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COVID-19 vaccination for children and adolescents? Fourteen aspects in search of a good way forward, using Germany as an example

Prof. Dr. med. David Martin[a,b], Prof. Dr. med. Arne Simon[c], Dr. med. Silke Schwarz[a]

[a]University of Witten/Herdecke, Witten, Germany

[b]University of Tübingen, University Hospital for Pediatrics and Adolescent Medicine, Germany

[c]Pediatric Oncology and Hematology, University Children's Hospital, Homburg/Saar, Germany; Vice-Chair of the German Society of Pediatric Infectiology

2nd Chairman of the German Society for Pediatric Infectiology (DGPI).

Corresponding author:

Prof. David Martin, MD,

Gerhard Kienle Chair of Medical Theory Department of Human Medicine

Faculty of Health, Witten/Herdecke University Tel: +49 2330 62 4760

Fax: +49 2330 62 3810

david.martin@uni-wh.de

"Acting is easy, thinking difficult, acting according to thought inconvenient."

J.W. Goethe, who is said to have been quite in favor of compulsory vaccination in the case of smallpox [1].

Abstract

Background: Whether children (0-11 years) and adolescents (12 to 18 years) should receive COVID-19 vaccinations is a topic of debate.

Methods: Through iterative and systematic engagement with the literature, aspects were collected that should be clarified collectively and individually before vaccines are recommended. These aspects were analyzed and discussed in a consensus process and sent to pediatric professional associations for comment. Feedback was fully considered.

Results: On the question of whether COVID-19 vaccination should be recommended for children in general, 7 child-related aspects and 7 society-related aspects to be considered were identified:

1. acute burden of disease,
2. sequelae (PIMS and Long-COVID vs. Long-Lockdown),,
3. mortality,
4. short-, medium-, and long-term side-effect spectrum of vaccines and ingredients,
5. immunity development to vaccination,
6. influence of vaccination on the emergence of immune escape mutations,
7. natural vs. vaccine-induced immunity.

The society-related aspects concern whether COVID-19 vaccination of children can be recommended for the good of the community, independent of (or even counter to) the good of children:

8. Role of children in the pandemic,
9. Reduction of transmission,
10. Vaccine-specific reduction of severe or fatal cases in adults by vaccinating children,
11. Environmental, economic, and social consequences of vaccination,
12. Impact of childhood vaccination on selection pressures,
13. Risk of shifting disease from childhood to later life, including the unlikelihood of eradicating SARS-CoV-2.
14. Access to community facilities and participation in social life.

Discussion: These 14 aspects provide a guideline for clarifying whether a particular vaccination should be recommended – for the respective age groups and in the context of the respective family, the respective country and its conditions. For Germany, there is currently no indication for a general vaccination recommendation for children and adolescents.

Key words: COVID-19, vaccination, children, adolescents, approval, recommendation

Background

Vaccination against severe courses of SARS-CoV-2 infection (against COVID-19) is a key measure to mitigate the pandemic in adults. Thus, the question arises whether children and adolescents < 16 years of age should be vaccinated [2], now that the EMA has approved the use of the mRNA vaccine COMIRNATY® (BNT162b2) for 12-15 year-olds in Europe.

Given the pressure to end the pandemic as quickly as possible, there is concern among some parents, as well as some pediatricians and adolescents, that the novel COVID-19 vaccines for children will be recommended, and administered in a fast-track process without careful benefit-risk evaluation and adequate knowledge of potentially rare serious side effects. On 05/05/2021, the German Medical Congress formulated the following in the resolution "Necessary COVID-19 vaccination strategy for children and adolescents 2021/2022": "The right to education with daycare and school attendance can only be secured in the winter of 2021/2022 with timely COVID-19 vaccination." And, "Families with children will regain equal participation in society only with vaccinated children."[3] This sounds like an "alternative-less" strategy, although visiting these community facilities would also be possible if all adult contacts wishing to do so were vaccinated or even if the suggested hygiene measures were consistently implemented. The aim of this publication is to evaluate the scientific background of these and similar claims and the issues that should be clarified before recommending vaccination against SARS-CoV-2 for children and adolescents.

Methods

Through iterative and systematic review of the literature, we collected aspects that should be clarified collectively and individually before vaccinations for children are approved, recommended and administered. These aspects were developed through a consensus process with colleagues and parents and then sent to representatives of pediatric professional societies for comment (see acknowledgments). All comments received were implemented. For their discussion, a systematic search for sources for the respective questions was carried out by all authors in as structured a manner as possible, sometimes repeated during the process. German- and English-language peer-reviewed sources were considered, as well as information from the websites of the Robert Koch Institute (RKI) and the German Societies for Pediatric Infectiology (DGPI).

Results

The literature search for "COVID-19 AND child AND vaccin*" yielded n=1,109 hits, and that for "Covid-19 vaccination AND child" yielded n=22 hits (PubMed, on 05/05/2021). The use of formal inclusion and exclusion criteria proved less helpful than reviewing the literature for information relevant to each question. Through dialogic expert exchange and discourse with colleagues and parents, 14 viewpoints were developed that also need to be discussed and carefully weighed in the case of a present drug regulatory approval for each country (related to the local risk of becoming severely ill or dying from COVID-19) for different age groups. This needs to be done before making a general recommendation for vaccination against SARS-CoV-2 in children and youth. These aspects are presented below in relation to the current situation in Germany.

Child-related aspects: Would COVID-19 vaccination in principle be in the best interest of children?

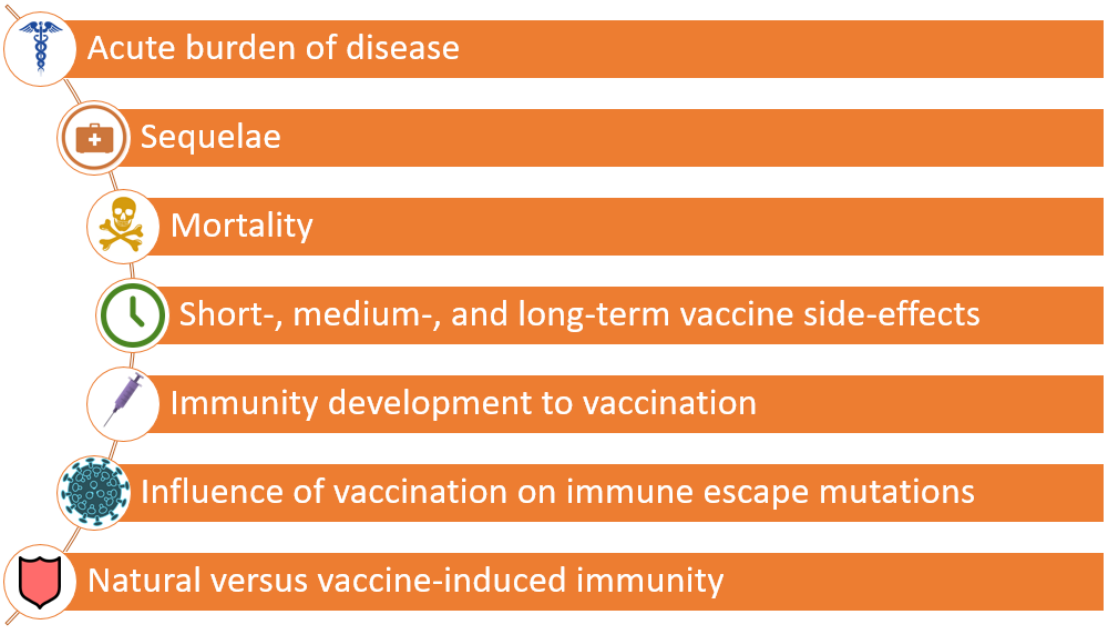

Figure 1: Seven child-related factors to consider when deciding on both individual and collective immunization recommendations for children and adolescents

1. Acute disease burden of children and adolescents

Children very rarely (<0.01% of rtPCR-positive)[1] become so severely ill with SARS-CoV- 2 infection that they require hospitalization for this infection [4][5]. Of all hospitalizations in 2021 in Germany,

[1]*The exact rate of hospitalizations is not known because, as in all age groups, reported (rtPCR confirmed) disease is only a subset of all infected individuals.*

(n=97,985), 925 (0.9%) were in 0-4 year olds and 725 (0.8%) were in 5-14 year olds (RKI reporting data, as of April 27, 2021) [6]). This is consistent with data from many other studies in which the proportion of hospitalized children among all hospitalizations of COVID 19 patients is less than 2%. In the Germany-wide DGPI registry (report week 16), 5% of the 1,373 hospitalized patients reported to date required children and adolescents of intensive care treatment, of these 6 children had sequelae [7]. These few sequelae need to be carefully investigated and published to consolidate the assessment basis for an individual vaccination decision. Importantly in the context of vaccination approval, of the hospitalized children with Sars-CoV-2 positivity, 30% were children less than 6 months of age and 60% were less than 6 years of age [7].

2. Sequelae of COVID-19 in children and adolescents

PIMS and long COVID are under discussion as pediatric sequelae. With a time latency of a few weeks, pediatric inflammation multisystem syndrome (PIMS) can occur after SARS-CoV-2 infection, especially in schoolchildren. In the DGPI PIMS Registry, 281 children and adolescents were registered (up to calendar week 16) who were hospitalized due to PIMS. None of these children died, but 43.6% still had residual symptoms at discharge and 6.5% had sequelae [8], which still require careful workup, also with regard to the time course in the next months. According to current knowledge, most cardiovascular sequelae after COVID 19 or PIMS are healed within 6 months in children [9, 10]. Reliable data on the occurrence of a "long COVID" symptom complex in children are not yet available from Germany [11][12]. Comparative studies comparing children with and without COVID-19 under lockdown conditions with regard to fatigue, depression, etc. are also lacking for other countries so far. Due to the considerable increase in child and adolescent psychiatric morbidity under lockdown conditions, only a contemporary prospective comparative study can answer the question of the prevalence of long COVID syndrome and "long lockdown" syndrome in children. Negative consequences of lockdown should also be considered in the just initiated survey of the DGPI [13].

3. Mortality from COVID-19 for children and adolescents

Because of its importance, part of the DGPI's statement on this point is reproduced here: "Every single case of a child becoming seriously ill or dying from SARS-CoV-2 infection is one case too many and an unbearable individual fate for child and family. The observation now made since the beginning of the pandemic that of the estimated 14 million children and adolescents in Germany, only about 1,200 with a SARS-CoV-2 infection required hospital treatment (<0.01%) and four died from their infection (<0.00002%) should be reason to relieve parents of excessive worries about a severe course of illness in their children. According to the Federal Ministry of Transport and Digital Infrastructure, the number of children killed in a traffic accident in 2019 was 55, and according to the German Lifesaving

Association (Deutsche Lebens-Rettungs-Gesellschaft (DLRG), the number of drowned children is 25. These figures should not and must not be set off against each other, but may help to classify them [4]]." As of 05/18/2021, 18 people under the age of 20 years had been reported to the RKI as having died from or with Sars-Cov-2. All 13 cases, according to current information, were known to have pre-existing conditions [14]. It is astonishing that in a country with so much research funding, the RKI and society learn so little about the exact associations when we are simultaneously considering vaccinating millions of children.

No child has died from Sars-Cov-2 associated PIMS in Germany to date [8].

4. Short-, medium-, and long-term side effect spectrum of vaccinations and ingredients in children and adolescents

Not every child has contact with the virus, not every of them gets infected, again only a small part of infected children develops symptoms and these are mostly mild. In contrast, general vaccination would cause forced iatrogenic exposure to a viral component (plus the additives and/or vectors contained in the vaccine) in all vaccinated children.

There is to date only one peer-reviewed publication of a trial of covid-19 vaccinations in 12-15 year-olds and none on younger children [15]. There were more intervention-related side effects (2.9% vs. 1.9%) and severe side-effects (0.6%, including one life-threatening event vs. 0.2%) in the intervention group than in the placebo group, although unfortunately no details are offered. A single serious side effect per 10,000 youth vaccinated would mean 340 serious side effects for 3.4 million 12-15 year olds in Germany.

The analysis of seven studies in adults in the 16-55 age group revealed that more than half of the subjects experience side effects. Younger participants have more problems with side effects after the first vaccination than older participants. After the second vaccination, side effects are evenly distributed among the age groups [17][18][19][20][21][22][23].

Differentiation of the short-, medium-, and long-term spectrum of adverse effects by age, ethnicity, and underlying disease is still pending. Many COVID-19 vaccines cause transient acute general reactions (fever, headache, aching limbs, sometimes chills), especially in younger individuals [24] [25] [26][19]. To date, there are insufficient data on the risk of thrombotic complications, which occur very rarely in adults, after SARS-CoV-2 vaccination with vector-based vaccines [19]. Very rarely, anaphylactic vaccine reactions occur, possibly caused by additives (solubilizers) contained in the vaccine. It should be borne in mind that these substances are by no means unique to these vaccines, but are present in numerous other clinically widely used drugs, as well as in cosmetics, etc.

In adults, the numbers of deaths reported in connection with COVID-19 vaccination (which still does not prove a causal relationship) rank between 1:14,000 (about 6,000 reported deaths [28] in about 88 million vaccinated people in Europe; as of 05 April 2021 [29]) and 1:58,000 [30]. The World Health Organization (WHO) makes no mention of death or mortality associated with vaccination on its vaccination side effects website to date [31]. For people who consider themselves at risk for severe COVID-19 disease, a vaccine-related risk in the order of 1:58,000 is acceptable. For healthy children and adolescents whose risk of dying from COVID-19 approaches zero (0.00002%), it is difficult to understand why policymakers, and even physicians, consider vaccination as a prerequisite for participation in school and community life [3]. The possible iatrogenic triggering of extremely rare but serious vaccination reactions requires a stronger justification than that for the application of the usual, comparatively well-tolerated vaccines against serious diseases in childhood.

5. Development of immunity against vaccination

In the case of virus-vector vaccines, there is the peculiarity that, in addition to the desired immunity against the vaccinated antigen, an immune response against the vector virus may also develop or already exist. This may, in principle, interfere with or render ineffective booster vaccinations and vaccinations against other diseases with such vector virus vaccines [32]. Immunity development does not seem to play a significant role so far in booster vaccinations with the other novel vaccines that are more relevant to children, such as mRNA vaccines COMIRNATY® (Biontech/Pfizer) or mRNA-1273 (Moderna Biotech).

6. Influence of vaccination on the emergence of immune escape mutations

SARS-CoV-2 is spread worldwide and infects millions of people. In the process (as with other respiratory viruses), mutations are constantly occurring, which in unfavorable cases give rise to so-called Variants of Concern (VOC). These are viral variants that are more contagious or pathogenic, or can evade the immune response to a previously undergone infection or vaccination [33–35]. It is not yet clear, either for adults or for children and adolescents, whether COVID-19 vaccinations increase or decrease the likelihood of VOCs, and if so, which ones.

7. Natural or vaccine-induced immunity development

There is no clinical evidence to date that vaccination induces stronger and more sustained immunity than infection with wild virus. Although higher titers of neutralizing antibodies have been repeatedly measured after vaccination [26], it is perhaps much more crucial that the bone marrow of people who have had Sars-Cov-2 infections contains dormant plasma cells that can be reactivated at any time to produce antibodies [36]. Thus, natural immunity, which attacks several components of the virus and

also includes mucosal immunity (IgA), could be broader and more sustainable [37]. Similarly, it is unclear whether natural or vaccine-acquired immunity is enhanced or maintained longer by renewed viral contact in the sense of boosting, and whether perhaps naturally acquired immunity in childhood is more flexible in adapting to viral mutations. In Israel, vaccinated adults – at least two weeks after the second vaccination – had an eightfold higher risk of being infected with VOCs B.1.1.7 or B.1.351 than non-vaccinated adults [38], although this could also be due to a more risky behavior of the vaccinated from an infectiological point of view. There is also evidence that prior contact with coronaviruses leads to a milder course of Sars-COV-2 infection [39], which may also contribute to the fact that teachers and educators are not disproportionately affected by COVID-19 [40–42].

In the only peer-reviewed published trial on 12-15 year-olds, there were 18 COVID-19 cases observed in the placebo group (n=1,129) and no cases in the vaccine group (n=1,131), which indicates an efficacy of between 75% and 100% [26], but says little about effectiveness, or about the number needed to be vaccinated to prevent one severe or fatal case of COVID-19, since that is dependent on background incidence and other factors [15]. In fact, the study was not designed to prove efficacy; its primary outcome parameter was non-inferiority in terms of antibody titers, which it showed in only 190 participants [26].

Society-related aspects: If vaccination were not useful for the benefit of children, yet proven to be safe in the short and long term, would a generally vaccination recommendation of children for the benefit of adults and especially for the benefit of high-risk groups be justified?

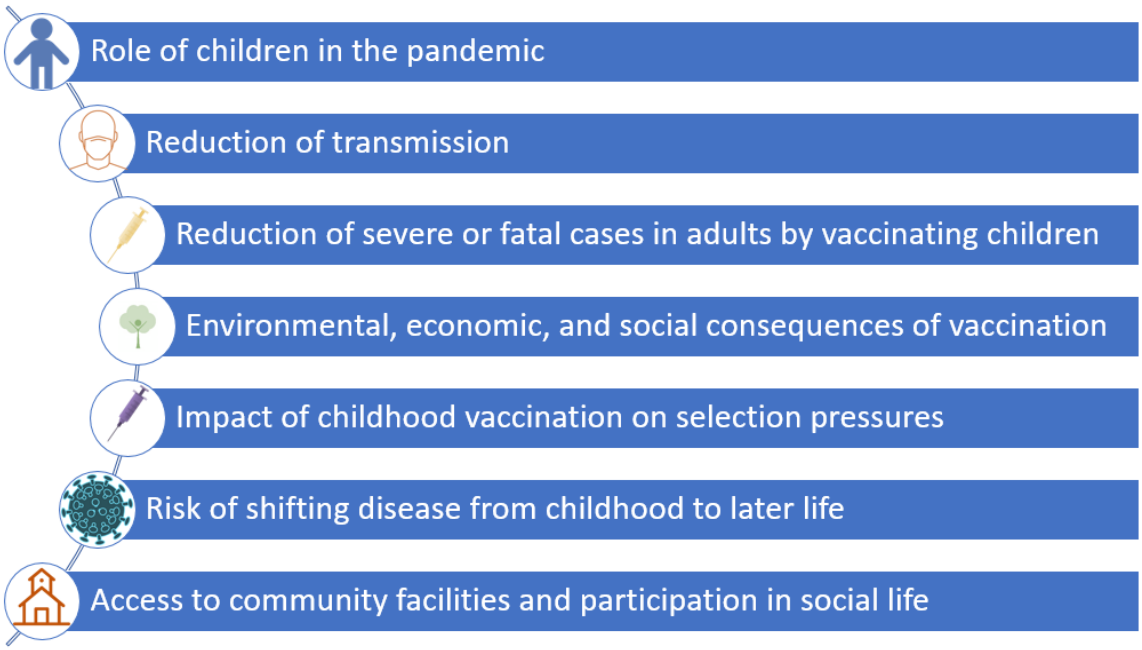

Figure 2: Seven society-related factors to consider when deciding on a collective vaccination recommendation for children for the benefit of others.

8. Role of children in the pandemic

The question to what extent SARS-CoV-2 infections in children contribute to the burden of disease by transmission to adult contacts at high risk for a complicated course is controversial and may need to be re-evaluated in view of the new mutations. Undoubtedly, such events do occur; whether they are quantitatively relevant to ICU occupancy and adult deaths is not known. In principle, children and adolescents must be distinguished, since adolescents tend to be more frequent carriers of corona viruses [43]. The study just cited comes from South Korea, a country that tracks infection numbers in the pandemic much more intensively than Germany. Only when the incidence in all age groups is again below 35 can individual infection chains be traced again reliably.

Teachers and educators, although classified as a risk group, are not affected by COVID-19 with above-average severity, as mentioned above [40–42]. With the more contagious variant B.117, more transmission from children to adults is observed and also reported by the RKI; however, the same is true for transmission from adults to children and from adults to other adults [6] .

In a school-screening in Berlin, for three of nine households with infection(s) detected at cross-sectional assessment, origin of the infection in school seemed possible. After one week, no school-related, secondary infections appeared in affected classes; the attack rate in connected households was 1·1%. [44]. Therefore, the question remains unanswered whether children contribute significantly to the severe illness or death of adults in the course of SARS-CoV-2 infection.

Schools in Germany have recently been ordered to conduct Corona self-testing for students in the classroom. Mandatory (antigen) testing twice a week as a prerequisite for participation in face-to-face classes is an essential part of the currently passed amendment to the Infection Protection Act [45]. This takes place despite a critical statement of pediatric societies and professional associations (German Society for Pediatric Infectiology DGPI, German Society for Pediatric and Adolescent Medicine DGKJ, Professional Association of Pediatricians and Adolescent Physicians BVKJ, German Society for Hospital Hygiene DGKH) [46]. The sensitivity of such antigen tests for the detection of SARS CoV-2 in asymptomatic children of different age groups has not been systematically investigated, but it is certainly significantly lower than that of rtPCR-based detection methods and there are false positive test results in addition to false negatives [47]. Despite these uncertainties, there is an association between testing frequency in schools and daycare centers and age-specific reporting rates for (rtPCR-confirmed) SARS-CoV-2 detections, following a multiplication of testing volume in recent weeks (e.g., Weeks 7-12 2021) [48]. In public discourse, the resulting "high detection rates" in children contribute to the attribution of a "driving" role in the pandemic to children and adolescents. In fact, SARS-CoV- 2

infection differs from influenza in that children have a minor role compared to adults. Children and adolescents up to 14 years of age accounted for 162,549 of 1,516,070 reported infections by calendar week 16 in 2021 (according to the RKI) (10.7%: distributed among 3.8% of 10-14 year olds, 3.8% of 5-9 year olds, and 3.1% of 0-4 year olds) [6].

Seroprevalence studies suggest that a substantial proportion of all SARS-CoV-2 infections in children (and also in adults, but less systematically studied there) are asymptomatic or only mildly symptomatic. According to the updated results of a prospective seroprevalence study of the Helmholtz Zentrum in Munich (screening study Fri1da), the RKI reporting rate underestimates the number of children who have actually undergone an infection by a factor of 3-6 [49], according to which significantly more children would have to be considered as "recovered" and thus the immunity situation of this age group is significantly underestimated.

It has now been shown several times that although young children are significantly less involved in virus transmission than adults, they probably make an age-dependent contribution to the distribution of the virus – which does not, however, justify school closures [50]. On the other hand, a study of 300,000 households found that the more children a family had, the less frequently severe COVID- 19 disease occurred in adults [51]. (This study could easily be replicated using secondary health insurance data in many countries).

9. *Vaccine-specific reduction in transmission*

Current understanding is that the risk of (re)infection is minimal in the first few months (we hardly know any longer than that) after complete vaccination, and fully vaccinated individuals contribute little to the spread of the virus even when tested positive, because the viral load is usually very low [52][53]. How high the transmission risk is in fully vaccinated children is unknown.

The group of people who may not receive COVID-19 vaccination for medical reasons is much smaller than for live measles vaccine, which is dangerous for immunocompromised people [54]. In immunocompromised people, morbidity and mortality resulting from SARS-CoV-2 infection are not comparable to that of measles or varicella infection, especially since measles and varicella are many times more contagious (baseline R0 of approximately 16-18 versus 2.5 to 3.5 for SARS-CoV-2). Therefore, the same arguments as for indirect measles vaccination would not be viable.

10. Reduction of severe or fatal cases in adults by vaccinating children

It is reasonable to expect that a vaccine-induced reduction in transmission in the community would lead to lower disease burden for all. It is not clear whether and, if so, to what extent and with which vaccines vaccinating children would lead to a reduction in severe disease or death in adults[55][56], especially since the increasingly small residual risk for people at risk for severe disease is low if they

use several different vaccines, and protective measures [57]. Not infecting at-risk near contact persons will be a strong motivator for many responsible young people to get vaccinated. The risk-benefit ratio needs to be analysed individually in medical consultation in such cases, depending on social mobility, background incidence, and general health and immune status of the people in question (only relevant if they cannot get properly vaccinated themelves) [15]. However, since eradication of Sars-CoV-2 by means of vaccination is highly unlikely, eventually virtually everyone will repeatedly come into contact with the virus and genetic variants, which means that individuals should not be pressured into vaccinating against their will for the sake of protecting others.

11. Ecological, economic and social consequences of vaccination

If one were of the opinion that the vaccination of all children worldwide would be an essential contribution to "herd immunity", it should be taken into account that one would then have to deal with approx. 1.9 billion children to be vaccinated, with all consequences regarding vaccination controls of (in)direct vaccination compulsions, possible booster vaccinations etc.. This would entail not only economic but also ecological costs, in terms of packaging, transport and not least hydrofluorocarbon gases used to freeze and transport the vaccines currently indicated for this purpose at very low temperature. Hydrofluorocarbon emissions result in up to 23,000 times more global warming than CO_2 [58][59]. Furthermore, it is questionable whether "herd immunity" will be achievable at all, since in many countries (e.g., the U.S.) there is now a decline in vaccination rates and, furthermore, since this can never be achieved by vaccination alone due to reservoirs outside of humans (domestic animals, bats, minks, etc.).

12. Influence of vaccination of children on selection pressure

The immune response to SARS-CoV-2 infection is much more extensive than that to vaccination. This is true in children even after asymptomatic or mild symptomatic infection [37]. Mothers secrete IgA against the virus in breast milk after infection during pregnancy. This does not appear to be the case after vaccination [60, 61]. Thus vaccination may boost VOC selection. The target antigen of available vaccines is susceptible to mutations (see VOCs) so that in vaccinated populations, the selection pressure for mutated virus variants increases. In this respect, vaccine adjustments and booster vaccinations will likely be required repeatedly in the future. In this regard, it is not clear whether a booster induced by non-vaccinated children would be beneficial or detrimental to adult vaccination titer.

13. Risk of shifting disease from childhood to later life, including the unlikelihood of eradicating SARS-CoV-2

Not all people respond to COVID-19 vaccination, and not all can or want to be vaccinated. In addition, SARS-CoV-2 has other reservoirs besides humans and is therefore unlikely to be eradicated. If vaccinations prevent natural exposure to the pathogen as a child and the immunity from vaccination eventually wears off, then the individual, now older, must either revaccinate in time, year after year, or expose himself to the pathogen at a higher, and therefore riskier, age. This argument holds even if natural immunity is not more durable than vaccine-induced immunity, because reinfection might be milder on the background of natural immunity acquired in childhood. Whether this is so is not yet known, i.e. whether a natural infection in childhood with a certain virus variant, e.g. B.1.117, would also be sufficient/useful if there were later new variants against which the current vaccinations did not help.

14. Access to community facilities and participation in social life

One argument in favor of immunization could be that immunity could restore children and adolescents' free access to community facilities and also to many other support services outside such facilities. This weighs heavily because children are impacted and disadvantaged by lack of or limited participation to a much greater extent than adults. In close contact with children, there are also (in fact, extremely rare) people who cannot be vaccinated because they cannot form a sufficient immune response to the vaccination. This was one of the central arguments for indirect compulsory measles vaccination in Germany. Since COVID-19 vaccination does not guarantee sterilizing immunity, there is only minimal safety gain by vaccinating children to protect people who cannot be vaccinated. Safety for these people is mainlyk achieved via adequate hygiene.

In view of the questions raised above, it is surprising that this argument is seriously raised in the public discussion and seems to become a normative force of fact. This is all the more so because it can only be considered should children and adolescents pose any serious danger at all in a world where most adults are fully vaccinated, which is almost certainly not the case in Germany at present.[2]

Conclusions and Discussion

Preliminary conclusion on the child-related aspects (would COVID-19 vaccination in principle be for the benefit of children?

[2] The normative force of the factual is a turn of phrase going back to Georg Jellinek, who sees the ground of validity of law not in reason but in the actual habits of historical-social life [62]. At this point, we can ask ourselves: do we want to make an effort to make reasonable and evidence-based decisions for and with children and adolescents, or do we want to uncritically follow a media-enhanced "normative force of the factual"?

While it is likely that vaccines also lead to immunity to COVID-19 in children, the risk-benefit ratio remains unclear to date. It was deemed “acceptable” by the authors of the registration study [26], without definition of what “acceptable” means. The serious short-term and long-term stress and damage that children are exposed to through interrupted participation in community facilities and events (culture, sport, etc.) is instrumentalized by the authors as a central argument in favor of vaccination [26]. The individual risk of severe COVID-19 or PIMS is very low in children, whereas so far the safety of general SARS-CoV-2 vaccination in children up to the age of 12 years (of which there are about 750,000 per cohort in Germany) cannot yet be described and at the age of 12-15 years, and 16 to 25 years only on the basis of very limited data from registration trials [26]. Simple analogies from populations of vaccinated adults are not permissible here.

Certainly, there are people in the age group of children and adolescents with an increased risk of a complicated course of SARS CoV-2 infection, in whom a risk-benefit assessment speaks for an indication of vaccination (see influenza). However, this does not affect the healthy among them and only a very small proportion of those with chronic diseases (no increased risk has been proven for children and adolescents with asthma or type 1 diabetes, for example). Here, the individual medical benefit of the individual child comes into play [2] and not the overall societal aspect in the context of pandemic containment. Although COVID-19 vaccines may become more tolerable over time, there must be serious arguments to replace naturally acquired polyvalent immunity competence with vaccination that may need to be renewed periodically. It is unclear, despite initial approvals by the FDA and EMA, whether healthy children or adolescents will sustainably benefit from COVID-19 vaccination. On the other hand, there are many concerns about such an indication.

*Preliminary conclusion on the society-related aspects (*can COVID-19 vaccination of children be recommended for the good of the community, independent of (or even counter to) the good of children?*)*

There is no evidence that vaccination in children would be necessary or even effective to protect the adult population still at risk after vaccination and self-protection, or to achieve "herd immunity." In Israel, the death rate associated with COVID-19 is currently declining to less than 1 person per day [63], without vaccination of children and adolescents – so do we need vaccination of children and adolescents at all?

The argument that not enough adults in Germany will get vaccinated to achieve "herd immunity" is neither supported by evidence (assumption from surveys) nor ethically sufficient to shift the risk of vaccination to children and adolescents [64]. It is not yet known how well and how long vaccines work in adults or children and adolescents. The use of the term "herd immunity" often overlooks the fact that it is probably not achievable with respect to COVID-19 [65] because, first, not

everyone will be vaccinated, second, vaccination is not 100% effective and does not confer completely sterilizing immunity, and third, the virus mutates and can replicate in (domestic) animals. Therefore, the question arises as to the basis on which "herd immunity" is calculated and defined. Even the WHO, with its politically motivated restriction of the term "herd immunity" to vaccinations a few months ago, does not provide any clear information on this [66].

Those who want to use the argument of "herd immunity" should keep in mind that the predominantly altruistic confrontation of a child with a) a painful medical measure accompanied by possible vaccination reactions and b) a medical measure whose true complication rate has not been evaluated could violate elementary children's and human rights, which could be unconstitutional. In this case, a person who is not yet legally capable of giving consent is subjected to an externally beneficial measure that is potentially harmful to him or her.

The argument remains that children and adolescents should urgently be allowed to move around freely again soon. It can be questioned whether adults have a right to expose children to the risk of long-term harm with potentially psychotoxic hygiene rules [67], especially since they (the adults) can protect themselves through appropriate hygiene and through vaccination. In an aging society such as Germany's, approximately 80% of the population is now over 14 years of age. If the majority of the population wants to bring about the forcing of a "herd immunity" – which can never be fully achieved anyway – then the dialogue can and must be conducted among those affected, i.e. the 16 to 100 -year-olds. Children can also be naturally immunized against SARS-CoV-2 and perhaps should be, as long as it is not proven that vaccine-generated spike protein immunity is better than natural immunity in the long term and in terms of mutants. For the nearly 2 billion children and adolescents worldwide, these aspects require thorough consideration adapted to country circumstances. In Israel, it is becoming apparent that an extensive interruption of the infection chains in COVID 19 is possible without vaccination of children and adolescents and with a proportion of vaccinated persons in the population well below 80%.

We found 14 issues to consider before making a general SARS-CoV-2 vaccination recommendation for children. A literature search revealed that there is only one publication to date that addresses a similar issue, and that is COVID-19 vaccination coverage in the school context. These authors list nine criteria: four vaccine-related criteria (safety and tolerability, effectiveness in terms of immunogenicity and population-based prevention, cost-effectiveness, increasing safety in the given setting) two disease-related criteria (reduction in mortality/morbidity, reduction in transmission) and three implementation-related criteria (acceptability to the medical community and society, administrative burden for distribution and tracking, adherence burden for vaccinators and vaccinated) [68]. The 14 aspects listed in this publication relate to recommendability rather than enforcement, and are primarily medical-ethical in nature rather than political or cost/administrative.

Opinion surveys at this time show that many parents already have very firm opinions about whether or not to have their child vaccinated against COVID-19. What unites both poles is concern for their children. Creating secure and trustworthy, matched-pair long-term registries could help both groups of parents feel they are contributing to better health and knowledge by regularly entering data and responding to health surveys, whether or not they have their children vaccinated. Because of the unresolved safety issues with Corona vaccines, off-label use poses serious liability risks for physicians. In the absence of licensure and low risk to children, all pediatricians and adolescents should be aware that these vaccines should not be recommended without sound justification. Vaccinating physicians have an unlimited liability risk if they vaccinate children outside of the approval and without a national vaccination recommendation with a vaccine for which safety and efficacy have not been tested in the long term.

Of course, the authors advocate risk-group-based research and, if the results are satisfactory, indications for vaccination for children with special risks as may be the case for children with Down syndrome or children with complex multimodal support needs due to severe underlying neurologic diseases [2]. However, again, it is not clear whether children, not just adults, with Down syndrome are also at higher risk for severe COVID-19 disease and how they tolerate vaccination. It is still unclear which children are really at risk but it appears that asthma [69] [70] and Type 1 Diabetes [71] do not represent a significant risk factor.- Children receiving immunosuppressive medications appear to have similar clinical involvement and outcomes as the pediatric general population, indicating that maintenance treatments should not be interrupted in suspect or confirmed SARS-CoV-2 infection [72].

Responsible development of effective vaccines is an important component of international strategies against epidemics or pandemics. Such vaccines should be accessible worldwide to people who want to protect themselves with them. The indication for travel-related vaccination willl depend on the conditions in the respective countries. However, imagine the safety standards and sample size that would have to be met by a pivotal trial of a COVID-19 vaccine for children to demonstrate that the vaccine has fewer side effects than a disease with a mortality rate of 0.0001% (to date, one in about 2 million infected children and adolescents have died safely from COVID-19) and a severe complication rate of 0.01%.

Containment of the pandemic and protection of vulnerable adults is sufficiently achievable without vaccination of children and adolescents younger than 16 years. Given the open safety and benefit/risk relationships, it seems wrong at this time, from a scientific and ethical perspective, to assume that children and adolescents should be vaccinated against SARS-CoV-2 as a matter of course, or that access to school or social life should be conditional on vaccination status.

May this publication contribute to the differentiating and contextualizing force of reason.

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