

# Childhood Vaccination

## Implications for Global and Domestic Public Health



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### KEYWORDS

• Vaccination • Neuroepidemiology • Public health

### KEY POINTS

- Vaccination is of indisputable importance in the control and prevention of endemic and emerging domestic and global disease.
- The immunologic basis of vaccination is related to the ability to passively activate the host immune system inducing a salutary host response leading to microbial-specific protective antibodies.
- There are different types of vaccines depending on the methodology used.
- The control of vaccine-preventable diseases is associated with measurable decline in preventable hospitalizations, increased morbidity and mortality, and increased health care costs.
- Improvement in state and local public health infrastructure along with innovative and targeted prevention efforts continues to yield significant progress in controlling infectious illnesses.

### INTRODUCTION

This is an era of intense change in exploration and understanding of the complexity of the human microbiome and the surrounding ecosystems. Although humans are hosts to a myriad of microorganisms that have assembled into complex communities outnumbering the human body by a factor of 10-fold providing many of the building blocks for shared immunity, there still exist certain pathogenic microorganisms that cause human and economic devastation, which if prevented by effective vaccination campaigns, could easily be eradicated. This article examines selected aspects of domestic and global vaccination. Vaccination was the topic of a recent book.<sup>1</sup>

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## HISTORICAL ASPECTS

During the twentieth century, the health and life expectancy of persons residing in the United States improved dramatically. Since the beginning of that century the average lifespan of persons in the United States increased by more than 30 years, with 25 years of the gain attributable to advances in public health. Vaccination of the US public is one of the 10 great public health achievements of the twentieth century.<sup>2</sup> At the beginning of that century, infectious diseases were widely prevalent in the United States and exacted an enormous toll on the population. With few effective antimicrobial treatments and preventative measures available, the first vaccine against smallpox, developed in 1796, was not widely used enough to fully control the disease exacting 894 fatalities of 12,064 reported cases. Four other vaccines against rabies, typhoid, cholera, and plague also developed a century earlier were not widely used by 1900. Since that time, vaccines have been developed or licensed against at least 21 other diseases in the United States, approximately one-half of which are recommended in selected populations at high risk because of areas of environmental factors, age, medical condition, or risk behaviors, whereas 13 are recommended by the Centers for Disease Control and Prevention (CDC) for use in all US children (**Table 1**).

Historically, national efforts to promote vaccines among eligible children began with the appropriation of federal funds for polio vaccination after introduction of the vaccine in 1955, and since then federal, state, and local governments and public and private health care providers have collaborated to develop and maintain the vaccine-delivery system in the United States. By the end of the twentieth century, vaccination coverage was at record levels, exceeding 90% for three or more doses of diphtheria-tetanus-toxoids-pertussis vaccine (DPT), three or more doses of poliovirus vaccine, three or more doses of *Haemophilus influenzae* type b (Hib) vaccine, and one or more doses of measles-containing vaccine. Coverage with four or more doses of DPT was 81% and 84% for three doses of hepatitis B vaccine. There was, however, lower coverage for the then recently introduced varicella vaccine (26%), for the combined series of four DPT/three polio/one measles-containing vaccine/three Hib.<sup>3</sup> By the end of the twentieth century, coverage for children age 5 to 6 years exceeded 95% each school year since 1980 for DPT, polio, and measles-mumps-rubella (MMR) vaccines.

Dramatic declines in morbidity were reported for nine vaccine-preventable diseases for which vaccinations were recommended in US children before 1990: smallpox, diphtheria, paralytic poliomyelitis, and measles caused by wild-type viruses declined 100%; and nearly 100% for pertussis, tetanus, mumps, rubella, congenital rubella, and Hib. The past decade additionally witnessed substantial declines in cases, hospitalizations, mortality, and health care costs associated with vaccine-preventable diseases.<sup>4</sup> In addition, new vaccines were introduced covering rotavirus, meningococcal disease, herpes zoster, pneumococcal bacteremia, and human papillomavirus infection, and tetanus, diphtheria, and acellular pertussis for adults and adolescents, bringing to 17 the number of disease targeted by US immunization policy. One economic analysis<sup>5</sup> showed that vaccination of each US birth cohort with the current childhood immunization schedule feasibly prevented approximately 42,000 deaths and 20 million disease cases, with net saving of nearly \$14 billion in direct costs and \$69 billion in total societal costs. Pneumococcal conjugate and rotavirus are the two vaccines implemented in the past decade that are particularly striking, preventing an estimated 13,000 deaths and up to 60,000 hospitalizations, respectively, each year, and advances made in the older hepatitis A and B, and varicella vaccines bringing reported cases to record low levels, and reducing age-adjusted mortality in

**Table 1**  
**CDC schedule of infant and childhood vaccinations**

Vaccine Name	Age at First Dose	Age at Second Dose	Age at Third Dose	Age at Fourth Dose
Hepatitis B (HepB)	Birth	1–2 mo	6–18 mo	—
Rotavirus (RV) RV1 (2-dose series); RV5 (3-dose series)	2 mo	4 mo	6 mo	—
Diphtheria, tetanus, and acellular pertussis (DTaP: <7 y)	2 mo	4 mo	6 mo	15–18 mo
Tetanus, diphtheria, and acellular pertussis (Tdap: >7 y)	11–12 y	—	—	—
<i>Haemophilus influenzae</i> type b5 (Hib)	2 mo	4 mo	6 mo	12–15 mo
Pneumococcal conjugate (PCV13)	2 mo	4 mo	6 mo	12–15 mo
Inactivated poliovirus (IPV: <18 y)	2 mo	4 mo	6–18 mo	4–6 y
Influenza (IIV; LAIV) 2 doses for some	6–18 mo annual vaccination (IIV only) 1 or 2 doses	2–8 y annual vaccination (LAIV or IIV) 1 or 2 doses	8–18 y annual vaccination (LAIV or IIV) 1 dose only	—
Measles, mumps, rubella (MMR)	12–15 mo	4–6 y	—	—
Varicella (VAR)	12–15 mo	4–6 y	—	—
Hepatitis A (HepA)	12–18 mo (2 dose series)	—	—	—
Human papillomavirus (HPV2, females only; HPV4, males and females)	11–12 y (3 dose series)	—	—	—
Meningococcal (Hib-MenCY >6 wk, MenACWY-D >9 mo; MenACWY-CRM >2 mo)	11–12 y	—	—	—

Data from Centers for Disease Control, Atlanta, GA. Available at <http://www.cdc.gov/vaccines/schedules>.

deaths per million population from hepatitis A from 0.38 by the end of the previous century to 0.26 by the end of the recent decade.<sup>6</sup>

Expanded vaccination coverage has also been historically the most cost-effective means to advance global welfare and one of the 10 great public health achievements worldwide in the past decade,<sup>7</sup> with an estimated prevention of 2.5 million deaths each year among children less than 5 years through use of measles, polio, and DPT vaccines. Polio eradication efforts through mandatory vaccination decreased the number of countries from 20 to 4, with fewer than 1500 cases reported in 2010. With the number of countries using hepatitis B vaccine increasing from 107 in 2000 to 178 in 2009, and global vaccination coverage of 70%, at least 700,000 deaths from cirrhosis and liver cases are expected to be averted in annual birth cohort in the 178 countries. Moreover, during 2000 to 2009, the number of countries using the Hib vaccine worldwide increased from 62 to 161, with a resulting global coverage of 38%, averting an estimated 130,000 pneumonia and meningitis deaths annually among children less than 5 years of age.

The combined achievements in vaccine-preventable diseases mirrored changes in the public health system. These included the greater quantitative capacity of epidemiology in study designs and period health surveys, methods of data collection that evolved from simple measures of disease prevalence to complex studies of precise analysis available in cohort, case-control, and randomized clinical trials to establish the efficacy of vaccination and demonstrate its low risk. The CDC in the United States, which assumed responsibility for collecting and publishing nationally notifiable disease data in 1998, now tracks more than 52 infectious illnesses. Today, public health represents the combined collaboration of governmental federal, state, county, and local governmental health departments, and nongovernmental organization to track infectious illness in the United States and rates of vaccination.

## IMMUNE BASIS OF VACCINATION

The human immune system and immunization are inextricably related. In practice, vaccines are most often comprised of an attenuated or weakened version of the pathogenic organism for which immunity is sought. This attenuation is accomplished in such a way that the foreign pathogen is rendered sufficient for invoking an immune response yet incapable of inducing infection. In essence, the immune system processes the immunization as if an infection were present.

Immunity was originally separated into two types, humoral and cell-mediated, based on the purported effects of immunization or vaccine against a given pathogen. Humoral immunity was deemed as the effect of immunization that resulted in definable changes in the cell-free body fluid or serum, whereas the cell-mediated type was ascribed to the observed protective effect associated with multiplication of specific cells. Two primordial types of immune cells are now recognized and contribute to vaccination-induced immunity. One lineage, termed B cells, which mature in the bone marrow, further differentiate into plasma cells and memory cells. Mature plasma cells are capable of producing antimicrobial antibodies capable of latching onto their target in a lock-and-key-specific fashion when their surface antibody receptors recognize other cells displaying foreign infectious antigens, whereas other B-cell types mature into memory B cells that circulate in the bloodstream. T cells, also derived in the bone marrow, pass instead through the thymus gland where they achieve their final immunoreactivity, and are thought to be most protective in recognizing virus-infected cells. These cells participate in the defense against intracellular bacterial, fungal, and protozoan infections; cancers; and transplant rejection. Other aspects of enhanced

cellular immunity include the secretion of cell-signaling molecules termed cytokines, which promote cell-to-cell communication in immune responses and stimulate the movement of cells toward sites of inflammation and infection. An important aspect of vaccination-induced immunity is the booster shot, which amplified the immune response by representing the foreign antigen to a nonnaive host immune system.

## **CATEGORIES OF VACCINES**

Vaccines are divided into different categories depending on the way they are prepared and therefore how they confer immunity, including live-attenuated, inactivated, subunit, conjugate, and toxoids. This has been reviewed elsewhere.<sup>8</sup>

### ***Live-Attenuated Vaccine***

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Most frequently used for viruses rather than bacterial illnesses, the method for preparing live-attenuated vaccines involves passing the viral agent through a succession of cell cultures to weaken it producing a form that is no longer able to replicate in human cells. Still recognized by the body's immune system, it protects against future infection. Examples includes MMR, varicella, and Hib vaccines. Although uncommon it is plausible that the introduced virus can cause illness if it has transformed into a more virulent form through mutation.

### ***Inactivated Vaccine***

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The microbe is inactivated by heat, irradiation, or certain chemicals to no longer cause illness on vaccination without altering its immune activation properties. Examples are poliovirus and hepatitis A vaccines. However, a disadvantage is the need for multiple boosters to augment efficacy.

### ***Subunit Vaccine***

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When only a portion of the microbe that acts as an antigen for immune surveillance is needed by the body to confer immunity, subunit vaccination is an appropriate methodology, such as influenza and hepatitis B subunit vaccines.

### ***Conjugate Vaccine***

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These types of vaccines are prepared from parts of the bacterium combined with a carrier protein, which when chemically linked together to the bacteria coat derivatives and generate a more potent host immune response, such as the pneumococcal vaccine.

## **DOMESTIC AND GLOBAL VACCINATION PROGRAMS**

Vaccination programs in the United States have generally been tied to school entry. The first national push to ensure that every state in the country had vaccination requirements for children entering schools occurred in the 1970s predicated on measles outbreaks during the preceding two decades.<sup>9</sup> Some states acted on their own accord and enacted vaccination laws. However, public opinion has at times been the most useful catalyst, especially outbreaks that remind one of the devastating potential of certain diseases that may have disappeared from public view because of infrequent occurrence. Indeed, a major advance in global public health was the launch of the World Health Organization Expanded Program on Immunization that promoted a schedule of basic vaccines for immunization against polio, measles, tuberculosis, and DPT according to the standard schedule similar to childhood programs in the United States (**Table 2**).

**Table 2**  
World Health Organization schedules of infant and childhood vaccinations

Vaccine Name	Age at First Dose	Age at Second Dose	Age at Third Dose	Age at Fourth Dose
BCG	Birth	—	—	—
Hepatitis B (Option 1)	Birth	4 wk	8 wk	—
Hepatitis B (Option 2)	Birth	4 wk	8 wk	12 wk
Polio (OPV + IPV)	6 wk	10 wk	14 wk	—
Polio (IPV/OPV Sequential)	8 wk	12–16 wk	4–8 wk after second dose	4–8 wk after third dose
Polio (IPV)	8 wk	12–16 wk	4–8 wk after second dose	—
DTP	6 wk	10–18 wk	4–8 wk after second dose	—
Hib (Option 1)	6 wk–59 mo	4 wk after first dose	4 wk after second dose	—
Hib (Option 2)	6 wk–59 mo	8 wk after first dose if 2 doses, 4 wk after first dose if 3 doses	4 wk after second dose	—
Pneumococcal (conjugate) (Option 1)	6 wk	10 wk	14 wk	—
Pneumococcal (conjugate) (Option 2)	6 wk	14 wk	—	—
Rotavirus (Rotarix)	6 wk	10 wk	—	—
Rotavirus (Rota Teq)	6 wk	10–16 wk	4 wk after second dose	—
Measles	9 or 12 mo	4 wk after first dose	—	—
Rubella	9 or 12 mo	—	—	—
Human papillomavirus	As soon as possible from 9 y	6 mo after first dose	—	—

Data from World Health Organization, Geneva, Switzerland. Available at: [http://www.who.int/immunization/policy/immunization\\_tables/en/](http://www.who.int/immunization/policy/immunization_tables/en/).

Vaccination as a method of disease prevention has been widely accepted globally. Goal Four of the United Nations Millennium Development Goals to reduce childhood mortality focuses on the delivery of effective vaccinations for children younger than age 5 years. Measles vaccination helped prevent nearly 15.6 million deaths worldwide between 2000 and 2013. The number of globally reported measles cases declined by 67% during the same period; about 84% of children worldwide received at least one dose of measles-containing vaccine in 2013, up 73% from 2000.<sup>10</sup> Chasing a disease down to the last few cases in lesser developed countries to the levels achieved in the more developed world remains a challenge. For example, the goal of malaria eradication faltered in the 1960s in part because of the resistance of *Plasmodium falciparum* to antimicrobial therapy and the development of mosquito vector resistance to insecticides resulting in a worldwide increase in cases. Virtually all vaccines against *P falciparum* (RTS, S/AAS01) have been designed using genetic sequences derived from the single well-characterized reference strain of West African origin (3D7).<sup>11</sup> A multivalent version of RTS, S with carefully chosen sporozoite protein variants, possibly combined with additional antigens, may offer broader protection.<sup>12</sup>

Even though most of the record decline of childhood infectious disease is attributed to increase in the use of vaccines, a small but significant minority of parents in the United States oppose the use of vaccines on children. Thus, the less than perfect effectiveness of certain US vaccination programs, such as childhood pertussis and measles that depend on widespread acceptance, resulted in a record number of cases in the United States in 2015.<sup>13</sup>

Valuable lessons have been learned from the worldwide campaigns to eradicate polio. In 1988, the World Health Assembly endorsed the goal of eradication of polio at a time when the number of new cases of paralysis approximated 350,000 and the disease was endemic in 125 countries.<sup>14</sup> The March of Dimes, established by President Franklin Roosevelt, was set up in the United States to end the epidemic that plagued the nation. Jonas Salk and Albert Sabin were two US scientists who took on the challenge of developing an effective vaccine against polio. To ensure efficacy against wild poliovirus infection, Salk methodically classified circulating polio strains before choosing the three in the final inactivated vaccine.<sup>11</sup> This methodology was implemented in the polio vaccine that achieved strain-specific protective immunity based on the inherent genetic diversity of the poliovirus. Wild-type poliovirus type 2 has since been eradicated in the United States with the last naturally occurring case detected in 1999, and type 3 seems to be close to eradication with virtually no new cases detected. Type 1 poliovirus, however, later emerged during the 2011 outbreak in China suggesting that eradication was incomplete. More recently cases of polio have been diagnosed in Syria, Nigeria, and Bangladesh caused by the disruption of populations by war and antivaccine sentiment expressed by some ultrareligious Muslims. As long as the polio virus circulates anywhere in the world, there is the potential for poliomyelitis to be exported to countries that are disease-free causing serious outbreaks.

## LEGAL CHALLENGES TO VACCINATION

### *The Lessons of Measles Vaccination*

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The hesitation or refusal of parents to vaccinate children was until recently on the rise in the United States with increasing exceptions granted from school-entry immunization mandates based on personal beliefs and nonmedical reasons. Buttenheim and colleagues<sup>15</sup> noted that while still below levels to maintain herd immunity against measles, there was a 2- to 10-fold underestimate of the true rate of vaccine refusal based on personal beliefs on school entry. This suggests a level of inadequate

understanding by parents as to the public imperative of measles immunization or a fear that the vaccine may itself be pathogenic in one form or another.

When an outbreak of measles cases was reported by the CDC in December 2014 at Disneyland in Orange County, California,<sup>16</sup> it was subsequently shown that 7% of children had received two or more MMR vaccinations, 45% were unvaccinated, and 43% had an unknown vaccination status.<sup>17</sup> These findings compelled two California State Senators, both with personal ties to health policy (one a pediatrician and the other the son of a polio survivor), to cosponsor and pass Bill SB 277 eliminating all nonmedical vaccine exemptions, and many other States began to follow California's lead.

There was no greater challenge for public health educators than trying to amend the misunderstanding of the risk of autism following MMR vaccination among concerned lay parent groups at the turn of the twentieth century in the United Kingdom. The basis for this misconception in causality was grounded in a publication in a major medical journal by a UK investigator that was subsequently retracted, which drew attention to cohorts of children with autism presumed to be a result of immune conditioning by early live-attenuated measles vaccination.<sup>18–20</sup> More than a decade later, a retracted US publication cited heightened risk for autism among only African American boys<sup>21</sup> citing a reanalysis of CDC data reported earlier showing no relation of autism in a population of school-matched subjects.<sup>22</sup> Further population-based studies<sup>19</sup> and a recent meta-analysis<sup>23</sup> of case-control and cohort studies have since found no strong evidence for a causal effect of autism by MMR vaccination.

Cawkwell and Oshinsky<sup>24</sup> studied the lessons learned from Mississippi, a state that consistently leads the United States in childhood vaccination with a greater than 99% MMR rate for children entering kindergarten. The fight against compulsory vaccination and the enduring success of Mississippi in repelling challenges to their vaccination requirements were traced to a State Supreme Court decision predicated on a 1972 State code that required vaccination before attending school. In 1979, Charles Brown sued the State of Mississippi claiming a strong religious belief against it, in order for his 6-year-old son to be admitted to Houston Elementary School despite not having been vaccinated. The Court upheld the validity of the State code but went a step further ruling that religious exemptions discriminated against children whose parents did not have those strong religious convictions thus violating the 14th Amendment, which called for equal protection of the law. This line of reasoning, which applied to philosophic and personal belief exemptions, removed any legal pathway to exemptions, with the exception of medical exemptions. The latter were so notoriously strict and required submission to the Department of Public Health by a licensed primary care physician that only 121 were approved in 2013 to 2014. There is no unanimous agreement among scientists and policy experts that removal of all nonmedical exemptions is the most logical path forward in ensuring acceptable rates of vaccination. Tea Party member Senator Chris McDaniel submitted in 2015 SB 2800, a bill that sought to amend the Mississippi code to allow for exemptions to vaccination on a contrary to belief stance that died in Committee. Subsequently, House Bill 130 surfaced supporting a parent's freedom to choose if their child is vaccinated, which although framed differently did not pass.

Strengthening childhood immunization laws is an important public health goal. There is legal precedent for the right of states to mandate vaccination for school entry to protect the public at large, as a social obligation to provide herd immunity, and to protect those who cannot be vaccinated recognizing that it is probably safer to be unvaccinated living in a highly vaccinated community than to be vaccinated but living in an unvaccinated one.<sup>9</sup>



## ASSESSING THE IMPACT OF VACCINES FOR ENDEMIC INFECTION

Assessing the impact of vaccination on an individual and population level requires an analysis of the direct and indirect effects of immunization. The theoretic concept of vaccine efficacy describes the individual level benefit or how much less likely an individual is to acquire infection following a given exposure. Most clinical trials, however, assess vaccine effectiveness at the population level. Both may fail to capture the indirect effect of vaccination accounting for the reduction in transmission to unvaccinated subjects in the wider population. Impossible to fully assess from clinical trial data alone, it is this combination of direct and indirect effects that should interest public health experts in fully evaluating the vaccination impact, especially because little may be known about the apparent or real vaccine impacts, and the risk of reinfection or mechanism of protection.

When performing statistical analysis of vaccine efficacy trials with heterogeneous exposure or susceptibility risk, care should be taken to account for the putative mechanism of the vaccine. Halloran and colleagues<sup>25</sup> used the term “leaky vaccine” inspired by the literature on malaria to describe a vaccine that exhibited failure in degree, and all-or-nothing vaccine for one that demonstrates failure in take. A vaccine that displayed only a failure in duration was called a waning vaccine. Farrington<sup>26</sup> cited the vaccine for pertussis as a possibly leaky vaccine, whereas vaccines for measles and rubella were termed all-or-nothing vaccines, and that for cholera as a waning vaccine.

Magpantay and colleagues<sup>27</sup> used mathematical modelling to extrapolate the epidemiologic efficacy and ramifications of such imperfect vaccines considering that an imperfect vaccine might exhibit failures in degree or leakiness and take or all-or-nothingness. These two extremes were reflective of their respective mechanisms of action from all-or-none complete protection of some fraction of subjects, with the remaining fraction remaining unaffected by it, and incomplete or leaky vaccines that reduced the per-exposure transmission rate for all recipients equally. Leaky vaccines again were those for which vaccine-induced protection reduced infection rates on a per-exposure basis, as opposed to all-or-none vaccines, which reduced infection rates to zero for some fraction of subjects, independent of the number of exposures. Leaky vaccines protected subjects with fewer exposures at a higher effective rate than subjects with more exposures. Edlefsen<sup>28</sup> noted that this simple dichotomy had serious implications for analysis of methodologies because leaky vaccines, which in effect protect highly exposed recipients at a lower rate, induce a violation of the proportional hazards condition that is often assumed in survival analysis.

Ragonnet and colleagues<sup>29</sup> applied a dynamic compartmental model to simulate vaccination for endemic infections studying several measures of effectiveness. They used mathematical derivations to calculate and compare the real and apparent impact of vaccination, and to assess the effect of a range of infection and vaccine characteristics on these measures. Their findings showed that vaccine impact was markedly underestimated in the following circumstances: when primary infection provided partial natural immunity, coverage was high, and postvaccination infectiousness was reduced. Leaky vaccines provided the same partial reduction of susceptibility to every vaccinated individual, whereas an all-or-nothing vaccine provided complete protection to a proportion of vaccinated individuals. All-or-nothing vaccines were more effective than leaky ones particularly in settings with high risk of reinfection and transmissibility. Accrued longer latent periods resulted in greater real impacts when risk of reinfection was high, but this effect diminished if partial natural immunity was assumed.

## MICROECONOMIC IMPACT OF VACCINATION

Jit and coworkers<sup>30</sup> analyzed the economic impact of vaccination. The authors noted that investment in immunization programs dramatically increased in developed and developing countries over the past two decades as a result of the development of new vaccines against major diseases,<sup>31</sup> and the emergence of new financing mechanisms. Organizations, such as Gavi, the vaccine alliance that subsidizes the cost of vaccines for some lesser developed countries, and the Pan American Health Organization, contributed to this economic feasibility and success of vaccination programs.<sup>32</sup> Spending growth heightened the importance of investing in immunization.<sup>33</sup>

Microeconomic evaluations can be used to facilitate decision-making by national and multinational stakeholders through comparisons of the economic cost of implementing vaccine program infrastructure, purchase, and delivery, against the health and economic benefits of vaccination. Economists have argued that improvements in health can lead to economic growth through longer term mechanisms, such as decreasing birth rates, strengthening macroeconomic stability, and improving educational outcomes.<sup>34,35</sup> Microeconomic theory has been applied to investments in immunization suggesting the separation of benefits into narrow and broad gains. Interest in particular in the former have included health gains; health care cost savings; reductions in the time costs of caring for the sick; and improved economic productivity because of prevention of mental and physical disabilities, improved child survival, the development of herd immunity, and prevention of antibiotic resistance. Bishai and coworkers<sup>36</sup> noted a significant reduction in the poverty-related gradient in younger than age 5 mortality by measles vaccination improving health equity directly. Using a cost-benefit analysis approach to assess the impact of Hib vaccination, Bärnighausen and colleagues<sup>37</sup> demonstrated that past economic evaluations had mostly adopted narrow evaluation perspectives, focusing primarily on health gains, health care cost savings, and reductions in the time costs of caring, while usually ignoring other important benefits including outcome-related productivity gains (improved economic productivity caused by prevention of mental and physical disabilities), behavior-related productivity gains (economic growth caused by declining birth rates because vaccination improves child survival), and community externalities (herd immunity and prevention of antibiotic resistance).

Although vaccination is most cost-effective in low-income groups and regions, the accrual of benefits of vaccination in the poorest countries may be difficult to ascertain, leading to exacerbation or narrowing of the indicators of equity. Using country-level rotavirus vaccination data from demographic and health surveys on within-country patterns of vaccine coverage and diarrhea mortality risk factors, Rheingans and colleagues<sup>38</sup> estimated distributional effects of rotavirus vaccination in 25 Gavi countries. The authors noted the greatest potential benefit of rotavirus vaccination in Gavi countries of the poorest quintiles, although existing rates of vaccination coverage were highly skewed toward the richest quintiles. Therefore, programs that added new vaccines to existing systems without mechanisms to ensure equity in uptake may actually exacerbate rather than reduce existing inequity. Simply adding new vaccines to existing systems could target investments to higher income children because of disparities in vaccination coverage. Maximizing health benefits for the poorest children, while ensuring the best value for money, may require increased attention to these distributional effects.

With an estimated 4% of global child deaths or approximately 300,000 deaths, attributed to rotavirus in 2010, and one-third occurring in India and Ethiopia, Verguet and colleagues<sup>39</sup> hypothesized that public financing of rotavirus vaccination in these

two countries could substantially decrease child mortality and rotavirus-related hospitalizations, prevent health-related impoverishment, and bring significant cost savings to households. Using extended cost-effectiveness analysis to evaluate a hypothetical publicly financed program for rotavirus vaccination in India and Ethiopia, the authors measured program impact along the averted dimensions of rotavirus deaths and household expenditures, financial risk protection afforded, and distributional consequences across the wealth strata of the country populations. Their analyses showed direct benefits of rotavirus vaccination in substantially decreasing rotavirus deaths mainly among the poorer, with reduced household expenditures across all income groups, and effective provision of financial risk protection that was concentrated among the poorest. The potential indirect benefits of vaccination of herd immunity would lead to increased program benefits among all income groups.

## SUMMARY

Vaccination is a domestic and global imperative not just to prevent certain microbial diseases but to eradicate them. Mass-vaccination campaigns have lowered the incidence of MMR in lesser developed countries to low levels but that may not be good enough because these diseases, like others, can bounce back. At least three big improvements underscore the argument for wider eradication and prevention campaigns, in a list of communicable diseases. The first is better techniques for locating and monitoring cases of disease globally. The second is improved medical technology that has produced superior drugs and vaccines. The third is a change in political attitudes that first sought to effectively deal with AIDS, and then Ebola, and by creating better medical infrastructures.

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