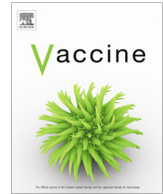




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Short communication

Potential impact of COVID-19 pandemic on vaccination coverage in children: A case study of measles-containing vaccine administration in the United States (US)



Cristina Carias^{a,*}, Manjiri Pawaskar^a, Mawuli Nyaku^a, James H. Conway^b, Craig S. Roberts^a, Lyn Finelli^a, Ya-Ting Chen^a

^a Merck & Co., Inc., Kenilworth, NJ, USA

^b University of Wisconsin-Madison, School of Medicine & Public Health, Dept. of Pediatrics, USA

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ABSTRACT

Background: The COVID-19 pandemic and stay-at-home orders have caused an unprecedented decrease in the administration of routinely recommended vaccines. However, the impact of this decrease on overall vaccination coverage in a specific birth cohort is not known.

Methods: We projected measles vaccination coverage for the cohort of children becoming one year old in 2020 in the United States, for different durations of stay-at-home orders, along with varying catch-up vaccination efforts.

Results: A 15% sustained catch-up rate outside stay-at-home orders (compared to what would be expected via natality information) may be necessary to achieve projected vaccination coverage similar to previous years. Permanent decreases in vaccine administration could lead to projected vaccination coverage levels below 80%.

Conclusion: Modeling measles vaccination coverage under a range of scenarios provides useful information about the potential magnitude and impact of under-immunization. Sustained catch-up efforts are needed to assure that measles vaccination coverage remains high.

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1. Introduction

The US Centers for Disease Control and Prevention (CDC) reported a significant decrease in vaccination coverage rates in March and April 2020, following stay-at-home orders due to the COVID-19 pandemic [1,2]. While the decreasing vaccination rates have been documented, the impact of stay-at-home orders on overall vaccination coverage is not yet known. A timely assessment of gaps in vaccination coverage can assist in understanding and communicating the urgency and magnitude of catch-up campaigns needed. Public health providers can use this information for planning and allocation of resources. As a result of this effort, infectious disease outbreaks might be anticipated and prevented. In the past, large measles outbreaks have occurred when vaccination coverage has declined to below 80% [3].

In this short communication, we propose a simple model that provides estimates of the impact of stay-at-home orders on vac-

nation coverage rates. We estimate vaccination coverage for the measles mumps and rubella (MMR) vaccine in the United States under a range of scenarios, discuss the potential impact of declines in coverage and methods to close the vaccination coverage gap.

2. Methods

We estimated the number of well-child visits impacted by stay-at-home orders using demographic information on births, population growth rates, and child mortality rates for a variety of stay-at-home and catch-up scenarios [4–6]. In particular, we progressed a cohort of infants through their first 24 months of life and estimated the number of infants eligible to attend a well-child visit and that were administered a vaccine in the months while stay-at-home measures were in place. The number of births was taken from publicly available data and adjusted to reflect childhood mortality [4,6]. Given latest demographic data, no growth in the number of births was assumed since 2018 [5]. Compliance with well-child visit schedule was assumed to occur as soon as the infant was eligible. Decrease in the number of vaccines administered was taken

* Corresponding author at: 351 N. Sumneytown Pike, North Wales, PA 19454, USA.

E-mail address: cristina.da.silva.carias@merck.com (C. Carias).

from pandemic specific data on vaccine administration for infants younger than 24 months [1].

We then projected vaccination coverage as the total number of doses administered to children eligible for their 12-month well-child visit in 2020, divided by the total number of eligible children [4]. This corresponds to projected vaccination coverage for children born in 2019 who become one year old in 2020.

We estimated the potential yearly reduction in projected vaccination coverage by accounting for the reduction in measles-containing vaccine administration during stay-at-home orders and considering the baseline as vaccination coverage for measles estimated in previous years for one-year-olds [1,7]. That is, the maximum projected vaccination coverage and the one achieved in the months prior to the Spring stay-at-home-orders was assumed to be 90%, equal to values previously published [7]. The reduction in doses administered was assumed to be relative to this baseline projected vaccination coverage. For the base-case scenario and consistent with published estimates on administration of measles-containing doses, we assumed a 50% reduction during stay at home orders, with upper and lower bounds considering a 60% and 40% reduction, respectively [1]. We assumed the first dose of measles-containing vaccine would be administered at 12 months of age, and >12 months of age for catch-up efforts [8].

In alternative scenarios, we varied the duration of stay-at-home orders and vaccination rates after the lifting of stay-at-home orders. In particular, we projected vaccination coverage considering: spring stay-at-home orders between March 14–May 20; Fall between September 15 and October 15; extended Fall stay at home orders between September 15 and November 15.

We also considered increases in vaccinations due to a catch-up strategy and a decrease in vaccinations due to persistent reduction in well-child visits after stay-at-home orders. The range of changes considered was –15% (decrease) to 15% (catch-up), which translates to percent variations in the number of one-year old well-child visits and consequent vaccinations when compared to what would be predicted by demographic information alone (0%). The final vaccination coverage estimates assume that the percent variations are sustained throughout the remainder of the year, in all the months when stay-at-home orders are not in place.

3. Results

Fig. 1 shows projected vaccination coverage. The x-axis corresponds to the difference between infants eligible to attend the 12 month well-visit and infants that attend and get vaccinated; a negative difference corresponds to reduction in attendance and vaccination related to permanent social distancing behaviors, while a positive difference corresponds to a proactive catch-up of individuals that missed their 12 month well-check. For each data-point, the line crosses the 50% reduction in administration for the base-case scenario, while the lower and upper bounds relay a 40 to 60% reduction.

For a two-month spring 2020 stay-at-home order with a reduction in measles-containing vaccine administration by 50% (base-case), we estimated a decline in projected vaccination coverage for infants born in 2019 from 90% to 82% for the first dose of the first measles-containing vaccine with no catch-up (Fig. 1). In scenarios with catch-up vaccination after stay-at-home orders are lifted, the projected vaccination coverage would increase to 85%, 88%, and 90% respectively, corresponding to a 5%, 10%, and 15% increase in the number of well-child visits over baseline for the remainder of the year.

In a scenario where voluntary social distancing or other concerns lead to persistent declines in well-child visits of 5%, 10% or 15% after stay-at-home orders are lifted, the annual projected vac-

ination coverage for this cohort rate would drop to 80% or below. Assuming declines in the vaccination rate similar to those observed in Spring 2020 for a second Fall 2020 stay-at-home order, the projected vaccination coverage could decrease below 75%, if there are ongoing decreases in vaccine administration between stay-at-home orders. In this case, catch-up vaccination up to 15% above well-child visits expected would be insufficient to achieve 90% coverage, which was the level of vaccination coverage for the first dose of measles-containing vaccine in previous years.

4. Discussion

Our model quantifies the impact of vaccination delay and catch-up efforts due to stay-at-home orders over several potential scenarios. Projected vaccination coverage could be significantly impacted if stay-at-home orders occur in the future due to a surge in cases in the COVID-19 pandemic, or if catch-up efforts are not implemented and sustained. Failure to organize intensive catch-up efforts increases the likelihood of community-wide measles outbreaks as daycares and schools reopen, and travel resumes.

Our model is inline with very recent reports on the decline in pediatric vaccination, that show a substantial impact of the pandemic on routine vaccination in the United States and across the world and concerns around decrease in vaccination worldwide [9–11]. Our results add to the literature by translating possible declines in vaccination to a common benchmark, recognized by infectious disease modelers and policy makers alike. Further, we quantify the extent of catch-up efforts needed and the need to sustain those efforts for vaccination coverage to remain at 90%; coverage levels widely perceived as the minimum to avoid widespread outbreaks [12,13].

Measles was eliminated in the US in 2002 due to high vaccination coverage rates [14]. However, there has been a resurgence in measles outbreaks in the last few years; the consequent health care resource and outbreak management costs are potentially high [15]. A previous modeling study estimated that a 5% decline in MMR coverage could lead to 3-fold increase in measles cases annually in children in the US; with an additional \$2.1 million in costs [16]. In 2019, 1282 measles cases were reported, which corresponds to the highest number in the last 25 years in the US [17]. To note, the 2018–2019 measles outbreak in New York City cost the New York City health department an estimated \$8.4 million and required 104,000 person-hours to manage [3].

Our model used demographic data for the United States to project vaccination coverage for a very diverse and heterogeneous population. In reality, prior to the pandemic, vaccination coverage in the United States varied per state, with vaccination coverage levels declining to levels as low as 85% [7,18]. In our model, reductions in vaccination relate to baseline vaccination coverage. Consequently, small geographic areas that have a lower baseline level than the national average could experience lower projected vaccination coverage than that projected in this analyses. Given the high herd immunity level necessary for measles, and observed clustering of children with low measles-containing vaccine coverage [18], our analysis suggests that special attention is needed to keep vaccination uptake levels similar to 90% in areas and populations where vaccination uptake is traditionally lower than national average. To note, there could also be substantial regional variation in future coverage based on local pandemic response policies and catch-up efforts, suggesting that continuous monitoring is necessary to understand impact on routine pediatric immunization.

Our projections have limitations. They are grounded on a demographic model, assume compliance with the well-child care visit for the first year, and are not based on reliable and representative survey data. We have assumed a perfect correlation between eligi-

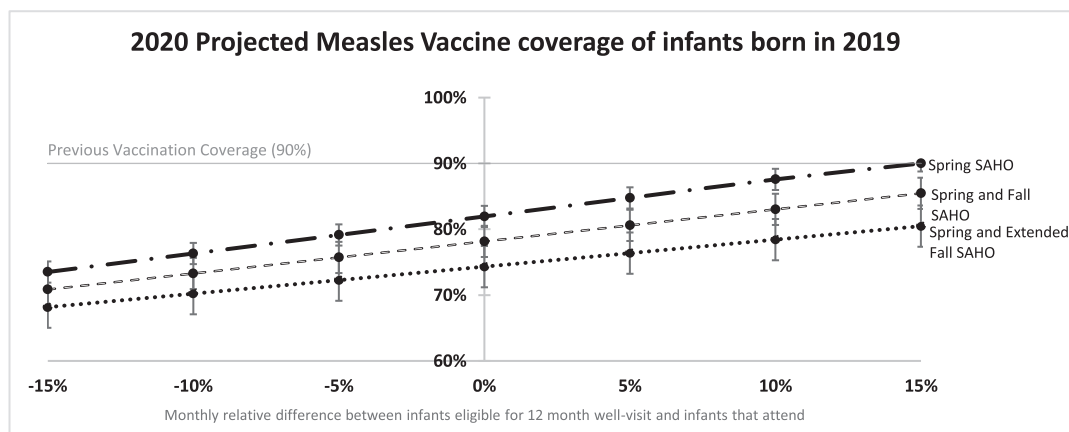


Fig. 1. Projected 2020 measles-containing vaccination coverage rates (VCR) in the US as a function of the relative difference between infants eligible for the 12-month visit and infants that attend and get vaccinated for different duration of stay-at-home orders (SAHO). Projected vaccine coverage calculated for infants born in 2019 turning 1 year old in 2020; estimated as the ratio between total doses administered and total infants eligible to attend the 12-month well-check and that get vaccinated. Different lines correspond to different duration and number of stay-at-home orders; the point estimate was estimated assuming a 50% reduction in the infants that attend well-visits while SAHO are in place, while the error bars consider a 40% and 60% reduction [1]. The x-axis corresponds to the difference between infants eligible to attend the 12 month well-visit and infants that attend; a negative difference corresponds to reduction in attendance related to permanent social distancing behaviors, while a positive difference corresponds to a proactive catch-up of individuals that missed their 12 month well-check.

bility for well-child visits and administration of measles-containing vaccine, which may not be the case. Additionally, providers and caregivers may choose to merge different well-child visits, and caregivers' attitudes towards sustaining routine infant care during the pandemic are not yet fully understood. While these factors may cause for an underestimation of the uncertainty associated with the projections, the multiple scenarios studied are consistent in suggesting the need to monitor vaccine catch-up administration for vaccination coverage levels to remain at 90% levels.

Notably, while we assumed that it would be possible to sustain catch-up efforts for the remainder of the year, this may not be feasible. In reality, health care resources are constrained and capacity may be limited during a pandemic. Scheduling catch-up visits in addition to those predicted by demographic eligibility may be unfeasible for providers already functioning at the limit of their capacity. Further, sustained catch-up efforts may not be possible if pandemic cases rise and compete for provider resources, or as more caregivers are themselves affected due to unemployment or disease. Additionally, outpatient clinics may be deployed to assist in pandemic vaccine administration [19]. This suggests that special care needs to be given to prioritize routine vaccination uptake during a pandemic.

A wide variety of methods may be employed to close gaps in vaccination coverage. Previously, "forgetting" a well-child visit has been identified as a cause of non-compliance with the well-child visit schedule [20]. Immunization reminder-recall systems allow providers to identify and notify families whose children are due or overdue immunizations through phone calls, text messages, or emails [21]. Additionally, providers may need to assuage parents' safety concerns, by communicating safety protocols implemented in the clinics. Offering additional days and special hours only for catch-up immunization could further encourage families to make in-person visits. Other methods include drive-through vaccination, and home visits by healthcare workers that might minimize the risk of infection and build patient/parent confidence.

Closing the gap in vaccination coverage will only be possible with accelerated and sustained catch-up immunization efforts [22]. Measles is one of the most infectious vaccine preventable diseases and high levels of vaccination coverage (>90%) are needed to

prevent outbreaks. While stay-at-home orders and pandemic concerns pose an additional challenge for the sustainability of high vaccination coverage, innovative strategies should be considered to support catch-up vaccination in order to avoid outbreaks of this infectious and potentially life-threatening disease.

Declaration of Competing Interest

CC, MP, MN, CR, LF, and YTC are employees and shareholders of Merck & Co. JHC reports personal fees from Merck Vaccines, grants from Sanofi Pasteur Vaccines, personal fees from GSK vaccines, personal fees from Pfizer vaccines.

References

- [1] Santoli JM, Lindley MC, DeSilva MB, et al. Effects of the COVID-19 Pandemic on Routine Pediatric Vaccine Ordering and Administration – United States, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:591–593.
- [2] Bramer CA, Kimmins LM, Swanson R, Kuo J, Vranesich P, Jacques-Carroll LA, et al. Decline in child vaccination coverage during the COVID-19 pandemic—Michigan Care Improvement Registry, May 2016–May 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:1–3.
- [3] Zucker JR, Rosen JB, Iwamoto M, Arciuolo RJ, Langdon-Embry M, Vora NM, et al. Consequences of Undervaccination – Measles Outbreak, New York City, 2018–2019. *New Eng Journal of Medicine* 2020; 382(11): 1009–17.
- [4] United States Department of Health and Human Services (US DHHS), Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Division of Vital Statistics, Natality public-use data 2016–2018, on CDC WONDER Online Database, September 2019. Accessed at <http://wonder.cdc.gov/nativity-expanded-current.html> on May 20, 2020.
- [5] United States Census Bureau, "Slower growth for nation's population". <https://www.census.gov/library/visualizations/2019/comm/slower-growth-nations-pop.html> Accessed at August 21st, 2020.
- [6] Centers for Disease Control, "Infant Mortality", <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/infantmortality.htm>. Accessed at October 15, 2020.
- [7] Hill HA, Singleton JA, Yankey D, et al. Vaccination Coverage by Age 24 Months Among Children Born in 2015 and 2016 – National Immunization Survey-Child, United States, 2016–2018. *MMWR Morb Mortal Wkly Rep* 2019;68(41):913–8.
- [8] Robinson CL, Bernstein H, Poehling K, Romero JR, Szilagyi P. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger – United States, 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69: 130–132.
- [9] Measles & Rubella Initiative. More than 117 million children at risk of missing out on measles vaccines, as COVID-19 surges. 2020 [cited 2020 August 18]; Available from: <https://measlesrubellainitiative.org/measles-news/more-than-117-million-children-at-risk-of-missing-out-on-measles-vaccines-as-covid-19-surges/>.

- [10] Mulholand K, Kretsinger K, Wondwossen L, Crowcroft L. Action needed now to prevent further increases in measles and measles deaths in the coming years. *Lancet Infect Dis* 2020.
- [11] Chandir S, Siddiqi DA, Mehmood M, et al. Impact of COVID-19 pandemic response on uptake of routine immunizations in Sindh, Pakistan: an analysis of provincial electronic immunization registry data. *Vaccine* 2020;38:7146–55.
- [12] European Centre for Disease Prevention and Control. Monthly Measles and Rubella monitoring reports. Accessed 11/20/20 at: http://ecdc.europa.eu/en/healthtopics/measles/epidemiological_data/Pages/measles_surveillance_reports.aspx.
- [13] World Health Organization. Global Measles and Rubella Strategic Plan, 2012–2020. Who Press, 2012, Switzerland. Accessed 11/20/20 at: http://apps.who.int/iris/bitstream/10665/44855/1/9789241503396_eng.pdf.
- [14] Papania MJ, Wallace GS, Rota PA. Elimination of endemic measles, rubella, and congenital rubella syndrome from the Western hemisphere: the US experience. *JAMA Pediatr* 2014;168(2):148–55.
- [15] Ortega-Sanchez IR, Vijayaraghavan M, Barskey AE, et al. The economic burden of sixteen measles outbreaks on United States public health departments in 2011. *Vaccine* 2014;32(11):1311–7.
- [16] Lo NC, Hotez PJ. Public health and economic consequences of vaccine hesitancy for measles in the United States. *JAMA Pediatr* 2017;171(9):887–92.
- [17] CDC Measles cases and outbreaks. 2020 July 10 2020; Available from:<https://www.cdc.gov/measles/cases-outbreaks.html>.
- [18] Smith PJ, Marcuse EK, Seward JF, et al. Children and adolescents unvaccinated against measles: geographic clustering, parents' beliefs, and missed opportunities. *Public Health Rep* 2015;130:485–504.
- [19] Carias C, Lehnert J, Greening B, et al. The PanVax tool to improve pandemic influenza emergency vaccination program readiness and partnership. *Am J Public Health* 2019;109:S322–4.
- [20] Jhanzee I, Saxeena D, Arora J, Gjerdingen DK. Parents' health and demographic characteristics predict noncompliance with well-child visits. *J Am Board Fam Pract* 2004;17:324–31.
- [21] American Academy of Pediatricians. "Strategies to improve immunization rates". Available at: <https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Practice-Management/Pages/Strategies-to-Improve-Immunization-Rates.aspx>. Accessed October 16, 2020.
- [22] Zucker ML, et al. Notes from the Field: Rebound in Routine Childhood Vaccine Administration Following Decline During the COVID-19 Pandemic—New York City, March 1–June 27, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69.