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Review

Covid-19 in children aged 5–11: Examining the issues surrounding vaccination and public health policy

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Educational aims

The reader will come to appreciate:

- Examine the effects of COVID-19 disease and restrictions in children aged 5-11 based on national data from Israel.
- Compare COVID risk and vaccine-associated myocarditis risk by age group.
- Examine reasons why parents might choose to vaccinate or not vaccinate their young children against COVID-19.

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ABSTRACT

Background: Children under 12 are now the largest unvaccinated group. Following FDA approval, vaccination of 5–11 year olds is now being encouraged in some countries. We present data on child COVID-related morbidity in Israel and discuss the complexities surrounding vaccinating children aged 5–11. *Methods:* Data were obtained from Israel's open COVID database regarding new confirmed daily COVID-19 cases, severe hospitalized cases and deaths by age group in Israel from February 2020-November 2021, as well as vaccination rate and adverse events following vaccination.

Results: In 5–11 year olds, there were 460 hospitalizations, including 72 moderate to critical (0.007% population rate), with 3 deaths (0.0003% population rate). Children (0–19) made up the largest proportion (41%) of cases, but comprised just <0.1% of deaths, and <1% of severe cases. Post-vaccine myocarditis was much lower than severe COVID risk except in boys aged 12–19 where it was equivalent to the risk of mechanical ventilation due to COVID in boys aged 10–19 (12 per 100,000). High numbers of children were quarantined.

Conclusions: COVID risk is minimal for most children though rare complications do occur. Israeli and US pediatric associations have recommended vaccinating children, particularly in high-incidence scenarios where risk–benefit balance is more clear-cut. However only a quarter of eligible parents have vaccinated their children. Parents may consider health grounds but also restrictions on children, population vaccination levels, waning immunity and new variants, and should be provided with clear information to help them make an informed decision. Policymakers should reevaluate the need for isolations, testing and mask-wearing in school age children, which are detrimental to their wellbeing.

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Abbreviations: CDC, Centers for Disease Control and Prevention; CFR, case fatality ratio; FDA, US Food and Drug Administration; MIS-C, Multisystem Inflammatory Syndrome in Children; MOH, Israel Ministry of Health.

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INTRODUCTION

With the majority of the adult population vaccinated against COVID in many countries, including Israel, children under 12 are now the largest unvaccinated group. Children are both susceptible to infection, but also subject to public health restrictions, including

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masks in schools, regular testing, isolation orders following exposure, and travel restrictions.

Following satisfactory results in Pfizer's clinical trial, the US Food and Drug Administration (FDA) granted emergency use of the Pfizer BioNTech COVID-19 vaccine in children aged 5–11 on October 29, 2021. On November 3rd, 2021 the US Centers for Disease Control and Prevention (CDC) recommended use of the vaccine in children aged 5–11 [1]. Results of Pfizer's clinical trial showed a robust immune response with one third of the adult dose, with a 91% efficacy rate against symptomatic infection. Of interest the trial reported no severe cases of COVID, nor hospitalizations, in either the vaccine or placebo groups [1]. Furthermore the trial was not large enough to assess the risk of rare adverse events, such as myocarditis, in this age group.

Over 8 million US children aged $5-11 (\sim 27\%)$ have already received the vaccine. In Israel the vaccination campaign began on 23rd November 2021 [2]; to date (28th February) around 25% of children aged 5–11 have received at least one dose of the vaccine [3,11].

US and Israeli health authorities are now encouraging parents to vaccinate their 5–11-year olds. The US CDC estimates that one million vaccines can prevent between 80 and 226 hospitalizations for children in this age group, based on a high-transmission scenario [4]. A risk-benefit analysis conducted in England found that benefit in preventing hospitalizations depends on case incidence level: with higher rates of circulating COVID the number of hospitalizations and deaths in children would rise, thus greater benefit of vaccinating children would be seen in a high-incidence scenario [5]. However, the authors state that the benefit of vaccination in preventing deaths and long COVID is independent of case incidence.

Data show that children's risk from COVID is low, but not zero. CDC data show a CFR of 0.009% (199 deaths out of 2,234,443 reported cases) in the 5–11 year age group. This figure is likely much lower in reality since true incidence of COVID-19 remains unknown due to lack of widespread testing in children [6]. Indeed, a report published by the Israel Ministry of Health (MOH) in September 2021 found 51–70% of children with a positive COVID test were asymptomatic, making it highly likely that significant numbers went undiagnosed [7].

Child mortality from COVID in different countries has ranged from 0.8 per million in the Netherlands to 5 per million in the USA (compared to 1000–3000 per million in adults). This is comparable in children to seasonal flu risk [8,9].

Beyond mortality, very low rates of hospitalization were reported in children < 18 years throughout 2020, compared to adults (COVID-NET [10]). Between March and July 2020, the cumulative hospitalization rate was 0.008%, with a weekly rate peaking at 0.001%. 42% of hospitalized children had at least one underlying condition, the most prevalent of which were obesity, chronic lung disease or a history of prematurity. Children with such chronic morbidity will likely see the most benefit from the vaccine.

Several questions surround the vaccination of young children. The current study presents data on child COVID-related morbidity in Israel; and discusses the complexities, controversies and potential ramifications of vaccinating children aged 5–11.

METHODS

Data were obtained from Israel's open-COVID database [3] regarding new confirmed COVID-19 cases, severe (including critically ill) hospitalized cases and deaths by age group, in Israel from February 2020 to November 2021. Severe cases were defined as those with SpO2 < 94% on room air, PaO2/FiO2 < 300 mm Hg, respiratory rate > 30 breaths/min, or lung infiltrates > 50%, in accordance with WHO guidelines. Additional data were obtained on

number of isolations reported, mean age of patients hospitalized with COVID-19, uptake of vaccinations and incidence of adverse events related to vaccination (specifically myocarditis).

RESULTS

COVID-19 morbidity and mortality

Israel Ministry of Health data show a total of 11 COVID-related deaths in children aged 0–19, out of 544,474 confirmed child cases, equating to a CFR of 0.002%, or a population mortality risk of 0.00037% (with 3 million children < 18) [3]. Two of the deaths were newborns of mothers hospitalized with severe COVID, eight had comorbidities and one had no comorbidities.

In the 5–11 age group, there were 460 hospitalizations, of which 72 defined as moderate to critical cases (0.007% population rate), with 3 deaths (0.0003% population rate).

Table 1 presents the cumulative number of confirmed cases, severely ill, patients on ventilators and deaths, by age group, and the percent represented by each age group, during 11 months since the vaccination drive began. While children (0-19) make up the largest proportion (41%) of cases, they comprise a negligible < 0.1% of deaths, and <1% of severe cases.

Mean age of patients hospitalized with COVID-19 in Israel throughout the pandemic remained between 55 and 65, with the mean age of ventilated patients slightly higher (not shown). Disease severity was much higher at older ages, with milder disease at a younger mean age.

Isolations

Aside from morbidity and hospitalizations – hundreds of thousands of people have had to quarantine due to COVID regulations. At the start of the school year in September 2021, the MOH reported that 150,000 school children were in isolation, including 110,000 due to contact with someone who tested positive. The actual number in quarantine was estimated to be closer to 280,000 since not all cases were reported by parents via the official MOH website [11]. Peaks occurred in September and January, with the highest daily number of isolations in children of 19,000 on September 15th 2021, and 18,000 on January 15th 2021. Children aged 5–11 had the greatest number of isolations relative to other age groups.

Vaccination uptake by age group

To date, over 80% of 16+ Israeli adults (and 90% of 40–89 year olds) have received at least one dose of the vaccine, however coverage is lower in the 12-15 age group with just 57% vaccinated with one dose, and 47% with two doses (Table 2).

Risk of myocarditis following vaccine was higher for males compared to females and was lower in the 12–15 age group than for older groups, with highest rates among 20–24 among females and 16–19 among males (Table 3).

Table 4 compares rates per 100,000 of reported events of myocarditis following vaccination, and of severe disease and ventilated status per 100,000 confirmed COVID cases. For most age groups, the risk of severe disease and ventilation is much higher from COVID than the risk of myocarditis following vaccination, with the exception of young males where the risk of myocarditis in boys aged 12–19 was equivalent to the risk of ventilation due to COVID in boys aged 10–19 (12 per 100,000). Age groups differ as vaccines were given so far only to children aged 12+, while morbidity is reported for 0–9 s and 10–19 s.

Table 1

Covid-19 related morbidity and mortality in Israel by age group, since beginning of vaccination: 19.12.20–15.11.21.

Age group	Gender	Number of confirmed cases	Percent of confirmed cases	Number of severe cases including critically ill	Percent of severe cases including critically ill	Number of patients on ventilators	Percent of patients on ventilators	Number of deaths	Percent of deaths
0-9	Female	128,249	9.7	37	0.2	9	0.2	3	0
0–9	Male	131,139	9.9	53	0.2	13	0.3	3	0
10-19	Female	144,393	10.9	56	0.3	13	0.3	4	0
10-19	Male	140,693	10.6	44	0.2	19	0.4	4	0
20-29	Female	121,117	9.2	230	1	47	1	16	0.2
20-29	Male	100,693	7.6	179	0.8	42	0.9	22	0.3
30–39	Female	101,742	7.7	489	2.2	83	1.8	31	0.4
30–39	Male	82,416	6.2	547	2.5	77	1.6	42	0.5
40-49	Female	82,491	6.2	812	3.7	119	2.5	62	0.8
40-49	Male	68,357	5.2	1219	5.5	212	4.5	99	1.2
50-59	Female	54,317	4.1	1299	5.9	200	4.2	158	1.9
50-59	Male	46,395	3.5	1943	8.8	446	9.5	313	3.8
60-69	Female	33,394	2.5	1776	8	395	8.4	440	5.4
60-69	Male	31,046	2.3	2679	12.1	768	16.3	805	9.9
70–79	Female	17,143	1.3	2062	9.3	445	9.4	780	9.6
70–79	Male	15,792	1.2	2834	12.8	818	17.3	1283	15.8
80-89	Female	9791	0.7	2135	9.6	345	7.3	1262	15.5
80-89	Male	7143	0.5	2090	9.4	479	10.2	1398	17.2
90+	Female	3570	0.3	1019	4.6	91	1.9	826	10.1
90+	Male	1743	0.1	651	2.9	97	2.1	590	7.2

Table 2

Cumulative proportion of vaccination* by age group and dose: 19.12.20–15.11.21.

Age group	% vaccinated with first dose	% vaccinated with second dose	% vaccinated with third dose	% unvaccinated	% out-of-date vaccines	% up-to-date vaccination
12-15	57.2	47	0.1	41.79	0.01	58.2
16-19	87.2	75.7	33.5	21.24	15.86	62.9
20–29	83.9	74.8	48.3	16.34	18.34	65.32
30–39	87.6	80.2	53.6	13.01	17.97	69.02
40-49	89.5	83.1	62	10.82	13.78	75.4
50-59	90.3	85	69	9.28	10.86	79.86
60–69	92.2	88.6	77	7.85	6.92	85.24
70–79	90.4	88.4	82.9	7.11	5.27	87.62
80-89	90.3	88	80.1	7.91	7.35	84.75
90+	83.6	80.5	71.2	12.31	12.88	74.81

*Adverse events following vaccination by age group.

DISCUSSION

Data from nearly two years of the pandemic show low risk from COVID in young children, similar to the risk of seasonal flu. Children comprise a large proportion of positive cases and of those in quarantine. However, they make up a very small proportion of severe disease and deaths. These figures are supported by global data which also show that children (aged 0–19) make up around 0.3% of global COVID deaths or a total of 8,700 deaths [8].

Parents will be weighing up the necessity and safety of vaccinating young children. While risk of serious illness is low in young children, some children require hospitalization, and rare complications do occur, including long-COVID, and Multisystem Inflammatory Syndrome in Children (MIS-C) [12]. In Israel, 2660 children (0-18) were hospitalized with COVID up to October 2021, including 398 with severe disease; the risk of hospitalization with moderate to severe disease was reported as 1 in 900 confirmed child cases [13]. In the 5–11 age group 460 children were hospitalized, of which 72 for severe disease (estimated risk 1 in 3,000), of which 3 died. In the USA over 5000 cases (45% in children aged 5-11) and 48 deaths resulting from MIS-C and positive for COVID-19 were reported in children [2]. In Israel, 150 children were hospitalized with MIS-C [13]. While long COVID has been reported in around 1% of children in Israel [13], some studies have shown reported symptoms to be in line with population prevalence [14]. Short- and long-term complications are less common in the pediatric population aged 5–12 than in adults. However, vaccinating children of all ages will protect them from the disease and its potential complications. Children with comorbidities, including asthma, obesity, cystic fibrosis, heart disease, diabetes and immunosuppression, are at higher risk of severe illness [2] and should be first in line for the vaccine. A study in 12–18 year olds found the vaccine to be 93% effective in reducing the risk of hospitalization, with 97% of those hospitalized being unvaccinated [15]. A more recent (preprint) study reported lower effectiveness against infection in 5–11 year olds from the Omicron variant a month following vaccination, but still protection against severe disease [16].

No significant short- or long-term side effects have emerged during the past year of vaccination, including millions of children over the age of 12. The trial in children aged 5–11 reported adequate safety, though sample size (1518 children who received the vaccine and 750 who received placebo) was insufficient to detect very rare adverse events. However, four million children have already been vaccinated in North America which provides greater support for the safety profile of the pediatric dose of the vaccine. Cases of myocarditis have been reported following COVID vaccination, particularly in young males, though most cases were mild and usually did not require special treatment with full recovery. In most age groups the risk of severe disease from COVID out-

Table 3

Incidence of myocarditis following COVID vaccination by age group.

Gender	Age group	First dose 0–21 days after vaccine			Second dose		Third dose 0–30 days after vaccine			
					0–30 days after va	ccine				
		Number of vaccination dose	Number of reported events of myocarditis	Rate per 100,000	Number of vaccination dose	Number of reported events of myocarditis	Rate per 100,000.	Number of vaccination dose	Number of reported events of myocarditis	Rate per 100,000.
Female	12-15	207,844	0	0.0	166,772	1	0.33	331	0	0.0
	16-19	250,629	0	0.0	223,402	2	0.69	106,338	0	0.0
	20-24	265,066	1	0.3	243,466	6	1.80	153,353	0	0.0
	25-29	248,314	0	0.0	229,839	2	0.64	139,418	0	0.0
	30+	2,131,311	3	0.12	2,032,615	7	0.29	1,581,032	1	0.04
Male	12-15	194,765	1	0.31	155,092	11	3.45	313	0	0.0
	16-19	256,067	3	0.99	224,406	36	11.92	104,162	6	1.99
	20-24	276,455	6	1.73	252,602	26	7.49	150,524	6	1.73
	25-29	258,610	3	0.94	240,024	20	6.27	143,931	1	0.31
	30+	1,986,677	10	0.44	1,900,434	31	1.37	1,484,868	12	0.53
Overall		6,075,738	27	0.29	5,668,652	142	1.51	3,864250	26	0.28

Table 4

Rates of myocarditis following vaccination vs rates of severe disease and ventilation resulting from COVID-19 by sex and age group.

Gender	Age group	First dose	Second dose	Third dose	Age	Severe disease rate			Ventilated rate	
		Rate of reported myocarditis per 100,000 vaccines	Rate of reported myocarditis per 100,000 vaccines	Rate of reported myocarditis per 100,000 vaccines		Number of severe cases	N confirmed	Rate per 100,000 confirmed	Number ventilated	Rate per 100,000 confirmed
	0–9	-	-	-	0–9	90	262,100	34.3	22	8.4
Female	12-19	0.0	0.76	0.0	10-19	55	145,270	37.9	13	8.9
	20-29	0.19	1.69	0.0	20-29	229	121,118	189.1	48	39.6
	30+	0.12	0.29	0.04	30+	9630	303,491	3173.1	1689	556.5
Male	12-19	0.88	12.38	5.7	10-19	46	141,404	32.5	18	12.7
	20-29	1.68	9.34	2.38	20-29	180	100,466	179.2	42	41.8
	30+	0.44	1.37	0.53	30+	11,986	253,167	4731.4	2904	1147

weighs the risk of myocarditis following vaccination [17]. Our findings support the advantage of preventing severe disease over the risk of myocarditis in most age groups although data show a reduced risk-benefit ratio in teenage boys.

Expert panels have ruled that the COVID vaccine will be recommended in young children age-5–11 [1]. Different countries have taken different stances: the Israel Pediatric Association concluded that the benefits of the vaccine in this age group outweigh any possible risks [13]; the American Association of Pediatrics recommends vaccination for all children age 5 and up and pediatricians are encouraged to actively promote the vaccine. In contrast, the Canadian Pediatric Society recommended that the vaccine may be offered to children [18], and that immunocompromised children should receive a series of three doses [19]. In the UK, the Royal College of Pediatrics and Child Health is recommending vaccination only for children at high risk of family members of immunocompromised patients, noting that "the risks and benefits around COVID-19 vaccination for children and young people are more finely balanced than for older age groups" [20]. Vaccination of children has begun in several European countries. In the US and Israel, around a quarter of eligible children in this age group have received at least one dose, with uptake plateauing in recent weeks.

Since morbidity in children is low, the decision whether to vaccinate children may be based to some extent on indirect benefits – reducing transmission in general and thus reducing older adults' risk; preventing isolations and school closures and the resultant indirect, long-standing cost to all children and even more so in vulnerable populations [21].

Besides individual protection, vaccination of children should reduce viral transmission, further protecting the elderly and unvaccinated, and possibly reducing the development of new variants. Israel has a high proportion of children, unable until now to get vaccinated, capping vaccine coverage at around two thirds - at the national level, therefore vaccination of additional groups is welcome. Beyond altruistic protection at the national level, vaccinating children can protect their older family members.

Several surveys have assessed parental willingness to vaccinate children < 12 years against COVID. In May 2020 the International COVID-19 parental attitude study reported that 65% intended to vaccinate their child when possible [22]. A study in Canada, USA, and Israel [23], found a correlation between parental willingness to vaccinate children and rate of adult vaccination. A survey of UK school students found 50% would opt to take the vaccination, 37% were undecided, and 13% would opt out [24].

Parents' decision to vaccinate will also be motivated by the promised removal of restrictions and isolations. Children have been affected by the pandemic, missing school, adapting to virtual learning, lockdowns, capsules, restricted social activities and maskwearing. In Israel in recent months, with high viral spread of the Omicron variant, children have been subject to an endless cycle of class quarantines. An effective vaccine will contribute to a return to routine and authorities should consider ending the regime of class quarantines and shutdowns. A recent study supported elimination of student quarantine following masked exposure to COVID-19 within school, due to exceptionally low secondary transmission, citing that it "further disrupts in-person learning with uncertain benefit" [25].

Parents may be reluctant to vaccinate due to low perceived risk and severity of the disease in children. According to the American Academy of Pediatrics, 0.01% of child cases resulted in death in the US [26]. In Canada, severe outcomes in children aged 5–11 were also very infrequent, with hospitalization and death occurring in <0.3% and <0.002%, respectively, of confirmed cases [19]. Disease severity with the newer Omicron variant appears to be milder than previous strains, further reducing parents' incentive to vaccinate. Risk from COVID in children may be compared with flu, also mild in most cases but leading to hospitalization and death in some cases. Flu-related hospitalization, admission to the intensive care unit, and mechanical ventilator use and death rates have been similar to those of COVID in children [9,27]. Flu Vaccine effectiveness (40% to 60%) [28] is far lower compared with that reported for the COVID-19 vaccine; yet flu vaccination is recommended for every-one over 6 months without contraindications. However, uptake is not high hovering around 20% in Israel for young children and just 10% for older children [29], reflecting similar difficulties of convincing parents to vaccinate young children.

Another factor influencing the decision to vaccinate is waning immunity – while COVID-19 vaccines have successfully reduced the risk of severe disease and death, immunity wanes after around 6 months, requiring a booster. Six months following a massive vaccine drive, Israel entered a new pandemic wave, which was subsequently reduced with a booster dose of the vaccine. A study of over a million patients at an Israeli HMO indeed found waning protection following 2 doses of the Pfizer vaccine in all age groups with those vaccinated earlier having a much higher infection rate [30]. While data clearly show the protective effect of the vaccine against severe disease, breakthrough infections following vaccination have somewhat undermined public faith in the vaccine [31]. A Mayo Clinic study demonstrated that in July 2021, m-RNA vaccine effectiveness against infection was lower, but has remained high against hospitalization [32].

The vaccine being offered now to children is thus not optimal and may need regular boosters to maintain efficacy. It remains to be seen whether immunity will wane in children as in adults and whether regular shots will be required, particularly with the advent of new variants such as Omicron.

Issues of health equity also surround COVID vaccination. A socioeconomic gradient has been noted in COVID vaccination of adults [33]. Indeed a Canadian survey of parents found a similar pattern, with lower income households less likely to accept vaccination of their children; and teenagers from the most deprived neighborhoods half as likely to be vaccinated as those from the least deprived [34]. This raises the question as to whether vaccines are being distributed equitably. Furthermore, child mortality was higher in some countries, for example 0.7% of total COVID mortality in Brazil. A nationwide Brazilian study found differences in mortality by socioeconomic variables – both social vulnerability index and regional Gini index [35]. Unlike mortality, incidence of cases was not significantly related to SES [35].

Beyond the direct effects of COVID, the indirect effects of lockdowns and public health restrictions also differentially effect the weakest populations and "in virtual learning environments, the achievement gap is widening for children who are disadvantaged" [36]. It is important that the most vulnerable children at high risk gain access to vaccines – indeed the provision of vaccines to children while many countries have yet been able to provide sufficient doses for the adult population is controversial – yet if child vaccines are being provided, perhaps they should be targeted to those most at risk.

LIMITATIONS

There are some limitations when assessing the data. (1) The number of positive cases in the population is a function of the rate of testing and is likely highly underestimated. (2) Considering the likelihood that there were many undiagnosed cases of COVID, the CFR is likely much lower than reported. (3) Furthermore, numbers of children hospitalized with COVID is likely to include those hospitalized for another reason but testing positive for COVID, resulting in overestimation of disease severity. 4) Data presented here

are aggregate data from existing MOH databases and not individual data.

CONCLUSION AND POLICY IMPLICATIONS

For the vast majority of children, COVID presents a minimal threat. Parents will need some reassurance that the vaccine is both safe and necessary before vaccinating their young children. They may also want reassurance that policy will change – that mask-wearing in schools will not be forever and that vaccinated children might be allowed more freedom.

Recommendations:

- Vaccines should be offered and encouraged, particularly in those with high risk and background morbidity (chronic health conditions or immunocompromised), and where COVID incidence is high, but made available for all.
- Due to the socioeconomic gradient in both morbidity and vaccination, it is important to make vaccines available in the geographic and socioeconomic periphery and to minority groups.
- Ensure parents keep sick children home and promote continued good hygiene.
- Reduce COVID testing among children; perhaps a better use of resources would be for pediatricians and parents to be aware of and monitor symptoms of severe disease or MISC, as with other seasonal viruses.
- In light of minimal risk to children, equivalent to other seasonal viruses, reevaluate and try to minimize quarantine and isolations and mask-wearing requirement in school-age children, all of which are detrimental to their wellbeing.

A precedent has been set during this pandemic involving school closures and enforced isolation of entire classes to deal with viral spread – while this may have been justified in the pre-vaccine era, in order to protect the elderly and vulnerable, we must re-examine whether these measures are still necessary. If children's risk from COVID is similar to risk from seasonal flu or other respiratory infections, as the data indicate, vaccines will not need to be mandated but should be offered to parents. In parallel, now that risk has been reduced for older vaccinated adults, we should consider removing restrictions on children.

In countries fortunate enough to have a majority of adults vaccinated, COVID in children may in the future be treated as any other viral disease – we may need reminding how we used to respond to seasonal viruses. It remains to be seen how willing parents are to vaccinate their young children, whether regular boosters will be needed, and whether the COVID vaccine may eventually become just another one of the routine childhood vaccines given to the majority of children.

DIRECTIONS FOR FUTURE RESEARCH

- National data should be made more transparent to allow risk comparisons in children of different viral illnesses, which could help parents to make an informed decision about vaccination.
- Parental surveys may be used more widely to assess current attitudes to COVID vaccination and to public health restrictions in children which could help provide targeted information and inform policy.

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CONFLICT OF INTEREST DISCLOSURE

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