Value of the Immunization Program for Children in the 2017 US Birth Cohort

Justin Carrico, BS,[a] Elizabeth M. La, PhD,[a] Sandra E. Talbird, MSPH,[a] Ya-Ting Chen, PhD,[b] Mawuli K. Nyaku, DrPh, MBA, MPH,[b] Cristina Carias, PhD,[b] Claire E. Mellott, BS,[a] Gary S. Marshall, MD,[c] Craig S. Roberts, PharmD, MPA, MBA[b]

abstract

BACKGROUND AND OBJECTIVES: We evaluated the economic impact of routine childhood immunization in the United States, reflecting updated vaccine recommendations and recent data on epidemiology and coverage rates.

METHODS: An economic model followed the 2017 US birth cohort from birth through death; impact was modeled via a decision tree for each of the vaccines recommended for children by the Advisory Committee on Immunization Practices as of 2017 (with annual influenza vaccine considered in scenario analysis). Using information on historic prevaccine and vaccine-era incidence and disease costs, we calculated disease cases, deaths, disease-related healthcare costs, and productivity losses without and with vaccination, as well as vaccination program costs. We estimated cases and deaths averted because of vaccination, life-years and quality-adjusted life-years gained because of vaccination, incremental costs (2019 US dollars), and the overall benefit-cost ratio (BCR) of routine childhood immunization from the societal and healthcare payer perspectives.

RESULTS: Over the cohort's lifetime, routine childhood immunization prevented over 17 million cases of disease and 31 000 deaths; 853 000 life years and 892 000 quality-adjusted life-years were gained. Estimated vaccination costs ($8.5 billion) were fully offset by the $63.6 billion disease-related averted costs. Routine childhood immunization was associated with $55.1 billion (BCR of 7.5) and $13.7 billion (BCR of 2.8) in averted costs from a societal and healthcare payer perspective, respectively.

CONCLUSIONS: In addition to preventing unnecessary morbidity and mortality, routine childhood immunization is cost-saving. Continued maintenance of high vaccination coverage is necessary to ensure sustained clinical and economic benefits of the vaccination program.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2021-056007

[a]*RTI Health Solutions, Research Triangle Park, North Carolina;* [b]*Merck & Co., Inc., Rahway, New Jersey; and* [c]*Norton Children's and University of Louisville School of Medicine, Louisville, Kentucky*

Mr Carrico, Ms Talbird, Ms Mellott, and Dr La conceptualized and designed the study, reviewed the literature and derived the model parameters, interpreted the results, drafted the initial manuscript, and/or reviewed and revised the manuscript; Dr Chen, Dr Nyaku, Dr Carias, and Dr Roberts conceptualized the study and provided input on the study design, secured funding, interpreted the results, and reviewed and revised the manuscript; Dr Marshall provided input on the model parameters, interpreted the results, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Dr La's affiliation is GSK, Philadelphia, Pennsylvania.

DOI: https://doi.org/10.1542/peds.2021-056007

Accepted for publication Jun 1, 2022

WHAT'S KNOWN ON THIS SUBJECT: Prior analyses have demonstrated that US childhood immunization is cost-saving, in addition to preventing unnecessary morbidity and mortality. Updated estimates of the public health impact of this program are needed, given changes in disease epidemiology and evolving childhood vaccination recommendations.

WHAT THIS STUDY ADDS: For the 2017 birth cohort, routine childhood immunizations prevented >17 million disease cases and 31 000 deaths. Vaccination costs ($8.5 billion) were fully offset by averted disease-related costs ($63.6 billion), with a benefit-cost ratio of 7.5 from the societal perspective.

To cite: Carrico J, La EM, Talbird SE, et al. Value of the Immunization Program for Children in the 2017 US Birth Cohort. *Pediatrics*. 2022;150(3):e2021056007

In 1995, the American Academy of Pediatrics and the US Advisory Committee on Immunization Practices (ACIP) first issued a unified pediatric vaccination schedule, targeting 9 vaccine-preventable diseases.[1] Since 2017 and through 2021, the ACIP-recommended schedule for routine childhood immunization has targeted 14 vaccine-preventable diseases: diphtheria, invasive *Haemophilus influenzae* type b, hepatitis A, hepatitis B, influenza, measles, mumps, pertussis, invasive Streptococcus pneumoniae, polio, rotavirus, rubella, tetanus, and varicella.[2]

The epidemiologic and economic impacts of routine childhood immunization on reducing disease burden in the United States have been well documented.[3–7] In the most recent evaluation, Zhou and colleagues[7] found that for the 2009 US birth cohort, routine childhood immunization prevented approximately 42 000 early deaths and 20 million cases of disease over the cohort's lifetime, resulting in a net savings of $68.8 billion (2009 US dollars [USD]) in societal costs and benefit-cost ratios (BCRs) of 3.0 and 10.1 for the healthcare payer and societal perspectives, respectively.[7] However, this analysis did not include the 13-valent pneumococcal conjugate vaccine (PCV13) and included only limited information on the impact of rotavirus vaccination.

The objective of the current study was to estimate the impact of childhood immunization in the United States, considering only the vaccines that are routinely administered from birth to age 10 years, as delineated in the 2017 vaccination schedule (which was largely unchanged as of 2021). This excludes vaccines that are recommended only for high-risk conditions (eg, meningococcal ACWY for asplenics), those that are recommended based on shared clinical decision-making (eg, meningococcal B for adolescents), those recommended only in certain geographical areas (eg, dengue vaccine), and those with allowances for starting earlier (eg, human papillomavirus vaccine at age 9 years). We update previous estimates by including recent observational evidence of the epidemiologic impact of the 13-valent pneumococcal vaccine[8–15] and rotavirus vaccination[16,17] as well as a scenario analysis of annual influenza vaccination (including the cost for 2 doses of influenza vaccine at first vaccination).

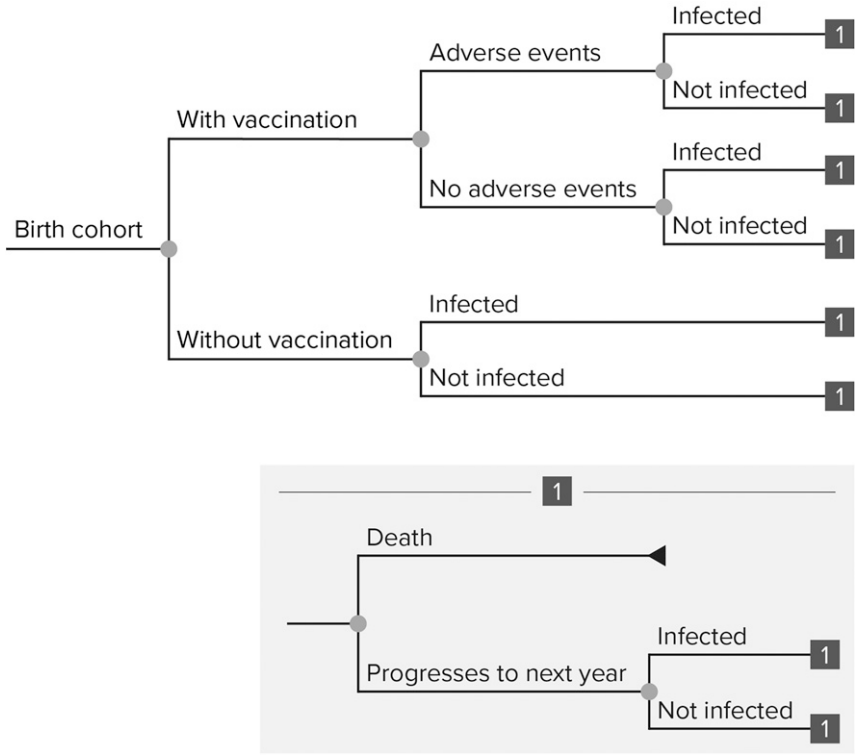

FIGURE 1
Decision-tree structure. This decision-tree structure was used for each of the vaccine-preventable diseases, with modifications as needed to account for disease-related death and long-term sequelae for certain diseases.

METHODS

Model Description

We developed a decision-tree model in Microsoft Excel (Microsoft Corporation; Redmond, Washington) to analyze the impact of vaccination on the 2017 US birth cohort (3 855 500 children)[18] during its lifetime (Fig 1), focusing on 9 childhood vaccines routinely administered from birth to age 10 years: diphtheria, tetanus, and acellular pertussis (DTaP); hepatitis A (HepA); hepatitis B (HepB); *Haemophilus influenzae* type b (Hib); inactivated polio vaccine (IPV); measles, mumps, rubella (MMR); PCV13; rotavirus; and varicella.[2] Since influenza vaccination is recommended for children and adults, vaccination impact cannot be attributed solely to the pediatric schedule. Additionally, both vaccination coverage and effectiveness vary year to year[19,20]; thus, annual influenza vaccine was included only in the scenario analyses. Vaccination of the 2017 cohort was assumed to follow the ACIP child immunization schedule, with coverage based on national estimates.[21]

For each disease, outcomes were calculated without and with

vaccination for every month until 12 months, and then for every year thereafter. From birth to 100 years, we subtracted the number of individuals who died because of all-cause or disease-specific mortality from that period's cohort and progressed the remaining individuals to the next period (month or, after 12 months, year). Age-specific all-cause mortality, disease incidence, treatment costs, and probability of different outcomes were used to parameterize the decision tree for each disease (see Supplemental Tables 5–25).

The model compared vaccination according to the recommended schedule against no vaccination. For each disease and for the vaccination and no-vaccination scenarios, we calculated the total number of cases of a given severity by multiplying the likelihood of different clinical outcomes by the total number of expected cases. Total disease-related costs were calculated by multiplying costs for a given clinical outcome by the number of clinical outcomes among the total number of disease cases and summing over the different clinical outcomes per disease (see Disease Costs and Quality of Life Impacts section). Surviving individuals who developed long-term complications for some diseases accumulated disability-related costs, which were discounted over their remaining lifetimes. Costs were inflated to 2019 USD using the healthcare component of the personal consumption expenditures index for treatment costs, the general component of the consumer price index for nonmedical costs such as transport costs,[22] and the employment cost index for productivity costs.[23] Costs and outcomes were calculated from the healthcare payer and societal perspectives and discounted using the standard annual discount rate of 3%.[24]

After calculating clinical outcomes for the vaccination and no-vaccination scenarios, we estimated the reductions in overall and age-specific cases of disease caused by vaccination. For the scenarios without and with immunization, treatment costs associated with disease cases were assumed to be based on current standard of care. Similarly, deaths caused by each disease were estimated in both scenarios, using the most recent mortality rates when available.

For each vaccination scenario, we reported the total disease-related cases, deaths, costs, life-years (LYs) and quality-adjusted life-years (QALYs). Then, we calculated averted cases by subtracting the number of cases with vaccination from the number of cases without vaccination. Similarly, we calculated LYs and QALYs gained by subtracting LYs and QALYs with vaccination from those obtained in the without vaccination scenario. We calculated the incremental cost-effectiveness ratio by dividing the net costs of the immunization program by incremental QALYs gained. The BCR was calculated by dividing the incremental disease-related cost-savings by the net costs of the immunization program.

Disease Incidence and Clinical Outcomes

We calculated cases before and after each vaccine was routinely recommended; these incidence estimates are described in a companion article.[25] Prevaccine incidence estimates were calculated from disease surveillance data (National Notifiable Diseases Surveillance System and Active Bacterial Core surveillance reports) or obtained from the literature. Vaccine-era disease incidence estimates were calculated as average values over the most recent 5 years of available data or obtained from estimates of cases averted or event rate reductions. Incidence estimates in each era were adjusted for underreporting when applicable.

Vaccination Program Costs

We calculated the costs of the vaccination program, which included vaccine acquisition, administration, and adverse event costs. Vaccination coverage, which was obtained from the 2017 National Immunization Survey-Child[21,26] and 2019 to 2020 state and local immunization program[27] data, was used to estimate the number of individuals vaccinated and number of doses administered.

Public and private vaccine acquisition costs were taken from the 2019 Centers for Disease Control and Prevention's Vaccine Price List for Children[28] (Table 1). The model assumed that 53% of childhood vaccines were purchased at the public price, such as through the Vaccines for Children program, and that 47% were purchased at the private price.[7] When multiple vaccines were available for the same disease (eg, HepA vaccines), vaccine acquisition costs per dose were estimated by averaging the price across brands, without accounting for market share of specific products. To account for combination vaccines, which typically have a small price premium, higher average vaccine acquisition costs were tested in sensitivity analyses. The vaccine wastage rate was assumed to be 5%.[7] Federal excise taxes for the Vaccine Injury Compensation Program were not included in vaccine acquisition costs, as they are collected from vaccine manufacturers.[29]

For vaccine administration costs, we assumed that 80% of vaccines were administered by private providers and that the remaining 20% of vaccines were administered in public clinics.[7] Unit costs of

TABLE 1 United States Childhood Immunization Schedule, Coverage Estimates, and Vaccine Acquisition Costs

Vaccine	Age at Vaccination	Coverage, %[a]	Acquisition Cost per Dose, by Purchasing Source[b]	
			Public, USD	Private, USD
DTaP	2, 4, 6, 15 mo, 4 y	94.9 fully vaccinated	17.90	27.45
HepA	12, 18 mo	59.7 fully vaccinated	19.44	32.31
HepB	Birth, 1, 6 mo	91.4 fully vaccinated	13.17	23.50
Hib[c]	3 dose: 2, 4, 12 mo	80.7 fully vaccinated	13.09	26.23
	4 dose: 2, 4, 6, 12 mo		9.44	13.53
MMR	12 mo, 4 y	95.2 fully vaccinated	21.05	75.04
PCV13	2, 4, 6, 12 mo	82.4 fully vaccinated	131.77	180.05
Polio (IPV)	2, 4, 6 mo, 4 y	92.7 fully vaccinated	13.30	33.53
Rotavirus[d]	2 dose: 2, 4 mo	73.2 fully vaccinated	92.85	117.45
	3 dose: 2, 4, 6 mo		70.49	82.89
Varicella	12, 18 mo	94.8 fully vaccinated	98.24	129.30

[a] DTaP, MMR, and varicella vaccination coverage for kindergarten-aged children in 2019 to 2020 were obtained from Seither and McGill.[27] All other coverage estimates were obtained from CDC data for 2017.[21]

[b] All vaccine acquisition costs were obtained from the CDC vaccine price list as of March 2019.

[c] A 50% market share for Hib vaccines was assumed for the 3-dose and 4-dose series.

[d] Market shares for rotavirus vaccines were assumed to be 20% and 80% for the 2-dose and 3-dose series, respectively.[70]

administration were obtained from the Centers for Medicare and Medicaid Services' Physician Fee Schedule[30] for privately administered vaccines, with the administration cost per dose dependent on the number of disease components included in each vaccine. For example, for the DTaP vaccine, which protects against 3 diseases, administration costs were equal to the costs associated with reimbursement for the initial disease component plus each of the 2 other disease components. Vaccines administered in a public setting incurred an administration cost of $8.40 per dose (2019 USD).[7]

We estimated the productivity loss costs associated with vaccination by multiplying 2 hours of lost caregiver time for each vaccination visit[7] by the hourly cost of caregiver time of $21.24.[31] Additionally, caregiver travel costs for each visit ($25.74) were applied.[7] For vaccines typically administered during routine well-child visits, and in the presence of a wide variation in indirect costs associated with pediatric vaccination, we assumed that 50% of caregiver time and travel costs were attributed to vaccination.[7,32–40]

Vaccinated individuals were assumed to experience adverse events and associated direct medical costs and disutilities (Supplemental Tables 5 and 6). Incidence, cost, and disutility estimates for vaccine-related adverse events were obtained from previous economic analyses[6,7,32,33,35,36,41–43] and validated with clinical expert opinion; events that were not considered causally attributable to vaccination by the Institute of Medicine were excluded.[44–53]

Disease Costs and Quality-of-Life Impacts

To capture the costs and impact of infectious diseases on quality of life, we used disease-specific severity distributions to calculate the number of clinical outcomes for each disease. The direct medical cost, disutility value, and duration of disease per clinical outcome were based on the published literature (Supplemental Table 21).

Productivity loss costs were calculated using the human capital approach.[6,7,54,55] Specifically, disease-related productivity costs were calculated as the number of cases at each age multiplied by mean workdays lost divided by 365, which was then multiplied by the age-specific market and nonmarket annual productivity[31] (Supplemental Tables 22 and 24). For disease cases resulting in long-term sequelae, the model assumed the percentage reduction in annual productivity was equal to the percentage reduction in health-related utility weights associated with the complication (Supplemental Table 23). Average age-specific estimates of annual productivity and life expectancy were used to calculate the discounted present value of lifetime productivity loss costs associated with disease-related mortality and long-term sequelae (Supplemental Tables 24 and 25).[31,56,57]

Analyses

In addition to base-case analyses, we conducted additional univariate scenario analyses to assess the robustness of health and economic outcomes to changes in key analysis assumptions. Scenarios considered variations to assumptions for the following: (1) 100% increase in vaccine administration costs, (2–3) 10% increase and reduction in the percentage of vaccines publicly purchased, (4) 5% increase in vaccine acquisition costs, (5) 100% of indirect costs for caregiver time and travel for vaccination at well-child visits attributable to vaccination, (6) 0% annual discount

rates, (7) 10% reduction in prevaccine disease incidence, (8) 50% increase in vaccine-era disease incidence, (9–10) 20% increase and decrease in healthcare payer disease-related costs, and (11) 20% reduction in case-fatality rates for modeled diseases. Another scenario (12) was conducted to include annual influenza vaccination and disease for children aged 0 to 10 years in the economic analysis. Annual influenza vaccination coverage was based on coverage from the 2017 to 2018 season (67.8% and 59.5% for ages <5 years and 5–10 years, respectively).[58] All children vaccinated received 2 doses at the time of their first influenza vaccination, per the ACIP-recommended schedule. Vaccine acquisition costs for influenza vaccines were obtained from the 2019 vaccines price list,[28] and an average cost across products was calculated ($14.24 and $18.73 for public and private purchasing sources, respectively). Details for disease-related inputs are presented in Supplemental Table 11.

An additional scenario (13) included the value of QALYs saved in the societal BCR calculation.[59] The value of QALYs saved was included in the benefits of vaccination by multiplying the number of QALYs saved by a willingness-to-pay threshold of $100 000 per QALY gained.[60] Finally, a worst-case scenario (14) was presented by combining all input variations that negatively impacted the BCR, which included scenarios 1, 3, 4, 5, 7, 8, 10, and 11.

RESULTS

Health Outcomes Without and With Vaccination

Over the lifetime of the 2017 US birth cohort, 21.2 million preventable disease cases were estimated without routine childhood immunization, resulting in 33 000 disease-related deaths, 876 500 LYs lost, and 931 400 QALYs lost. When vaccine-preventable diseases were modeled with routine childhood immunization, 3.4 million cases and 1600 disease-related deaths occurred, with 23 400 LYs and 39 800 QALYs lost. As a result, routine childhood immunization was associated with 17.8 million disease cases averted, 31 400 disease-related deaths averted, and an incremental gain of 853 000 LYs and 891 600 QALYs (Table 2). Incremental results varied by disease, with the most cases averted for pneumococcal disease, measles, and varicella and the most deaths averted for pneumococcal disease, diphtheria, and measles. Gains in LYs and QALYs were largest for diphtheria, pneumococcal disease, and measles (Table 2).

Undiscounted outcomes are shown in Table 2. For each disease evaluated, inclusion of the associated vaccine in the routine childhood immunization program reduced the number of cases; reductions ranged from approximately 47% for rotavirus cases to 100% for polio cases. More than 90% reduction in cases was achieved for 10 of the 13 diseases evaluated.

TABLE 2 Base-Case Health Outcome Results, Overall and by Disease

Disease	Cases Averted (Thousands)	Deaths Averted	LYs Gained (Thousands)	QALYs Gained (Thousands)
Diphtheria	219	21 870	655	580
Tetanus	<1	70	2	2
Pertussis	1693	700	21	43
Hepatitis A	21	<10	<1	<1
Hepatitis B	40	220	4	13
Haemophilus influenzae type b	17	650	20	34
Measles	2915	2330	70	83
Mumps	1694	<10	<1	8
Rubella	1371	20	<1	7
Streptococcus pneumoniae[a]	5851	5230	72	95
Polio	25	240	6	8
Rotavirus[b]	1280	20	<1	4
Varicella	2641	50	1	16
Total	17 769	31 412	853	894[c]
Total (Undiscounted)	21 900	74 240	2787	2650[c]

All health outcomes were discounted at an annual rate of 3%.

[a] *Streptococcus pneumoniae* cases are defined as the sum of cases of invasive pneumococcal disease, Streptococcus pneumoniae pneumonia, and Streptococcus pneumoniae acute otitis media.

[b] Rotavirus cases are defined as a sum of rotavirus-related hospitalizations, emergency department visits, outpatient visits, and nonmedically attended cases. The sum of these cases may be an overestimate of total rotavirus cases in the population, as some events may have multiple rotavirus-related visits.

[c] Total discounted QALYs gained from cases of disease averted is ∼894 000; when accounting for incremental QALYs from vaccine-related adverse events, total QALYs gained is ∼892 000. Similarly, total undiscounted QALYs gained from cases of disease averted is ∼2 650 000, whereas total QALYs gained are ∼2 648 000 when adjusting for incremental QALYs from vaccine-related adverse events.

Economic Outcomes Without and With Vaccination

Lifetime societal disease-related costs for the 2017 birth cohort were $66.8 billion without childhood immunization, which included $22.4 billion in healthcare payer costs to treat cases of disease, $8.4 billion in productivity losses caused by cases of disease and long-term sequelae, and $36.0 billion in productivity losses caused by disease-related mortality (Fig 2). With routine childhood immunization, lifetime societal disease-related costs were $3.2 billion, including $1.3 billion in healthcare payer costs to treat cases of disease, $0.9 billion in

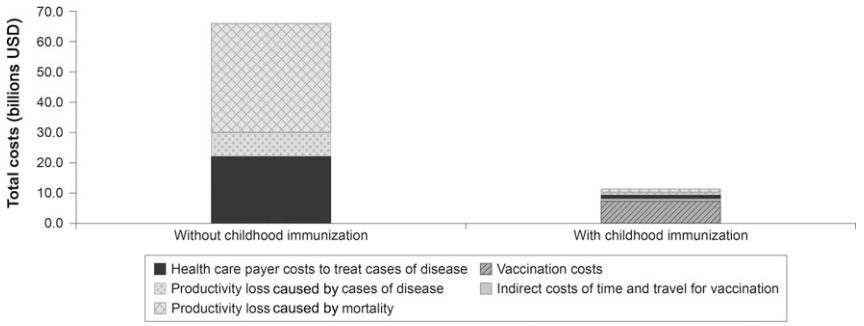

FIGURE 2

Base-case total societal perspective costs, overall and by type of cost. Total lifetime cost outcomes for the 2017 US birth cohort were discounted at an annual rate of 3% and are presented in 2019 US dollars.

productivity losses caused by cases of disease and long-term sequelae, and $1.0 billion in productivity losses caused by disease-related mortality.

Thus, societal disease-related cost-savings totaled $63.6 billion, with the highest savings being caused by averted cases of diphtheria, measles, and pneumococcal disease (Fig 3). For disease-related costs averted, direct medical costs to treat acute cases and long-term sequelae accounted for 33% of the savings, whereas the remaining costs averted were from productivity losses caused by cases and long-term sequelae (12%) and productivity loss caused by mortality (55%) (Table 3).

The societal costs of the US routine vaccination program were $8.5 billion for the 2017 birth cohort. Most societal vaccination costs were from vaccine acquisition (62%), administration (23%), and caregiver time and travel (13%); adverse events constituted a small proportion of costs (2%). As a result of the disease-related costs averted, the US childhood immunization program was associated with a net savings of $55.1 billion and a BCR of 7.5 from the societal perspective. This BCR indicates that every dollar invested in the childhood immunization program is expected to result in $7.50 in savings to society. A BCR of 2.8 was observed from the healthcare payer perspective. Incremental costs per LY and per QALY saved were not applicable because the immunization program was cost-saving. However, using a willingness-to-pay threshold of $100 000 per QALY saved,[60] the value of total QALYs saved by the childhood immunization program was approximately $89.2 billion.

Scenario Analyses

BCRs were most impacted by variations of annual discount rates, vaccine administration costs, and direct medical costs of disease cases (Table 4). Healthcare payer and societal BCRs were minimally impacted when assumptions impacting vaccine acquisition costs were varied. The economic value of routine childhood immunization was lower when annual influenza vaccination for children aged 0 to 10 years was included in the economic analysis, with healthcare payer and societal BCRs of 2.6 and 5.8 (compared with 2.8 and 7.5 in the base case), respectively. The societal BCR substantially increased when the value of QALYs saved was included in the BCR calculation (BCR = 18.0). When the scenarios negatively impacting the BCR of childhood immunization were simultaneously observed (ie, worst-case scenario), the healthcare payer and societal BCRs were 1.5 and 3.8, respectively.

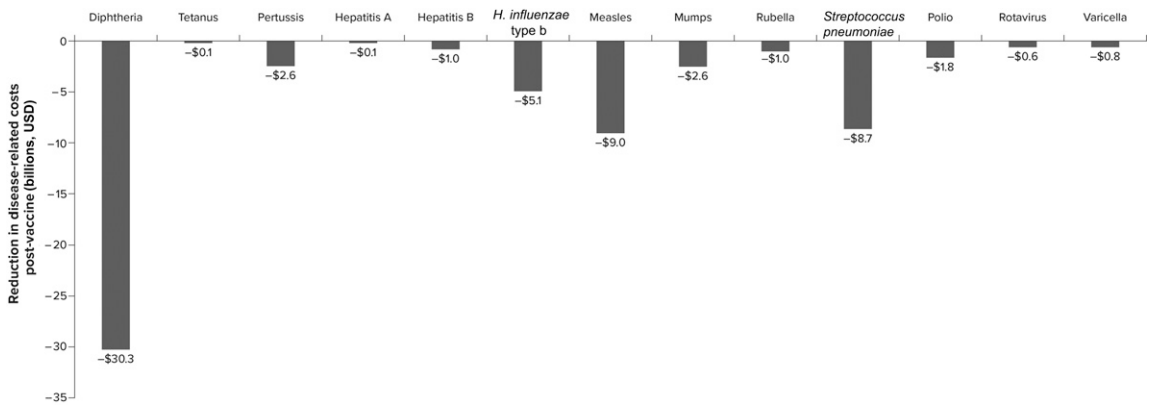

FIGURE 3

Base-case incremental societal disease-related costs, by disease. Incremental lifetime cost outcomes for the 2017 US birth cohort were discounted at an annual rate of 3% and are presented in 2019 US dollars.

TABLE 3 Base-Case Economic Results for Routine Childhood Immunization Program Compared With No-Vaccination Program

Incremental Outcome	Healthcare Payer Perspective (Millions USD)	Societal Perspective (Millions USD)
Vaccination costs		
Acquisition	5298	5298
Administration	1941	1941
Adverse events	175	175
Time and travel for vaccination	—	1084
Disease-related costs		
Disease treatment	−21 067	−21 067
Productivity loss caused by disease	—	−7555
Productivity loss caused by disease-related mortality	—	−34 950
Total incremental costs	−13 652	−55 072
Benefit-cost ratio	2.8	7.5
Incremental cost per QALY gained	Cost-saving	Cost-saving
Value of QALYs saved[a]	—	89 329

Data presented in US dollars unless otherwise indicated. —, not applicable.
[a] Value of QALYs saved were calculated by multiplying the total QALYs saved with childhood immunization (Table 2) by a willingness-to-pay threshold of $100 000 per QALY gained.[60]

DISCUSSION

We estimated that routine childhood immunization averted 17.8 million cases and 31 400 disease-related deaths for the 2017 US birth cohort over its lifetime, resulting in a net savings of $55.1 billion (BCR of 7.5) and $13.7 billion (BCR of 2.8) from a societal and healthcare payer perspective, respectively. Results were robust to variations in key input values. These estimates could be used to aid US national vaccination goals for increasing public awareness of the individual and societal benefits of the childhood immunization program,[61,62] which are particularly important given recent decreases in childhood vaccination rates observed in the United States during the COVID-19 pandemic.[63]

TABLE 4 Scenario Analysis Results

Scenario	Healthcare Payer BCR	Societal BCR
Base case	2.8	7.5
Scenario 1: 100% increase in vaccine administration costs	2.3	6.1
Scenario 2: 10% increase in public purchase of vaccines	2.9	7.7
Scenario 3: 10% reduction in public purchase of vaccines	2.8	7.3
Scenario 4: 5% increase in vaccine acquisition costs	2.7	7.3
Scenario 5: 100% of indirect costs for caregiver time and travel for vaccinations at well-child visits attributable to vaccination[a]	2.8	6.6
Scenario 6: 0% annual discount rates	5.3	21.0
Scenario 7: 10% reduction in pre-vaccine disease incidence	2.5	6.7
Scenario 8: 50% increase in vaccine-era disease incidence	2.8	7.3
Scenario 9: 20% increase in healthcare payer disease-related costs	3.4	8.0
Scenario 10: 20% reduction in healthcare payer disease-related costs	2.3	7.0
Scenario 11: 20% reduction in disease case-fatality rates	2.8	6.7
Scenario 12: annual influenza vaccination and disease included in economic analysis	2.6	5.8
Scenario 13: inclusion of value of QALYs saved in societal BCR	2.8	18.0
Scenario 14: worst-case scenario[b]	1.5	3.8

[a] A total of 50% of indirect costs for caregiver time and travel for vaccinations at well-child visits were assumed to be attributable to vaccination in the base-case analysis.
[b] The worst-case scenario combined the input variations observed in Scenarios 1, 3, 4, 5, 7, 8, 10, and 11.

Previous analyses have evaluated the economic impact of prior US pediatric vaccination schedules.[6,7] From the healthcare perspective, the current BCR was similar to results previously obtained (2.8 versus 3.0 from Zhou and colleagues[7]); from a societal perspective, however, the estimated BCR was lower (7.5 versus 10.1 from Zhou and colleagues[7]). The difference in the societal BCR could be explained by the current model's higher lost productivity caused by vaccination-related caregiver time and transport costs; we also calculated lower reductions in lifetime productivity losses from long-term complications and death.

Our analysis is useful for health economists, policy makers, and other stakeholders interested in ascertaining the benefits and observed impacts of childhood vaccination. Additional analyses should evaluate the impact of childhood vaccination among racial and ethnic groups that may be at increased risk for vaccine-preventable disease or that may have lower vaccination rates. Our analyses could not explore the impact of childhood vaccination within specific population strata because data on differences among racial and ethnic groups in vaccine coverage and disease incidence estimates are scarce and/or based on small population size. Further, continued changes to the ACIP vaccination schedule over time and the epidemiologic impacts of changes to vaccination patterns justify periodic economic evaluations of the childhood vaccination program. Future updates to these evaluations are of particular importance after a shock or disruption to a vaccination program, such as the COVID-19 pandemic, which may impact both disease incidence and population-level vaccination rates.

Some limitations of this analysis must be considered. Our model followed a birth cohort over its

lifetime but modeled only pediatric vaccines and did not include the impact or cost of adolescent, adult, maternal, or booster vaccines relevant to our analysis (eg, influenza, TDaP booster, pneumococcal vaccines); this may overestimate the value of childhood immunization. However, our model did not capture the reduced incidence and associated cost-savings of diseases avoided for age groups outside the birth cohort through herd immunity. This was a conservative approach, thus underestimating the value of childhood immunization. Similarly, for the scenario including annual influenza vaccination, influenza incidence and vaccination were modeled only in children aged 0 to 10 years and therefore only captured direct protection of the influenza vaccine.

Prevaccine incidence estimates, for some diseases, corresponded to different historic periods, with possible differences in contact patterns affecting transmission. Vaccine-era incidence estimates use an average across multiple years, thus capturing but not accurately reflecting seasonal fluctuations or periodic outbreaks in a given year. This analytic framework also limits the analysis results to the time periods compared, and as such, our analysis does not account for potential changes in disease incidence over time. In addition, estimates of case-fatality ratios and disease management costs in the vaccine era could not be obtained for diseases that are nearly or fully eradicated. Of note, our sensitivity analyses showed that cost-savings from the childhood vaccination program were robust to variations in assumptions across these parameters.

In addition, each disease was modeled separately and did not allow for interaction across the diseases. For example, disease-related deaths for diphtheria did not reduce the size of the cohort modeled for tetanus. However, during prevaccine periods, children were exposed to multiple infectious disease risks and could die of multiple causes. Thus, the model expresses the value of reducing infectious disease morbidity and mortality across a variety of diseases. Additionally, this analysis did not capture all extended benefits of vaccination, such as increased educational attainment and productivity, reduced household financial risk, and reduced use of antimicrobial agents because of the averted cases of diseases that would have warranted such treatment.[64–66] Furthermore, some aspects of vaccination impact are difficult to capture in models and may lead to underestimation of vaccination benefits. For example, natural measles infections may negatively affect immunologic memory for other pathogens[67–69]; this phenomenon is not observed in individuals with vaccine-induced immunity.[68] Thus, our results serve as a conservative estimate of the value of the childhood immunization program.

CONCLUSIONS

From the healthcare payer and societal perspectives, the US childhood immunization program results in cost-savings caused by reductions in cases of disease and disease-related costs. This highlights the continued value of routine childhood immunization in reducing the clinical and economic burden of vaccine-preventable disease. Sustaining high levels of vaccination coverage and adherence to the recommended vaccination schedule are necessary to continue observing the benefits of the vaccination program.

ACKNOWLEDGMENTS

Thank you to Kate Lothman of RTI Health Solutions, who provided medical writing support for the development of this manuscript and whose services were funded by Merck Sharp and Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ.

ABBREVIATIONS

ACIP: Advisory Committee on Immunization Practices
BCR: benefit-cost ratio
DTaP: diphtheria, tetanus, and acellular pertussis vaccine
HepA: hepatitis A vaccine
HepB: hepatitis B vaccine
Hib: *Haemophilus influenzae* type b vaccine
IPV: inactivated polio vaccine
LY: life-year
MMR: measles, mumps, rubella vaccine
PCV13: 13-valent pneumococcal conjugate vaccine
QALY: quality-adjusted life-year
USD: United States dollars

Address correspondence to Mawuli Nyaku, DrPh, MBA, MPH, Merck & Co., Inc., 126 East Lincoln Avenue, PO Box 2000, Rahway, NJ 07065. E-mail: mawuli.nyaku@gmail.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FUNDING: This study was funded by Merck Sharp and Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ.

CONFLICT OF INTEREST DISCLOSURES: Mr Carrico, Ms Talbird, and Ms Mellott are employed by RTI Health Solutions, which received funding for the conduct of this study. Dr La was an employee of RTI Health Solutions when this study was conducted and is now an employee and shareholder in the GSK group of companies. Dr Chen, Dr Carias,

and Dr Roberts are employees of Merck Sharp and Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ, USA, and are shareholders in Merck and Co., Inc., Rahway, NJ, USA. Dr Nyaku was an employee of Merck Sharp and Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ, USA, and a shareholder in Merck and Co., Inc., Rahway, NJ, USA, when this study was conducted. Dr Marshall has been an investigator on clinical trials funded by GlaxoSmithKline, Merck, Pfizer, Sanofi Pasteur, and Seqirus, and he has received honoraria from these companies for service on advisory boards and/or nonbranded presentations.

REFERENCES

1. Gindler J; American Academy of Pediatrics and the Advisory Committee on Immunization Practices. Recommended childhood immunization schedule United States–1995. *J Natl Med Assoc.* 1995;87(8):537–543
2. Centers for Disease Control and Prevention (CDC). Recommended child and adolescent immunization schedule for ages 18 years or younger, United States, 2020. Available at: https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Accessed September 8, 2020
3. Centers for Disease Control and Prevention (CDC). Impact of vaccines universally recommended for children–United States, 1990-1998. *MMWR Morb Mortal Wkly Rep.* 1999;48(12):243–248
4. Roush SW, Murphy TV; Vaccine-Preventable Disease Table Working Group. Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. *JAMA.* 2007;298(18):2155–2163
5. van Panhuis WG, Grefenstette J, Jung SY, et al. Contagious diseases in the United States from 1888 to the present. *N Engl J Med.* 2013;369(22):2152–2158
6. Zhou F, Santoli J, Messonnier ML, et al. Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001. *Arch Pediatr Adolesc Med.* 2005;159(12):1136–1144
7. Zhou F, Shefer A, Wenger J, et al. Economic evaluation of the routine childhood immunization program in the United States, 2009. *Pediatrics.* 2014;133(4):577–585
8. Centers for Disease Control and Prevention (CDC). Active bacterial core surveillance report, emerging infections program network, Streptococcus pneumoniae, 2013. Available at: https://www.cdc.gov/abcs/reports-findings/surv-reports.html. Accessed May 11, 2020
9. Centers for Disease Control and Prevention (CDC). Active bacterial core surveillance report, emerging infections program network, Streptococcus pneumonia, 2014. Available at: https://www.cdc.gov/abcs/reports-findings/surv-reports.html. Accessed May 11, 2020
10. Centers for Disease Control and Prevention (CDC). Active bacterial core surveillance report, emerging infections program network, Streptococcus pneumoniae, 2015. Available at: https://www.cdc.gov/abcs/reports-findings/surv-reports.html. Accessed May 11, 2020
11. Centers for Disease Control and Prevention (CDC). Active bacterial core surveillance report, emerging infections program network, Streptococcus pneumoniae, 2016. Available at: https://www.cdc.gov/abcs/reports-findings/surv-reports.html. Accessed May 11, 2020
12. Centers for Disease Control and Prevention (CDC). Active bacterial core surveillance report, emerging infections program network, Streptococcus pneumoniae, 2017. Available at: https://www.cdc.gov/abcs/reports-findings/surv-reports.html. Accessed May 11, 2020
13. Tong S, Amand C, Kieffer A, Kyaw MH. Trends in healthcare utilization and costs associated with pneumonia in the United States during 2008-2014. *BMC Health Serv Res.* 2018;18(1):715
14. Kawai K, Adil EA, Barrett D, Manganella J, Kenna MA. Ambulatory visits for otitis media before and after the introduction of pneumococcal conjugate vaccination. *J Pediatr.* 2018;201:122–127.e1
15. Kaur R, Morris M, Pichichero ME. Epidemiology of acute otitis media in the postpneumococcal conjugate vaccine era. *Pediatrics.* 2017;140(3):e20170181
16. Getachew HB, Dahl RM, Lopman BA, Parashar UD. Rotavirus vaccines and health care utilization for diarrhea in US children, 2001 to 2015. *Pediatr Infect Dis J.* 2018;37(9):943–948
17. Krishnarajah G, Demissie K, Lefebvre P, Gaur S, Sheng Duh M. Clinical and cost burden of rotavirus infection before and after introduction of rotavirus vaccines among commercially and Medicaid insured children in the United States. *Hum Vaccin Immunother.* 2014;10(8):2255–2266
18. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: final data for 2017. *Natl Vital Stat Rep.* 2018;67(8):1–50
19. Centers for Disease Control and Prevention (CDC). Coverage by season. Available at: https://www.cdc.gov/flu/fluvaxview/coverage-by-season.htm. Accessed October 22, 2021
20. Centers for Disease Control and Prevention (CDC). CDC seasonal flu vaccine effectiveness studies. Available at: https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm. Accessed October 22, 2021
21. Centers for Disease Control and Prevention (CDC). ChildVaxView interactive. Available at: https://www.cdc.gov/vaccines/imz-managers/coverage/childvaxview/data-reports/index.html. Accessed April 22, 2019
22. US Bureau of Labor Statistics. Consumer price index - all urban consumers: all items [CUSR0000SA0]. Available at: https://www.bls.gov/cpi/data.htm. Accessed March 25, 2019
23. US Bureau of Labor Statistics. Employment cost index - total compensation for all civilian workers in all industries and occupations, index, 2001-2019. Available at: https://www.bls.gov/ncs/ect/home.htm#data. Accessed August 22, 2019
24. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA.* 2016;316(10):1093–1103

25. Talbird SE, Carrico J, La EM, et al. Impact of routine childhood immunization in reducing vaccine-preventable diseases in the United States. *Pediatrics*. 2022;150(3):e2021056013

26. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19–35 months — United States, 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(40):1123–1128

27. Seither R, McGill MT, Kriss JL, et al. Vaccination coverage with selected vaccines and exemption rates among children in kindergarten — United States, 2019–20 school year. *MMWR Morb Mortal Wkly Rep*. 2021;70(3):75–82

28. Centers for Disease Control and Prevention (CDC). CDC vaccine price list. Available at: https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html. Accessed March 25, 2019

29. Thompson KM, Orenstein WA, Hinman AR. Performance of the United States vaccine injury compensation program (VICP): 1988-2019. *Vaccine*. 2020;38(9):2136–2143

30. Centers for Medicare and Medicaid Services. Physician fee schedule – 2019. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched. Accessed March 25, 2019

31. Grosse SD, Krueger KV, Pike J. Estimated annual and lifetime labor productivity in the United States, 2016: implications for economic evaluations. *J Med Econ*. 2019;22(6):501–508

32. Zhou F, Ortega-Sanchez IR, Guris D, Shefer A, Lieu T, Seward JF. An economic analysis of the universal varicella vaccination program in the United States. *J Infect Dis*. 2008;197(Suppl 2):S156–S164

33. Zhou F, Reef S, Massoudi M, et al. An economic analysis of the current universal 2-dose measles-mumps-rubella vaccination program in the United States. *J Infect Dis*. 2004;189(Suppl 1):S131–S145

34. Hankin-Wei A, Rein DB, Hernandez-Romieu A, et al. Cost-effectiveness analysis of catch-up hepatitis A vaccination among unvaccinated/partially-vaccinated children. *Vaccine*. 2016;34(35):4243–4249

35. Widdowson MA, Meltzer MI, Zhang X, Bresee JS, Parashar UD, Glass RI. Cost-effectiveness and potential impact of rotavirus vaccination in the United States. *Pediatrics*. 2007;119(4):684–697

36. Miller MA, Sutter RW, Strebel PM, Hadler SC. Cost-effectiveness of incorporating inactivated poliovirus vaccine into the routine childhood immunization schedule. *JAMA*. 1996;276(12):967–971

37. De Wals P, Petit G, Erickson LJ, et al. Benefits and costs of immunization of children with pneumococcal conjugate vaccine in Canada. *Vaccine*. 2003;21(25–26):3757–3764

38. O'Brien MA, Prosser LA, Paradise JL, et al. New vaccines against otitis media: projected benefits and cost-effectiveness. *Pediatrics*. 2009;123(6):1452–1463

39. Rosenthal EM, Hall EW, Rosenberg ES, Harris A, Nelson NP, Schillie S. Assessing the cost-utility of preferentially administering Heplisav-B vaccine to certain populations. *Vaccine*. 2020;38(51):8206–8215

40. Thompson KM, Tebbens RJ. Retrospective cost-effectiveness analyses for polio vaccination in the United States. *Risk Anal*. 2006;26(6):1423–1440

41. Ekwueme DU, Strebel PM, Hadler SC, Meltzer MI, Allen JW, Livengood JR. Economic evaluation of use of diphtheria, tetanus, and acellular pertussis vaccine or diphtheria, tetanus, and whole-cell pertussis vaccine in the United States, 1997. *Arch Pediatr Adolesc Med*. 2000;154(8):797–803

42. Meltzer MI, Shapiro CN, Mast EE, Arcari C. The economics of vaccinating restaurant workers against hepatitis A. *Vaccine*. 2001;19(15–16):2138–2145

43. Prosser LA, Bridges CB, Uyeki TM, et al. Health benefits, risks, and cost-effectiveness of influenza vaccination of children. *Emerg Infect Dis*. 2006;12(10):1548–1558

44. Institute of Medicine. *Adverse Effects of Vaccines: Evidence and Causality*. Washington, DC: The National Academies Press; 2011

45. Rubin JL, McGarry LJ, Strutton DR, et al. Public health and economic impact of the 13-valent pneumococcal conjugate vaccine (PCV13) in the United States. *Vaccine*. 2010;28(48):7634–7643

46. Anyiwe K, Richardson M, Brophy J, Sander B. Assessing adolescent immunization options for pertussis in Canada: a cost-utility analysis. *Vaccine*. 2020;38(7):1825–1833

47. Kamiya H, Cho BH, Messonnier ML, Clark TA, Liang JL. Impact and cost-effectiveness of a second tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine dose to prevent pertussis in the United States. *Vaccine*. 2016;34(15):1832–1838

48. Tu HA, Deeks SL, Morris SK, et al. Economic evaluation of meningococcal serogroup B childhood vaccination in Ontario, Canada. *Vaccine*. 2014;32(42):5436–5446

49. Kuppermann M, Nease RF Jr, Ackerson LM, Black SB, Shinefield HR, Lieu TA. Parents' preferences for outcomes associated with childhood vaccinations. *Pediatr Infect Dis J*. 2000;19(2):129–133

50. Martin A, Batty A, Roberts JA, Standaert B. Cost-effectiveness of infant vaccination with RIX4414 (Rotarix) in the UK. *Vaccine*. 2009;27(33):4520–4528

51. Lee GM, Salomon JA, LeBaron CW, Lieu TA. Health-state valuations for pertussis: methods for valuing short-term health states. *Health Qual Life Outcomes*. 2005;3:17

52. Philipson TJ, Thornton Snider J, Chit A, et al. The social value of childhood vaccination in the United States. *Am J Manag Care*. 2017;23(1):41–47

53. Fowler A, Stödberg T, Eriksson M, Wickström R. Long-term outcomes of acute encephalitis in childhood. *Pediatrics*. 2010;126(4):e828–e835

54. Weisbrod BA. The valuation of human capital. *J Polit Econ*. 1961;69(5):425–436

55. Wateska AR, Nowalk MP, Zimmerman RK, Smith KJ, Lin CJ. Cost-effectiveness of increasing vaccination in high-risk adults aged 18-64 years: a model-based decision analysis. *BMC Infect Dis*. 2018;18(1):52

56. Centers for Disease Control and Prevention (CDC). Underlying cause of death 1999-2017 on CDC WONDER online database. Available at: https://wonder.cdc.gov/ucd-icd10.html. Accessed April 10, 2019

57. Arias E, Xu JQ. United States life tables, 2017. *Natl Vital Stat Rep.* 2019;68(7):1–66

58. Centers for Disease Control and Prevention (CDC). Estimates of flu vaccination coverage among children — United States, 2017–18 flu season. Available at: https://www.cdc.gov/flu/fluvaxview/coverage-1718estimates-children.htm. Accessed March 25, 2019

59. Park M, Jit M, Wu JT. Cost-benefit analysis of vaccination: a comparative analysis of eight approaches for valuing changes to mortality and morbidity risks. *BMC Med.* 2018;16(1):139

60. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness–the curious resilience of the $50,000-per-QALY threshold. *N Engl J Med.* 2014;371(9):796–797

61. US Department of Health and Human Services. Vaccines national strategic plan: 2021–2025. Available at: https://www.hhs.gov/sites/default/files/HHS-Vaccines-Report.pdf. Accessed April 20, 2021

62. Ackerson BK, Sy LS, Glenn SC, et al. Pediatric vaccination during the COVID-19 pandemic. *Pediatrics.* 2021;148(1):e2020047092

63. Kujawski SA, Yao L, Wang HE, Carias C, Chen YT. Impact of the COVID-19 pandemic on pediatric and adolescent vaccinations and well child visits in the United States: a database analysis. *Vaccine.* 2022;40(5):706–713

64. Jit M, Hutubessy R, Png ME, et al. The broader economic impact of vaccination: reviewing and appraising the strength of evidence. *BMC Med.* 2015;13:209

65. Bloom DE, Brenzel L, Cadarette D, Sullivan J. Moving beyond traditional valuation of vaccination: needs and opportunities. *Vaccine.* 2017;35(Suppl 1):A29–A35

66. Lakdawalla DN, Doshi JA, Garrison LP Jr, Phelps CE, Basu A, Danzon PM. Defining elements of value in health care-A health economics approach: an ISPOR special task force report. *Value Health.* 2018;21(2):131–139

67. Wesemann DR. Game of clones: how measles remodels the B cell landscape. *Sci Immunol.* 2019;4(41):eaaz4195

68. Mina MJ, Kula T, Leng Y, et al. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. *Science.* 2019;366(6465):599–606

69. Petrova VN, Sawatsky B, Han AX, et al. Incomplete genetic reconstitution of B cell pools contributes to prolonged immunosuppression after measles. *Sci Immunol.* 2019;4(41):eaay6125

70. Rogers MAM, Kim C, Hofstetter AM. Geospatial variation in rotavirus vaccination in infants, United States, 2010-2017. *Emerg Infect Dis.* 2019;25(10):1993–1995