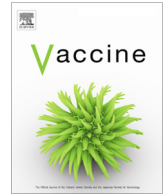




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## Short communication

# Childhood vaccinations: Hidden impact of COVID-19 on children in Singapore



Youjia Zhong<sup>a</sup>, Hannah Eleanor Clapham<sup>b</sup>, Ramkumar Aishworiya<sup>a,\*</sup>, Ying Xian Chua<sup>c</sup>, Jancy Mathews<sup>c</sup>, Mabel Ong<sup>c</sup>, Jingji Wang<sup>a</sup>, Belinda Murugasu<sup>d</sup>, Wen Chin Chiang<sup>d</sup>, Bee Wah Lee<sup>a,e</sup>, Hui-Lin Chin<sup>a</sup>

<sup>a</sup> Khoo Teck Puat – National University Children's Medical Institute, National University Health System, Singapore

<sup>b</sup> Saw Swee Hock School of Public Health, National University of Singapore, Singapore

<sup>c</sup> National University Polyclinics, Singapore

<sup>d</sup> Mount Elizabeth Medical Centre, Singapore

<sup>e</sup> Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

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## ABSTRACT

Although the direct health impact of Coronavirus disease (COVID-19) pandemic on child health is low, there are indirect impacts across many aspects. We compare childhood vaccine uptake in three types of healthcare facilities in Singapore – public primary care clinics, a hospital paediatric unit, and private paediatrician clinics – from January to April 2020, to baseline, and calculate the impact on herd immunity for measles. We find a 25.6% to 73.6% drop in Measles-Mumps-Rubella (MMR) uptake rates, 0.4 – 10.3% drop for Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza (5-in-1), and 8.0–67.8% drop for Pneumococcal conjugate vaccine (PCV) across all 3 sites. Consequent herd immunity reduces to 74–84% among 12-month- to 2-year-olds, well below the 95% coverage that is protective for measles. This puts the whole community at risk for a measles epidemic. Public health efforts are urgently needed to maintain efficacious coverage for routine childhood vaccines during the COVID-19 pandemic.

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## 1. Introduction

The coronavirus disease pandemic has infected more than 9 million people and killed more than 400 000 by the time of writing on 24 June 2020. Despite its scale, the overall direct health impact on the paediatric population has been small. Only 1.2–5% of reported cases thus far are children between 0 and 19 years of age, of whom 90% are either asymptomatic or have mild disease [1].

Like previous epidemics such as the 2014 Ebola outbreak, the true impact of COVID-19 on the paediatric population may lie in its indirect health impacts [2]. Contributory factors include rationing of healthcare resources, physical distancing measures, and fear of exposing children to COVID-19 at healthcare facilities [3,4]. Reports of reduction in vaccine uptakes in developing countries

have already emerged despite warning from international agencies to not neglect essential childhood vaccines [5], and to take efforts to safeguard supply chains [6,7]. Quantitatively, this reduction has been measured in England, where Measles-Mumps-Rubella (MMR) vaccination rates fell after introduction of physical distancing measures in March 2020 [4], and in the United States, where sharp drops in non-influenza vaccines were demonstrated after the declaration of national emergency [3].

Singapore instituted public health measures targeted at COVID-19 subsequent to the first reported case on 23 January 2020. These were increasingly restrictive through January to March 2020, culminating in border closures on 23 March and a near-lockdown called the “Circuit Breaker” (CB) mandating cessation of non-essential services and school closure on 7 April [8,9]. Routine childhood vaccinations from 0 to 18 months of age were considered essential and remained available during this period [10]. Baseline coverage for routine childhood vaccines in Singapore is high; coverage for MMR in 2018 was 95.6% for primary dose and 88.0% for booster dose [11]. No significant outbreak of vaccine-preventable diseases (VPDs) has been reported in the last 15 years [11].

The progressive pandemic measures undertaken in Singapore between January to April 2020 present a unique opportunity to study the effects of a pandemic on the uptake of routine childhood

*Abbreviations:* Circuit Breaker, CB; Confidence intervals, CIs; Coronavirus disease, COVID-19; Measles-Mumps-Rubella, MMR; Measles-Mumps-Rubella-Varicella, MMRV; Pneumococcal conjugate vaccine, PCV; Vaccine-preventable diseases, VPDs.

\* Corresponding author at: Khoo Teck Puat National University Children's Medical Institute, National University Health System, Department of Paediatrics, National University Hospital, Singapore.

E-mail address: [aishworiya\\_ramkumar@nuhs.edu.sg](mailto:aishworiya_ramkumar@nuhs.edu.sg) (R. Aishworiya).

vaccinations. The aim of this study is to examine vaccination uptake in 3 types of healthcare facilities from January to April 2020 compared to the baseline rates in January to April 2019. Using measles as an example, we estimate how this translates into lowered herd immunity in the 1 to 2-year age group.

## 2. Methods

This was a multi-center retrospective cohort study, which represents a convenience sampling of the 3 types of healthcare facilities available in Singapore: 5 public primary care clinics under the National University Polyclinics group (“polyclinics”), the pediatric outpatient clinic at National University Hospital, Singapore (“hospital”), and 3 private pediatric practices (“private clinics”). Parents can opt to take their child to any of these 3 types of healthcare facilities in Singapore for each vaccine dose. 70% of children get their vaccinations from the public sector, comprising polyclinics and hospitals, and 30% from private clinics. The polyclinics sampled comprised all the polyclinics under one of the 3 major healthcare clusters, and the hospital is one of 2 tertiary pediatric centers in the country. Vaccines studied were the MMR vaccine, including the Measles-Mumps-Rubella-Varicella (MMRV) vaccine, the pentavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza (5-in-1) vaccine, including the hexavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza-hepatitis B (6-in-1), and the 13-valent Pneumococcal conjugate vaccine (PCV). All administered vaccine doses were counted. Primary outcome was the month-on-month number of doses of MMR/MMRV, 5-in-1/6-in-1 and PCV administered in January to April 2020, compared to January to April 2019. Data from the same periods in 2017 and 2018 was also collected. Data for the first 3 months of the year January to March (T1) was analyzed separately from April (T2) as the CB was implemented on 7 April 2020.

### 2.1. Statistical methods

We combined January-March vaccination numbers for each vaccine at each site for 2019 and separately, for 2020. We calculated the percent change in vaccines given in T1 2020 and in T2 2020 when compared to 2019. We used the Wilson method for confidence intervals [12].

As data on the number of missed vaccinations by primary or booster was not available, the percentage of the population that missed a vaccination and hence not fully protected was calculated. From data on vaccination numbers in different sectors in Singapore [13], we found that approximately 70% of vaccinations are done in the public sector and 30% in private sector. We therefore assumed that 70% of individuals would have vaccinations in the public sector, and used the polyclinic data to estimate how many total individuals missed vaccination in this 70% of the populations. We did the same for the 30% of the population in the private clinics. Combining these numbers give us the total missed vaccinations in the total population. We assumed that the baseline vaccine numbers represented 95% coverage as this is the reported coverage, therefore the drops in vaccination were relative to 95% coverage [11]. We assumed that the month of May had the same vaccination uptake as April, as the CB continued. Therefore, to calculate the percentage of the entire cohort who missed a vaccine, we assumed that for 3 out of 12 months the vaccine reduction was the weighted (missed vaccines in each sector weighted by the proportion of individuals who are vaccinated in that sector) January-March reduction in vaccination coverage (relative to baseline coverage) and for 2 out of 12 months this was the weighted April to May reduction (which is relative to 95% coverage). For the rest of the year

(7/12 months) we assessed two scenarios: 1: vaccines return to baseline levels (95% coverage), or 2: vaccines return to January-March 2020 levels (reduced coverage). This calculation models the coverage in this vaccine cohort, not in the overall population.

All analysis was performed in R-3.6.2.

### 2.2. Ethics

This study was conducted with the oversight of the Domain Specific Review Board, National Healthcare Group, Singapore (No. 2020/00375), with waiver of consent.

## 3. Results

### 3.1. Polyclinics

In polyclinics, all vaccines recorded a drop in T1 2020, with a more significant drop in T2 2020; this was 25.6% (95% confidence intervals (CIs): 23.3 to 28.1) for MMR/MMRV, 10.3% (95% CIs: 9.1 to 11.5) for 5-in-1/6-in-1 and 8.0% (95% CIs: 6.8 to 9.4) for PCV [Table 1, Fig. 1].

### 3.2. Hospital

In the hospital, MMR/MMRV numbers dropped mainly in T2 2020 by 57.3% (95% CI 50.0 to 65.0). 5-in-1/6-in-1 numbers, however, increased by 22.0% (95% CI 19.0 to 25.4) in T1 2020, and remained similar for T2 2020. PCV numbers increased by 8.8% (95% CI 6.7 to 11.5) in T1 2020, and decreased by 12.9% (95% CI 8.9 to 18.3) in T2 2020.

The trends for January to April 2017 and 2018 were also analyzed to evaluate whether the year-on-year vaccination numbers were stable in the years prior to 2020; these were stable for polyclinics and private clinics, but in the hospital there was an increasing trend of number of vaccines administered between 2017 and 2019, which could be related to expansion of hospital services in the same time period [Supplementary material, Table 1].

### 3.3. Private clinics

In private clinics, MMR/MMRV vaccines dropped by 52.16% (95% CI 47.2 to 57.1) in T1 2020 compared to 2019, and even more in T2 2020, by 73.6% (95% CI 65.1 to 81.0). 5-in-1/6-in-1 vaccines dropped slightly in T1 2020, but significantly in T2 2020 by 47.8% (95% CI 50.0 to 56.1). PCV dropped 27.9% (95% CI 22.9 to 33.5) in T1 2020, and even more in T2 2020 by 67.8% (95% CI 57.4 to 77.0).

### 3.4. MMR/MMRV

The detailed trend for January to April 2017 to 2020 is shown in Fig. 2 for MMR/MMRV; note that data was not available for the Hospital in 2017. By April 2020, the number of MMR / MMRV vaccines administered in all 3 types of healthcare facilities was the lowest in all the months studied. This trend was more pronounced for the private clinics and the polyclinics; however, as the Hospital was in the process of expanding its outpatient capacity from 2017 onwards, an increase in number of administered vaccines was expected and thus the observed trend of slight decrease is significant.

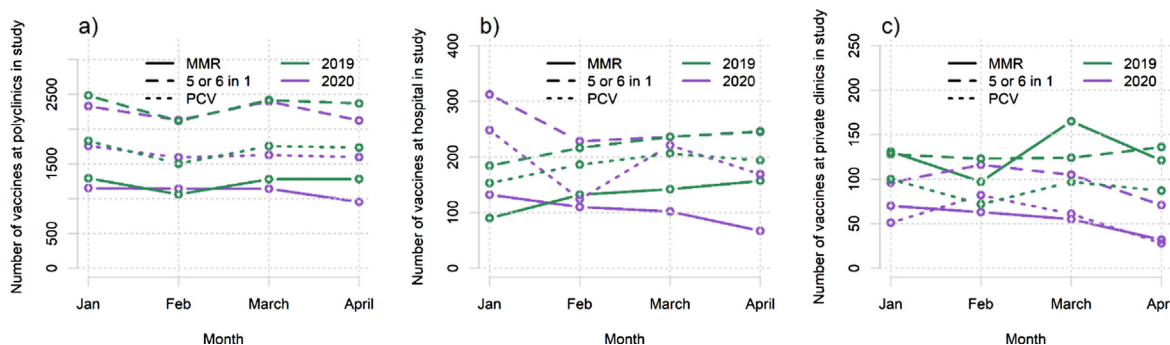
### 3.5. Impact analysis

We modelled the impact of this drop for MMR/MMRV. We used 5% drop in public sector numbers and 50% drop in private numbers

**Table 1**  
Number of vaccines given for January to March 2020 compared to the baseline in January to March 2019, and for April 2020 compared to the baseline in April 2019, with the estimates of the percentage change in number of vaccines between time periods, at each type of healthcare facility.

Vaccine	Place	Number of vaccines Jan - March 2019	Number of vaccines Jan-March 2020	% Difference January - March 2019–2020 (95% confidence interval)	Number of vaccines April 2019	Number of vaccines April 2020	% Difference April 2019–2020 (95% confidence interval)
MMR / MMRV	Polyclinics	3634	3436	-5.5 (-6.2 to -4.8)	1283	954	-25.6 (-28.1 to -23.3)
MMR / MMRV	Hospital	364	344	-5.5 (-8.3 to -3.6)	157	67	-57.3 (-65.0 to -50.0)
MMR / MMRV	Private clinics	393	188	-52.2 (-57.1 to -47.2)	121	32	-73.6 (-81.0 to -65.1)
5-in-1 / 6-in-1	Polyclinics	7015	6855	-2.3 (-2.7 to -2.0)	2367	2123	-10.3 (-11.5, to -9.1)
5-in-1 / 6-in-1	Hospital	636	776	22.0 (19.0 to 25.4)	246	245	-0.4 (-2.3 to -0.1)
5-in-1 / 6-in-1	Private clinics	375	317	-15.5 (-19.5 to -12.2)	136	71	-47.8 (-56.1 to -40.0)
PCV	Polyclinics	5087	4977	-2.2 (-2.6 to -1.8)	1735	1596	-8.0 (-9.4 to -6.8)
PCV	Hospital	545	593	8.8 (6.7 to 11.5)	194	169	-12.9 (-18.3 to -8.9)
PCV	Private clinics	269	194	-27.9 (-33.5 to -22.9)	87	28	-67.8 (-77.0 to -57.4)

MMR = Measles-Mumps-Rubella vaccine, MMRV = Measles-Mumps-Rubella-Varicella vaccine, 5-in-1 = pentavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza vaccine, 6-in-1 = hexavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza-Hepatitis B vaccine, PCV = 13-valent Pneumococcal conjugate vaccine, Polyclinics = 5 public primary care clinics under the National University Polyclinics group, Hospital = Specialist Outpatient Clinic of the Khoo Teck Puat National University Children’s Medical Institute, National University Hospital, Singapore, Private clinics = 3 private paediatrician practices.



**Fig. 1.** Number of vaccines given by month, for each facility, for January to April 2019 and 2020. Footnote: MMR = Measles-Mumps-Rubella vaccine, MMRV = Measles-Mumps-Rubella-Varicella vaccine, 5-in-1 = pentavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza vaccine, 6-in-1 = hexavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza-Hepatitis B vaccine, PCV = 13-valent Pneumococcal conjugate vaccine, Polyclinics = 5 public primary care clinics under the National University Polyclinics group, Hospital = Specialist Outpatient Clinic of the Khoo Teck Puat National University Children’s Medical Institute, National University Hospital, Singapore, Private clinics = 3 private paediatrician practices).

from January to March, and 25% drop in public and 73% drop in private clinics in April and May. As the public sector in Singapore mainly comprises polyclinics, we used drops observed in polyclinics to represent the public sector. We gave the public sector a weightage of 70% and private sector 30% as mentioned in “Methods”, and started with the baseline coverage of 95.6% [11]. [Supplementary material](#) Table 2 gives a step-by-step breakdown of our calculations. If we assume these reductions in vaccine uptake to be representative of public and private sectors in Singapore, we estimate that the proportion of the cohort of 1 to 2-year-olds that are fully immunized against measles at the end of May 2020 to be 84% (95% CIs: 82 to 86%). The vaccine coverage will remain at this level if vaccination returns to baseline (2018) levels [11] (Fig. 1 Scenario 1). If the COVID-19 pre-CB (January-March) trends continue for the rest of 2020, the fully immunized population will decrease further to 74% (95% CIs: 72 to 77%) (Fig. 3 Scenario 2). This modelling is only for the 1 to 2-year-old age group, which is eligible for MMR vaccination, not for the total population. To prevent an outbreak of measles, WHO recommends 95% of any population should be fully vaccinated (Fig. 3).

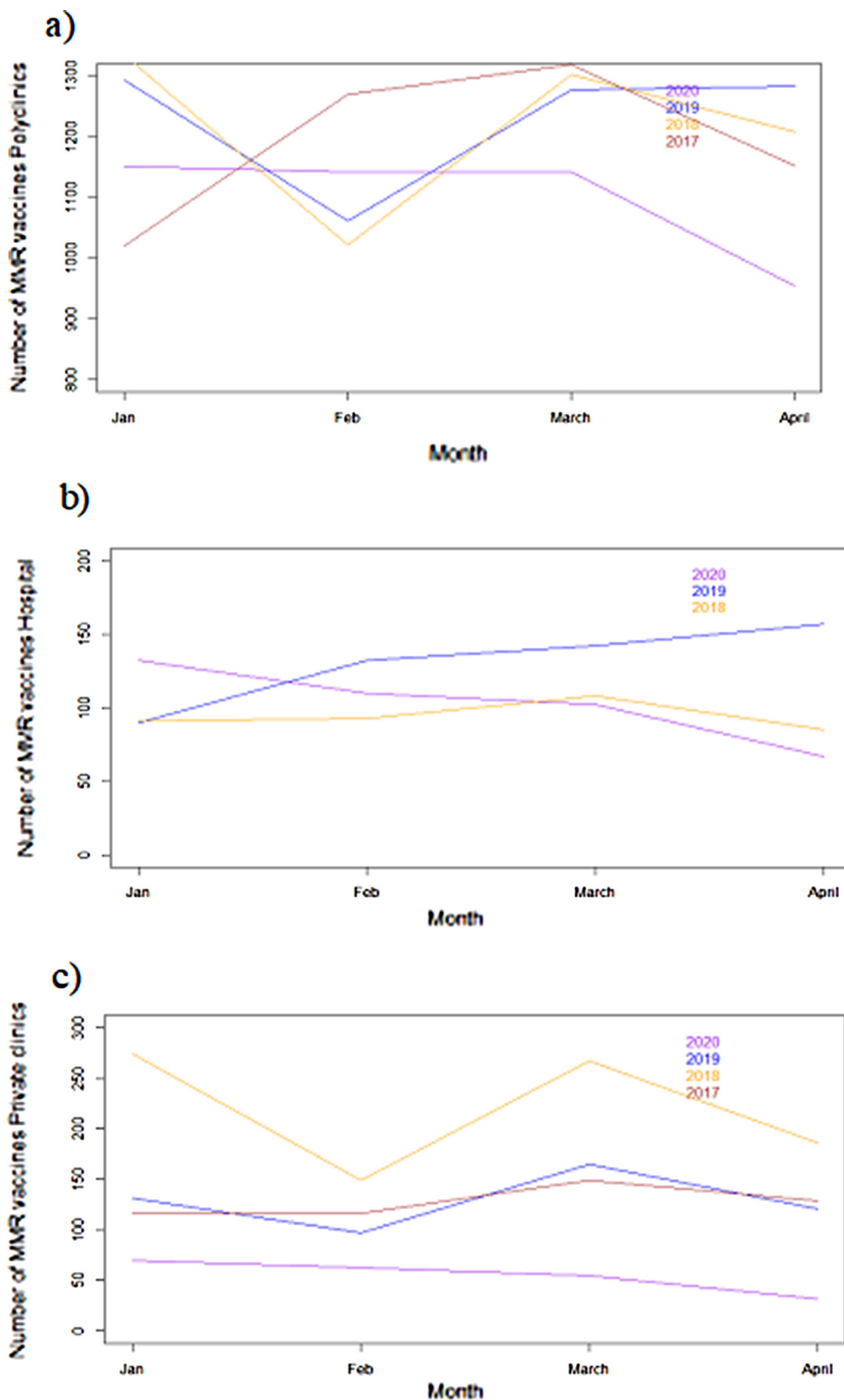
**4. Discussion**

Amidst the increased demands on healthcare services during a pandemic, governments and healthcare institutions need to ensure

the continuity of essential healthcare services, including childhood vaccinations. In Singapore, the Ministry of Health has provided for this throughout this period [10]. Despite this, we show a significant reduction in the vaccination rates for all the vaccines studied since the start of the pandemic, across 3 different healthcare settings.

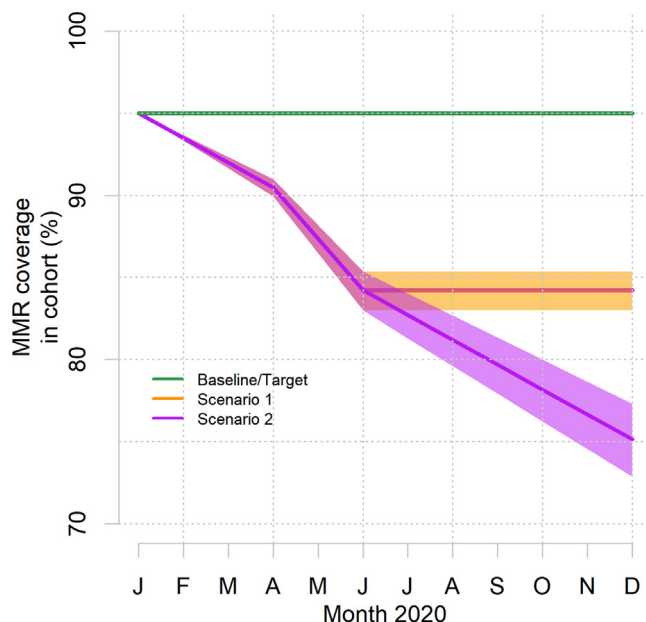
The most significant drop was for MMR/MMRV in the month of April 2020; this was less drastic but still significant for 5-in-1/6-in-1 and PCV. The drop was most noticeable in private clinics, and least in the hospital.

The most likely reason for this observation is parental hesitance to visit healthcare facilities due to perceived risk of acquiring the contagion; reduced health-seeking behavior has been observed during past epidemics [14]. During COVID-19, reports have emerged citing reduction in healthcare and emergency medicine attendances in Europe [15]. This concern may be greater for toddlers above 12 months of age, who are more mobile than infants, which explains why MMR/MMRV (given at 12 and 15 months) suffered a greater impact than 5-in-1/6-in-1 (given at 3, 4, 5 months). Additionally, strict physical distancing measures may pose logistical challenges; for example, each child is only allowed one accompanying caregiver in most clinics during the pandemic. The effect on pandemic vaccination coverage being less pronounced in infants compared to toddlers is interesting, since no healthcare facilities in Singapore prioritized any age group over another within the childhood vaccinations in the under-2-year age bracket.



**Fig. 2. Number of MMR / MMRV vaccines given by month, for each facility for January to April 2018 – 2020.** Footnote: MMR = Measles-Mumps-Rubella vaccine, MMRV = Measles-Mumps-Rubella-Varicella vaccine, 5-in-1 = pentavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza vaccine, 6-in-1 = hexavalent Diphtheria-Tetanus-Pertussis-inactivated Polio-Haemophilus influenza-Hepatitis B vaccine, PCV = 13-valent Pneumococcal conjugate vaccine, Polyclinics = 5 public primary care clinics under the National University Polyclinics group, Hospital = Specialist Outpatient Clinic of the Khoo Teck Puat National University Children’s Medical Institute, National University Hospital, Singapore, Private clinics = 3 private paediatrician practices).





**Fig. 3. Coverage of Measles-Mumps-Rubella (MMR) for the rest of 2020 year based on two scenarios after circuit breaker ends in May 2020:** Scenario 1: vaccination coverage returns to baseline, and Scenario 2: vaccination coverage returns to what it was during pandemic in January to March 2020.

Instead, this could reflect greater parental concern resulting in prioritization of vaccination for infants compared to their older toddlers.

The reduction of vaccination rates across healthcare facilities was heterogeneous. We observed the lowest drop in the hospital; in fact, there was an initial increase for 5-in-1/6-in-1 and PCV, although these both subsequently dropped in April 2020. The hospital is a tertiary center which sees children with chronic conditions, while the other two serve the general pediatric population. We postulate that parents of children with chronic illnesses are more likely to prioritize vaccinations. Interestingly, the steepest drops in vaccination rates were in private clinics. Reduced international patients from border closures likely augmented this drop; international patients access our private clinics routinely as Singapore is a regional hub for medical tourism.

Our findings also show that if the missed MMR/MMRV doses are not eventually administered, the complete vaccine coverage in 1 to 2-year-olds will be estimated at 84%, well below the 95% target required for herd immunity. The coverage can also further drop to 74% if the vaccine uptake rate persists at the same rates in T1 2020 for the rest of the year.

Measles outbreaks have occurred in developed countries in recent years due to reduced vaccine coverage [16], and outbreaks can occur from just a single index case even in highly-vaccinated populations [17]. Though a drop in vaccine coverage in 1 to 2-year-olds may not greatly alter the overall population immunity, the spatial clustering of unvaccinated individuals has been shown to cause large measles outbreaks in the United States, as well recently in Tanzania [18]. 1 to 2-year-olds who are insufficiently vaccinated do not mix homogeneously with the rest of the population but preferentially with each other, in childcare centers and playgrounds, a classic example of spatial clustering. As they often live in multi-generational households in Singapore, this then specifically endangers the elderly or immunocompromised individuals at home.

The main limitation of our study is the relatively short period of analysis which did not allow differentiation between cancelled and postponed visits. However, as Singapore has extended its CB to

include May 2020, with a phased relaxation of physical distancing measures extending to December 2020, vaccine postponement may also inadvertently be for many months, if parental perceptions remain. Moreover, even with mere postponement of vaccines, the susceptibility of the community to VPDs during the immediate ensuing months remain. Traditionally, vaccination coverage is the metric used to assess vaccine usage. Our study represented a sample of the entire Singaporean population and so there is risk of biased sampling, and also could not differentiate between whether missed vaccines were primary or booster doses. However, administered doses in 3 representative healthcare facilities is an immediately available proxy measure [3]. The population coverage, including whether doses were primary or booster, could be gleaned from the Communicable Diseases Centre Surveillance Singapore for 2020, for which a late 2021 publication can be anticipated.

Our findings reflect the effects of COVID-19 on a developed country with a world-class healthcare system but are applicable worldwide. Outbreaks of highly infectious diseases like measles are even more consequential in resource-limited settings. There is an urgent need to ensure that vaccine uptake rates are maintained despite the pandemic. Targeted efforts should be taken to educate parents on the consequences of a missed or delayed vaccine. Parents should be reassured of the safety of visiting a healthcare facility that has adequate infection control measures. Mobile vaccination centers can be used to reach children in the community [19]. Catch-up campaigns should be launched for children with missed vaccines. Healthcare providers should take every opportunity to vaccinate eligible children.

Fortunately, social distancing measures and compulsory mask-wearing in Singapore during the COVID-19 pandemic can help to mitigate the potential for a measles outbreak to some degree. Closure of borders also decreases risk of imported cases. However, measles is airborne and much more transmissible than COVID-19, and pandemic measures will be relaxed in due time. If catch-up vaccination to an adequate level does not occur before that, the population is vulnerable to a significant measles outbreak.

**5. Conclusion**

Amidst the global focus on COVID-19, it is critical that children are not unintentionally afflicted by VPDs. Our findings suggest a frightening reduction in vaccine uptake in a developed country where vaccine availability is not affected, rendering an epidemic like measles a real possibility. Efficacious vaccine coverage must be maintained everywhere, to safeguard the health of our children and vulnerable populations.

**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2020.12.054>.

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