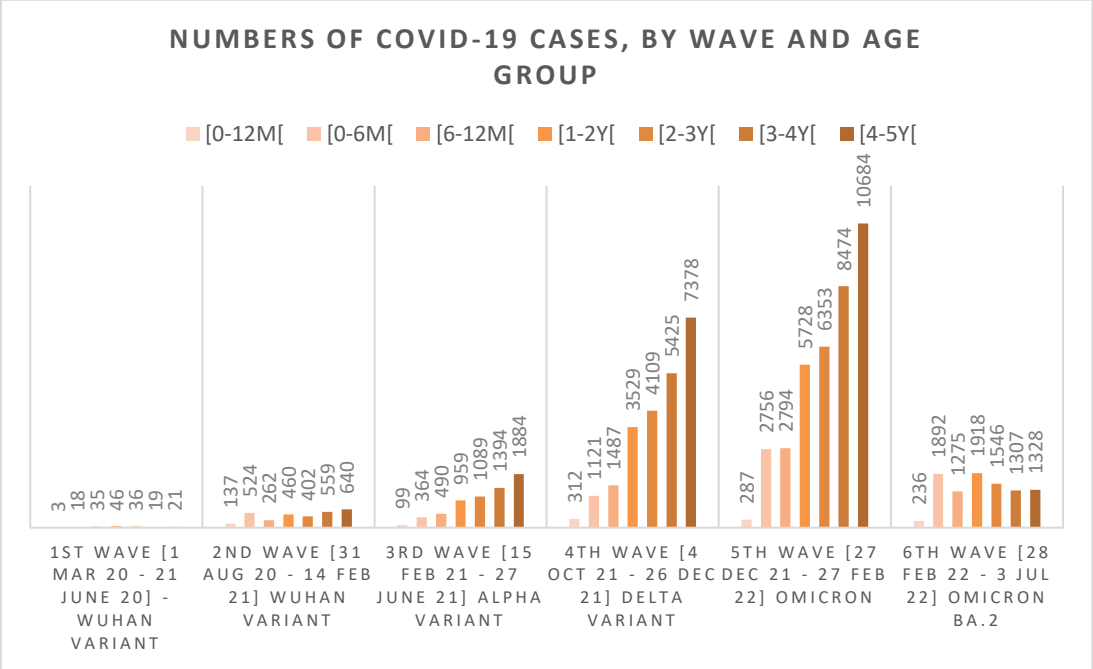
1 COVID-19 among children aged 6 months to 5 years old

1.1 Belgian epidemiology (Sciensano, preliminary report September 2022)

1.1.1 Numbers of infections

Since the beginning of the pandemic (week 9 of 2020) and until the 26th week of 2022, 82,820 COVID-19 infections occurred among children aged 6 months to 4 years-old.

The graph below shows the number of cases, by age group and by COVID-19 wave. The [0-12M[[3] category refers to children for whom the date of birth is unavailable but who are registered by the laboratory (and as such, age at testing is entered by the lab). The dates defining the waves of the COVID-19 pandemic are those determined and used within Sciensano.



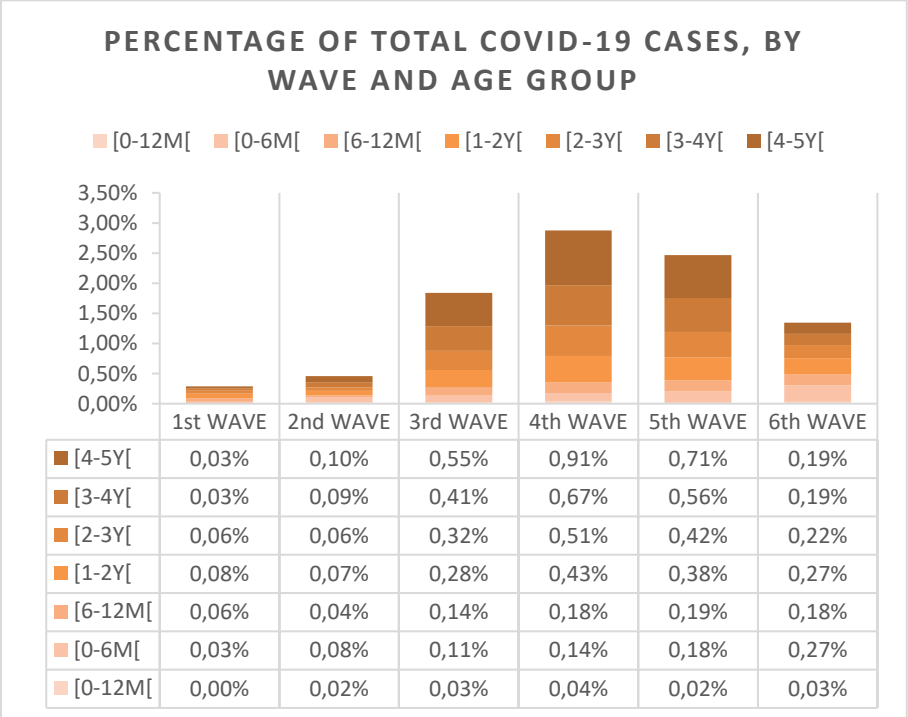
The table below shows the number of tests performed as well as the positivity rate, by age group and by COVID-19 wave, for children aged 0-4 years old. **While the positivity rate was low in the first three waves, it became higher in more recent waves (in particular during the 5th wave (Omicron), ranging from 20-41%).** This increase in positivity rate was visible in all age groups due to the higher circulation of the virus, however it was more pronounced in the younger age groups.

[3] [0-12m[indicates that the group includes children <1 year / [0-12m] would mean children <= 1 year

	1ST WAVE [1 MAR 20 - 21 JUNE 20]		2ND WAVE [31 AUG 20 - 14 FEB 21]		3RD WAVE [15 FEB 21 - 27 JUNE 21]		4TH WAVE [4 OCT 21 - 26 DEC 21]		5TH WAVE [27 DEC 21 - 27 FEB 22]		6TH WAVE [28 FEB 22 – 3 JUL 22]	
	TESTS	P.R	TESTS	P.R	TESTS	P.R	TESTS	P.R	TESTS	P.R	TESTS	P.R
[4-5Y[	3606	0,6%	16878	3,8%	40948	4,6%	48139	15,3%	26190	40,8%	10979	12,1%
[3-4Y[	4186	0,5%	16578	3,4%	41903	3,3%	44326	12,2%	24454	34,7%	12428	10,5%
[2-3Y[	5347	0,7%	14171	2,8%	34133	3,2%	37253	11,0%	22359	28,4%	13626	11,3%
[1-2Y[	8068	0,6%	17502	2,6%	32744	2,9%	35049	10,1%	23411	24,5%	16221	11,8%
[6-12M[	4375	0,8%	8898	2,9%	15653	3,1%	15543	9,6%	11849	23,6%	11404	11,2%
[0-6M[	2245	0,8%	8499	6,2%	12699	2,9%	11510	9,7%	9731	28,3%	12031	15,7%
[0-12M[	458	0,7%	2196	6,2%	2651	3,7%	2755	11,3%	1407	20,4%	1776	13,3%

P.R. = Positivity Rate

The graph below presents the contribution of 0-4 year olds to all COVID-19 cases, by age group and wave. The proportion of small children was very low during the first two waves. Mainly hospitalised people were tested then due to limited testing capacity at the beginning of the pandemic; as a result, testing among young children was very limited. **The highest proportion was found during the 4th (Delta) wave, although the contribution was still lower than 3%.**



	1st WAVE	2nd WAVE	3rd WAVE	4th WAVE	5th WAVE	6th WAVE
[4-5Y[	0,03%	0,10%	0,55%	0,91%	0,71%	0,19%
[3-4Y[	0,03%	0,09%	0,41%	0,67%	0,56%	0,19%
[2-3Y[	0,06%	0,06%	0,32%	0,51%	0,42%	0,22%
[1-2Y[	0,08%	0,07%	0,28%	0,43%	0,38%	0,27%
[6-12M[	0,06%	0,04%	0,14%	0,18%	0,19%	0,18%
[0-6M[	0,03%	0,08%	0,11%	0,14%	0,18%	0,27%
[0-12M[	0,00%	0,02%	0,03%	0,04%	0,02%	0,03%

1.1.2 Numbers of hospitalizations and ICU admissions

Hospitalisation data is derived from the Clinical Hospital Survey, a **non-exhaustive** surveillance system which collects clinical data on patient level and allows the requested distinction by age groups. The difference between the 2 tables below lies in the definition of inclusion: the left table presents the profiles of patients admitted to the hospital **for** COVID-19 (symptomatic) and the table on the right includes profiles of hospitalised patients **for and with** COVID-19 ("*with COVID*" refers to asymptomatic patients identified by routine screening).

All patients admitted

During the 4th wave (from the 4th of October until the 26th of December 2021), there were 386 hospitalisations among children aged 0 to 4 years old (for those admitted **for** COVID), with a median length of stay of 2 days (IQR of 2-3 days). A large majority did not present with comorbidities (95,6%), but for those who had at least one, the highest proportion was found for cardiovascular diseases.

Within the 5th (start the 27th of December 2021) and 6th waves (from the 28th February 2022 until the 29th of May 2022), there were 1,631 hospitalisations for children aged 0 to 4 years old (for those admitted **for** COVID), with a median length of stay of 2 days (IQR of 1-3 days). The large majority did not present with comorbidities (97,2%). For those who had one or more comorbidities, the main comorbidity group was cardiovascular diseases, followed by immunodeficiency disorders and renal disease.

For the 7th wave (data included until the 31st of August 2022), there were 470 hospitalisations among children aged 0 to 4 years old (for those admitted **for** COVID), with a median length of stay of 2 days (IQR of 1-3 days). As for the previous waves, the large majority did not present with a comorbidity (97,7%). For those who had at least one, the highest proportion was for renal disease.

For all 3 periods, the median length of stay was low (only 2 days), which implies that children aged 0-4 years were generally kept under observation after admission to the hospital, rather than being admitted because of a severe clinical course.

	0-4			0-4		
	4th wave (N=386)	5th and 6th wave (N=1631)	7th wave (N=470)	4th wave (N=523)	5th and 6th wave (N=2093)	7th wave (N=566)
Age						
Median [Q1, Q3]	0 [0, 1.00]	0 [0, 1.00]	0 [0, 0]	0 [0, 1.50]	0 [0, 1.00]	0 [0, 1.00]
Gender						
Femme	160 (41.5%)	719 (44.1%)	206 (43.8%)	223 (42.6%)	911 (43.5%)	259 (45.8%)
Homme	224 (58.0%)	905 (55.5%)	252 (53.6%)	298 (57.0%)	1172 (56.0%)	295 (52.1%)
Autre	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vaccination status						
Not vaccinated	353 (91.5%)	1520 (93.2%)	438 (93.2%)	475 (90.8%)	1941 (92.7%)	530 (93.6%)
Partially vaccinated	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fully vaccinated	2.00 (0.5%)	1.00 (0.1%)	1.00 (0.2%)	3.00 (0.6%)	1.00 (0.0%)	1.00 (0.2%)
Fully vaccinated + booster	1.00 (0.3%)	3.00 (0.2%)	0 (0%)	1.00 (0.2%)	4.00 (0.2%)	0 (0%)
Unknown	30.0 (7.8%)	107 (6.6%)	31.0 (6.6%)	44.0 (8.4%)	147 (7.0%)	35.0 (6.2%)
Number of comorbidities						
0	369 (95.6%)	1585 (97.2%)	459 (97.7%)	500 (95.6%)	2028 (96.9%)	553 (97.7%)
1	12.0 (3.1%)	31.0 (1.9%)	9.00 (1.9%)	17.0 (3.3%)	48.0 (2.3%)	11.0 (1.9%)
2	2.00 (0.5%)	8.00 (0.5%)	1.00 (0.2%)	2.00 (0.4%)	9.00 (0.4%)	1.00 (0.2%)
3	0 (0%)	1.00 (0.1%)	1.00 (0.2%)	1.00 (0.2%)	1.00 (0.0%)	1.00 (0.2%)
4+	3.00 (0.8%)	1.00 (0.1%)	0 (0%)	3.00 (0.6%)	1.00 (0.0%)	0 (0%)
Length of hospital stay (days)						
Median [Q1, Q3]	2.00 [2.00, 3.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	2.00 [2.00, 3.00]	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]

	0-4			0-4		
	4th wave (N=386)	5th and 6th wave (N=1631)	7th wave (N=470)	4th wave (N=523)	5th and 6th wave (N=2093)	7th wave (N=566)
Cardiovascular disease	10.0 (2.6%)	9.00 (0.6%)	2.00 (0.4%)	12.0 (2.3%)	12.0 (0.6%)	4.00 (0.7%)
Diabetes	1.00 (0.3%)	2.00 (0.1%)	1.00 (0.2%)	2.00 (0.4%)	2.00 (0.1%)	1.00 (0.2%)
Renal disease	3.00 (0.8%)	5.00 (0.3%)	5.00 (1.1%)	3.00 (0.6%)	6.00 (0.3%)	5.00 (0.9%)
Liver disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Immunodepressed	2.00 (0.5%)	7.00 (0.4%)	1.00 (0.2%)	3.00 (0.6%)	9.00 (0.4%)	1.00 (0.2%)
Hematological cancer	1.00 (0.3%)	3.00 (0.2%)	0 (0%)	1.00 (0.2%)	4.00 (0.2%)	0 (0%)
Transplant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nursing home resident	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Regarding data on Intensive Care Units (ICU) admissions for COVID-19, the following is available regarding patients admitted to the ICU **for and with** COVID-19 for admissions during the 4 waves described before:

- 11 children transferred to ICU during the 4th wave with a median length of stay of 12 days (interquartile range 5,5-16,5 days). The majority (8 out of 11) did not present with any comorbidity.

- 13 children transferred to ICU during the 5th and 6th waves with a median length of stay of 3 days (interquartile range 2-9 days). The majority (11 out of 13) did not present with any comorbidity.

Sciensano does not have access to reliable information on the number of MIS-C that occurred within this age group.

Patients with a length of stay longer than 2 days

For the 4th wave, there were 143 hospitalisations longer than 2 days among children aged 0 to 4 years old (for those admitted **for** COVID), which represent 37% of total hospital admissions for this age group during this wave, and the median length of stay is 3 days (Interquartile range - IQR of 3-4,5 days). 91,6% of children admitted did not present a comorbidity but for those who had at least one comorbidity, the highest proportion was found for cardiovascular disease.

Within the 5th and 6th waves, there were 499 hospitalisations longer than 2 days among young children of 0 to 4 years old (for those admitted **for** COVID), which represent 30,5% of total hospital admissions for this age group during these waves, and the median length of stay is 3 days (IQR of 3-5 days). The large majority do not present comorbidities (95,8%). For those who had one or more comorbidities, the main comorbidity group was immunodeficiency disorders and renal disease, followed by cardiovascular disease and haematological cancer.

During the 7th wave, there were 117 hospitalisations longer than 2 days among children aged 0 to 4 years old (for those admitted **for** COVID), which represent 24,9% of total hospital admissions for this age group during this wave, and the median length of stay is 3 days (IQR of 3-5 days). The large majority did not present with comorbidities (95,7%), but for those who had at least one comorbidity, the only one reported was renal disease.

	0-4			0-4		
	4th wave (N=143)	5th and 6th wave (N=499)	7th wave (N=117)	4th wave (N=205)	5th and 6th wave (N=674)	7th wave (N=138)
Age						
Median [Q1, Q3]	0 [0, 1.00]	0 [0, 1.00]	0 [0, 1.00]	0 [0, 2.00]	0 [0, 1.00]	0 [0, 1.00]
Gender						
Femme	61.0 (42.7%)	234 (46.9%)	50.0 (42.7%)	89.0 (43.4%)	309 (45.8%)	61.0 (44.2%)
Homme	82.0 (57.3%)	264 (52.9%)	64.0 (54.7%)	116 (56.6%)	364 (54.0%)	74.0 (53.6%)
Autre	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vaccination status						
Not vaccinated	131 (91.6%)	468 (93.8%)	111 (94.9%)	184 (89.8%)	625 (92.7%)	130 (94.2%)
Partially vaccinated	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fully vaccinated	0 (0%)	1.00 (0.2%)	0 (0%)	1.00 (0.5%)	1.00 (0.1%)	0 (0%)
Fully vaccinated + booster	1.00 (0.7%)	2.00 (0.4%)	0 (0%)	1.00 (0.5%)	3.00 (0.4%)	0 (0%)
Unknown	11.0 (7.7%)	28.0 (5.6%)	6.00 (5.1%)	19.0 (9.3%)	45.0 (6.7%)	8.00 (5.8%)
Number of comorbidities						
0	131 (91.6%)	478 (95.8%)	112 (95.7%)	188 (91.7%)	644 (95.5%)	131 (94.9%)
1	7.00 (4.9%)	15.0 (3.0%)	4.00 (3.4%)	11.0 (5.4%)	24.0 (3.6%)	6.00 (4.3%)
2	2.00 (1.4%)	4.00 (0.8%)	1.00 (0.9%)	2.00 (1.0%)	4.00 (0.6%)	1.00 (0.7%)
3	0 (0%)	0 (0%)	0 (0%)	1.00 (0.5%)	0 (0%)	0 (0%)
4+	3.00 (2.1%)	1.00 (0.2%)	0 (0%)	3.00 (1.5%)	1.00 (0.1%)	0 (0%)
Length of hospital stay (days)						
Median [Q1, Q3]	3.00 [3.00, 4.50]	3.00 [3.00, 5.00]	3.00 [3.00, 5.00]	3.00 [3.00, 5.00]	3.00 [3.00, 5.00]	3.00 [3.00, 5.00]

	0-4			0-4		
	4th wave (N=143)	5th and 6th wave (N=499)	7th wave (N=117)	4th wave (N=205)	5th and 6th wave (N=674)	7th wave (N=138)
Cardiovascular disease	7.00 (4.9%)	2.00 (0.4%)	0 (0%)	9.00 (4.4%)	3.00 (0.4%)	2.00 (1.4%)
Diabetes	1.00 (0.7%)	1.00 (0.2%)	0 (0%)	2.00 (1.0%)	1.00 (0.1%)	0 (0%)
Renal disease	3.00 (2.1%)	3.00 (0.6%)	3.00 (2.6%)	3.00 (1.5%)	4.00 (0.6%)	3.00 (2.2%)
Liver disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Immunodepressed	2.00 (1.4%)	3.00 (0.6%)	0 (0%)	3.00 (1.5%)	4.00 (0.6%)	0 (0%)
Hematological cancer	1.00 (0.7%)	2.00 (0.4%)	0 (0%)	1.00 (0.5%)	3.00 (0.4%)	0 (0%)
Transplant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nursing home resident	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Children who stayed longer than 2 days in the hospital represent around a quarter to a third of the total admissions among children, and for the different waves, the median length of stay is 3 days (compared to 2 days for all children aged 0 to 4 years old). This implies that most admissions of children aged 0 to 4 years old in hospital also seem to be hospitalised for surveillance of symptoms rather than for severe outcomes caused by COVID-19 infections.

1.1.3 Numbers of deaths

Since the beginning of the pandemic and until now, less than 5 deaths have occurred among children aged 6 months to 4 years old; these events occurred between the 1st wave (1st of March 2020 – 21st of June 2020) and the 3rd one (15th of February 2021 – 27th of June 2021).

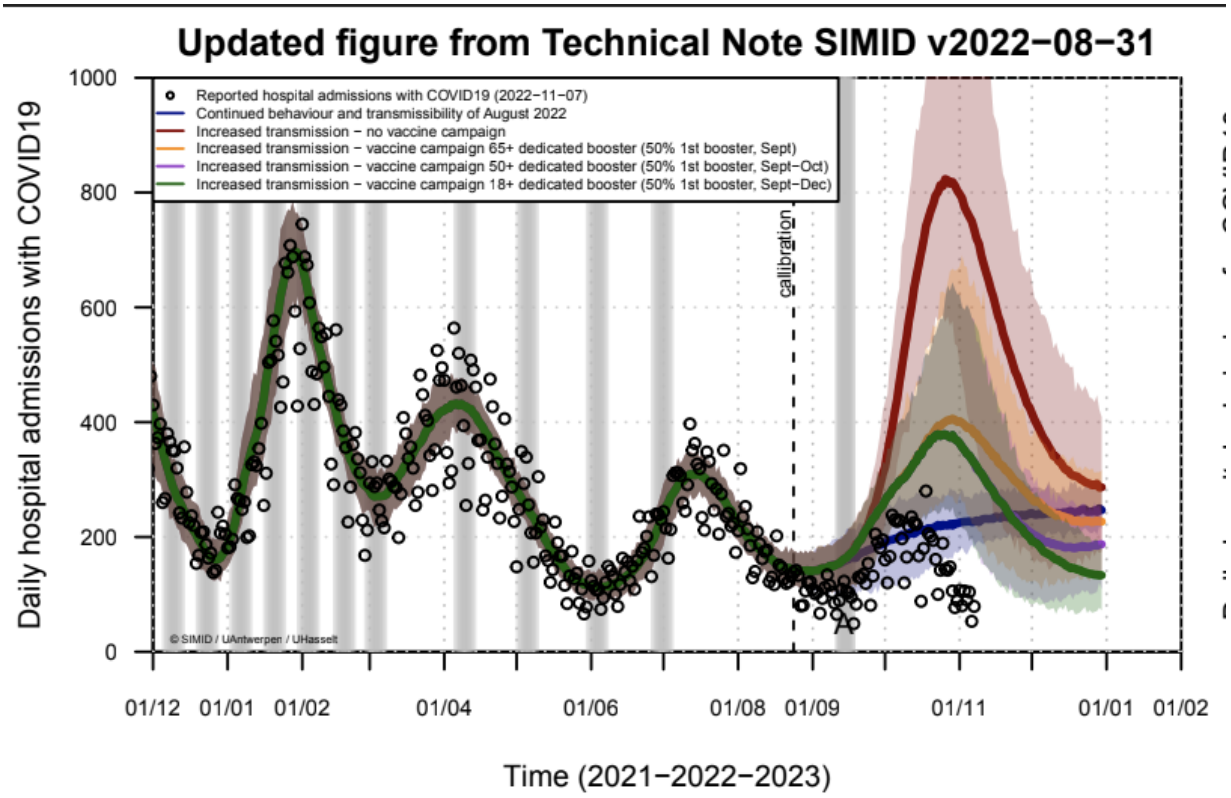
1.1.4 Data on Long-COVID from Belgium

Sciensano's COVIMPACT project on long-COVID-19 has received the approval of an ethical committee to collect self-reported health data on people aged 18 and over. To our knowledge, there are no research projects or data in Belgium on long-COVID in people under 18 years. In general, there is few research on long-COVID in children, and even less in children aged 5 years and under.

1.1.5 Model simulations on childhood and adult vaccination (by the SIMID)

On August 31 2022, the SIMID consortium published a new technical note (v2022-08-31) containing the estimates of a stochastic dynamic transmission model using observational data up to August 23, 2022:
http://www.simid.be/wp-content/uploads/2022/09/20220831_technical_note_SIMID.pdf

These scenario analysis shows a new wave in October-November 2022 as a result of resuming societal activities and seasonality. **However, a booster vaccine campaign with an Omicron dedicated booster and coverage of at least 50% of the oldest population (65 years and older) with already one booster shows a substantial impact on the size thereof**. More specifically, including vaccination in the scenario analysis results in a wave moderate in size, near the level of the latest Omicron wave in June. Projections with subsequent vaccination campaign targeting the 18 years and older population show the lowest hospital admission rates in December 2022. While we focus on hospital admissions, high infection rates could lead to significant absenteeism and pressure on primary care.



A booster vaccine campaign with an Omicron dedicated booster and coverage of at least 50% of the oldest population (65 years and older) with already one booster shows a substantial impact on hospital admission with COVID-19. The incremental value of vaccinating younger age groups seems limited.

1.2 International publications and data

1.2.1 Severe outcome of SARS-CoV-2 in children

Children often experience mild or asymptomatic COVID-19 (Bhopal et al., 2021). The risk of onset of severe disease resulting in hospitalisation or death is lower than in adults (Kortz et al., 2021). During the two-month period (3 August 2020 to 3 October 2021) of one study from 10 EU countries, there were approximately 117 hospitalisations (of which eight required ICU admission and respiratory support) for every 10,000 reported symptomatic pediatric cases (Bundle et al., 2021).

The majority of children hospitalised due to COVID-19 do not have comorbidities, but comorbidities increase the risk of severe disease, hospitalisation, and death in children (Bundle et al., 2021). Children made up an increasing proportion of hospitalisations as adult vaccination coverage increased (and thus rates of adult hospitalisations decreased). Also, child hospitalisations have increased during periods of high transmission. However, rates of hospitalisations of notified SARS-CoV-2 cases among children remain low (ECDC, 2021).

In persons < 18 years, Whitakker an collaborators (2022), found a decrease in risk of hospitalization in the Delta (aRR: 0.53, 95% CI: 0.30-0.93) and Omicron wave (aRR: 0.40, 95% CI: 0.24-0.68), compared to the Alpha wave.

Overall decreased risk of Omicron hospitalisation compared to Alpha in unvaccinated children < 18 years (Whittaker et al., 2022)

1.2.2 Multisystem inflammatory syndrome (MIS-C)

Multisystem inflammatory syndrome in children (MIS-C) is a condition in which different body parts can become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs.

A register-based cohort study including > 2 million children and adolescents >19 years in Sweden found increased risks for MIS-C in children with male sex, age 5-11 years, foreign-born parents, asthma, obesity, and life-limiting conditions (Rhedin et al., 2022).

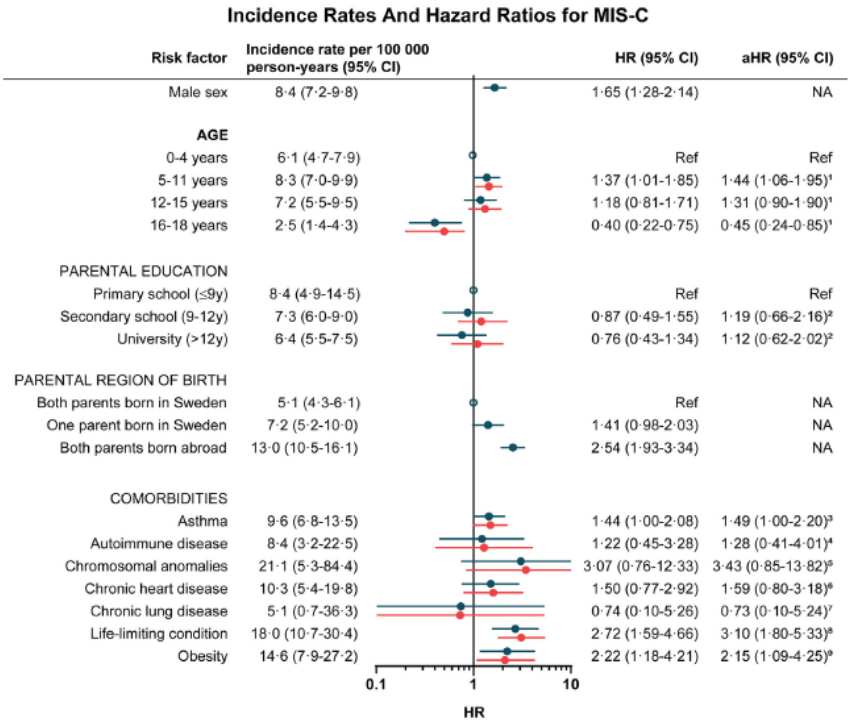


Figure 2. Risk factors for MIS-C in children. Crude (blue) and adjusted (red) hazard ratios for MIS-C. [1]Adjusted for parental education, parental region of birth. [2]Adjusted for parental region of birth, siblings. [3]Adjusted for age, sex, parental education, parental region of birth siblings, maternal smoking during pregnancy, chronic lung disease. [4]Adjusted for age, sex, parental education, parental region of birth, siblings, maternal smoking during pregnancy. [5]Adjusted for age, sex, parental education, parental region of birth, siblings, maternal smoking during pregnancy. [6]Adjusted for age, sex, parental education, parental region of birth, maternal smoking during pregnancy, chromosomal anomalies. [7]Adjusted for age, sex, parental education, parental region of birth, maternal smoking during pregnancy, asthma. [8]Adjusted for age, sex, parental education, parental region of birth, maternal smoking during pregnancy. [9]Adjusted for age, sex, parental education, parental region of birth, maternal smoking during pregnancy. Abbreviations: CI, confidence interval; HR, hazard ratio; MIS-C, multisystem inflammatory syndrome in children; NA, not applicable.

A study from the USA compared the odds of being fully vaccinated (two doses of BNT162b2 vaccine ≥28 days before hospital admission) between 304 MIS-C patients and 502 controls who tested negative for SARS-CoV-2. Children with MIS-C had a lower likelihood of being vaccinated (aOR, 0.16; 95% 13 CI, 0.10-0.26 - Zambrano et al., 2022).

Nygaard et al. estimated the VE against MIS-C was 94% (Delta context) in individuals aged 5-17 years (Nygaard et al., 2022).

In Israel, in persons younger than 18 years, a drastic reduction in MIS-C incidence was reported during the Omicron wave compared to the Alpha and Delta wave (Levy et al., 2022):

Table 2. Nationwide Data on the Incidence of MIS-C During the Alpha, Delta, and Omicron Waves in Israel

Pandemic wave data[a]	Alpha	Delta	Omicron	Total
MIS-C cases, No. (%)[b]	103 (40.5)	115 (45.3)	36 (14.2)	254
SARS-CoV-2 infections in persons younger than 18 y, No.[c]	188 800	233 585	946 779	1 369 164
MIS-C incidence rate[d]	54.5	49.2	3.8	
MIS-C incidence rate ratio (95% CI)[e]	14.34 (9.81-20.96)	12.94 (8.90-18.81)	1 [Reference]	

[a] Each wave was a 16-week period: Alpha, December 20, 2020, to April 10, 2021; Delta, July 18, 2021, to November 13, 2021; and Omicron, November 21, 2021, to March 12, 2022.

[b] Cases of multisystem inflammatory syndrome in children (MIS-C) were limited to patients aged 0 to 18 years.

[c] According to the Israel Ministry of Health SARS-CoV-2 data set.

[d] Incidence rates were calculated using number of cases as numerator, with number of SARS-CoV-2 pediatric infections as denominator, per 100 000.

[e] Incidence rate ratios use the rate of MIS-C cases in the Omicron wave as a referent group, with 95% CIs.

These results are confirmed in other studies (Cohen et al. 2022 ; Whittacker et al., 2022).

- Risk of MIS-C is highest for 5-11 year olds

- Drastic reduction in both the risk of MIS-C and the clinical severity of MIS-C with Omicron

- Vaccination has been shown to reduce the risk of MIS-C, especially in the Delta context, but also during Omicron

1.2.3 Long-COVID in children aged 6 months to 4 years old

Long-COVID in children is rare and mainly of short duration.

The impact and prevalence of post-COVID-19 condition (Long-COVID) in children in the EU is unclear due to the lack of high-quality pan-European studies and a clear case definition (Zimmermann et al., 2021). Several studies have reported post-COVID-19 condition in children (Zimmermann et al., 2021 ; ECDC 2022). Children who experience severe COVID-19 are more likely to experience long-term symptoms, and there may be an increased risk in children older than 10 years and those with certain underlying medical conditions (ECDC 2022).

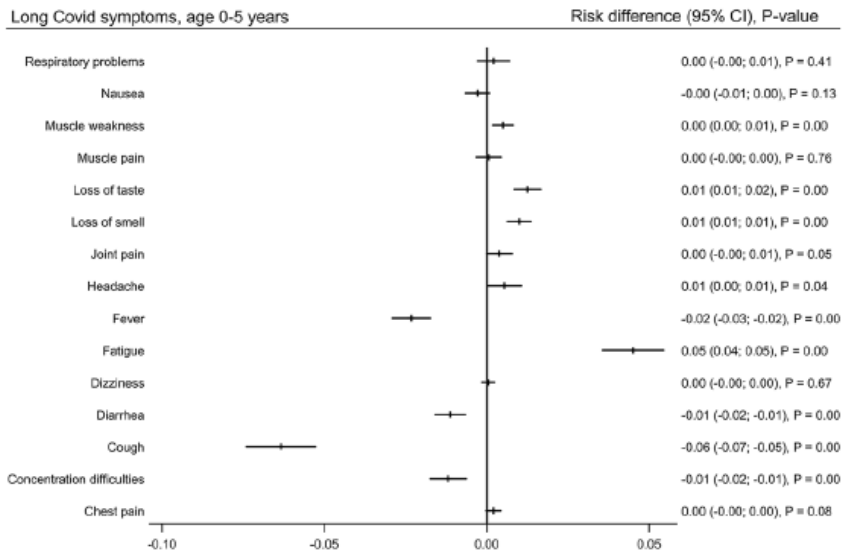
In June 2022, a systematic review and meta-analysis (Lopez-Leon et al., 2022) estimated the prevalence of long-COVID in children and adolescents (aged 0 to 18 years old) at 25.24%; where long-COVID was defined by the presence of one or more symptoms more than 4 weeks following a SARS-CoV-2 infection. The most prevalent clinical manifestations were: mood symptoms like sadness, tension, anxiety etc. (16.50%), fatigue (9.66%), sleep disorders (8.42%), headache (7.84%) and respiratory symptoms (7.62%). The review reported that, like adults, the pediatric population's risk factors associated with long-COVID are older age, female gender, severe COVID-19, overweight and obesity, and long-term comorbidities.

A report[4] by the Office for National Statistics (ONS) UK in April 2021 found that children aged 2-16 years were significantly less likely than adults to self-report symptoms of long-COVID-19. The same study estimated that among 2-16 year olds, 7.4% reported symptoms 3 months after infection. The ONS estimates were subsequently reviewed with a control group of children not infected with SARS-CoV-2. In September 2021, a new report[5] was published by the ONS. This report shows a lower proportion of long-COVID in children infected with SARS-CoV-2 (3.3%), and a similar proportion (3.6%) of long-COVID symptoms in the control group. This result shows that long-COVID symptoms are common to other diseases in children not infected with SARS-CoV-2 (as in adults), and that prevalence/proportion estimates for long-COVID should therefore be interpreted with caution. A study published in August 2021 (Molteni et al., 2021) found that 1.8% of SARS-CoV-2 infected children aged 5-17 years had at least one symptom of long-COVID 28 days after infection (study of a sample of 1,379 children in England).

A Danish cohort study evaluated symptoms and duration of 'long-COVID' in 37,522 children aged 0–17 years. According to this study, SARS-CoV-2 pre-school children (age 0-5 years) more often suffered from fatigue RD 0.05 (CI 0.04–0.06), loss of smell RD 0.01 (CI 0.01–0.01), loss of taste RD 0.01 (CI 0.01–0.02) and muscle weakness RD 0.01 (CI 0.0–0.01 - Figure below - Borch et al., 2022).

[4] https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/previousReleases
[5] https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/technicalarticleupdatedestimatesoftheprevalenceofpostacutesymptomsamongpeoplewithcoronaviruscovid19intheuk/26april2020to1august2021

Panel **B**



ECDC, 14 June 2022

For children, the risk of infection and severe disease from SARS-CoV-2 is low. There is, however, an increased risk of severe disease in children with comorbidities.

Vaccination is of particular importance for children at higher risk of severe disease. The implementation of multi-layered mitigation measures in schools, particularly during periods of high community transmission, is important to ensure the safe operation of schools and limit transmission in children.

Most currently available data in peer-reviewed studies and systematic reviews are from before the widespread circulation of the Delta and Omicron VOCs, limiting the certainty of the conclusions that can be drawn.

1.3 Potential impact of vaccinating young children on transmission of SARS-CoV-2

The role that very young children play in transmission within households remains difficult to estimate because of their high prevalence of asymptomatic infection and the changing transmissibility of new variants (Cheng et al., 2022).

In the context of Omicron and variants currently in circulation there are no studies on the effect of vaccination young children on transmission. Vaccination was associated with a smaller reduction in transmission of the Delta variant than of the Alpha variant, and the effects of vaccination decreased over time (Eyre et al., 2022).

A Swedish study found a protective association between preschool children at home and hospitalisation due to COVID-19 during the first and third waves compared with only older children or no children at all, with ORs (95% Cis) 0.63 (0.46 to 0.88) and 0.75 (0.68 to 0.94) respectively (Geijerstam et al., 2022).

In contrast, a large cohort study performed in the UK found the opposite: living with children of any age was associated with an increased risk of recorded SARS-CoV-2 infection (hazard ratio 1.06 (95% confidence interval - CI 1.05 to 1.08) for living with children aged 0-11 years; 1.22 (1.20 to 1.24) for living with children aged 12-18 years) and covid-19 related hospital admission (1.18 (1.06 to 1.31) for living with children aged 0-11; 1.26 (1.12 to 1.40) for living with children aged 12-18). In UK (wave 1 - 1 February to 31 August 2020), some evidence existed of increased risk of reported SARS-CoV-2 infection and covid-19 outcomes among adults living with children during wave 2 (1 September to 18 December 2020). However, this did not translate into a materially increased risk of covid-19 mortality, and absolute increases in risk were small (Forbes et al., 2022).

In the context of Omicron and variants currently in circulation, there are scarce studies on the effect of vaccinating young children on transmission.

1.4 Primary vaccination schedule against COVID-19 with mRNA vaccines (pediatrics formulations not yet adapted to Omicron) for infants and children from 6 months of age

1.4.1 EMA (19/10/2022) recommends approval of Comirnaty® and Spikevax® COVID-19 vaccines for children from 6 months of age.

https://www.ema.europa.eu/en/news/ema-recommends-approval-comirnaty-spikevax-covid-19-vaccines-children-6-months-age

EMA's CHMP has recommended extending the use of Comirnaty® and Spikevax® targeting the original strain of SARS-CoV-2. The Committee recommended including the use in children aged 6 months to 4 years for Comirnaty® and use in children aged 6 months to 5 years for Spikevax®. Comirnaty® and Spikevax® are already approved in both adults and children aged from 5 and 6 years, respectively.

Compared to the doses for already authorised age groups,1 the doses of both vaccines in these new younger age groups will be lower. In children from 6 months to 4 years of age, Comirnaty® can be given as primary vaccination consisting of three doses (of 3 micrograms each); the first two doses are given three weeks apart, followed by a third dose given at least 8 weeks after the second dose. In children from 6 months to 5 years of age, Spikevax® can be given as primary vaccination consisting of two doses (of 25 micrograms each), four weeks apart. For children within these age groups, both vaccines are given as injections in the muscles of the upper arm or the thigh.

For Comirnaty®, a main study in children from 6 months to 4 years of age showed that the immune response to the lower dose of Comirnaty® (3 micrograms) was comparable to that seen with the higher dose (30 micrograms) in 16- to 25-year-olds. **For Spikevax®, a main study in children from 6 months to 5 years of age showed that the immune response to the lower dose of Spikevax® (25 micrograms) was comparable to that seen with the higher dose (100 micrograms) in 18- to 25-year-olds**. Both studies evaluated the immune response triggered by the vaccines by measuring the level of antibodies against SARS-CoV-2.

The most common side effects for both vaccines, in children aged from 6 months to 4 or 5 years, **were comparable to those seen in older age groups**. Irritability, sleepiness, loss of appetite, rash and tenderness at the injection site were also common side effects in children aged 6 to 23 months with Comirnaty®, while irritability, crying, loss of appetite and sleepiness were common side effects in children aged 6 to 36 months with Spikevax®. For both vaccines, these effects **were usually mild or moderate and improved within a few days of vaccination**.

The CHMP therefore concluded that the benefits of Comirnaty® and Spikevax® in children aged from 6 months to 4 and 5 years, respectively, outweigh the risks.

The safety and efficacy of both vaccines, in children and adults, will continue to be monitored closely as they are used in vaccination campaigns in EU Member States through the EU pharmacovigilance system and ongoing and additional studies conducted by the company and coordinated by European authorities.

The originally authorised vaccines, Comirnaty® and Spikevax®, are both effective at preventing severe disease, hospitalisation and death associated with COVID-19 and continue to be used within vaccination campaigns in the EU, in particular for primary vaccinations.

National authorities in the EU Member States will determine who is recommended to be vaccinated and when, taking into account factors such as infection and hospitalisation rates, the risk to vulnerable populations, vaccination coverage and vaccine availability.

The CHMP recommendations will now be sent to the European Commission, which will issue final decisions applicable in all EU Member States.

How the vaccines work

Both vaccines work by preparing the body to defend itself against COVID-19. Each vaccine contains a molecule called messenger RNA (mRNA) which has instructions for making the spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells.

When a person is given the vaccine, some of their cells will read the mRNA instructions and temporarily produce the spike protein. The person's immune system will then recognise this protein as foreign and produce antibodies and activate T-cells (white blood cells) to attack it.

If, later on, the person comes into contact with the SARS-CoV-2 virus, their immune system will recognise it and be ready to defend the body against it.

The mRNA from the vaccine does not stay in the body but is broken down after vaccination.

Where to find more information

The product information approved by the CHMP for Comirnaty® and Spikevax® contains prescribing information for healthcare professionals and a package leaflet for members of the public.

Assessment reports, with details of EMA's evaluations of the use of Comirnaty® and Spikevax® in children from 6 months of age, will be published on the EMA website.

The studies in children were carried out in accordance with the paediatric investigation plan (PIP) for each vaccine, which was agreed by EMA's Paediatric Committee (PDCO). Clinical trial data submitted by the companies in their applications for the paediatric extensions of indication will be published on the Agency's clinical data website in due course.

More information is available in the overviews of the vaccines in lay language, including a description of the vaccine's benefits and risks and why EMA recommended their authorisation in the EU.

Monitoring the safety

In line with the EU's safety monitoring plan for COVID-19 vaccines, Comirnaty® and Spikevax® are closely monitored and subject to several activities that apply specifically to COVID-19 vaccines. **Independent studies of COVID-19 vaccines coordinated by EU authorities will give more information on the vaccines' long-term safety and benefits in the general population.**

These measures allow regulators to swiftly assess data emerging from a range of different sources and take appropriate regulatory action to protect public health if needed.

1.4.2 Comirnaty® (adopted from ACIP, WWWR, FDA – **for information only**)

FDA: The Pfizer-BioNTech COVID-19 Vaccine is a suspension for intramuscular injection.
https://www.fda.gov/media/159312/download
https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccines

Immunogenicity, efficacy and safety

The body of evidence regarding immunogenicity, efficacy, and safety of the Pfizer-BioNTech COVID-19 vaccine among children aged 6 months–4 years was composed of data from one randomized, double-blind, placebo-controlled phase II/III clinical trial in which 4,526 participants aged 6 months–4 years were enrolled and randomized 2:1 to receive either vaccine or saline placebo. The protocol initially specified 2 doses of vaccine (3 µg) or saline placebo separated by an interval of 3 weeks. Per protocol, participants were unblinded 6 months after dose 2 or at age 5 years (whichever occurred first). Based on an interim analysis where the predefined criteria for immunobridging and efficacy of the trial were not met after 2 doses, a protocol amendment was implemented on February 1, 2022, to include a third dose of either vaccine (3 µg) or saline placebo, administered ≥56 days after dose 2. Dose 3 was offered to blinded and unblinded participants in the vaccine arm, and blinded participants in the placebo arm were offered a third dose of placebo. Among trial participants, 1,456 (32.2%) received a blinded third dose and were included in a 3-dose efficacy analysis (992 in the vaccine arm and 464 in the placebo arm). The median interval between doses 2 and 3 was 16 weeks among children aged 6–23 months and 11 weeks among children aged 2–4 years. Safety analyses included blinded participants and assessed outcomes starting at dose 1. Interim findings from this clinical trial were based on data from participants with a median blinded follow-up of 35 days after dose 3 for children aged 6–23 months and 40 days for children aged 2–4 years.

Vaccine efficacy was supported by two types of evidence: 1) direct efficacy of 3 doses against symptomatic laboratory-confirmed COVID-19 and 2) immunobridging data. Vaccine efficacy ≥7 days after dose 3 was 80.0% (95% CI = 22.8%–94.8%) in preventing symptomatic, laboratory-confirmed COVID-19 in children aged 6 months–4 years with and without evidence of previous SARS-CoV-2 infection, based on infection in three vaccine recipients and seven placebo recipients, none of whom were hospitalized. In the immunobridging analysis, the measure of immune response to 3 doses (3 µg each) of the Pfizer-BioNTech COVID-19 vaccine in children aged 6 months–4 years without evidence of previous SARS-CoV-2 infection was at least as high as the response observed in persons aged 16–25 years who had received 2 doses (30 µg each) of the Pfizer-BioNTech COVID-19 vaccine, with a GMR for 50% neutralizing antibody titer of 1.19 (95% CI = 1.00–1.43) for children aged 6–23 months and 1.30 (95% CI = 1.13–1.50) for children aged 2–4 years, satisfying the noninferiority criteria for both age groups.

Among vaccine recipients aged 6 months–4 years, reactogenicity, defined as solicited local injection site or systemic signs or symptoms during the 7 days after vaccination, were common (47.8% reported any local reaction, and 63.8% reported any systemic reaction); most reactions were mild to moderate. Local and systemic reactogenicity symptoms were usually less frequent in children aged 6 months–4 years (63.8%) than in children aged 5–11 years (86.2%) . Severe local and systemic adverse reactions (grade 3 or higher, defined as interfering with daily activity) occurred in 4.3% and 3.6% of vaccine recipients and placebo recipients, respectively. The most commonly reported reactions of grade 3 or higher among vaccine recipients aged 6–23 months were fever (4.0%) and irritability (1.3%), and among recipients

aged 2–4 years, were fatigue (0.8%) and fever (2.2%). Overall, reactions of grade 3 or higher were also more commonly reported after the second dose than after the first or third dose. Serious adverse events were uncommon and occurred with similar frequency among recipients of vaccine (1.0%) and placebo (1.5%), with no statistically significant difference in frequency. Two serious adverse events in one participant in the vaccinated group were determined to be potentially related to vaccination. No specific safety concerns were identified among vaccine recipients aged 6 months–4 years. A detailed summary of safety data, including information on reactogenicity, is available at https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html.

- Antibody levels after 3 doses in children ages 6 months–4 years produces similar antibody levels after 2 doses in individuals ages 16–24 years
- Reactogenicity post-vaccine similar after each of the 3 vaccine doses, and similar to reactions seen in placebo recipients
- Efficacy estimates difficult to interpret given small numbers and limited follow-up time

1.4.3 Spikevax® (adopted from NACI, FDA – **for information only**)

The Moderna COVID-19 Vaccine is a suspension for intramuscular injection.
https://www.fda.gov/media/159307/download
https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccines

The Moderna Spikevax COVID-19 vaccine was evaluated in pediatric participants aged 6 months to 5 years as part of an ongoing, Phase 2/3, randomized, observer-blind, placebo-controlled study. For all analyses, the participants were split into two age-based subgroups; ages 6 to 23 months and 2 to 5 years. Participants were recruited from the US and Canada beginning November 2021 and 25nrolment is ongoing. Participants were randomly assigned to receive either two doses of the vaccine (25 mcg mRNA) or two doses of a placebo, administered 28 days apart.

Across both age groups and between the vaccine and placebo groups, approximately 50% of participants were female. Among participants that received the Moderna Spikevax vaccine, the majority were between 1 and <5 years of age, whereas about 8% were aged 6 months to 11 months and about 2% were age 5 years to < 6 years.

At data cut-off (February 21, 2022), median follow up after the second dose was 68 days for participants aged 6 to 23 months and median follow up time was 72 days for participants aged 2 years to 5 years.

Efficacy

Vaccine efficacy was assessed among children aged 6 months to 5 years following one and two doses of Moderna Spikevax (25 mcg) mRNA COVID-19 vaccine during a time when Omicron was the predominant variant of SARS-CoV-2 in the US and Canada (data cut-off February 21, 2022). The per-protocol population (negative baseline SARS-CoV-2 status and received two doses of either vaccine or placebo) included 5,476 participants who received two doses of either vaccine or placebo (for participants 6 months through 23 months, 1,511 participants in the vaccine group, 513 in the placebo group; for participants 2 years through 5 years, 2,594 in the vaccine group, 858 in the placebo group).

Efficacy estimates among participants without evidence of prior SARS-CoV-2 infection (per-protocol population)

Efficacy against confirmed symptomatic SARS-CoV-2 infection starting 14 days after dose 2 was estimated at 50.6% (95% CI: 21.4 to 68.6%) among study participants aged 6 to 23 months and 36.8% (95% CI: 12.5 to 54.0%) among participants aged 2 to 5 years..

Efficacy against asymptomatic SARS-CoV-2 infection starting 14 days after dose 2 was estimated at 3.8% among study participants aged 6 to 23 months and 22.9% among participants aged 2 to 5 years; however, in both age groups, the CI around the point estimate was wide and included zero (95% CI: -111.5 to 52.8% and 19.5 to 49.3%, respectively).

The estimate of vaccine efficacy against asymptomatic infection after 2 doses should be interpreted with caution as cases were identified among participants that were seronegative at baseline prior to dose 1 and who later had a positive reverse transcription polymerase chain reaction (RT-PCR) test or serology result at varying time points starting 14 days after dose 2; however, there was a limited number of participants providing samples for serology at later time points. Therefore, this finding could reflect infection acquired at any time after dose 1 prior to the time of sample collection, and may be an underestimation of 2 dose efficacy.

Efficacy against confirmed symptomatic SARS-CoV-2 infection from 14 days after dose 1 until dose 2 was estimated at -11.4% among study participants aged 6 to 23 months and 17% among participants aged 2 to 5 years. However, estimates of 1-dose vaccine efficacy should be considered with caution, as few cases were reported during this two-week time frame, and accordingly the CI around the point estimate was wide and included zero (95% CI: -529.8 to 71.3% and -161.2 to 69.6%, respectively).

Efficacy estimates among participants with or without evidence of prior SARS-CoV-2 infection

Efficacy against confirmed symptomatic SARS-CoV-2 infection starting 14 days after dose 2 was also determined among participants regardless of evidence of prior to SARS-CoV-2 infection and was estimated at 50.6% (95% CI: 21.4 to 68.6%) among study participants aged 6 to 23 months and 36.5% (95% CI: 12.5 to 54.0%) among participants aged 2 to 5 years.

Efficacy estimates against severe outcomes of COVID-19

There were no deaths or cases of severe COVID-19 or MIS-C among trial participants that received the vaccine; however, one case of MIS-C was reported after the February 21, 2022 data cut-off in a participant that received the placeboFootnote18. Therefore, efficacy against outcomes of severe COVID-19 or MIS-C was not evaluated.

Real world evidence suggests mRNA vaccines in older age groups have high vaccine effectiveness (VE) at preventing severe outcomes of COVID-19 including hospitalization and death. Additionally, mRNA vaccines have high VE against hospitalization due to MIS-C in adolescent populations.

Estimates of Moderna Spikevax vaccine efficacy against symptomatic disease during the Omicron wave in children aged 6 months to 5 years are consistent with VE reported for Pfizer-BioNTech Comirnaty (10 mcg) vaccine among children 5 to 11 years of age during the Omicron waveFootnote25. However, waning of immune responses over time are well documented in older age groups and may also contribute to lower VE estimates when calculating VE at longer intervals following vaccination or infection. VE against any future variants is unknown.

For further information on the VE of mRNA COVID-19 vaccines against severe outcomes of COVID-19 including hospitalization due to MIS-C, please refer to the COVID-19 vaccine chapter in the Canadian Immunization Guide (CIG).

VE estimates are consistent with VE estimates in adults during the time of the Omicron surge (Tseng et al., 2022; Andres et al., 2022)

Immunogenicity

Immunogenicity as per protocol among participants without evidence of prior SARS-CoV-2 infection
The humoral immune response to Moderna Spikevax (25 mcg) was non-inferior in children aged 6 months to 5 years compared to young adults, meeting pre-established non-inferiority criteria (lower bound of the 2-sided 95% CI for the geometric mean ratio [GMR] >0.67; point estimate ≥0.8). SARS-CoV-2 neutralizing antibody titers (ID50) were assayed 28 days following dose 2, and the GMR of neutralizing antibody titres in children 2 to 5 years of age (n=264) and 6 to 23 months of age (n=230) relative to young adults (18 to 25 years of age; n=291) was 1.01 (95% CI: 0.88 to 1.17%) and 1.280 (95% CI: 1.12 to 1.47%), respectively. The neutralizing seroresponse rates (SRR) among children 2 to 5 years and children 6 to 23 months old were 98.9% and 100% respectively, with differences compared to young adults of -0.4% (95% CI: -2.7 to 1.5%) and 0.7% (95% CI: -1.0 to 2.5%), respectively, meeting non-inferiority success criteria (lower bound of the 95% CI of the SRR difference > -10%).

Immunogenicity in participants based on SARS-CoV-2 serology at baseline

Approximately 9% of participants 2 to 5 years of age and 6% of participants 6 to 23 months of age had serologic evidence of prior SARS-CoV-2 infection at the start of the study and were thus excluded from immunobridging analyses. Neutralizing antibody titres increased in these participants 28 days after dose 2. In seropositive children 2 to 5 years of age, antibody titres increased by 37-fold compared to pre-vaccination titres. In seropositive children 6 to 23 months of age, antibody titres increased by 49-fold compared to pre-vaccination titresFootnote26. Antibody titres for seropositive children aged 2 to 5 years and 6 to 23 months were at least 4- or 6-fold higher 28 days after dose 2 compared to seronegative children.

In both seronegative and seropositive participants, antibody titres were generally higher in children 6 to 23 months of age compared to children 2 to 5 years of age.

As an immunological correlate of protection has not been determined for COVID-19 at this time, it is unknown how the immune response levels that have been reported in clinical trials are related to the prevention of SARS-COV-2 infection or disease or the ability to transmit to others.

Safety

The Moderna Spikevax (25 mcg) COVID-19 vaccine was well tolerated in children aged 6 months to 5 years. Safety data were collected in a still ongoing Phase 2/3 clinical trial that included children 6 months through 5 years of age. The safety data analyzed was based on a February 21, 2022 data cut-off. At the time of data cut-off, the safety analysis set included 375 subjects who were 6 months to < 1 year of age, 1,373 subjects who were 1 to < 2 years of age, and 3,007 subjects who were 2 to < 6 years of ageFootnote20. No safety signals were identified after a median of 103 days after dose 1 and 71 days after dose 2 for ages 2 to 5 years, and 98 days after dose 1 and 68 days after dose 2 for children 6 months to < 2 years of age. Duration of participant follow-up ranged from 0 to 127 days after dose 1 and from 0 to 99 days after dose 2 as the study was still recruiting participants at time of data cut off.

Overall, the safety profile of Moderna Spikevax (25 mcg) vaccine was consistent with the known safety and reactogenicity profile of the 50 mcg and 100 mcg Spikevax formulations authorized for use in older age groups. Events reported in the vaccine group were consistent with events commonly reported for other pediatric vaccines authorized for use in children 6 months to 5 years of age.

Local and systemic adverse events

Data on solicited local and systemic adverse reactions included 4,792 participants 6 months to 5 years of age who received at least one dose of vaccine, and 1,596 participants who received at least one dose of placebo. Solicited local adverse reactions within 7 days, including grade 3 events, were reported at a higher frequency in the vaccine group than in the placebo group in both the 2 to 5 year and the 6 months to < 2 year age groups, particularly after the second dose. Solicited systemic adverse reactions within 7 days reported after dose 1 were similar when compared to placebo in both age groups, but were reported at a higher frequency in the vaccine group than in the placebo group after the second dose, including grade 3 events. The majority of solicited local and systemic adverse reactions were grade 1 or 2 and occurred within the first 2 days after any dose of vaccine and persisted for a median of 2 to 3 days. The incidence of grade 3 solicited adverse reactions was infrequent in both vaccine and placebo groups in both age groups (< 5% after any dose).

The most frequently reported solicited local and systemic adverse reactions were irritability/crying, pain, sleepiness, and loss of appetite. Fatigue (48.4%) was the most frequently reported systemic adverse reaction in the participants 37 months to 5 years of age.

Any type of AE that occurred in at least 1% of study participants aged 6 months to <2 years of age who received vaccine and at a rate at least 1.5-fold higher than in the placebo group, included acute otitis media (1.4% versus 0.7%), injection site lymphadenopathy (1.4% versus 0.2%) and injection site erythema (1.1% versus 0.2%). In children 2 to 5 years of age, only injection site erythema occurred in ≥ 1% in the vaccine arm and at a rate at least 1.5-fold higher than placebo (1.3% versus 0.2%).

Serious adverse events and other adverse events of interest

For participants 2 to 5 years of age: Serious adverse events (SAEs) up to and beyond 28 days since last dose were reported at a frequency of 0.3% (n=9) for the vaccine group and 0.2% (n=2) for the placebo group. None of the reported SAEs were considered related to the vaccine. The incidence of medically attended events up to 28 days after any dose was similar in the vaccine group (662/3031; 21.8%) compared with the placebo group (221/1007; 21.9%). No participants in either group discontinued the study due to an adverse event.

For participants 6 months to <2 years of age: SAEs up to and beyond 28 days since last dose were reported at a frequency of 0.9% (n=15) for the vaccine group and 0.2% (n=1) for the placebo group. In the vaccine group, there was 1 participant with two SAEs considered related to the vaccine (a grade 3 fever that occurred 6 hours after dose 1, which was followed by a febrile convulsion). None of the other reported SAEs were considered related to the vaccine. The incidence of medically attended events up to 28 days after any dose were also similar in the vaccine group (486/1761; 27.6%) compared with the placebo group (161/589; 27.3%). One participant in each group discontinued study vaccination.

There was 1 event of anaphylaxis attributed to a concurrent medication in the 2 to 5 year age group (32 days after vaccination), and 2 events of egg or food product related-anaphylaxis unrelated to the vaccine in the younger age group 6 months to < 2 years (15 and 18 days after vaccination).

There were no deaths, no cases of MIS-C, and no cases of myocarditis and/or pericarditis reported in any participant during the study period. Given the trial was limited to n=4,792 participants randomized to receive the Moderna Spikevax (25 mcg) vaccine, it is unlikely that any AE occurring at a frequency less often than 6 in 10,000 would be detected.

-The safety profile of Moderna Spikevax® vaccine was consistent with the safety and reactogenicity profile of the Spikevax® formulations used in older age groups
- Events reported in the vaccine group were consistent with events commonly reported for other vaccines used in children 6 months to 5 years of age. The most frequently reported solicited local and systemic adverse reactions were irritability/crying, pain, sleepiness and loss of appetite. Fatigue (48.4 %) was most frequently reported systemic adverse reaction.
- The majority of reactions onset by 1-2 days and lasted 2-3 days
-The risk of any rare or very rare adverse events such as myocarditis and/or pericarditis, is unknown at this time.

V REFERENCES

Antoon JW, Hall M, Howard LM, et al. COVID-19 and Acute Neurologic Complications in Children [published online ahead of print, 2022 Aug 11]. Pediatrics. 2022;10.1542/peds.2022-058167. Doi:10.1542/peds.2022-058167

Bhopal SS, Bagaria J, Olabi B, Bhopal R. Children and young people remain at low risk of COVID-19 mortality. The Lancet Child & adolescent health. 2021 May;5(5):e12-e3.

Borch L, Holm M, Knudsen M, Ellermann-Eriksen S, Hagstroem S. Long COVID symptoms and duration in SARS-CoV-2 positive children – a nationwide cohort study. Eur J Pediatr. 2022;181(4):1597-1607. Doi:10.1007/s00431-021-04345-z

Bundle N, Dave N, Pharris A, Spiteri G, Deogan C, Suk JE. COVID-19 trends and severity among symptomatic children aged 0-17 years in 10 European Union countries, 3 August 2020 to 3 October 2021. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin. 2021 Dec;26(50)

Chen F, Tian Y, Zhang L, Shi Y. The role of children in household transmission of COVID-19: a systematic review and meta-analysis. Int J Infect Dis. 2022;122:266-275. Doi:10.1016/j.ijid.2022.05.016

Cohen JM, Carter MJ, Ronny Cheung C, Ladhani S; Evelina PIMS-TS Study Group. Lower Risk of Multisystem Inflammatory Syndrome in Children (MIS-C) with the Delta and Omicron variants of SARS-CoV-2 [published online ahead of print, 2022 Jul 5]. Clin Infect Dis. 2022;ciac553. Doi:10.1093/cid/ciac553

European Centre for Disease Prevention and Control. SARS-CoV-2 in children (14 June 2022). https://www.ecdc.europa.eu/en/all-topics-z/covid-19/latest-evidence/sars-cov-2-children

European Centre for Disease Prevention and Control. Latest evidence: Clinical characteristics of COVID-19. Stockholm: ECDC; 2022. Available at: https://www.ecdc.europa.eu/en/covid19/latest-evidence/clinical

European Centre for Disease Prevention and Control. Joint ECDC-ESPID webinar on post COVID-19 condition in children. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/news-events/webinar-post-covid-19-condition-children

Eyre DW, Taylor D, Purver M, et al. Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants. N Engl J Med. 2022;386(8):744-756. Doi:10.1056/NEJMoa2116597

Fleming-Dutra KE, Wallace M, Moulia DL, et al. Interim Recommendations of the Advisory Committee on Immunization Practices for Use of Moderna and Pfizer-BioNTech COVID-19 Vaccines in Children Aged 6 Months-5 Years – United States, June 2022. MMWR Morb Mortal Wkly Rep. 2022;71(26):859-868. Published 2022 Jul 1. Doi:10.15585/mmwr.mm7126e2

Forbes H, Morton C E, Bacon S, McDonald H I, Minassian C, Brown J P et al. Association between living with children and outcomes from covid-19: OpenSAFELY cohort study of 12 million adults in England BMJ 2021; 372 :n628 doi:10.1136/bmj.n628

Geijerstam A, Mehlig K, Hunsberger M, Åberg M, Lissner L. Children in the household and risk of severe COVID-19 during the first three waves of the pandemic: a prospective registry-

based cohort study of 1.5 million Swedish men. BMJ Open. 2022;12(8):e063640. Published 2022 Aug 11. Doi:10.1136/bmjopen-2022-063640

Hoge Gezondheidsraad. Aanbevelingen voor het prioriteren van subgroepen van patiënten jonger dan 65 jaar voor vaccinatie tegen SARS-CoV-2 (fase Ib). Brussel: HGR; 2021. Advies nr. 9618.

Kortz TB, Connolly E, Cohen CL, Cook RE, Jonas JA, Lipnick MS, et al. Diagnosis and Acute Management of COVID-19 and Multisystem Inflammatory Syndrome in Children. Pediatric emergency care. 2021 Oct 1;37(10):519-25

Levy N, Koppel JH, Kaplan O, et al. Severity and Incidence of Multisystem Inflammatory Syndrome in Children During 3 SARS-CoV-2 Pandemic Waves in Israel. JAMA. 2022;327(24):2452-2454. Doi:10.1001/jama.2022.8025

Lopez-Leon S, Wegman-Ostrosky T, Ayuzo Del Valle NC, Perelman C, Sepulveda R, Rebolledo PA, Cuapio A, Villapol S. Long-COVID in children and adolescents: a systematic review and meta-analyses. Sci Rep. 2022 Jun 23;12(1):9950. doi: 10.1038/s41598-022-13495-5. PMID: 35739136; PMCID: PMC9226045.

Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Antonelli M, Murray B, Kläser K, Kerfoot E, Chen L, Deng J, Hu C, Selvachandran S, Read K, Capdevila Pujol J, Hammers A, Spector TD, Ourselin S, Steves CJ, Modat M, Absoud M, Duncan EL. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. Lancet Child Adolesc Health. 2021 Oct;5(10):708-718. doi: 10.1016/S2352-4642(21)00198-X. Epub 2021 Aug 3. Erratum in: Lancet Child Adolesc Health. 2021 Aug 31;: PMID: 34358472; PMCID: PMC8443448.

Nygaard U, Holm M, Hartling UB, et al. Incidence and clinical phenotype of multisystem inflammatory syndrome in children after infection with the SARS-CoV-2 delta variant by vaccination status: a Danish nationwide prospective cohort study. *Lancet Child Adolesc Health*. 2022;6(7):459-465. Doi:10.1016/S2352-4642(22)00100-6

Rhedin S, Lundholm C, Horne A, et al. Risk factors for multisystem inflammatory syndrome in children – A population-based cohort study of over 2 million children. Lancet Reg Health Eur. 2022;19:100443. Doi:10.1016/j.lanepe.2022.100443

SIMID: http://www.simid.be/wp-content/uploads/2022/09/20220831_technical_note_SIMID.pdf

Superior Health Council. Vaccination against COVID-19 of children aged 5-11 years in Belgium. Brussels: SHC; 2021. Report 9680.

Superior Health Council. Booster vaccination against COVID-19 for immunocompromised patients. Brussels: SHC; 2022. Report 9691.

Superior Health Council. COVID-19 vaccination: Autumn / Winter season 2022 – 2023. Brussels: SHC; 2022. Report 9721.

Wang L, Berger NA, Kaelber DC, Davis PB, Volkow ND, Xu R. Incidence Rates and Clinical Outcomes of SARS-CoV-2 Infection With the Omicron and Delta Variants in Children Younger Than 5 Years in the US. JAMA Pediatr. 2022;176(8):811-813. doi:10.1001/jamapediatrics.2022.0945

Whittaker R, Greve-Isdahl M, Bøås H, Suren P, Buanes EA, Veneti L. COVID-19 Hospitalization Among Children <18 Years by Variant Wave in Norway. Pediatrics. 2022;150(3):e2022057564. doi:10.1542/peds.2022-057564

Zambrano LD, Newhams MM, Olson SM, et al. BNT162b2 mRNA Vaccination Against COVID-19 is Associated with Decreased Likelihood of Multisystem Inflammatory Syndrome in U.S. Children Ages 5-18 Years [published online ahead of print, 2022 Aug 4]. Clin Infect Dis. 2022;ciac637. doi:10.1093/cid/ciac637

Zimmermann P, Pittet LF, Curtis N. How Common is Long COVID in Children and Adolescents? The Pediatric infectious disease journal. 2021 Dec 1;40(12):e482-e7.

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).

The following experts were involved in endorsing this advisory report by mail by 18 October 2022 or during the NITAG meeting of 20 October 2022. The *ad hoc* working group was chaired by Anne **TILMANNE** and Petra **SCHELSTRAETE**. The NITAG was chaired by Yves **VAN LAETHEM**; the scientific secretary Veerle MERTENS and Fabrice PETERS.

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DAELEMANS Siel	Pediatric pulmonology, infectology	UZ Brussel
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ROBERFROID Dominique	Epidemiology	KCE, UNamur

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VAN LAETHEM Yves	Infectiology, vaccination, travel clinic	CHU Saint-Pierre
VEKEMAN Veerle	Communicable Diseases General	Kind en gezin
VERHAEGEN Jan	Microbiology, Bacteriology	UZ Leuven

The following administrations and/or ministerial cabinets were heard:

DAEMS Joêl	Directorate Drugs	RIZIV-INAMI
MENDEZ Murielle	Health Officer, Health coordinator,	Kaleido Ostbelgien
THEETEN Heidi	Vaccinology	VAZG
VANDEN DRIESSCHE Koen	Pediatric infectious diseases	UZA

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.

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