THE CHALLENGE OF VACCINATION HESITANCY AND ACCEPTANCE: AN OVERVIEW

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INTRODUCTION

Vaccination is one of the world's most important medical interventions. Generally safe, effective, and relatively inexpensive, vaccines save about three million lives every year and protect hundreds of millions of people against acute and chronic infections and their consequences (World Health Organization [WHO], 2017). While administering a vaccine is a fairly simple process, the enterprise of vaccination is complex. To invent, test, and produce a vaccine is difficult, and protecting a population of people against infectious diseases requires high levels of organization and participation.

Vaccination programs aim to protect individuals—often children—and to provide population-wide barriers of immunity that will shield vulnerable individuals for whom vaccination is not possible, recommended, or effective. Vaccine-preventable infectious diseases can be controlled without 100% vaccine coverage, but the rates must be high—generally in the 80–95% range, depending on the disease in question (Plotkin, Orenstein, & Offit, 2004)—to reliably protect against outbreaks. The WHO estimates that one in seven children around the world are unvaccinated or under-vaccinated, and that three lives are lost to vaccine-preventable diseases every minute (WHO, 2017).

Immunization programs face many overlapping, context-related logistical, economic, and sociocultural challenges that contribute to sub-optimal and uneven coverage. Health systems sometimes struggle to effectively engage caregivers and communities, leading to weak demand and acceptance of vaccination, inequities in coverage, and stagnating

or declining coverage rates (Strategic Advisory Group of Experts on Immunization, 2017). The root causes of suboptimal vaccination uptake are numerous; one analysis groups these challenges as the "5As": access, affordability, awareness, acceptance, and activation (Thomson, Robinson, & Vallée-Tourangeau, 2016). The salience of each obstacle to reaching vaccination goals depends on many interrelated factors. As in clinical medicine, proper diagnosis is key before initiating a treatment plan. If little affordable vaccine is available, or people are unaware of its availability or can't get to where it is being administered, a community's willingness to be vaccinated isn't necessarily relevant.

Vaccine supply and demand go hand in hand. Gaps in demand or acceptance—and gaps between caregiver intention to vaccinate and actual follow-up—contribute to stagnating or declining coverage rates. As new initiatives have expanded global access to vaccines, new challenges to their acceptance have arisen. Over the past 2 decades, parental doubts about the importance and safety of vaccines, and the growing politicization of the issue, have increasingly threatened efforts to eradicate or control vaccine-preventable disease (Gowda & Dempsey, 2013). In response, immunization programs and partners are amplifying efforts to build awareness of the value and acceptance of vaccines, even as they continue to expand and strengthen delivery and access to them.

It is important to note that vaccination hesitancy and skepticism are not the major causes of missed vaccinations on a global scale; a host of other factors come into play. In Pakistan, to cite one recent example, 35% of parents who did not vaccinate a child were simply unaware of the need to do so (Riaz et al., 2018). Nonetheless, the current global measles outbreak, characterized by a tripling of cases around the world in 2019, has focused renewed attention on the role of vaccination hesitancy and skepticism in the broader context of under-vaccination. Measles epidemics—from Congo to Ukraine, France to the United States—sickened hundreds of thousands of people, mostly children, and caused thousands of deaths and disabilities. In the United States, where measles had been declared eliminated in 2000 (defined as the absence of continuous disease transmission for more than 12 months), the Centers for Disease Control (CDC) reported more than 1,282 cases in 31 states in 2019, the highest number in 27 years (CDC, 2020b). Most of the local outbreaks were linked to cases imported from epidemic areas of the world into inadequately vaccinated U.S. communities.

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Measles is among the most contagious diseases, yet it can be prevented effectively with two doses of vaccine. As such, many experts see measles outbreaks as an indicator of inadequate primary health care (WHO, 2016), and symptomatic of gaps in national immunization programs. Though the current global measles epidemic has multiple causes (WHO, 2019b), this setback has focused the world's attention on vaccine hesitancy, leading the WHO (2019c) to declare it one of 10 major threats in 2019.

In this paper, we refer to "vaccination" rather than "vaccine" hesitancy, acceptance, and demand because these behaviors are not solely determined by vaccines or antigens, but by a host of influences. It would be unwise to suggest that the responsibility for vaccination rests completely with the caregiver or parent. Hesitancy is complex and determined by a range of factors that lie outside their control, including the quality of immunization services and the actions of government authorities and manufacturers that provide and administer them. In this context, the term "hesitancy" may divert attention from the fuller picture. Parental decision-making plays a role, but health services have the responsibility to provide equitable, accessible, high-quality, affordable, and appealing immunization services to their constituents. Hesitancy as a concept is here to stay in the vaccine world, but we insert a caveat to acknowledge the broader context.

VACCINATION HESITANCY

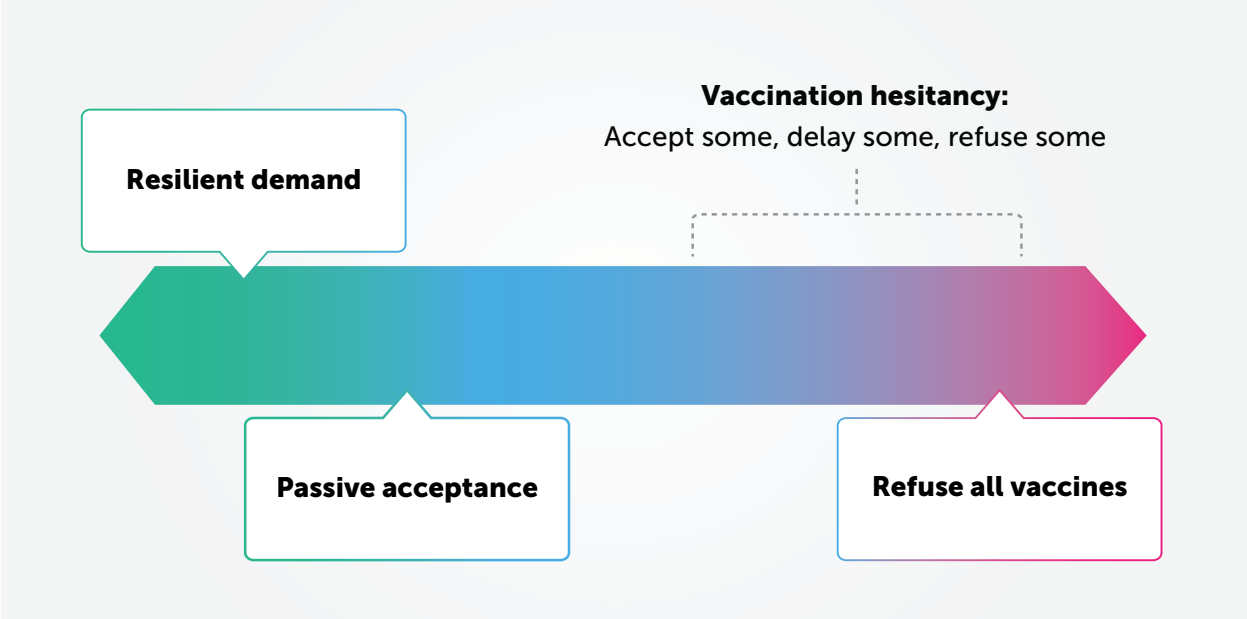
Trepidation about vaccines is as old as vaccination itself, as demonstrated by a letter that Massachusetts landowner Adam Winthrop wrote while struggling with the decision to have his grandson vaccinated during a smallpox epidemic in 1721. "I should have less distress in burying many children by the absolute acts of God's providence," Winthrop wrote, "than in being the means of burying one by my own act and deed" (Allen, 2007). The risk/benefit equation of vaccination, and the overall confidence in medicine's efficacy, have improved significantly since Winthrop's time, yet hesitancy remains in many guises.

A WHO expert panel has defined hesitancy as a "delay in acceptance or refusal of vaccines despite availability of vaccination services," in which "complacency, convenience and confidence" play a role (MacDonald & the SAGE Working Group on Vaccine Hesitancy, 2015). The extent of parental acceptance of vaccines lies on a continuum, with vaccination-hesitant parents (and other caregivers) falling along the middle range (Figure 1). Vaccination

hesitancy is by no means equivalent to vaccination rejection, which is generally confined to a very small percentage of parents who refuse all recommended vaccines. Vaccination hesitancy is complex and context-specific, varying across time, place, and vaccines (Opel et al., 2011). Vaccination-hesitant individuals are a heterogeneous group, and the roots of their hesitancy range from physical fear of vaccination to distrust of government, science, and the pharmaceutical industry. Some parents accept all vaccines but remain concerned; others may refuse or delay some vaccinations while accepting others. Some doubt vaccination in general but accept it in some specific instances (Leask et al., 2012).

Vaccination acceptance tends to be greatest in countries where the perception of risk from vaccine-preventable diseases is highest (Wellcome Global Monitor, 2019), although the phenomenon has not been rigorously examined in all regions of the world. A review of studies from the United States, Europe, Australia, and New Zealand characterizes 30–40% of parents as "unquestioning vaccine acceptors," with another 25–35% vaccinating their children despite minor concerns. An additional 20–30% also vaccinate but have significant concerns, typically based on safety allegations, such as those levied against the measles-mumps-rubella (MMR) vaccine. In this group, trust in the clinician is particularly key. Up to 27% of parents delay vaccination or accept only some recommended vaccines, while about 2% decline any vaccination—with higher percentages in given places and times (Leask et al., 2012).

Figure 1. The vaccination behavior continuum



Source: UNICEF and the WHO Regional Office for Africa's Regional Immunization Technical Advisory Group (RITAG), January 2019; Presentation.

The Three Cs

The 2014 report by the WHO's Strategic Advisory Group of Experts (SAGE) on vaccination hesitancy offers a framework for understanding hesitancy in terms of the "three Cs"—*convenience*, the logistical arrangements available to individuals, and their awareness of them; *complacency*, which is determined by the perception of vaccine-preventable diseases in a given setting; and *confidence* in the efficacy and safety of vaccines, the system that delivers them, and the motivation of policymakers who decide how and when to administer them (WHO, 2014).

Reluctance to accept vaccination because of fear or mistrust of the vaccine itself—or those who produce, recommend, administer, or order it—is not the only barrier to acceptance. Especially in resource-poor countries or populations, complacency and convenience play important roles. This suggests that those responsible for immunization campaigns should be sure to look for shortcomings in their own performance before assuming that a less-than-desired uptake is the fault of parents or those who prey on their doubts.

Convenience. In principle, convenience is a discrete problem of logistics that can be identified and dealt with in a relatively straightforward fashion (though it may be anything but easy). Yet the importance of the convenience factor is hard to understate, and it may overlap with, or compound, lack of confidence as an obstacle to vaccine uptake.

Research into hesitancy in the United States has shown clearly that inaction is easier than action when it comes to vaccination. For example, states that make it easier to obtain a philosophical or religious exemption for childhood vaccination than to get the child vaccinated (e.g., Colorado, Oregon) have higher rates of exemption—and vaccine-preventable diseases—than those in which the decision not to vaccinate requires additional effort (Omer et al., 2006). And when states, such as California, have made it more difficult to get exemptions, vaccination rates have increased (Pingali et al., 2019).

Not all missed vaccinations are due to fully conscious parental actions; technology also plays a role in convenience. Influences here include the degree of difficulty in getting a pediatrician to report a vaccination to a child's school; the availability of pharmacies as an alternative to a doctor's visit (Finnegan, 2012); more convenient vaccine delivery methods, such as micro-array patches that could obviate the need for children to get shots; and enhanced training of nurses to make inoculation less painful (UNICEF, 2018).

A recent study in Australia (Beard, Hull, Leask, Dey, & McIntyre, 2016) found that among the population of under-vaccinated children, 40% of the failures to vaccinate were due to an active decision on the part of the parents and 60% to simple inaction, which, in part, suggests a lack of convenience. The framework used by Gavi, the Vaccine Alliance to generate demand stresses that delivery of high-quality vaccine services is key to ensuring positive parent and child experiences in vaccination settings. It is also crucial that players in the vaccination enterprise improve community awareness and knowledge, creating and continually reinforcing positive social norms toward immunization and providing reminders and nudges through appropriate communications media. While community demand is fostered by governments, immunization program managers, clinicians, and local leadership and civil society organizations (Hickler, MacDonald, Senouci, Schuh, & the Informal Working Group of Vaccine Demand, 2017), convenience may make it easier for a parent who is inchoately hesitant about vaccination to carry through with it.

Complacency. Complacency is a complex issue. Like any medical procedure, vaccines require the consent and participation of the patient or, in the case of children, a parent or guardian. But unlike procedures used to treat an existing malady, vaccines are a tool of prevention whose purpose is not always obvious. This is especially so in countries where vaccination programs and campaigns have succeeded to the extent that the diseases they target have largely disappeared or no longer appear as significant threats. Even where they do occur, intensive-care medicine has lowered the death rate from common vaccine-preventable illnesses (Offit, 2015). Yet success against infectious disease is never permanent, as shown by the 2018-19 measles resurgence in the United States. When a community stops worrying about a disease threat, complacency can paradoxically cause it to resurface.

Confidence. The third "C"—confidence and its component parts—has attracted research interest in recent years. There is growing awareness in the public health sector of the need for more study of the attitudes that lie at the heart of an individual's trust or mistrust of vaccines. Medical authorities have traditionally viewed popular education and scientific understanding as key to the success of vaccines; one could also say that scientific understanding of people is just as important. Unfortunately, behavioral research has yet to yield a silver bullet in the form of a communications approach that always increases trust in science or in vaccines.

THE FOUNDATION OF MISTRUST

Attitudes toward health systems and vaccines "are wrapped in context," stated one of the authors of a recent Wellcome Global Monitor report (Wellcome Global Monitor, 2019), the world's largest study of how people around the world view science and major health challenges. If scientists don't understand the context, they aren't likely to bridge the gap in trust (Allen, 2019a). This fourth "C" of context includes the social norms around vaccination, which may stray under a variety of social, political, and cultural influences. To take a drastic example, health workers administering Ebola vaccines in the midst of the 2019 outbreak in Congo were attacked by crowds of villagers who simply didn't trust outsiders because they had repeatedly been brutalized by military and paramilitary forces.

The Wellcome report, released in June 2019, gathered views about science—and in particular, about vaccination—from some 145,000 people in 144 countries. As suggested by previous studies, the highest levels of vaccine mistrust exist in Europe and North America, where the mortality from vaccine-preventable diseases is lowest. The study found that 79% of the world's population "somewhat" or "strongly" agreed with the statement that vaccines are generally safe. That figure was 72% in North America, 59% in Western Europe, and only 50% in Eastern Europe, while 95% of South Asians and 88% of Central Americans agreed with the statement.

Confidence in vaccines, the Wellcome survey indicates, does not necessarily correlate with trust in all component parts of vaccination programs. Trust in government institutions was generally low where trust in vaccines was low. However, while vaccination programs generate lower levels of trust in developed countries, trust in doctors and nurses, and in

science in general, is higher. The reverse appears true as well. Confidence in science overall was lowest in Latin America, one of the regions with the highest confidence in vaccines. The survey appeared to validate the WHO's focus on doubts about vaccine safety, and the welter of data it produced suggested some causes. The authors note that France, the country with the highest percentage of people who disagreed with a statement that vaccines are generally safe (one in three), has faced a series of vaccine scares and allegations of pharmaceutical influence over national vaccine programs. These appear to play a key role in the relatively low social confidence in vaccination campaigns in that country (Warren, 2019).

Some of the foundations of mistrust in vaccines are intrinsic to human psychology, while others are contextual and depend on education levels, news media accounts, social norms, and social networks. In many cases, misinformation plays a role by creating scares or feeding into doubts that parents may already have developed. The global measles resurgence can be traced, in part, to a 1998 article in *The Lancet* by a British gastroenterologist, Andrew Wakefield, which suggested that measles vaccination caused childhood autism (Wakefield et al., 1998). The article was later retracted, and Wakefield's medical license revoked for fraud and malpractice (General Medical Council Preliminary Proceedings Committee, 2010), but the meme of a vaccine-autism link continues to circulate in social media. Another major factor undercutting vaccination is the perception in many communities that the diseases targeted by vaccines are no longer a threat to children's health. Fewer clinicians have seen the diseases, which undercuts their ability to give parents a vivid, convincing sense of the dangers those vaccines prevent. As vaccine-preventable diseases fade in perceived importance, possible vaccine harms loom larger (Jacobson, St. Sauver, & Finney Rutten, 2015).

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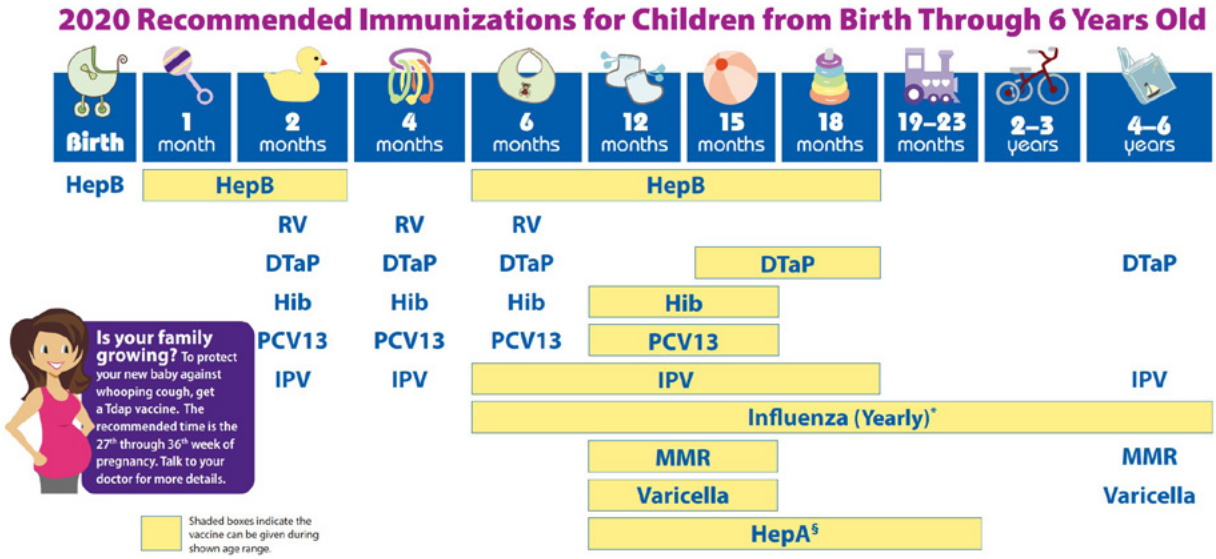
Parental hesitancy about vaccination has a large psychological component (Brewer, Chapman, Rothman, Leask, & Kempe, 2017). Research on risk assessment has shown that vaccination anxiety far exceeds the actual risks because it keys into uncertainty, dread, and the tendency to favor inaction over action in an ambiguous situation (Wroe, Bhan, Salkovskis, & Bedford, 2005). Ironically, the biomedical advances that have enabled the development, licensure, and widespread use of numerous vaccines has resulted in a vaccine schedule that alarms parents, who can intuitively be swayed by the argument that "too many vaccines, too soon" may "overwhelm" a child's immune system (Rodriguez, 2016).



Source: Centers for Disease Control and Prevention, February 2020.

Parents may have difficulty digesting the scientific response: that today's vaccine schedule exposes children to lower quantities of pathogenic particles than in the 1970s, and that a child's immune system is primed every day by exposure to organisms that dwarf the immunologic "challenge" of vaccines (Offit et al., 2002). Cognitive science has provided many explanations for why parents may prefer to go with a "gut" reaction over scientific evidence (Kolbert, 2017). Survey research indicates that parents with needle anxiety, conviction of moral purity, or openness to conspiracy theories are particularly likely to delay or shun vaccination for their children (Browne, 2018; Callaghan, Motta, Sylvester, Lunz Trujillo, & Blackburn, 2019). The Dunning-Kruger effect (over-regard for one's understanding of an issue) can also lock in a false understanding of the safety risks of vaccines (Kruger & Dunning, 1999).

In much of the world, vaccination hesitancy is associated with inequities arising from poverty, geographic remoteness, security problems, gender discrimination, and other barriers. Mothers are typically the primary caregivers of children, but their lower status in many communities limits their capacity to act on their own behalf and that of their children. In conflict settings, fear and mistrust of vaccines and the authorities who administer them intensifies with increased fear and suspicion of outsiders. Such tensions have perhaps been a factor in the 2019 measles outbreak in Congo, which caused some 2,000 deaths and 115,000 cases in the first 6 months of the year (WHO, 2019d). That was a more deadly result than the concurrent, and much more well-publicized, Ebola outbreak (WHO, 2019a).

Hesitancy, in general, is a potential threat to any vaccination program at any time, anywhere. Misinformation has been linked to increased vaccine refusals in Afghanistan, Indonesia, Malaysia, and Pakistan (Ahmed et al., 2018). Disinformation drove a boycott of polio vaccination in Nigeria (Kaufmann & Feldbaum, 2009) and a neonatal tetanus vaccination program in Kenya (Kenya Conference of Catholic Bishops, 2014). Media-fed and advocacy-led safety concerns caused human papilloma virus (HPV) vaccine coverage to collapse in Japan (Okuhara, Ishikawa, Okada, Kato, & Kiuchi, 2019), Denmark (Suppli et al., 2018), and Ireland; a similar panic triggered decreased vaccination rates in Colombia (Simas, Munoz, Arregoces, & Larson, 2018). The anti-vaccine movement is very small, but when parents are susceptible to fear, it can have great influence by providing false information that appears to confirm their worries.

Since 2010, vaccine-preventable disease outbreaks have been reported in marginalized, hard-to-reach populations in Europe, including anthroposophical communities in Germany and Switzerland; ultra-Orthodox Jewish groups in Belgium, Israel, and the United Kingdom; and Roma and Sinti populations in southeastern Europe. But outbreaks have not been exclusively the province of isolation, as there have also been more generalized outbreaks in France (2011), the United Kingdom (2014), Germany (2015), and Ukraine (2018–19).

THE STRUCTURE AND GROWTH OF VACCINATION PROGRAMS

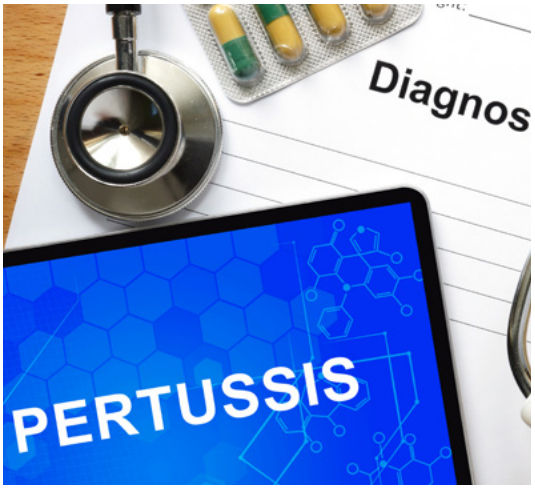
The formidable logistical challenges of vaccination include creating effective vaccines and testing them extensively for safety and efficacy in real-world settings; these requirements are particularly high for vaccines intended for healthy children. Once national or global agencies have accepted a vaccine as appropriate for a given population, batches must be successfully produced and transported from the manufacturer to individuals and communities in far-flung places. Vaccination programs require extensive planning and resources to address everything from cost to proper storage to the arrangements required to get vaccines and vaccinators to the places they are needed in a timely fashion. Any failure in these arrangements can affect the demand for vaccines and confidence in the enterprise.

Although cruder immunization techniques preceded him, Edward Jenner kicked off what we consider to be the era of vaccination in the late 18th century when he discovered that infection with cowpox, a virus carried by cattle, could protect people against smallpox (Baxby, 1999). Largely thanks to Jenner's vaccine, the deadly scourge of smallpox, which killed up to 500 million people in the 20th century alone, was declared eradicated globally in 1980 (WHO, 2020b). Vaccination against diphtheria, tetanus, and pertussis (DTP) became widespread starting in the 1950s in the United States and later in Europe; the successful trial of the inactivated polio vaccine in 1955 was a landmark in the reputation of vaccination, given its efficacy against a widely feared disease that paralyzed and killed people of all ages and classes (Baicus, 2012). Vaccines against measles, mumps, and then rubella were introduced in the 1960s in the United States, followed in the 1980s by vaccines against Haemophilus influenzae type B (HiB), and, in the 1990s, by hepatitis B, with hepatitis A, chickenpox, rotavirus, pneumococcus, influenza, and HPV following. The result is that children now generally receive multiple vaccinations against at least 14 diseases (Children's Hospital of Philadelphia, 2019).

Beginning in the 1970s, the addition of new antigens dramatically expanded the size and complexity of vaccine schedules. Some vaccines, such as DTP, are administered up to five times in the first four years of a child's life. In the United States, a child could theoretically receive nine vaccinations during a single physician's visit. In 1984, a child might have gotten three DTP shots, an MMR shot, and two sugar cubes with oral polio vaccine during her first two years of life; today, she might get 22 shots and three doses of oral rotavirus vaccine in that same period (CDC, 2020a). As vaccination programs expand, they increasingly attack childhood diseases that parents are less likely to view as life-threatening—such as mumps and chickenpox—or are unlikely to have heard of, such as rotavirus and pneumococcal disease.

Although the newer vaccines were introduced more slowly in routine schedules—and in Europe, some were not initially included at all—by 2019, most countries recommended routine vaccination against most of these diseases (Vaxopedia, 2017). In each case, the new vaccine was introduced after significant analyses demonstrated the health and health care burden of the targeted disease and the cost-effectiveness of introducing vaccination.

VACCINE SCARES AND THE ROLE OF ANTI-VACCINE MOVEMENTS



Aspects of vaccination that frequently alarm parents often originate in belief systems, or theories of harm, that the anti-vaccine movement has mined in ways that further aggravate such fears. Some of these tropes have existed since the 18th century; they tap into deep-seated ideas about purity, contamination, and conspiracy, and have a rich textual and visual history (Durbach, 2005). These include religious or spiritual beliefs asserting that vaccination contravenes divine will or sullies the body by introducing an unnatural or foreign substance; that drug companies, governments, and health care providers are indifferent to or conspiring to cover up harms from vaccines (Coulter, 1990); and that vaccination mandates abridge liberty or parental authority.

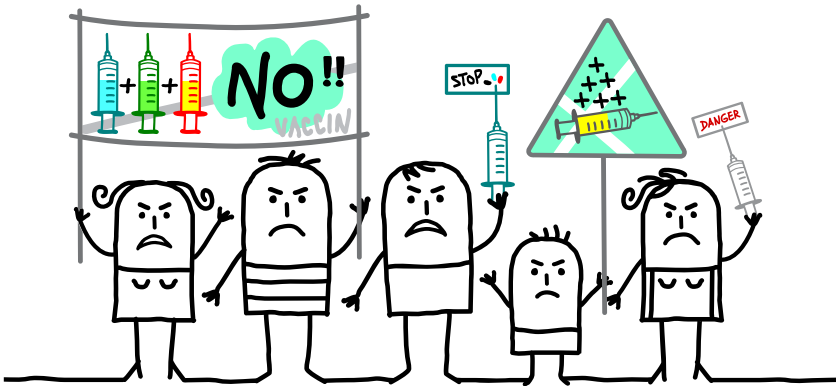
Whatever their ideological or philosophical bent, anti-vaccination materials inevitably come with claims that vaccines are hurting large numbers of healthy children and are often accompanied by personal stories of vaccine injury. Anti-vaccination activists "tell a good story," often about a healthy child who suffers a heartbreaking physical or mental reversal following vaccination (Brewer et al., 2017).

Compelling anti-vaccine messages in the media are not new (Rosner, 2012); indeed, they are nearly as old as vaccination itself. But current media structures have expanded and deepened the reach of troubling messages about vaccines and made them more vivid. Search engine and social media algorithms put anti-vaccine propaganda at virtually anyone's fingertips, and the internet is something of a hall of mirrors that confirms and expands fearful assumptions (Strandberg, Himmelroos, & Grönlund, 2017). The technology readily allows anti-vaccine activists to expand their movements by carefully targeting users with information in response to their previous browsing habits.

Contemporary Western anti-vaccine movements emerged in the 1970s in response to statements by scientists examining the toxicity of the whole-cell pertussis (whooping cough) vaccine, which produced frequent febrile seizures (Barlow et al., 2001). Although the vaccine had significantly reduced whooping cough, a study by Gordon Stewart claimed that "not less

than 1 in 50,000" pertussis shots resulted in permanent brain damage (Stewart, 1979). Large epidemiological studies eventually concluded that such events were much rarer (Institute of Medicine, 1991), but, to quote Jonathan Swift, "Falsehood flies, and truth comes limping after it, so that when men come to be undeceived, it is too late; the jest is over, and the tale hath had its effect."

Concerns about the safety of the DTP vaccine provoked a global scare, growing anti-vaccine activism, and dramatic declines in vaccination, perhaps most notably in Sweden and Japan (Baker, 2003), which suspended vaccination against whooping cough altogether. Use of the vaccine declined in England and Wales from 77% to 30% from 1974 to 1978 (CDC, 1982). In all three countries, whooping cough quickly returned as a routine childhood disease. Five thousand English children were hospitalized with it during a 1977–79 epidemic, and hundreds of children were hospitalized in Sweden each year until a new vaccine, lacking the reactivity of the previous one, was introduced in the mid-1990s. Nearly 20% of those hospitalized with pertussis suffered pneumonia or neurological damage (Romanus, Jonsell, & Bergquist, 1987).



The scare reached the United States in the form of a 1982 television "exposé" of the supposed dangers of the shot, accompanied by many lawsuits against the pharmaceutical industry by parents of disabled children. The resulting liability concerns led many vaccine makers to leave the market, threatening the supply of DTP and other essential vaccines (Hinman, 1984). Worried that manufacturers would withdraw from the vaccine business and threaten supplies, Congress created a no-fault administrative court in 1986 to consider allegations of vaccine harm and provide monetary awards on a case-by-case basis, shielding manufacturers from responsibility (Cook & Evans, 2011).

In the late 1990s, two new theories arose alleging that vaccines were responsible for a burgeoning incidence of childhood autism. Andrew Wakefield's 1998 *Lancet* paper was widely discussed in the news media, although it was quickly refuted, and an investigation found his work to be fraudulent and unethical. About the same time, federal officials and the American Academy of Pediatrics urged manufacturers to provide DTP, hepatitis B, and Haemophilus influenzae type B (Hib) vaccines in single-dose vials that did not contain the

mercury-containing preservative thimerosal (Halsey, 1999). The July 1999 recommendation reflected an abundance of caution in response to Environmental Protection Agency (EPA) data on potential neurodevelopmental impacts of mercury exposure. But few other countries followed suit, and repeated studies have not supported a link between autism and either the MMR vaccine or thimerosal (Baker, 2008).

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Yet the idea of neurological problems resulting from vaccination continues to circulate in corners of social media where allegations of government and scientific cover-ups prosper and has often become a political issue. Wakefield, environmental lawyer Robert F. Kennedy Jr., and others have traveled around the United States filing suits against states and manufacturers in a well-funded effort to encourage parents to shun vaccination (Kim, 2019).

The theory of an autism link to vaccines caught hold among parents worried about environmental contaminants and their impact on child development. The scare corresponded with a rapid increase in the diagnoses of autism and a community of parents seeking explanations for that. Although changes in diagnostic criteria and guidelines aimed at earlier recognition and interventions to treat autistic children were largely responsible for the growing incidence (Spence, Sharifi, & Wiznitzer, 2004), a secular increase has not been ruled out (Arvidsson, Gillberg, Lichtenstein, & Lundström, 2018). Older parenting, maternal viral infections, and exposure to environmental toxins are generally considered the most likely contributors to any true increase. Nonetheless, lacking clear answers, some parents concluded they should avoid "too many" vaccines "too soon" (Cooke & Lewandowsky, 2012).

While fears of cognitive damage dominate in the United States, other anxieties have aroused suspicion of vaccination campaigns elsewhere. In Kenya, a Catholic doctors' association has accused the government of putting an abortifacient chemical in tetanus vaccines (Kenya Conference of Catholic Bishops, 2014) and in some Muslim countries, allegations that polio vaccines are laced with HIV or birth control drugs have spread (Murakami et al., 2014). Vaccine scares seldom remain confined to the country in which they originate, although they don't spread uniformly. For example, the MMR vaccine scare found traction in the Somali immigrant community in Minnesota, while Japan's HPV scare spread to Denmark, Colombia, and Ireland (Larson, Wilson, Hanley, Parys, & Paterson, 2014).

SOCIAL MEDIA AND PUBLIC HEALTH RESPONSE

Vaccination programs rely on fragile networks of trust, especially when public confidence in the government and the pharmaceutical industry is weak. This means that public health officials may need to carefully consider whether some approaches to vaccine promotion could backfire by feeding public perceptions of an unholy alliance among manufacturers, public health, and doctors.

Politicians have, at times, openly instrumentalized disease and vaccine scares for political purposes. In 1976, Gerald Ford was worried about appearing weak during his presidential campaign when he pushed for swine flu vaccination of the entire country, long after it became evident that the virus was not nearly as serious as public health officials had originally feared. In Ukraine in 2009, Prime Minister Yulia Tymoshenko, then running for office, closed schools and banned mass gatherings in an overwrought response to the possibility of another swine flu epidemic (Hong, 2014). In these and similar instances, exaggerating the threat of a vaccine-preventable disease hurt confidence in the reliability of the government's advocacy for vaccination. Similarly, the political opposition in Indonesia (Rose, 2018) and India (Purnell, 2019) have spread false rumors about vaccines on social media in attempts to paint governments in a bad light.

Sometimes, the underlying concerns about vaccination are aggravated by governmental missteps. In 2013, the Japanese government suspended its recommendation for routine HPV vaccination after a series of alleged adverse events were reported in the Japanese news media. As in the thimerosal episode in the United States, an initial precautionary step appears to have increased fears of the vaccine despite subsequent and swift reassurances that the vaccine was safe (Larson et al., 2014). In the Philippines, deaths during a vaccination campaign against dengue fever, allegedly caused by cross-reactivity with existing dengue fever antibodies, undermined confidence in vaccination campaigns in general. In a country whose immunization system was already flawed, the dengue vaccine scare contributed to a plunge in acceptance of measles vaccination; significant outbreaks quickly followed (Seeman & Mukerjee, 2019), with 37,000 measles cases reported in 2019 alone (WHO, 2020a). In Pakistan, the revelation that the CIA had used a fake hepatitis B vaccination campaign in

2011 to locate Osama bin Laden caused militants to target vaccinators as suspected foreign spies (Gostin, 2014). This and other factors have contributed to low levels of trust in the polio vaccination campaign along the Afghan-Pakistan border, where scores of vaccinators have been killed (Hussain, Boyle, Patel, & Sullivan, 2016).

Fragile confidence in immunization campaigns puts public health officials in difficult positions as they consider how to communicate potential risks that surface during post-marketing monitoring of vaccination campaigns. Following the swine flu epidemic of 2009, critics accused European health officials of having suppressed or ignored evidence of an increased risk of narcolepsy in children who received the Pandemrix flu vaccine, which contained a new adjuvant designed to improve immune response (Doshi, 2018). Confidence was also undercut by claims that the WHO had exaggerated the threat of the H1N1 virus in order to boost the income of vaccine makers (Schnirring, 2010).

Mistaken policies can cause mistrust in the vaccine enterprise in less dramatic ways as well. When Merck attempted to accelerate the rollout of its new HPV vaccine in 2006 with an ad and lobbying campaign, it provoked criticism, not only from parents concerned about the supposed "moral hazard" of a vaccine against a sexually transmitted virus, but also from public health figures accustomed to more gentle introduction of pediatric vaccines for widespread use. Noting that HPV infections did not spread in schools, and complaining of the $300 cost for three doses, some officials saw the push as rushed and imprudent (Schwartz, Caplan, Faden, & Sugarman, 2007).

Vaccination campaigns may also generate resentment and opposition in the context of poor overall health care services. Repeated polio eradication campaigns in poor areas of India and Pakistan have sometimes encountered outrage because health systems in these areas aren't meeting basic needs (Alexander, Zubair, Khan, Abid, & Durry, 2014). Similar distrust may arise when vaccines against diseases that are not generally understood as life-threatening, such as rotavirus or chickenpox, are introduced in communities where people struggle with basic health care coverage.
One author has written that while "harmonizing vaccine schedules across countries in Europe might please politicians, it doesn't impress parents." Blaming vaccine hesitation on

anti-vaccine activists "obscures the possibility that resistance to vaccination may somehow reflect failings in the way vaccination programs work, or still more fundamental anxieties," such as a more diffuse sense of dissatisfaction and concern about "increasingly technological and dehumanized medical practice" (Blume, 2017).

HESITANCY IN A NEW MEDIA ENVIRONMENT

The anti-vaccine movement is still tiny, but in some places, aided by the amplifying power of the internet and social media, which makes tendentious, distorted, or incorrect information readily available, it has gained prominence out of proportion to its size. Still, it is important not to equate those who have doubts and questions about vaccines with vaccination's foes. A high degree of vaccination hesitancy does not automatically equate with low vaccine uptake if the logistical, legal, and cultural supports for vaccination are strong enough in a given country or setting.

That said, the media structures that inform popular understandings pose new challenges, though it is not clear that sources of bad information have become more influential than they were in the past. Until recently, when Google altered its search algorithm, anti-vaccine websites appeared prominently in routine searches about vaccines. The same was true of Facebook and Instagram before they began filtering anti-vaccine misinformation. Vaccine queries on Amazon still steer the searcher immediately to anti-vaccine literature. Social media are structured to intensely focus and channel information to affinity groups based on friendship, neighborhoods, and parental status, as well as on cultural (lifestyle) and political affiliations. Influential parties on social media often cherry-pick findings that fit preconceived notions and create spurious patterns of fact (Evrony & Caplan, 2017). The spread of tendentious information accelerates when opponents of vaccination use the anonymity of social media to multiply false or conflicting messages (Kata, 2012).

Although most anti-vaccine propaganda originates in groups with genuine anti-vaccine beliefs, researchers recently discovered that social media trolls affiliated with a Russian intelligence service had been spreading pointed commentaries about vaccines, with the apparent intent of sowing discord around an issue perceived to be divisive in the United States (Broniatowski et al., 2018). In public health and

medicine, fears of vaccination are countered with scientific evidence for vaccine safety. But since proponents of an anti-vaccine message also claim to use "evidence" to make their case, confidence in vaccines may be modulated through an individual's trust in the authority of the government, established medicine, and the prescription drug industry. Because cases of vaccine-preventable illness are hard to find in countries where the disease burden is low and parents of unvaccinated children who become ill may be reluctant to share their stories, it can be difficult to offer a counter-narrative to claims about children allegedly hurt by vaccines. As DiResta and Wardle (this volume) point out, science-based information on vaccines is seldom produced by people who are inclined to create "content that is engaging, dynamic, and is designed to touch people's emotions." But, clearly, there is an unmet need for stories to counter the alarm generated by foes of vaccination.

Clearly, there is an unmet need for stories to counter the alarm generated by foes of vaccination.

People tend to reject information that runs counter to their existing biases or the beliefs of their affinity groups (Bahns, Crandall, Gillath, & Preacher, 2017). Such confirmation bias is an increasing threat in an environment of intensifying political and cultural polarization. As sociologist Damon Centola has noted, just the knowledge that a social media post is from someone of a different political party is often enough to turn an individual off to its message (Guilbeault, Becker, & Centola, 2018). In the United States, vaccination advocates have grown concerned that political polarization could alter social norms around vaccination. The issue surfaced during the 2018–19 measles outbreak, which led 24 states to consider tightening vaccine exemption laws. In many of these states, legislators have taken sides along partisan lines, with Republican legislators arguing that new limits on vaccine exemptions would unjustifiably sacrifice parental rights (Allen, 2019b). While beliefs are polarized around the duties of parents to vaccinate their children, a high percentage of Americans of both parties distrust the drug industry (Politico & Harvard T.H. Chan School of Public Health, 2019), and there is no evidence they consider vaccine manufacturers differently (Reich, 2016).

The easy availability of medical information of widely varying quality has forced clinicians to reassess how they manage communications with parents (Neuberger, 2000). In many subcultures, there is an expectation that patients—or in this case, parents—will educate themselves before accepting medical recommendations. Medical paternalism is no longer routinely accepted. In the United States, the increased consolidation of medicine into large group practices, frequent changes in medical staff, administrative workload, and consequent

medical burnout are seen by many as having weakened the patient-doctor bond (Enke, 2018). The growth of customer ratings puts pressure on doctors to "please" their patients, and could, in principle, lead them to bend the vaccine schedule in response to parental doubts. It might also improve attentiveness to parental concerns and questions, but this is tempered by time pressures, which limit the ability of pediatricians to engage in lengthy conversations. Yet numerous studies have shown that a parent's relationship with their child's provider is key to instilling trust in vaccination (Larson, 2018).

WHAT WE KNOW AND DON'T KNOW, AND WHAT WE STILL NEED TO DO

In response to the 2014 SAGE report's call for better metrics on hesitancy, the WHO has sought information from member countries about vaccination concerns. Meanwhile, several groups have created survey tools to assess the nature and degree of hesitancy (Betsch et al., 2018), and a number of recommendations for reducing it have been advanced. More research is needed to understand the problem, because there is not yet strong evidence to recommend interventions that effectively address vaccination hesitancy in every situation and setting.

A continuum of approaches, ranging from entirely voluntary to gently coercive mandates, has shown different degrees of efficacy in increasing immunization rates.

Much of what we have learned so far about improving vaccine confidence centers on what *doesn't* work. The latter includes many strategies to change parents' thoughts and feelings about vaccines, and efforts to try to convince people to vaccinate their children if they have already decided against it (Thomson et al., 2016; Brewer et al., 2017). Studies of Europe's vaccination hesitancy landscape over the past decade found that confrontation and adversarial situations rarely change outcomes. Public health officials and governments have recognized that there is no single solution, given the relevance of local context. The efficacy of evidence-based practices or communication strategies for convincing vaccine-hesitant parents is not well-established, but it is essential to address the widely heterogeneous group. Mandates may be effective in raising vaccine uptake but can also bring a level of discord to public discussions. An in-depth 2018 Sabin Vaccine Institute study of recent legislation in Europe found that a continuum of approaches, ranging from entirely voluntary to gently coercive mandates, has shown different degrees of efficacy in increasing immunization rates. This study, too, concluded that no one approach could be appropriate for all settings (Sabin Vaccine Institute, 2018).

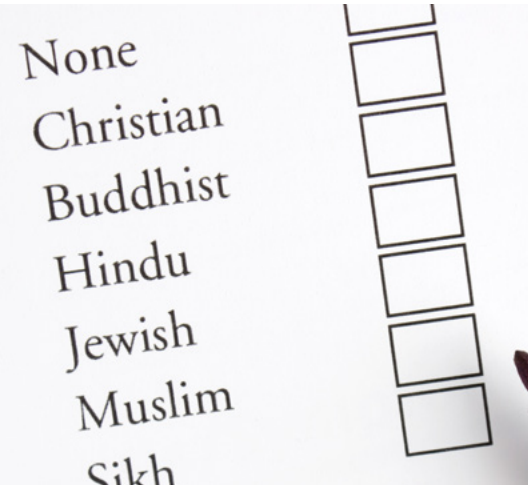
MANDATES AND INCENTIVES

In addition to efforts that build on favorable intent—such as reducing logistical barriers to vaccination and providing reminders, based on the presumption that parents intend to vaccinate their children—policymakers may consider shaping behavior through mandates, incentives, or sanctions. These range in severity from pay incentives to physicians to withholding public benefits or even jailing parents who refuse vaccination for their children. Mandates are a controversial area, one in which policymakers must be attuned to national traditions and attitudes on vaccination responsibilities. Studies generally show that requiring vaccination can improve vaccine uptake in high-income countries, but there is limited evidence of the impact in low- or middle-income countries (Omer, Betsch, & Leask, 2019). Compulsory vaccination programs have had varying degrees of success, and experts who have studied them recommend that policymakers pay careful attention to context and ethical concerns before creating or enforcing mandates.

The first efforts to require vaccination were harsh and created a major backlash. Beginning in 1853, Britain confiscated property and declined to make welfare payments to those who refused smallpox vaccination. The vaccines of the time frequently caused severe adverse reactions, and the laws inspired a nationwide protest movement that reviled mandatory vaccination as illiberal, iniquitous, and a violation of citizens' privacy (Durbach, 2005) until the law was lifted in 1907. In the United States, 19th-century German immigrants' disgust with their home country's harsh vaccination regime was so intense that they shunned the smallpox vaccine in their adopted country merely because the federal Public Health Service ordered it (Leavitt, 1996).

Mandatory vaccination has been an element of the U.S. public health system for more than a century, with increasing enforcement since the late 1960s. At that time, federal officials pursuing the elimination of measles nudged states to enforce school-age vaccination requirements, and by 1980, those laws were on the books in all 50 states (Hinman, Orenstein, & Papania, 2004). While officials frustrated by lagging vaccination in certain communities have on occasion called for federal mandates (Parmet, 2019), state laws, while not uniform, have fostered local control and cultural accommodation, coupled with competition among neighboring states to keep vaccination levels strong.

Most countries outside the United States do not mandate childhood vaccines as a condition of school entry, although Argentina, China, France, Italy, and several Eastern European countries are notable exceptions (Holzmann & Wiedermann, 2019). In Japan and most of Western Europe, governments offer recommended vaccines for free but do not require them; in many countries, the government funds required vaccines while private sources must be used to cover others. In the United Kingdom, the state incentivizes general practitioners who provide recommended vaccinations to a certain percentage of their patients. A trend toward tightening vaccine requirements or adding vaccines to required schedules has emerged in a few European countries and in Australia in recent years (Bozzola et al., 2018).



All U.S. states allow children with medical contraindications to avoid vaccination, but California, Maine, and New York recently joined Mississippi and West Virginia in banning all non-medical exemptions. Forty-five U.S. states permit religious exemptions to vaccination, and 15 allow philosophical (sometimes called "personal belief") exemptions (National Conference of State Legislators, 2020). Mandatory school-age vaccination laws are generally regarded as a success in the United States because high rates of vaccination have maintained herd immunity against most diseases, despite the controversies in some communities. Australia, Belgium, France, Italy, and other countries that have enforced mandates for some vaccines have also found evidence that this leads to higher uptake (Ricciardi, Boccia, & Siliquini, 2018). During the whooping cough vaccine scare of the 1970s and 1980s, and again during the autism controversy, U.S. public health officials could point to relatively stable vaccination levels among American children. In the United Kingdom, by contrast, plunging DTP vaccination uptake in 1974 caused a massive increase of infections and hospitalization; likewise, the autism scare of the early 2000s coincided with a decline in MMR vaccination, thousands of reported measles cases, and some deaths.

Mandatory vaccination regimens can cause unintended harm if they are associated with other unpopular policies. The former Soviet bloc countries had strong vaccination requirements and high uptake rates, but with the collapse of the Soviet Union, alternative theories and disinformation challenged relatively weak states and damaged their authority to implement the vaccination rigor that had been associated with the Communist past.

For years, Ukraine has had the lowest childhood vaccination rate in Europe, with frequent measles epidemics that also sparked outbreaks in other countries (McDonald et al., 2019). Because of an MMR scare, a measles vaccination campaign that targeted 7.5 million Ukrainians reached only 116,000. Romania, Serbia, and Poland have each seen large protests against compulsory vaccination laws (Miner, 2018). And in Germany, angry reactions to limited compulsory vaccination requirements actually increased resistance to vaccines that are recommended, but not required (Betsch & Böhm, 2015).

Some authors have argued that while compulsory vaccination may be effective, mandates will generally be accepted only if they are accompanied by strong immunization programs that guarantee reliable access to an adequate supply of safe and effective vaccines—as well as a compensation program for those who suffer post-vaccination injuries (MacDonald et al., 2018; Salmon et al., 2006).

However, few countries have such compensation programs in place (Attwell, Drislane, & Leask, 2019). Mandates are often inspired by the perception among politicians and the public that vaccine refusal by parents is the biggest barrier. But poverty, social exclusion, and access difficulties also depress rates; in many settings, that has a more significant impact than refusal. In Germany, for example, barriers to access probably explain why children of immigrant parents have a 10% lower immunization rate for booster doses (such as for tetanus or HPV) than children who were born there (Giambi et al., 2019).

As mandates went into effect in the 1970s in the United States, critics observed that they were an exception to the general trend away from paternalism in medicine in democratic countries (Larson, Cooper, Eskola, Katz, & Ratzan, 2011), since school-entry requirements in effect offer most parents little choice (Colgrove, 2006). The bioethicist LeRoy Walters argued in 1978 that mandates obliged the state to provide an easy-to-navigate system for people who believed their children were harmed by required vaccines (United States Congress, 1999). Eventually, such a system was established in the United States, but it was fundamentally designed to protect the vaccine industry from lawsuits. Some have argued that the most effective approach to mandating vaccination is to allow non-medical exemptions, but to make them hard to obtain (Salmon & Omer, 2006). Otherwise, such mandates may place unfair demands on individuals who have logistical difficulties accessing vaccination. Penalties for failure to comply are likely to worsen inequity by disproportionately affecting the poor, and in undemocratic countries, restrictive laws and regulations can easily be abused, they point out. Finally, creating more difficulties for exemption is likely to increase the anger and activism of those who refuse vaccination (Omer et al., 2019).

CONCLUSION

Experts at Gavi, the WHO, UNICEF, and elsewhere believe it is important not to make the countering of anti-vaccine messages the focus of immunization campaigns (WHO, 2018). Instead, doubts should be supplanted with confidence and appeals to the benefits of vaccination, with the idea of building a broad social movement that embraces it. Gavi calls for well-designed and well-executed interventions that engage and mobilize caregivers, communities, and others to increase coverage and equity and reduce dropout and missed opportunities to vaccinate, while building resilience against vaccine safety scares, rumors, and misinformation (Gavi, the Vaccine Alliance, 2020).

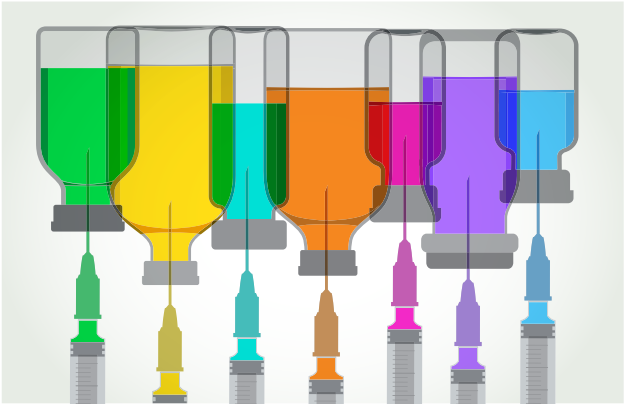
Global vaccine agencies and non-governmental organizations increasingly frame vaccination acceptance as "demand promotion." Demand promotion aims to ensure that all parents, caregivers, and other key partners value and trust immunization; have the necessary information, capacity, and motivation to seek out services; and actively pursue immunization for their children. The goal of demand promotion is to help build up vaccination as a positive social norm—one that embodies resilient and sustained demand across the life-course of individuals and throughout the community.

> Building a consensus about the soundness of vaccination campaigns is key to bolstering demand and support for vaccines.

Most people in any setting passively accept vaccination as a normative behavior. In general, this serves society well by maintaining high levels of vaccination. However, passive acceptance is vulnerable to vaccine safety fears, poor service quality, out-of-pocket expenses, misperceptions and myths, any of which can lead to hesitancy or outright refusal to vaccinate (Faulkner, Brown, & Quinn, 2018). A study on the impact of climate change denial showed that people who believe scientists disagree on global warming also feel less certain that it is occurring, and are less supportive of restorative climate policy. The authors argue that this indicates the potential importance of correcting misperceptions about the scientific consensus on global warming (Ding, Maibach, Zhao, Roser-Renouf, & Leiserowitz, 2011). The same might be said for vaccination; building a consensus about the soundness of vaccination campaigns is key to bolstering demand and support for vaccines. Creating resiliency in lower-income countries will hopefully prevent mistrust of vaccines from developing into the serious issue it has become in the United States or Europe.

Scholars who have recently examined the hesitancy issue agree that vaccination programs and providers need more evidence-based tools to efficiently convince vaccine-hesitant patients and parents. This clearly requires communication strategies that consider the context of science and vaccine literacy, social media, and other sources of popular information and influence. Recently, scholars at the London School of Hygiene & Tropical Medicine created the Vaccine Confidence Project, an effort to track vaccine confidence around the world and provide insights into the causes of hesitancy and effective social and behavioral science approaches to deal with them.

While few strategies have been evaluated, there is a growing consensus about the need to bolster awareness of the positive impact of vaccination. One new strategy is to add educational materials about vaccination to health programs for middle-school and older children. Since vaccine scares can derail immunization programs in ways that are costly to repair, interventions that promote demand and community resilience in favor of vaccination are key. Resilience, in the context of public health campaigns, might be defined as the degree to which a system or community expresses capacity for learning and adaptation, and the ability to bounce back in the face of turbulence. A resilient community is one in which demand for vaccination is an inherent part of the community; for this reason, UNICEF in 2018 created a Demand Hub to support collaborative efforts on immunization demand among immunization partners, donors, and countries, and to improve the support and technical assistance offered to countries to drive and maintain demand (UNICEF, 2018).



Gavi's partners have likewise designed a framework to generate demand. This includes enhancing service quality and accountability to ensure that parents and caregivers have a positive experience at a health facility; engaging communities to continually reinforce positive social norms toward immunization while providing reminders and nudges for vaccination; and managing risks and building resilience by having rapid response plans in place to counter scares, with ongoing media monitoring and social listening to stay on the qui vive. They also recommend that immunization programs

build political will from the grassroots level upward to make sure vaccination programs are prioritized and resourced. The framework includes a call for countries to develop strategies for understanding vulnerable populations and the barriers they face, and equipping health care providers with tools to communicate with parents about vaccines. In some communities, awareness of the right to be vaccinated may be key (Gavi, the Vaccine Alliance, 2020).

While research to identify optimal approaches remains critical, positive action to reinforce vaccination can't wait for perfect solutions. Recognizing that context is crucial to any action plan, public health officials, clinicians, and others dedicated to the benefits of vaccination need to deepen their outreach to affected groups as they continue to pursue new strategies for rebuilding confidence in vaccination.

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