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Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications

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Despite being recognized as one of the most successful public health measures, vaccination is perceived as unsafe and unnecessary by a growing number of parents. Anti-vaccination movements have been implicated in lowered vaccine acceptance rates and in the increase in vaccine-preventable disease outbreaks and epidemics. In this review, we will look at determinants of parental decision-making about vaccination and provide an overview of the history of anti-vaccination movements and its clinical impact.

KEYWORDS: anti-vaccination • parents • vaccination decisions • vaccine hesitancy • vaccine refusal**Background**

Immunization is widely considered to be one of the greatest achievements of public health. Immunization programs have contributed to the major decline in mortality and morbidity of selected infectious diseases, and are responsible for the worldwide eradication of smallpox and the elimination of poliomyelitis in the Americas [1–3]. To be successful in reducing the prevalence and incidence of vaccine-preventable diseases (VPD), immunization programs rely on high vaccine uptake [4,5]. Not only does this provide direct protection for vaccinated individuals, but high immunization coverage rates also induce indirect protection (herd immunity) for the overall community for VPD that are spread person to person [6].

The high rate of childhood vaccination coverage in most countries indicates that vaccination remains a widely accepted public health measure [7]. However, national estimates of vaccination coverage do not reflect variability within a country. Undervaccinated individuals tend to cluster together, leading to increased transmission of VPD [8]. Many studies have also shown that even parents who vaccinate their children can have doubts and fears about immunization [9–12]. Therefore, national estimates of vaccine coverage

rate are limited in their ability to reflect anti-vaccine sentiment [13].

In this review, we will illustrate how the interrelation between context, politics, science, public health and the media have played (and continue to play) a role in fuelling anti-vaccination sentiments. We will show that the anti-vaccine movement has been present since vaccines were developed, how some of the anti-vaccine negative arguments have not changed while others have evolved over time and why their arguments are very appealing to some parents. Before looking at the history of anti-vaccination movements and their clinical impact, we will briefly summarize the main determinants of parents' vaccination decisions.

Parental vaccination decisions

Many studies have shown that parental decisions to use or avoid immunization for their children are complex and multi-dimensional. Several recently published reviews have examined the factors associated with vaccination acceptance or refusal among parents [13–18]. While these reviews had different objectives and scopes, similar determinants of vaccination acceptance or refusal emerged including: contextual determinants (broad influences such as communication and media, religious values, social norms, health policies, etc.); organizational determinants (or

factors related to the accessibility and quality of vaccination services) and individual determinants (such as parents' knowledge, attitudes and beliefs or sociodemographic characteristics) (TABLE 1).

Studies examining parental vaccination decision-making have led to several proposed models of acceptance and resistance to vaccination [19–26]. These studies have also shown that vaccination acceptance behaviors appear to be on a continuum ranging from active demand for vaccines to complete refusal of all vaccines rather than as a dichotomous 'pro- versus anti-vaccination' perspectives. Between these extremes and along a continuum are vaccine-hesitant parents [22,27]. Vaccine-hesitant parents may refuse some vaccines, but agree to others; they may delay vaccines or accept them according to the recommended schedule, but feel unsure in doing so [22,28,29]. While only a very small proportion of parents are estimated to have strong anti-vaccination convictions and be outright refusers (less than 5% [30]), a larger proportion are vaccine hesitant (e.g., around one-third in the US studies [28,31]). There is a growing concern that immunization program uptake success may be losing momentum [12].

In high-income countries (HIC) with well-established immunization programs, it is often argued that vaccines are 'victims of their own success' with the decline in VPD resulting in parents having no direct experience with these illnesses anymore [32–34]. Thus, fear of risks of vaccine maybe be more prominent than fear of the diseases vaccines prevent. However, in low- and middle-income countries (LMIC), where VPD still pose a more imminent threat to health, this argument does not explain the decrease in acceptance of some or all vaccines in these settings [35–38].

Erosion of parents' trust in vaccines is also linked to the many controversies and scares that have been brought to the public attention by the media and kept alive by anti-vaccination activists [39,40]. These controversies have affected vaccine acceptance to varying degrees within and across countries. Some have occurred within a particular context; such as the purported association between the hepatitis B vaccine and multiple sclerosis in France that resulted in the suspension of the universal vaccination program in the 1990s, in spite of many studies finding no evidence of a causal association [41]. Some vaccination scares have transcended frontiers; the most well-known concerned autism and the purported link to measles mumps and rubella immunization. This later proved fraudulent, the claim was at first highly publicized in the UK by Andrew Wakefield, and then rapidly diffused worldwide [42]. Despite numerous scientific studies showing no link between measles–mumps–rubella (MMR) vaccination and autism [43–45] – and Wakefield being discredited as a researcher and losing the right to practice medicine in the UK [46]; fear of autism continues to be a frequently cited MMR vaccine safety concern among parents in different settings [47,48]. Many have suggested that the Internet, which permits a faster and larger diffusion of anti-vaccination content, has contributed to the increase of vaccine hesitancy and refusal among parents [12,49–51].

Anti-vaccination movements: from pamphlets to tweets

To understand modern-day anti-vaccination movements, it is necessary to look back briefly to the opposition to vaccination since its origin as a medical technique in the 1790s and then widespread use in the 1800s. FIGURE 1 presents an abridged timeline of major milestones in the history of vaccination.

Anti-vaccination in the past

Widespread vaccination began in the early 1800s after Jenner's demonstration that cowpox could protect against smallpox¹, a deadly disease that had plagued human populations for centuries [53]. Despite the dramatic consequences of smallpox (30% of cases ended in death, most survivors had some degree of permanent scarring and loss of lip, nose, ear tissue and in some blindness), many criticized the use of this vaccine [54,55], including the prominent co-discoverer of natural selection, Alfred Russel Wallace [56,57]. That an anti-vaccine cartoon would be published in the influential British weekly satire magazine *Punch* illustrates how widely the concerns had spread (FIGURE 2).

In the UK, in order to control smallpox, Vaccination Acts were passed between 1840 and 1853 to make the vaccination compulsory, with cumulative penalties for non-compliance [58]. These acts were met with immediate resistance from individuals who refused state control over their bodies and claimed these acts as an unacceptable invasion of personal liberty [59]. Anti-vaccination leagues, such as the Leicester Anti-Vaccination League [60], were formed and numerous anti-vaccination tracts, books and journals appeared in the 1870s and 1880s [53]. In the decades that followed, similar movements flourished across Europe [53,61].

In North America, at the end of the 19th century, smallpox outbreaks also led to intensive vaccine campaigns. Attempts to persuade adults and children into accepting vaccination resulted in vigorous opposition. Anti-vaccination activists fought public health authorities using pamphlets, court battles and instigating riots [53,62,63]. The 1902 smallpox epidemic led to a landmark legal case of *Jacobson v. Massachusetts*² in the

¹Noting the common observation that milkmaids were generally immune to smallpox, Jenner postulated that the pus in the blisters that milkmaids received from cowpox (a disease similar to smallpox, but much less virulent) protected them from smallpox. On 14 May 1796, Jenner tested his hypothesis by inoculating James Phipps, an 8-year-old boy who was the son of Jenner's gardener. He scraped pus from cowpox blisters on the hands of Sarah Nelmes, a milkmaid who had caught cowpox from a cow called Blossom. Jenner inoculated Phipps in both arms that day, subsequently producing in Phipps a fever and some uneasiness, but no full-blown infection. Later, he injected Phipps with variolous material, the routine method of immunization at that time. No disease followed. The boy was later challenged with variolous material and again showed no sign of infection [52].

²Henning Jacobson's arguments that the compulsory inoculation violated his right to care for his own body and health was rejected by the Massachusetts courts, including the Supreme Judicial Court. Jacobson was supported by the Massachusetts Anti-Compulsory Vaccination Association.

Table 1. Main determinants of parents' vaccination decisions.

Main determinants	Illustration from studies
Contextual determinants	
Historical, political and sociocultural influences • Past public health crisis (e.g., mad cow disease) • Politics and policies (e.g., mandates) • Religion (e.g., vaccination is against God's will) • Ethnicity (e.g., feeling of alienation because not in the majority group) • Gender (e.g., limited autonomy of women) • Social norms, social pressure • Social network • Unequal power relations and/or differences in culture between healthcare personnel and patients	Streefland <i>et al.</i> use the expression 'local vaccination cultures' to characterize how 'shared beliefs about disease etiology, ideas about the potency and efficacy of modern medicine and views on the need for preventive measures' as well as 'local health services experiences and vaccination settings' influence the individual decision about vaccination. These authors also have shown that 'people have their children vaccinated because everybody does so, and it seems the normal thing to do' [21] Authors of a retrospective qualitative study on the origin, development and impact of a rumor linking vaccines and sterilization in Cameroon concluded that 'the rumor and the dramatic events it caused emerged at the intersection of several contexts, involving public health services, the state, a local rhetoric of reproductive threat, and the increasingly strained position of women in a period of economic and political turmoil'. Vaccinated girls interviewed in this study described their experience as one of submission to authority: they assented vaccination because they feared not being admitted to exams or because the school gates were locked [87]
Communication and media environment • Promotion/communication about vaccination • Influential leaders/anti-vaccination and pro-vaccination lobbies • Rumors • Social media and Internet	A recent study conducted in the USA showed that parents who intentionally delayed vaccines for their child were significantly more likely to have heard or read negative information about vaccination when compared with parents who followed the recommended childhood vaccination schedule [191] Brunson studied the impact of social networks on parent's vaccination decisions in the USA. Findings from her study has illustrated that parents who did not conform to the recommended vaccination schedule had a significantly greater number of network members than parents who conformed. In addition, the variable most predictive of parents' vaccination decisions was the percent of parents' people networks recommending non-conformity [192]. Many studies have shown that individuals who delayed or refused vaccines are significantly more likely to have looked for vaccine information on the Internet [193,194]. For instance, a recent study has shown that parents who used the Internet to get vaccination information were significantly less likely to consider healthcare providers and health authorities as trusted sources of vaccination information [195]
Individual determinants	
Sociodemographic characteristics • Education level • Socioeconomic status • Maternal age • Family composition (family size, birth order, lone-parent/blended family, living with extended family members) • Recent/seasonal migrants	A recent study conducted in the USA showed that parents who intentionally delayed vaccines for their child were significantly more likely to live in a high-income household (e.g., household with an annual income 400% superior of the US federal poverty level) [194]. Whereas many studies, mostly from LMIC, found that parents' higher education level was positively associated with vaccination acceptance, other studies, mostly from HIC, identified an association between parents' higher education level and anti-vaccination attitudes [196] Results of a large survey conducted in the USA has shown that, although most of the 1552 parents who responded agreed that vaccines protect their child from diseases, more than half were concerned that vaccines could cause serious adverse effects and a quarter, that vaccines could cause autism [48]
Knowledge and attitudes • Knowledge and awareness about immunization (who, when, where) • Perceptions of the safety of vaccines (fear of adverse events) • Perceptions of the efficacy of vaccines • Perceptions of the risk of VPD (perceived risk of VPD – susceptibility to VPD severity of VPD) • Beliefs about immunity (preference for 'natural' immunity; 'too many, too soon' and immune system overload; perceived contradiction to vaccinate the child) • Health priorities/perceptions of the importance of vaccination for child's health/general attitudes about health and prevention (e.g., preference for 'natural health') • Anticipated regret (e.g., anticipating feeling of guilt if the child contracts a VPD or suffers from an adverse event)	Two studies, one ethnographic and one based on a questionnaire, have identified a 'lay theory of immunity'. This theory is based on a view of the immune system as an individual characteristic needing individualized healthcare and on the idea that there is a possible risk of immune overload due to individual 'weakness' of a child [131,197]. Qualitative studies have shown that parents who refuse to vaccinate their child often share a particular worldview regarding health (e.g., a preference for natural immunity, the belief that VPD are needed to build a strong immune system, the idea that it is possible to control exposure to disease or the belief that good hygiene and personal habits can make vaccination unnecessary) [130,198]

LMIC: Low- and middle-income countries; VPD: Vaccine-preventable diseases.

Table 1. Main determinants of parents' vaccination decisions (cont.).

Main determinants	Illustration from studies
Individual determinants	
Past experiences with health and vaccination services • Past encounters with healthcare providers (e.g., unpleasant experiences at health services) • Fear of needles/child's pain after immunization • Negative events after past vaccination of the child (real or perceived)	Authors of an ethnographic study conducted in Nouna (Burkina Faso) concluded that: 'when a mother is harshly criticized (by vaccination officer) in front of other mothers for failure to keep her (vaccination) booklet in good condition, this can create a genuine aversion to the whole vaccination process' [199] A recent US study showed that the vaccine concern listed most often by parents was a child's pain from the shots [200]
Trust in health system and healthcare providers • Recommendations from healthcare providers • Communication with healthcare providers • Perceived conflicted interest of healthcare providers and public health authorities (e.g., financial rewards to meet target, etc.) • Distrust of the medical community • Distrust of the pharmaceutical industry	A recent US study has shown that how healthcare providers initiate discussion about vaccination with parents has an influence on parents' acceptance. Fewer parents opposed the initial providers recommendations when a presumptive tone was used (we will do the shots) rather than a participatory tone (what do you want to do about the shots). Also, when providers pursue their original vaccine recommendations in the face of parental resistance, many parents subsequently agree to vaccination [186] Authors of a study conduct in The Netherlands concluded that trust in the objectivity of the doctor was highly influential on parents' decisions. Some parents believed that doctors only inform them about the advantages of vaccination and not about possible side effects. Parents were also doubtful about whether doctors themselves were knowledgeable about vaccines' side effect [201]
Organizational determinants	
Availability and quality of vaccination services • Distance/geographic barriers • Costs (direct and indirect) • Reliability of vaccine supply (e.g., stock outs, cold chain) • Convenience of vaccination services delivery (e.g., waiting time, limited days/hours, time pressure) • Missed opportunities (e.g., false contraindications)/integration of vaccination with other health care services • Incentives • Mode of delivery (e.g., routine program vs campaigns)	Results from a review of studies conducted in 51 LMIC including India, Pakistan, Turkey, Bangladesh, Brazil, Nigeria, Burkina Faso, Uganda, China, Columbia, Cambodia, Kenya and South Africa have indicated that lack of access to vaccination services was the most frequent reason for underimmunization in children [17] Across five cohort studies (n = 2293), perceived contraindications on the appointment day were cited as a reason for not vaccinating by 34% of vaccine decliners [14]. The frequency of polio vaccination campaigns has been linked to vaccine refusal in different studies [202,203]
Health staff motivation and attitudes • Trained and competent health staff • Ability to communicate with parents (e.g., language barrier, social connection, accurate and sensitive delivery of information to parents)	Findings of a review on determinants of nurses' practices regarding influenza vaccination indicate a relationship between knowledge, attitudes and vaccination practices. In the 12 research studies included in this review, higher knowledge and positive attitudes toward influenza vaccination were positively associated with vaccination coverage among nurses and there was also an association between nurses' vaccination status and their reported promotion of vaccination to their patients [204] Results of an ethnographic study conducted in Nigeria showed that health officials attributed vaccine refusal to the lack of training of health team members as well as some negative attitudes. Health officials reported cases of health staff that refused to follow local practices, such as veiling, which would have increased their local acceptability, whereas some were opposed to polio immunization program but 'needed a job' [205]
Vaccines-specific issues • Vaccination schedule (multiple injections in a single visit, combination vaccine) • Introduction of a new vaccine or formulation • Mode of administration (nasal, injection, oral) • Mode of delivery (vaccination campaigns vs routine programs)	Results of an Internet-based survey of a nationally-representative sample of US parents of young children have shown that more than 1 out of 10 parents was following an alternative vaccination schedule. More worrying were results about opinions of parents who were following the regular schedule: one out of five agreed that delaying vaccine doses was safer than following the recommended schedule and nearly one out of four of these parents disagreed that the best vaccination schedule to follow was the one recommended by vaccination experts [206]. The authors of an Indian study noted a difference of 16 percentage points in children who had received the three doses of oral polio vaccine (45%) when compared with the children who had received the three doses of DPT (29%). The authors have concluded that the emphasis on the polio program has detracted parents from routine immunization, rather than increasing it [207]

LMIC: Low- and middle-income countries; VPD: Vaccine-preventable diseases.

USA, ruling that the state could pass laws requiring vaccination in order to protect the public against communicable diseases [64].

The golden age of vaccination acceptance

Then, in the first decades of the 20th century, the anti-vaccination movements slowly declined but not before the

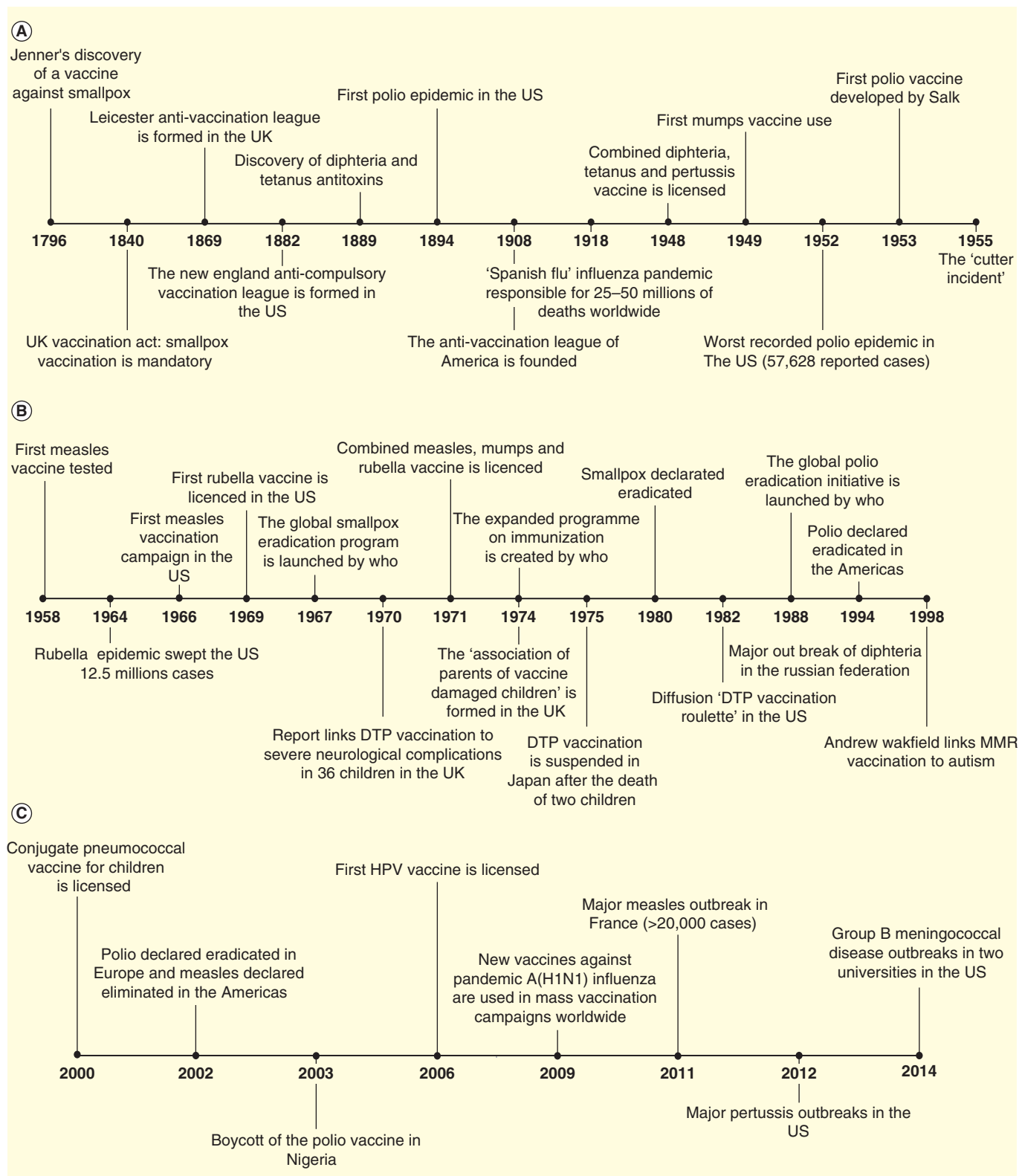


Figure 1. Abridged timeline of vaccination history. (A) 1796–1955, (B) 1958–1998 and (C) 2000–2014[†]. Most dates of vaccine licensure/discovery are based from the USA. Data taken from [62].



Figure 2. Anti-vaccine cartoon, *The Punch*.

In this cartoon published in 1802, the British satirist James Gillray caricatured a scene at the Smallpox and Inoculation Hospital at St. Pancras, showing cowpox vaccine being administered to frightened young women, and cows emerging from different parts of peoples' bodies. Opponents of vaccination had depicted cases of vaccinees developing bovine features and this is picked up and exaggerated by Gillray.

Reproduced with permission from [190].

anti-vaccination activists in the UK had successfully secured a conscience clause (British Vaccination Act of 1898 [58]) that effectively dismantled the compulsory vaccination laws [59]. In the USA, after the mid-1920s, court challenges to compulsory laws became rare [59]. In HIC, the 1950s and 1960s were the 'golden age of vaccination acceptance' with the introduction of new universal vaccination programs against poliomyelitis, measles, mumps and rubella [61]. Although opposition to vaccination still existed [65], parents widely accepted and used vaccines resulting in major decreases in vaccine preventable disease outbreaks, illnesses and deaths [61]. Even the major polio vaccine manufacturing problem, the Cutter Incident, where incomplete killing of polio virus leading to live polio virus in the killed vaccine, resulted in 5 child deaths and 51 children being permanently paralyzed due to polio [66], did not significantly impact on overall parental acceptance of killed polio vaccine for their children.

The 1970s saw the beginning of the push for large vaccination programs to control infectious diseases in LMIC. The Expanded Programme on Immunization was initiated by WHO in May 1974 with the objective to vaccinate all children throughout the world against six killer diseases: polio, diphtheria, tuberculosis, pertussis, measles and tetanus. At this time, less than 5% of the world's children were immunized against these diseases during their first year of life [67]. Following this initiative, vaccine coverage of the third dose of diphtheria, tetanus and polio (DTP) vaccine increased globally from 20% in 1980 to 75% coverage by 1990 [68].

However, this period of relatively wide and enthusiastic acceptance of infant and childhood vaccines did not last.

The resurgence of anti-vaccination movements

The pertussis vaccine controversy that started in the mid-1970s is often considered the match that lit the resurgence fire of active anti-vaccination opposition in modern days [69,70]. The controversy started in the UK after the publication of a report from the Great Ormond Street Hospital for Sick Children in London, alleging that 36 children suffered serious neurological conditions following DTP immunization [71]. This report garnered much media attention and triggered waves of public concerns [72]. The Association of Parents of Vaccine Damaged Children was founded in the UK in 1974 and played a key role in drawing attention to this purported safety problem with the whole-cell pertussis vaccine [73]. By 1977, child coverage in the UK had declined from 77 to 33%. Three major epidemics of pertussis followed soon thereafter with over 100,000 cases and the deaths of at least 36 children [69]. Despite reassurance about the vaccine's safety by the UK Joint Commission on Vaccination and Immunization that was based on a large study that had looked at every child hospitalized in the UK with neurological diseases [74], great opposition to the vaccine continued. Attempts to reassure the public continued but by the mid-1980s the controversy had swept through most Europe and Japan, the USA, the Soviet Union and Australia [75]. In 1975 in Japan, after the death of two children who had just received DPT vaccine, the Ministry of Health and Welfare suspended the use of the whole-cell pertussis vaccine for infants. This was followed by major outbreaks of pertussis [76,77]. This angst about the safety of whole-cell pertussis vaccine spurred on the development of less reactogenic acellular pertussis vaccines [78–80].

In the USA, the anti-vaccine controversy began with the Emmy winning 1982 documentary entitled '*DTP: Vaccination Roulette*' that alleged the pertussis component was causing severe brain damage, seizures and mental retardation. As in the UK, concerned and angry parents formed victim advocacy groups, such as the National Vaccine Information Center, which is still active today [81]. Several lawsuits against vaccine manufacturers were instigated, resulting in increased vaccine prices and a drop in the number of companies producing vaccines [70]. In response, the US Congress, in 1988, passed the National Childhood Vaccine Injury bill to protect manufacturers from lawsuits by establishing and maintaining an accessible and efficient no-fault alternative program to the traditional tort system for individuals found to be injured by certain vaccines. The Vaccine Adverse Event Report System, a passive surveillance system where suspected side effects of vaccines could be reported by parents and health professionals, was also created by this Act [82].

Nearly 25 years after the DTP controversy, the UK was again the site of another major public crisis in vaccine confidence, this time ignited by a purported link between MMR vaccination and autism noted above (Box 1). Measles immunization rates in children plummeted from over 90% in 1997 to less than 80% in 2004 [83]. As with the previous pertussis vaccine scare with its associated drop in immunization rates, the

MMR scare with dropped rates was followed by measles outbreaks and deaths [84].

While vaccination initiatives have generally been welcomed in LMIC, these settings were not immune to vaccine scares. In parts of Asia and Africa, over the past 20 years, several different vaccination controversies have led to decreased vaccination rates and even failure of an immunization program [85,86]. For example, in Cameroon in 1990, rumors and fears that public health officials were administering a range of childhood vaccines to sterilize women thwarted the country's immunization efforts [87]. Similarly, in the Philippines in the 1990s, the Catholic Church raised concerns about tetanus immunizations, sparking sterilization rumors and halting the campaign [88]. One of the most striking examples was the boycott of the polio vaccine in northern Nigeria in 2003 (Box 2). An underlying feature in all of these events was the asymmetrical power relationship between the target groups to be vaccinated and those responsible for the implementation of the campaigns that led in these instances to the attribution of undisclosed negative motives to these vaccination campaigns by local leaders in these communities. Indeed, in LMIC, as argued by Taylor, resistance to vaccination could be seen as a way for economically and politically deprived communities to express their discontent [37].

Anti-vaccination in the digital era

The popularization of the Internet at the beginning of the 2000s has offered an unprecedented opportunity for anti-vaccination activists to diffuse their messages to a much wider audience and recruit new members [89,90]. For instance, individuals who are opposed to vaccination are very active in news forums, resulting in a minority of users generating a disproportionate amount of anti-vaccination content [91]. In addition, issues about the safety and efficacy of some vaccines have been raised in scientific studies [92,93]. By enabling people to easily share links to scientific abstracts and articles, the Internet allows the diffusion of studies' findings outside of the scientific community, often using punchy titles and without presenting the details of the scientific information³ or the context. In fact, studies examining vaccination-related content on websites or social media platforms have shown that the quality of

³The authors' conclusions were that: 'Prior receipt of 2008–09 TIV was associated with increased risk of medically attended pH1N1 illness during the spring–summer 2009 in Canada. The occurrence of bias (selection, information) or confounding cannot be ruled out. Further experimental and epidemiological assessment is warranted. Possible biological mechanisms and immunoepidemiologic implications are considered' [94]. In an anti-vaccination website, the study was used in support allegations that vaccination against a disease will increase the risk to contract other diseases: 'Why Getting a Vaccine for One Disease Could Make You More Likely to Catch Another. Remember that ALL vaccines are immune suppressing, meaning they lower your immune functions. The chemicals and adjuvants in the vaccines depress your immune system; the viruses present depress immune function, and the foreign DNA/RNA from animal tissues depresses immunity – that is the trade-off you are risking' [95].

Box 1. Andrew Wakefield and the MMR vaccine.

Andrew Wakefield is a former British surgeon who first attracted attention when he published a paper proposing a link between the measles virus and Crohn's disease in 1993 [208] and 2 years later, in the prestigious medical journal *The Lancet*, between the measles vaccines and Crohn's disease [209]. Subsequent researches failed to confirm these two hypotheses [210]. While he was still conducting researches on Crohn's disease, Wakefield was approached by the parent of an autistic child who was seeking help with for bowel problems. Wakefield turned his attention to researching possible connections between the MMR vaccine and autism [211]. In 1998, Wakefield published with 12 other colleagues a paper about 12 autistic children in *The Lancet* [212] (Retracted). In this paper, the author claimed that they add 'identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers' [212] (Retracted).

At the time of his MMR research study, Wakefield was senior lecturer and honorary consultant in experimental gastroenterology at the Royal Free Hospital School of Medicine. Although the paper said that no causal connection had been proven, before it was published, Wakefield made statements at a press conference and in a video news release issued by the hospital, calling for suspension of the triple MMR vaccine until more research could be done [213,214]. This was immediately controversial, leading to widespread publicity and a drop in vaccination rates in the UK. That was the beginning of the MMR vaccination scare that swept throughout the world [215].

Following Wakefield's claim, multiple epidemiological studies were undertaken; all found no link between MMR vaccination and autism [45,216–219].

In February 2004, after a 4-month investigation, reporter Brian Deer wrote in *The Sunday Times* of London that, prior to submitting his paper to *The Lancet*, Wakefield had received £55,000 from legal firms seeking evidence to use against vaccine manufacturers, that several of the parents quoted as saying that MMR had damaged their children were also litigants and that Wakefield did not inform colleagues or medical authorities of the conflict of interest [220].

In March 2004, immediately following the news of the conflict of interest allegations, 10 of Wakefield's 12 co-authors retracted [221].

In 2007, Wakefield and two of his co-authors were charged by the General Medical Council (GMC), which is responsible for licensing doctors and supervising medical ethics in the UK, of serious professional misconduct. On 28 January 2010, the GMC panel delivered its decision on the facts of the case: Wakefield was found to have acted 'dishonestly and irresponsibly' and to have acted with 'callous disregard' for the children involved in his study, conducting unnecessary and invasive tests [222]. Wakefield lost the right to practice medicine in the UK. Soon afterward, *The Lancet* took the very uncommon step of retroactively retracting his article [223].

Box 2. The Boycott of polio vaccination.

In 1988, WHO had embarked on the Global Polio Eradication Initiative with the goal of eradicating the disease by the year 2000 [224]. In 1996, the 'Kick Polio Out of Africa' was launched by Nelson Mandela with the goal to vaccinate 50 millions of children in this same year [225]. The initiative was highly successful, with a drop from 350,000 polio cases worldwide in 1988 to less than 500 in 2001 [86]. However, in 2003, political and religious leaders of five states in Northern Nigeria brought the immunization campaign to a halt by calling on parents not to allow their children to be immunized due to fears that the vaccine was a Western plot to spread infertility and HIV among Muslims [226]. While the boycott was short-lived in most states, the state of Kano maintained the ban for 11 months [225], leading to a resurgence of polio in Nigeria that then spread to at least 15 countries that had been previously polio-free [86]. While negative rumors about polio vaccine had circulated for years before the boycott, several historical, cultural, political and contextual factors triggered this crisis: past attempts to regulate population and fertility, history of unethical testing of drugs by pharmaceutical companies in the region, distrust of southern-led central government and the West and the re-election of a southern President over the northern Muslim candidate [86,202,225,227].

information was highly variable, with a substantial amount of inaccurate information [49,96–100].

As the Internet has become an important health information source for the public, this problem of accuracy and a bigger platform and voice for anti-vaccine comments is of growing concern [101–104]. In 2012, it was estimated that 2.4 billion people accessed the Internet. This is an explosive 566% increase in access from 2000 [105]. Furthermore, the 'digital divide' between HIC and LIC is also shrinking [106]. Even more worrisome is the growing trend to seek health information from user-generated sites (Web 2.0), such as online news groups and blogs rather than more traditional evidence-based vaccine information sites [100,107–109]. The Internet is also cited as one of the main sources of information on immunization for parents in studies conducted in different countries [44,110]. Immunization experts are concerned that, as the vaccination debate on the Internet intensifies, 'many parents may shift from vaccine hesitancy to vaccine resistance, and from vaccine resistance to outright opposition' [111].

The information available about parents' use of online vaccination information and its influence on their decision regarding childhood immunization is still limited [112–114]. The few studies in this area have been experiments based on fictitious websites and/or hypothetical vaccines [50,115,116]. Results of these experiments have demonstrated that viewing anti-vaccination websites and reading personal stories about negative consequences of immunization increased users' risk perceptions about immunization [50,115,116]. For instance, Betsch *et al.* showed that viewing an anti-vaccination website increased negative beliefs about immunization, whereas

viewing a provaccination website had a minimal effect on beliefs. Five months after the study, vaccine coverage rates of children in the experimental group (anti-vaccination website) were significantly lower than those of children in the control group (provaccination website) [50].

To summarize, despite changes in time periods, safer and more effective vaccines, as well as enhanced surveillance of adverse events following vaccination, vaccine opposition is still deeply rooted as it was two centuries ago. Some of the arguments used by the anti-vaccination activists in the 1800s are still used today: vaccines are ineffective or cause diseases; vaccines are used to make profit; vaccines contain dangerous substances; harms caused by vaccines are hidden by the authorities; vaccination mandates violate civil rights; natural immunity is better than immunity induced by vaccines or natural approaches to health and alternative products (e.g., homeopathy, vitamins) are superior to vaccines to prevent diseases [53].

However, there are distinct differences between anti-vaccine promoters then and now. Whereas in the past anti-vaccination activists were mostly proletarians who were opposed to the state intervention in their bodies and their children's bodies [59,117], anti-vaccination groups in today's world, at least in HIC, are mostly well-educated middle- and upper-income parents who claim the right to make an 'informed decision' about vaccination [81]. Many contemporary anti-vaccination groups were also formed by parents who believed that their child has been seriously harmed by vaccine in order to seek compensation from the industry or the government. Other anti-vaccination groups are lead by alternative practitioners who are opposed to biomedicine and who sell 'natural solutions' to replace vaccination [118]. The Internet also provides a bigger platform and louder voice than was possible a 100 years ago and it offers the potential to reach and influence many more parents. Another difference is the 'marketing strategy' of anti-vaccination groups. In the past, opponents of vaccination were referring to themselves as 'anti-vaccine'. However, in today's world, these marketing savvy groups try to distance themselves from this label by claiming that they are not anti-vaccine, but pro 'safe' vaccine or pro 'informed-decision' about vaccines [119]. Indeed, contrary to the anti-vaccination leagues of the 1800s, most contemporary anti-vaccination groups use neutral names such as 'Vaccination News', the 'National Vaccine Information Center' or the 'Australian Vaccination Network' [120,121], thus appearing as vaccine information websites not anti-vaccine political websites (Box 3).

Influences of anti-vaccination movements on parental vaccination decisions

First, it is important to note that, despite trying to mimic the science, the anti-vaccination movements rely mostly on rhetorical arguments [122,123]. In many ways, anti-vaccinationism can be seen as part of a larger phenomenon of 'denialism' or 'the employment of rhetorical arguments to give the appearance of legitimate debate where there is none, an approach that has the ultimate goal of rejecting a proposition on which a scientific

consensus exists' [124]. Whether it is to deny evolution, climate change or the fact that vaccines do not cause autism, Diethelm and McKee have shown that denialists employ similar tactics such as relying on 'conspiracy theories', using fake experts, purposively selecting only supportive evidence and discrediting all other, creating impossible expectations of what research can deliver or using logical fallacies [124]. In addition, as argued by Kata [107], other means used by anti-vaccination claims include: shifting hypotheses (or continuously proposing new theories to attribute risks to vaccines); censoring the opinions of those who are criticizing these theories and attacking their detractors either by personal insults or by filing legal actions [107]. It is thus unlikely that accumulation of scientific evidences disproving the causal association between vaccination and different diseases or conditions (e.g., sudden infant death syndrome, autism, diabetes, etc.) will ever stop the anti-vaccination movements. This is well illustrated by the shifting hypothesis linking the measles component of the MMR to autism: once disproved by science, a new hypothesis was generated that focused on additives in vaccines, and then after that, on 'too many, too soon' [42]. Evidence alone does not help reshape these anti-vaccine beliefs.

So, why are the anti-vaccination arguments so appealing to parents? Psychosocial researches have indicated that many cognitive biases, or heuristics, can influence parents' perceptions about vaccination. Heuristics are used by everyone when faced with complex decision-making, implying judgments about risks and are intuitive, automatic and often unconscious [125]. For instance, many studies have shown that individuals are more averse to the risks associated with an action – getting a possibly 'unsafe' vaccine – than to the risks associated with inaction – taking a chance of contracting a vaccine preventable disease when there are no cases locally. This is known as the 'omission bias' [126]. Another important bias that could be triggered by anti-vaccination activists is the 'co-incidence dragon' or the propensity to attribute every event occurring *after* immunization to be *caused by* vaccination, such as the false association between vaccination and sudden infant death syndrome (because of the timing of childhood vaccination both events have high probability to occur subsequently) [123,127]. Viewing anti-vaccination content could also influence parents to consider vaccines as risky because of the 'availability bias' or the propensity to judge something as frequent if it is easily recalled. For instance, a recent study looking at the potential impact of conspiracy theories on vaccination intentions has highlighted that exposure to anti-vaccine conspiracy theory (pharmaceutical companies manipulated research data on vaccine efficacy to make profits) was associated with reduced parental vaccination intentions [128].

Indeed, the arguments of anti-vaccination activists can convince parents because they are simple to understand and provide explanations for the etiology of medical conditions that science and medicine have yet to fully explain. Many anti-vaccination activists also appeal to emotion by presenting personal stories of parents who strongly believe that their child has

Box 3. From the Australian Vaccination Network to the Australian Vaccination-Skeptics Network.

In 2011, the New South Wales Health Care Complaints Commission (HCCC) had begun investigating the activities and online publications of the Australian Vaccination Network (AVN) after having received complaints from medical professionals, scientists and citizens, including parents of a child who died from pertussis. The HCCC found the AVN guilty of providing information that is 'misleading, incorrect, inaccurate and entirely taken out of context' as well as to 'use fears to influence people' [228]. In July 2010, the HCCC recommended that the AVN include a statement in a prominent position on its website stating that the purpose of the AVN is to provide information against vaccination [229]. The AVN was also ordered by the New South Wales Supreme Court to change its name because it was 'misleading and a detriment to the community' [229]. In March 2014, after long-lasting court battles, the AVN finally complied with the court request and changed its name for the 'Australian Vaccination-Skeptics Network' [230]. Despite facing strong criticisms by government departments and medical authorities, the group is still active and diffuses its anti-vaccination messages on its website, Facebook page and Twitter account, using the same acronym (AVN), showing how difficult it could be to stop anti-vaccination movements in the digital era [230]. However, the court also stripped AVN of its charitable status so there may be less money over time to keep the website and social media accounts as active as it has been.

been seriously harmed by vaccination [90,118,129]. Evidence statements on statistics and probabilities, often used in public health communication about vaccination, are not nearly as powerful as emotive anecdotes. Furthermore, many studies have shown that popular interpretation of risk is not usually based on a rational assessment of evidence, but rather on an 'uncertainties and ambiguities' approach where doubts remain even in the face of empirical evidence [130,131]. Finally, parents think of risk for their own child rather than from a population-based approach often used in public health: what does this risk mean for my family and me?

Clinical impact of anti-vaccination

We are equally at risk of the 'co-incidence dragon' problem when quickly drawing a direct causal association between anti-vaccination activism and the decline in vaccine uptake, because many factors contribute to the parental decision to delay or refuse some, many or all vaccines, as noted above. However, there are several studies showing the negative influence of traditional media controversies on vaccine uptake [75,132,133]. Gangarosa *et al.* found that in countries where anti-vaccination pertussis vaccine safety concerns were especially prominent and widely circulated by the media (e.g., Sweden, Japan, the UK, The Russian Federation, Ireland, Italy, the former West Germany and Australia), vaccine uptake plummeted and the incidence of pertussis was 10- to 100-times higher than in countries less affected by this scare

and high coverage was maintained (e.g., Hungary, Poland and the USA) [75].

Many recent outbreaks of VPD, including measles [134–140], mumps [141], rubella [142], poliomyelitis [143] and pertussis [144], have been linked to undervaccinated or non-vaccinated communities [145].

Measles

From January 2008 to May 2012, over 22,000 cases of measles were reported in France, leading to almost 5000 hospitalization and 10 deaths. This epidemic was largely attributed to insufficient and heterogeneous vaccination coverage with pockets of susceptible people that allowed measles virus to easily circulate beyond France [146]. In 2013, there were 29,150 cases of measles in the WHO European region, and most were among unvaccinated persons [147]. Even with a vaccination coverage of over 95% in The Netherlands, a measles outbreak started in May 2013 with most cases occurring in orthodox Protestants who opposed vaccination on religious grounds [148]. In the USA, despite measles having been declared eliminated in 2000, three large outbreaks were reported in 2013. From January to August 2013, 159 cases were reported in 16 states, of which 99% were imported. More than 90% of cases were in persons who lacked vaccination or had unknown vaccination status [149]. A similar situation happened in Quebec, Canada, with 21 measles importation cases that then spread to 725 others. A super spreading event triggered by one importation resulted in sustained transmission and 678 cases [135]. In 2014, more local outbreaks have been reported in the USA and Canada again usually started by importation into an area with low MMR vaccine uptake [150,151]. Given that measles is so contagious, these examples are not surprising. Outbreaks will continue to occur as long as an imported measles case has the opportunity to expose others who are not immunized. Since measles cases are infectious via infected droplets or airborne spread from 4 days before the rash appears, that is, before any signs or symptoms of measles, others in the home or local community may be easily exposed through routine acts of daily living.

Rubella

From January to April 2013, Poland reported 21,283 rubella cases (55.2 per 100,000 inhabitants), the highest number since 2007. Some 81% of cases were among 15- to 29-year-old males, a phenomenon that reflects the history of Polish rubella immunization policies, selective vaccination of adolescent girls since 1989, then universal two-dose MMR vaccination since 2004, with no catch-up program for boys [152]. In 2012, an outbreak of rubella also occurred in Sweden with the 50 cases occurring mostly in an anthroposophic community known to be opposed to vaccination [147]. In The Netherlands, an outbreak in 2013 led to 54 cases, all linked to an orthodox Protestant denomination opposed to immunization [147]. From 2011 through 2013, a rubella outbreak occurred in Romania

involving 1840 probable and confirmed cases among mainly unvaccinated adolescents [153].

Mumps

In 2011, 5261 mumps cases were recorded in the Federation of Bosnia and Herzegovina, leading to an incidence of 225.8 per 100,000 population [141] and occurred mainly in the unvaccinated or those unaware of their vaccination status likely related to immunization program failures during the war and post-war period (1992–1998). This example highlights the importance of local conflicts as a factor that undermines routine immunization uptake with or without anti-vaccine sentiments being prominent.

In the USA, between 2009 and 2010, a total of 3502 outbreak-related cases of mumps were reported, mostly among orthodox Jewish persons [154]. Despite high vaccine coverage with two doses of almost 90%, transmission was focused within Jewish schools for boys where students spend many hours daily in intense face-to-face interaction [154]. Even two doses of mumps vaccine do not give 100% immunity in the face of this intense exposure.

Pertussis

In 2012, 48,277 cases of pertussis were reported in the USA, including 20 pertussis-related deaths. The majority of deaths occurred among infants younger than 3 months of age, too young to be fully immunized [155]. The US major outbreaks in the past few years have been attributed to the cyclical nature of pertussis, improved diagnosis and waning immunity of the acellular pertussis vaccine [156]. Clustering of unvaccinated individuals appears to also have played an important role [157]. For example in 2010, 9120 cases of pertussis were reported in California, the largest number since 1947 with cases clustered spatially and temporally in areas with high rates of non-medical vaccine exemptions leading to local concentrations of unvaccinated children [158].

To summarize, VPD are still today a major cause of morbidity and mortality. In 2010, WHO estimated the number of deaths caused by traditional VPD (diphtheria, measles, neonatal tetanus, pertussis and poliomyelitis) at 0.4 million [159]. Over half of unvaccinated children lived in only three countries: India, Nigeria and Indonesia, where poor health infrastructure may explain much of the undervaccination, but parental refusal is also an important factor [160]. In other countries, HIC, MIC and LIC, vaccine refusals also threaten the success of current vaccination programs [161]. In the USA, between 2004 and 2011, the mean state-level rate of non-medical exemption increased from 1.48 to 2.2% [162]. While this overall rate may appear low, exemptions are highly clustered at the county, neighborhood and school levels. In Washington State, for example, exemption rates in some counties were up to 25.3% [163], diminishing the potential for added herd immunity protection. Spatial clustering of un- or undervaccinated individuals has been linked to the growing risk of outbreaks [8].

Expert commentary

While a minority of parents holds strong anti-vaccination sentiment, the proportion categorized as vaccine-hesitant may be increasing as noted above [162]. This is of concern because maintenance of vaccination successes requires high immunization uptake. It needs to be seen as normal parental behavior to have your child immunized on schedule and on time. Vaccination is an individual measure that benefits not only the individual, but also produces a common good: herd immunity. Unlike many other health prevention interventions, if a parent refuses to vaccinate his or her child, it is not only this child who will be at risk of suffering from the negative consequences of this decision, but the risk to the whole community increases. Thus, vaccine hesitancy and vaccine opposition needs to be addressed both at the individual and community levels. The broader social, cultural and political context in which parents are living needs to be considered.

For example, Colgrove and Bayer in their analysis of the different consequences of the MMR and autism controversy in the UK and the USA have shown that breakdown of public trust in a vaccine could be explained by contextual factors, such as media coverage, vaccination policies, past health crisis or scandals and health professionals' perceptions and support [59]. Looking retrospectively at vaccination confidence crisis, Larson *et al.* showed that early signs of public concern were often available well before their most serious effects on vaccination programs occurred, but were not acted on, largely because the negative results were not expected [164]. As argued by Colgrove and Bayer, 'to view anti-vaccinationists as simply paranoid or reactionary obscures the significance of their fight within the broader social and political environment' [59].

Context is the key, and context is changing. In recent years, there has been an explosion in the number of new vaccines licensed and commercialized [165]. In the USA, the number of vaccines included in the publicly funded vaccination program for children from birth to 18 years of age has more than tripled between 1990 and 2012 [165]. This increase in the number and the consequent decline in vaccine-preventable illnesses have focused attention by both health professionals and parents on vaccine need (if the diseases are gone does my child really need this vaccine?) and safety [41,166–169]. The increase in the number of vaccines has given rise to complicated and differing vaccine schedules raising many parental questions. Some have argued that differences between vaccination schedules and programs adopted in different countries, or even in different jurisdictions of the same country, could increase individuals' negative perception of the relevance of particular vaccines or vaccine schedules [33,51]. Some new vaccines prevent diseases that the parents perceive to be mild and of low risk for serious complication (e.g., chickenpox or gastroenteritis), which may further compromise parental belief in their need and acceptance.

These changes in childhood vaccination schedules and rapid developments in the field of vaccines have also

happened concurrently with many societies' increasing preoccupation with the safety and the future, thus generating more concerns about risk [170]. The value and legitimacy of science, expertise and medical authority is also being questioned [107]. Some well-publicized cases of licensed drugs with major side effects (such as thalidomide or, more recently, VioxxTM) [171,172] have made many people suspicious of government and pharmaceutical industry motives in general and are often used by anti-vaccination activists in analogy to support their claims. Management of past crisis, where industries and government agencies tried to hide critical data on some important health issues, like the 'Tainted Blood Scandal' or the 'Mad-Cow Disease Crisis' [173], could also explain the increased distrust toward authorities and medical experts by some members of the general public. In today's 'risk-averse' world, people are increasingly encouraged to take responsibility over their own lives, to stay continuously aware of risks and benefits in order to make their future more secure [174]. Notions of empowerment and individual choices are predominant health themes. 'Consumerism' in healthcare is growing. Patients want to be involved in their own health decisions [13,175]. The rise of the informed patient has shifted the traditional locus of power from doctors as sole directors of patient care to shared decision-making between health professionals and patients who want to be active participants in decisions concerning their health. In addition, with the Internet, health information based on individual experience ('experience-based') has gained legitimacy and credibility similar to scientific information based on research data ('evidence-based') [176,177]. Eysenbach uses the concept of '*apomediation*' to refer to the observation that individuals are relying more heavily on social media and social networks than on experts and institutions to gather useful and trustworthy health information in an accessible format [178]. With social media, Internet users' personal stories add a new dimension to health information: the knowledge and emotional experience of disease and treatments as well as their physical and psychological consequences [179]. These powerful tools have been widely used by anti-vaccination activists [100,107].

In the past decades, despite significant efforts, few, if any, public health strategies have effectively and long-lastingly succeeded in countering anti-vaccination movements. To respond to parents' concerns about vaccination, vaccine advocates have relied on education and information. However, even when provided with evidence-based information about the effectiveness and safety of vaccines, some parents still believe vaccines to be useless and even harmful [180]. The time has come to move beyond the 'knowledge deficit model' to develop innovative responses to address anti-vaccination sentiment [30,113]. Vaccine-hesitant parents should be targeted as they make up a larger at-risk group for poor immunization uptake rates and are more amenable to change their attitudes toward vaccination than outright vaccine-refusers parents who currently represent a much smaller proportion [30]. Trust

of parents who accept vaccination should also be carefully nurtured and supported.

A first and important step to developing effective strategies is to have a good understanding of both the *causes* and of the *contexts* leading to vaccine hesitancy and refusal [13,181,182]. Increasing awareness of the public about the extent of surveillance of vaccine safety; increasing transparency in the decision-making process that lead to vaccination policies and/or including vaccination in school education programs are among the novel strategies that have been proposed to counter anti-vaccination movements (for detailed discussion, see [114]). Finally, the crucial role of health providers in maintaining confidence in vaccination cannot be understated [12,183,184]. One of the main predictors of acceptance of a vaccine is the recommendation for vaccination by a healthcare professional [44,183,185], and how the healthcare provider presents immunization [186]. For example, results of a large US study indicated that the largest proportion of parents who changed their minds about delaying or not getting a vaccination for their child listed 'information or assurances from healthcare provider' as the main reason [29]. This is also found in LMIC [187]. Many articles in the literature have stressed the importance of health providers addressing concerns of vaccine-hesitant patients in a well-managed way and authors have given their tips to providers on how to do so [26,184,188,189]. Although the approaches presented in these articles vary, they do share some common characteristics, such as the importance of maintaining a trustworthy patient-provider relationship and the importance of tailoring the communication to specific patients' concerns and doubts.

Five-year view

Anti-vaccination sentiment is as old as vaccination itself. Despite the fact that anti-vaccine movements have had some salutary effects, such as pressure for the development of even safer vaccines, for the implementation of large-scale surveillance systems for licensed vaccines and for the development of vaccine-injury compensation programs [42,75], they have also incited fears among parents, leading to increased vaccine refusal and lowered community vaccine uptake followed by increased VPD and deaths [119].

Anti-vaccination movements are unlikely to disappear. The development of new vaccines, additives and adjuvants combined with the enhancement of the anti-vaccine platform

with the Internet and social media are likely to spur on the anti-vaccine movement [40]. Despite significant efforts, 'knowledge deficit model' public health strategies to date have not effectively succeeded in countering anti-vaccination movements. It is time to move beyond these strategies and to develop more innovative responses to address anti-vaccination sentiment. One possibility suggested in the 2012 Global Vaccine Action Plan is to build on the potential offered by social media [159]. Social media platforms not only offer opportunities to the anti-vaccine movement, but also to public health [100]. While this strategic opportunity merits attention, more will be needed as there is unlikely to be one strategy that will effectively counteract the anti-vaccine movements' impact on parental decision-making. To achieve high vaccine uptake rates needed to protect individuals and communities, multiple strategies will be required as many factors are at play across the broad continuum of vaccine hesitancy between full acceptance of all vaccines and outright refusal. The first step must include determination of why vaccine uptake rates for a specific or all vaccines are not being achieved in a group or subgroup (i.e., to diagnose what factors are driving hesitancy). The EURO Region of the WHO's Guide to Tailoring Immunization Program-TIP can help in the process [181]. A tailored intervention or prevention strategy that then fits the problem can be developed. As well, public health messaging needs to be tailored to fit the intended group: reinforcement of those who fully accept vaccine, responses to those who are hesitant and very different approaches for those who outright refuse all vaccines [180].

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Key issues

- The high rate of childhood vaccination coverage in most countries indicates that vaccination remains a widely accepted public health measure. However, these national estimates may hide clusters of undervaccinated individuals.
- Many recent outbreaks of vaccine-preventable diseases have been linked to undervaccinated or non-vaccinated communities.
- Many studies have shown that parental decisions to use or avoid immunization for their children are complex and multi-dimensional, including contextual determinants, determinants related to the vaccination services and individual determinants, such as parents' knowledge, attitudes and beliefs or sociodemographic characteristics.
- While minority of parents hold strong anti-vaccination sentiment, the proportion categorized as vaccine-hesitant may be increasing; even parents who vaccinate their child can have important doubts and fears regarding immunization.
- Anti-vaccination is as old as vaccination itself and is not likely to disappear. With the Internet, the anti-vaccination movements are more powerful than ever and have the potential to reach and influence many parents.
- Despite significant efforts, few, if any, public health strategies have effectively and long-lastingly succeeded in countering anti-vaccination movements. It is time to move beyond the 'knowledge deficit model' to develop innovative responses to address anti-vaccination sentiment.
- A first and important step to develop effective strategies is to have a good understanding of both the *causes* and of the *contexts* leading to vaccine hesitancy and refusal.
- Interventions must be tailored to address the specific concerns in a given context, time and vaccine.

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