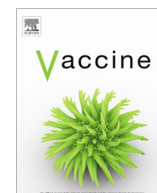


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Vaccine strategies: Optimising outcomes



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ABSTRACT

Successful immunisation programmes generally result from high vaccine effectiveness and adequate uptake of vaccines. In the development of new vaccination strategies, the structure and strength of the local healthcare system is a key consideration. In high income countries, existing infrastructures are usually used, while in less developed countries, the capacity for introducing new vaccines may need to be strengthened, particularly for vaccines administered beyond early childhood, such as the measles or human papillomavirus (HPV) vaccine. Reliable immunisation service funding is another important factor and low income countries often need external supplementary sources of finance. Many regions also obtain support in generating an evidence base for vaccination via initiatives created by organisations including World Health Organization (WHO), the Pan American Health Organization (PAHO), the Agence de Médecine Préventive and the Sabin Vaccine Institute. Strong monitoring and surveillance mechanisms are also required. An example is the efficient and low-cost approaches for measuring the impact of the hepatitis B control initiative and evaluating achievement of goals that have been established in the WHO Western Pacific region. A review of implementation strategies reveals differing degrees of success. For example, in the Americas, PAHO advanced a measles-mumps-rubella vaccine strategy, targeting different population groups in mass, catch-up and follow-up vaccination campaigns. This has had much success but coverage data from some parts of the region suggest that children are still not receiving all appropriate vaccines, highlighting problems with local service infrastructures. Stark differences in coverage levels are also observed among high income countries, as is the case with HPV vaccine implementation in the USA versus the UK and Australia, reflecting differences in delivery settings. Experience and research have shown which vaccine strategies work well and the factors that encourage success, which often include strong support from government and healthcare organisations, as well as tailored, culturally-appropriate local approaches to optimise outcomes.

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Abbreviations: AMP, Agence de Médecine Préventive; DTP, diphtheria-tetanus-pertussis; EPI, Expanded Programme on Immunisation; GAVI, Global Alliance for Vaccines and Immunisation; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; HPV, human papillomavirus; MMR, combined measles-mumps-rubella vaccine; MVP, Meningitis Vaccine Project; NESI, Network for Education and Support in Immunisation; NITAG, National Immunisation Technology Advisory Group; PAHO, Pan American Health Organization; SAVIC, South African Vaccination and Immunisation Centre; SIA, supplementary immunisation activities; WHO, World Health Organization.

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1. Introduction

Successes in the eradication of smallpox offered high hopes for vaccines and the control of infectious diseases [1]. This experience contributed to the Expanded Programme on Immunisation (EPI), which was introduced in 1974 by the World Health Organization (WHO) [2]. Comprehensive vaccination programmes were developed and became the cornerstone of good public health intervention [3].

Although progress has been impressive, global vaccination coverage rates show there is room for improvement, with nearly 19 million infants not receiving routine immunisation, such as three doses of diphtheria-tetanus-pertussis (DTP) vaccine, in 2014 [4]. More than 60% of these children live in 10 countries in Africa

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and Asia, indicating regional disparities [4,5], although outbreaks of vaccine-preventable diseases in high-income regions show that there is a need to expand or adapt vaccination strategies worldwide [1,6].

The benefits of successful vaccination strategies are clear, providing not only direct protective effects but also sometimes indirect effects among unvaccinated individuals (herd protection) [7,8]. The consequences of under-vaccination include a shift of infection to different age groups and rebound effects [9].

Strategies to address vaccine hesitancy are discussed in an accompanying paper [6]. This paper provides an overview of the vaccine introduction strategies and the key factors underlying their effectiveness.

2. Key principles of vaccination strategies

The main objective of all vaccination strategies is to meet disease reduction goals by achieving high levels of immunity in the targeted population via adequate immunisation coverage and vaccine effectiveness (Box 1) [10]. The strategy varies according to the target of a vaccination programme, which may be selected groups or whole populations (Table 1). Theoretically, targeting subjects with the highest risk of disease or its complications would be most effective, since the rate of prevented cases per administered dose

would be maximised. Unfortunately, vaccine-preventable diseases are often not exclusively present in risk groups or there is no particular risk condition for their acquisition (for instance, measles, rubella, varicella and rotavirus). The other difficulty lies in the ability to reach all those at risk, since healthcare systems may fail to ensure patients receive all recommended vaccines, as discussed in an accompanying paper [11]. Consequently, age-based strategies complemented by risk group strategies have been found to be most effective for disease reduction [12].

For most vaccine-preventable diseases, a single cohort approach is used in which immunisation is started at a given age (for example, 2–3 months for DTP) and the targeted population receives all recommended doses at specific times. Sometimes a double-cohort approach is useful to speed up the impact of a vaccination programme, for instance, simultaneous vaccination of infants and adolescents or young adults [13,14]. Mass vaccination occurs when a large number of people are immunised within a short period of time for efficient disease reduction and generation of herd protection, depending on the mode of disease transmission [15]. It may be used in response to an emerging or existing epidemic, such as polio in the 1950s [16] and, more recently, meningococcal, measles and yellow fever epidemics in sub-Saharan Africa and Latin America [15]. This programme may also be employed to prevent a predicted epidemic, such as the annual influenza campaign in industrialised countries [15]. For catch-up vaccination, in addition to routine immunisation of an age cohort, other population groups are actively offered vaccination, usually for a limited time.

Various factors are considered when determining the feasibility of the immunisation strategy in the targeted population. This includes the demographic composition of the population to immunise, the age at which most disease cases occur and the biological and social factors underlying infection transmission that determine the basic reproductive rate (R_0) of the infectious agent [8,9]. Calculation of the disease burden, expressed in terms of incidence and prevalence rates, associated hospitalisations, disability and mortality, provides valuable information on the particular disease and its importance or seriousness compared with other health conditions [10]. Detailed mathematical models can help make inferences on the total disease burden when such data are incomplete, as well as on spread of infection and critical vaccination coverage [17].

Assuming vaccination is feasible, the strategy for its introduction must take into account the structure and strength of the local healthcare system, service funding and means of monitoring success. Each of these factors is considered below.

Box 1

Main elements of vaccination strategies.

Programmatic objectives	<ul style="list-style-type: none"> • Meet disease reduction goals in targeted population via <ul style="list-style-type: none"> – Adequate immunisation coverage – Adequate vaccine effectiveness
Factors for an effective vaccination strategy	<ul style="list-style-type: none"> • Structure and strength of local healthcare system <ul style="list-style-type: none"> – Infrastructure for vaccine distribution and administration – Compatibility with existing immunisation calendar – Political will • Immunisation service funding • Surveillance and monitoring systems for disease impact and vaccine coverage
Implementation aspects	<ul style="list-style-type: none"> • Strategy and planning • Human resources • Supportive framework • Advocacy and communication

Table 1

Main vaccination strategies and disease reduction goals.

Vaccination strategy ^a	Example vaccine	Goals
Routine vaccination (selective immunisation)		To eradicate, eliminate or contain disease
Single birth cohort	DTP, Rotavirus HBV	
Double cohort (e.g., infants and adolescents)		
Mass immunisation (entire population in affected area or priority risk groups ^b)		
Response to an emerging epidemic	Yellow fever	To rapidly limit morbidity and mortality due to the documented presence of a vaccine-preventable disease
Response to a predicted epidemic	Influenza	To establish population immunity before risk occurs
Response to a diseases outbreak	Hepatitis A	To establish population immunity and reduce number of cases after several cases are reported in a certain area/group of people
Catch-up vaccination	MMR	To protect individuals whose vaccinations have been delayed or missed
Specific immunisation campaigns/supplemental immunisation activities	OPV	To eradicate, eliminate or contain disease, where not achieved by routine vaccination

Abbreviations: DTP = diphtheria-tetanus-pertussis, HBV = hepatitis B virus, MMR = measles-mumps-rubella, OPV = oral poliovirus.

^a A combination of strategies may be appropriate, most commonly age-based complemented by risk group strategies.

^b Priority risk groups: groups at highest risk of disease morbidity or mortality, such as young children, pregnant women, older adults, healthcare professionals.

2.1. Structure and strength of the local healthcare system

The structure and strength of local or national healthcare systems vary widely, with many developing countries lacking the means to access, evaluate and implement new vaccines [5,10]. In the assessment of existing immunisation programmes, areas for improvement are identified as well as the feasibility of the proposed vaccination schedule in terms of number of clinic visits required and compatibility with vaccine schedules already in the immunisation calendar. Political issues also play an important role [10,18]: strong decision making and political will is needed for immunisation calendar updates, integration of policies into national health plans and social mobilisation measures. Infrastructures may need to be strengthened or new systems developed for vaccines administered to age groups beyond early childhood [19], such as vaccines against human papillomavirus (HPV) types that cause of cervical cancer. Around 85% of cervical cancer cases and deaths occur in less developed countries [20], predominantly because of a lack of preventive measures [21–23]. Demonstration projects conducted in India, Peru, Uganda and Vietnam beginning in 2006 found that high coverage could be achieved using a variety of delivery strategies, including school- and health centre-based strategies, as well as those coupling HPV vaccination with other health interventions [24]. In India, however, problems were encountered with unconfirmed adverse events and claims that the project was an experimental clinical trial [25]. The adverse events were formally investigated and no deaths were determined to be caused by the HPV vaccine. Despite this, the trial was shut down by the government. This shows how a local healthcare system with adequate structure and strength for delivering a successful vaccination programme may be undermined by politics, suspicion of the motives of outside organisations and public distrust.

The factors that are important for successful introduction of HPV immunisation in low-resource settings were summarised by Kane et al. (see Box 2) [26]. In particular, investment is often required to improve infrastructure to ensure efficient vaccine

Box 2

Important factors in the policy process for human papillomavirus (HPV) vaccine introduction in low-resource settings [26].

Policy environment	<ul style="list-style-type: none"> • National disease data on the burden of cervical cancer • Priorities of women's health and cervical cancer control • Priorities in adolescent health • National immunisation programmes: infrastructures and policies
HPV vaccine-specific issues	<ul style="list-style-type: none"> • Safety and efficacy data • Economic modelling of cost-effectiveness and impact • Demonstration projects in country or region • Behaviour of other countries regionally and globally • Cost and 'affordability' of the vaccine to the country • Social perception of vaccine
Policy development and implementation	<ul style="list-style-type: none"> • National capacity for HPV vaccine introduction • Vaccine financing • International guidelines from WHO, GAVI, UNICEF and donors at global, regional and national levels • Training on cervical cancer for the staff involved in HPV vaccination • Information, education and communication material • Appropriate implementation and monitoring

GAVI, Global Alliance for Vaccines and Immunisation; UNICEF, United Nations Children's Fund; WHO, World Health Organization.

delivery and good coverage, and to reduce vaccine wastage [21]. This includes sufficient centralised vaccine storage space, refrigerators to store vaccines at health centres, and walk-in coolers for vaccination at delivery points (schools or elsewhere). Nurses and doctors need to be trained in HPV vaccination and in assessing and managing any side effects or complications. For implementation through schools, a strategy to reach non-attending girls must be in place. Achieving these goals requires long-term political support since, as with other vaccines, HPV vaccination is a long-term prevention strategy, the benefits of which may only become evident beyond a government's term of office.

2.2. Service funding

Immunisation services can only realise their potential to improve health if there is adequate and reliable funding to ensure continuity and increases in coverage. Insufficient funding is one of the main barriers to providing access to vaccines in low income countries, which often need external sources of finance to supplement government budgets. However, high income countries may also struggle to keep immunisation budgets sustainable, particularly when new vaccines need to be introduced.

Although most national governments are investing more in their national immunisation programmes, new vaccines and higher target coverage rates are driving costs up [27]. It is therefore important to assess financial sustainability. For example, a cost comparison of vaccine introductions in Rwanda found that delivery costs of pneumococcal and rotavirus vaccines were similar since both were delivered using existing healthcare infrastructure while the cost of delivering HPV vaccine was higher because a new vaccine delivery system had to be created for a new target population [28].

To avoid a large financing gap, policy makers in many countries have had to examine the options available to support immunisation. This includes initiatives by the Pan American Health Organization (PAHO), Global Alliance for Vaccines and Immunisation (GAVI), the International Finance Facility for Immunisation and the Advanced Market Commitment, which together with various governments, international agencies and charitable foundations have provided funds to the world's poorest countries [29,30]. For example, the PAHO EPI Revolving Fund allows several countries with the same vaccine needs to apply for vaccine supplies together, resulting in a decreased vaccine cost, and handles most aspects of procurement using a common fund to pay producers before being reimbursed by countries [30,31].

Various countries have developed other public and private financing solutions [27]. In countries such as Tajikistan, Vietnam and Haiti, resources for immunisation are raised through tax levies on luxury goods, alcohol and tobacco. In Costa Rica, proceeds from the November drawing of the national lottery are earmarked for the National Immunisation Fund, providing a minor but stable proportion of the immunisation budget. Other innovative sources of financing include taxes on exported food products, airline tickets, mobile phone usage, residential tax and vehicle tax discs. Also, financing from private sources can be an effective option. In Bhutan, the government established the Health Trust Fund, with the goal of eliminating funding unpredictability and generating sufficient income to meet the cost of critical components of the country's health services [32]. Private and public donor contributions to the fund are matched by the Bhutanese government. This approach has been an important tool in ensuring the timely availability of vaccines and essential drugs.

2.3. Monitoring success

Surveillance mechanisms allow for continuous evaluation of the coverage, safety and effectiveness of the vaccine [33] and can be

used to identify ways to enhance the efficiency and effectiveness of the programme.

The importance of a strong monitoring programme can be illustrated by the experience in Germany following the introduction of routine vaccination with a single dose of monovalent varicella vaccine for young children in 2004 [34]. A sentinel surveillance system used to monitor the epidemiology of varicella disease showed vaccination brought a steep downward trend in disease prevalence over time, with 55% fewer varicella cases in the 2008–2009 season compared with 2005–2006 [35]. However, during the same period, a rising number of breakthrough infections was reported and an investigation of varicella outbreaks in daycare centres in 2008 and 2009 found vaccine effectiveness after one dose was only 62% [36]. Germany's National Immunisation Technology Advisory Group (NITAG) responded by examining these monitoring data, new vaccine immunogenicity data, and epidemiological information and experiences from other countries. Particularly relevant information came from the USA, where a single dose of monovalent varicella vaccine had been administered to children aged 12–18 months since 1996. Despite 80–85% effectiveness in preventing varicella [37], disease outbreaks still occurred, leading to recommendation in 2007 of a second dose of varicella vaccine for children [38]. In Germany, after considering all available evidence and the feasibility of changing the immunisation schedule, the NITAG recommended in 2009 that the varicella vaccine should be administered twice [39]. Evidence from regions that adopted the new dosing schedule showed the number of varicella cases decreased, indicating that the recommended change was effective [40].

3. Supportive framework for implementation of vaccine strategies

Different groups and organisations provide supportive frameworks that encourage successful implementation of vaccine strategies. These focus on various elements including generation of the evidence base for vaccination, effective presentation of evidence to policy decision makers and activities to strengthen the capacity of immunisation programmes.

Policy decisions to introduce new vaccines require an evidence base that reflects national, and sometimes local, conditions [41]. Many countries generate this evidence base with support from organisations involved with global immunisation activities, such as PAHO, the USA Centres for Disease Control and Prevention, PATH, the Sabin Vaccine Institute, the Agence de Médecine Préventive (AMP) and the WHO. For example, in Latin America and the Caribbean, the ProVac Initiative was introduced by PAHO in 2004 to train ministry of health technical staff on economic evaluations for introducing rotavirus, pneumococcal and HPV vaccines [42]. These organisations often collaborate with NITAGs, which are composed of expert committees that make recommendations on vaccination programmes to national authorities. The SIVAC (Supporting Independent Immunisation and Vaccine Advisory Committees) initiative, which is led by the AMP in collaboration with the WHO and funded by the Bill & Melinda Gates Foundation [43], assists in the establishment or strengthening of functional, sustainable independent NITAGs in GAVI-eligible and middle income countries. Another AMP initiative, the Health Policy and Institutional Development unit, encourages systematic use of evidence-informed policy-making processes in immunisation, collaborates with the WHO on scaling-up initiatives and facilitates the exchange of information within the immunisation community [44].

NITAGs have been established to guide immunisation policies in most industrialised and some developing countries: in 2015, a NITAG was in place in 124 countries of which 82 met six basic

WHO criteria relating to administrative and legislative practices, areas of expertise, frequency of meetings and meetings preparation [45]. A highly functioning NITAG is instrumental in enabling its national government to form evidence-based vaccination strategies and policies [46]. However, approaches towards providing immunisation advice vary widely among countries and few NITAGs have published their model for advice and vaccine funding in peer-reviewed journals [47,48]. Survey data suggest more NITAGs need to use health economic assessments as part of their vaccine recommendation processes, in low income countries as well as in high and middle income countries; a survey of 28 European countries in 2014 showed 20 used health economic assessments, while mathematical modelling as part of the recommendation process was conducted in only 18 countries [48]. This is particularly important, in addition to the epidemiology of disease, for cost-benefit considerations relating to choice of dosage regimen (such as the decision to administer two or three priming doses of pneumococcal conjugate vaccine with or without booster dose [49]) and target population, such as high-risk groups (as for seasonal influenza vaccine in some countries [50]) versus immunisation of the wider population, or number of age cohorts to be included in catch-up vaccination programmes. To help address inconsistencies in approaches, the NITAG Resource Centre has been developed by the Health Policy and Institutional Development unit of the AMP [45]. This online resource aims to provide centralised access to NITAG related tools, NITAG recommendations from around the world as well as the background documents used to issue them, such as systematic reviews and technical reports, and information on upcoming immunisation events.

Many capacity-building organisations also contribute to successful immunisation programmes. Examples include the South African Vaccination and Immunisation Centre (SAVIC), which is an academic-public alliance between the Sefako Makgatho Health Sciences University (previously University of Limpopo) and the University of Antwerp, Belgium [51], Network for Education and Support in Immunisation (NESI) based at the University of Antwerp [52], Vaccines for Africa Initiative based at the University of Cape Town, South Africa [53], the International Vaccine Institute in the Republic of Korea [54] and the more recently established East Africa Centre for Vaccines and Immunisation, administered from Egerton University, Kenya, and Makerere University College of Health Sciences, Uganda [55]. These organisations provide inter-country vaccinology courses and experience exchange workshops on the introduction of new vaccines, targeting NITAG members and policy-makers, as well as EPI managers and staff. Specific training (including the development of training materials) for healthcare workers delivering the new vaccine may be conducted as well. The activities aim to strengthen immunisation programme capacity with technical assistance, training, development of tools and information sharing, and promote evidence-based decision-making on new vaccine introduction and efficient management of immunisation programmes. An example is a two-year capacity building project entitled 'Improving skills and institutional capacity to strengthen country adolescent immunisation programmes and health systems in the African Region' [56]. Using HPV vaccine as a case study, this project was implemented in 2014 in eastern and southern Africa by SAVIC, the South African Medical Research Council and NESI, funded by the Belgian government and with support from the WHO regional office for Africa. Through various experience exchange activities, the project has developed immunisation training materials that can be easily adapted to specific country needs and is helping create a multidisciplinary team of experts to support and advocate for the introduction of HPV vaccines in the region.

Other organisations assist with the managerial structures and processes for delivering vaccination services, such as the newly

constituted International Association of Immunisation Managers [57]. To support the uptake of vaccination and encourage better public understanding of its importance, civil society groups (mostly non-state voluntary organisations, such as health-, child- or patient-focused advocate groups) can play an important role [58]. As discussed in an accompanying paper [6], healthcare providers also have an essential role in optimising vaccine uptake [59]. The collaboration of various public health sector partners is necessary to ensure immunisation programmes are supported sufficiently, including partnership with vaccine manufacturers. Transparent processes are being introduced for developing, manufacturing and monitoring the safety and effectiveness of vaccines, as well as strategies for providing accurate and reliable information on vaccines' benefit-risk profiles [33].

4. Implementation strategies in different parts of the world

Table 2 outlines some of the many vaccine implementation strategies that have been employed in different regions with vary-

ing degrees of success [60–72]. A few of these strategies are discussed in more detail below, highlighting the challenges faced as well as reasons for success.

In the Americas, PAHO advanced a rubella elimination strategy from 2003, which was combined with a measles elimination strategy [61]. This aimed to achieve at least 95% coverage with rubella-containing vaccine, mainly measles-mumps-rubella (MMR) vaccine, for children aged 12 months in all countries ('keep up' campaign). Supplementary immunisation activities (SIAs) included implementation of a one-time mass campaign among adolescents and adults ('speed up' campaign), catch-up campaigns in children aged 1–14 years and periodic follow-up campaigns among children younger than 5 years. By 2010, all countries routinely vaccinated children against rubella, an estimated 450 million people had been vaccinated against measles and rubella in SIAs and rubella transmission had been interrupted, with the last confirmed endemic rubella case reported in 2009. Comparison of different strategies showed this combined vaccination strategy with a universal approach was more effective than strategies that focused on

Table 2
Examples of implementation strategies that have been assessed in relation to uptake of vaccines or other outcomes.

Intervention tested (year)	Vaccine	Age group	Setting/country	Main findings/outcomes	Reference
National multivaccination campaign; national polio immunisation day (2012)	IPV-OPV (sequential schedule)	<5 years	Brazil	Rapid uptake of vaccines (from 5% in August to 67% in December for two IPV doses) despite challenges with local vaccine supply due to high wastage rates	[60]
Mass campaigns targeting children, adolescents and adults; follow-up campaign targeting unvaccinated children (2003–2009)	Rubella-containing	Children, adolescents, adults	Americas	High vaccination coverage (93–94% for first MMR dose at age 12 months; estimated 450 million people vaccinated during supplementary immunisation activities) led to elimination of rubella and congenital rubella syndrome	[61]
Routine immunisation (2011–2013)	MMR	<5 years	Mesoamerica	Vaccination coverage 45–80% (at least one dose). Missed vaccinations possibly due to vaccine shortages, failures to immunise at all well-child clinic visits, inadequate knowledge of current immunisation schedules, lack of immunisation documentation	[62]
Mass vaccination campaign, supplemental immunisation activities (2010)	Measles	≤14 years	South Africa	Heterogeneity in vaccination coverage (of 52 districts, 8 had coverage <80% for first vaccine dose). Reduction in routine immunisation coverage associated with supplemental immunisation activities, which might have a negative impact on functioning of health systems	[69]
Vaccine-preventable disease control goal (2005–2012)	HBV	≥5 years	WHO Western Pacific region	Adopting the regional goal led to greater political commitment and reduced inequalities in HBV vaccination between and within countries. Major progress in provision of HBV birth dose	[63]
Vaccination during pregnancy (2013)	Pertussis	Pregnant women	England	Vaccination coverage 60–78%. High vaccine effectiveness among neonates <3 months old: 78% fall in confirmed cases and 68% fall in related hospital admissions	[64]
Vaccination of parents in neonatal ICU (2007)	Pertussis	Parents of neonates	New York, USA	Vaccination coverage 87%; 11% refused vaccination citing pertussis as an insignificant threat or disbelief in vaccination. Short length of ICU stay (<3 days) was logistic barrier	[65]
Schoolchild immunisation programme (1962–1994)	Influenza	School-age	Japan	Schoolchild programme contributed to reduced influenza-associated mortality rate among younger children and people aged 65 years or older	[66]
Mass vaccination campaign (2008–2011)	Influenza	Primary healthcare workers	Spain	Low vaccination coverage (49–58%): vaccination rates decreased over time, especially after pandemic season	[67]
Phased mass vaccination campaign for priority groups (2010)	Pandemic influenza	Priority groups	Brazil	Immunisation target (80%) achieved by 86% of groups overall and surpassed among several groups, including very young children, healthcare workers, persons with chronic illness. Conducting the campaign in phases facilitated vaccine distribution and service delivery despite limited vaccine stocks	[68]
School-based programme (2012–2014)	HPV	Girls 12–13 years old	England	Vaccination coverage >86% for 3-dose course. Reduction in prevalence of HPV 16/18 infections consistent with high vaccine effectiveness and herd protection	[70]
School-based catch-up programme (2007–2009)	HPV	Girls 12–17 years	Australia	Vaccination coverage 70% for 3-dose course	[71]
Vaccination in medical clinic (2014)	HPV	Girls 13–17 years	USA	Vaccination coverage 40% for 3-dose course	[72]

Abbreviations: HBV, hepatitis B virus; HPV, human papillomavirus; ICU, intensive care unit; IPV, inactivated poliovirus; MMR, measles-mumps-rubella; OPV, oral poliovirus; WHO, World Health Organization.

women and children, which were associated with a more than 5-fold greater incidence of rubella in men and disease outbreaks [73].

There is however evidence that the most vulnerable groups are still not receiving the MMR vaccine in parts of the Americas. In a recent study of MMR immunisation of children younger than 5 years in low income areas of El Salvador, Guatemala, Honduras, Mexico, Nicaragua and Panama, conducted for the Mesoamerican Health Initiative [74], vaccine coverage was 45–80% and the data indicated that families were bringing their children to health facilities but they were not receiving all appropriate vaccines during visits [62]. This highlighted major problems that need to be addressed to prevent missed opportunities: a shortage of vaccines, failures to immunise at all well-child clinic visits, inadequate knowledge of current immunisation schedules and a lack of documentation of vaccinations by healthcare professionals.

Another example of a region-wide policy towards disease prevention involves the response in the WHO Western Pacific region to a disproportionate burden of hepatitis B virus (HBV) infection [75]. Most HBV-related deaths occur in adults and common routes of transmission include perinatal, early asymptomatic childhood infection, sexual contact, blood transfusions and unsafe injection practices [76]. Universal vaccination of newborns with three doses of HBV vaccine, the first within 24 h of birth, was identified as the most feasible and cost-effective vaccination strategy and was incorporated into the EPI. In 2005, the Western Pacific region became the first to adopt the goal of reducing the prevalence of chronic HBV infection, as indicated by seroprevalence of hepatitis B surface antigen (HBsAg), to less than 2% in children at least 5 years of age by 2012 [63]. A time-bound supranational control goal was chosen to create a sense of political urgency for strengthening routine immunisation services and improving access to vaccines. Moreover, rather than relying on surveillance systems, the WHO encouraged national serologic surveys to be conducted to measure HBsAg prevalence in children since disease outcomes after infection are usually delayed by decades [77]. Also, a regional verification process was established to ensure standard and independent mechanisms for assessing achievement of HBV control targets, which is conducted by a WHO expert panel, takes approximately 3 months and is an efficient and low-cost approach to measuring impact [77]. Adopting the regional goal led to greater political commitment and reduced inequalities in HBV vaccination between and within countries, with major progress in providing timely birth doses [63].

The impact of discontinuing a specific vaccination strategy is illustrated by the experience in Japan with influenza vaccination [66]. In 1962, the Japanese government introduced a programme based on the theory that influenza epidemics could be reduced by vaccinating schoolchildren. It was abandoned in 1994 because of a lack of evidence that it had limited the spread of influenza in the community. However, comparison of influenza-related mortality in Japanese people aged 65 years or older during the vaccination programme with mortality after the programme was discontinued showed a 36% increase among Japanese seniors, corresponding to around 1,000 additional deaths annually [78]. There was also an increase in influenza-associated deaths among younger children following discontinuation of the schoolchild vaccination programme, with an estimated 783 excess deaths among children aged 1–4 years from 1990 to 2000 [79]. When the vaccination programme was in effect, Japanese schoolchildren therefore appear to have served as a barrier against the spread of influenza in the community.

The response to a pertussis (whooping cough) outbreak provides an example where different strategies to decrease disease transmission were evaluated. In England, pertussis-containing vaccines had been administered at 2–4 months of age since 1990 with

good coverage but in 2011, a national increase in pertussis cases was reported, initially in adolescents and adults but extending to young infants in 2012 [80]. Since infants are at particular high risk for pertussis-related complications and death [81], their protection was of high priority. Strategies to optimise control of pertussis in infants that were considered included vaccination of pregnant women, adolescents or close contacts ('cocooning') [80,82]. There was little evidence that an adolescent booster had an impact on infant pertussis. Cocooning can be very costly and resource-intensive to implement because of the need to vaccinate all individuals who have close contact with infants younger than 6 months, and acceptance of vaccination by all close contacts can be challenging [82]. There was however sufficient evidence of protection by maternal antibodies following vaccination in pregnancy [80]. Consequently, the UK Department of Health recommended a temporary maternal pertussis immunisation programme to minimise morbidity and prevent further infant deaths. An observational study of the programme showed high vaccine effectiveness, with a 78% fall in confirmed cases of pertussis in infants younger than 3 months and 68% fall in related hospital admissions [64]. This and other demonstrations of the effectiveness and safety of maternal vaccination against pertussis has led the Global Pertussis Initiative to recommend immunisation during pregnancy as the primary strategy to prevent pertussis in infants [82]. Moreover, a recent analysis of the temporary programme in England found that it was highly cost effective in 2012 and, compared with the existing paediatric vaccination programme, had the major benefit of offering direct protection of the highly vulnerable infant population [83]. Policymakers therefore decided in 2014 to keep maternal vaccination in place in the UK for at least another 5 years, with re-evaluation of its cost effectiveness in light of the future epidemiology of pertussis.

The impact of employing different strategies is demonstrated by the dramatically different approaches to HPV vaccination across high income countries, such as the USA versus the UK and Australia [25]. In the USA, most vaccines, including HPV vaccine, are delivered to individual patients in medical clinic settings. High vaccination rates are typically achieved through laws enacted in each state requiring receipt of certain vaccines for school entry but few states have school-entry requirements for HPV vaccination. As a result, HPV vaccination rates in the USA remain relatively low, with 2014 national data indicating that 40% of 13–17 year-old girls had completed the three-dose series [72]. In contrast, the UK and Australia have delivered HPV vaccines principally via school-located programmes, which allow for immunisation of large groups of youths over a relatively short span of time. In these countries, the three-dose completion rate for girls ranges from about 70–86%, much higher than rates in the USA [70,71]. Also, evidence from the hepatitis B school-located vaccination programme in the USA suggests that the cost of vaccinating via school can be significantly lower than immunising adolescents via a health maintenance Organization [84].

5. Importance of communication strategies

The communication strategy that accompanies an immunisation programme should encourage sustained support by healthcare policy makers and demand for the vaccine from healthcare workers and the public. Support from policy makers is encouraged via a communication and advocacy strategy that ensures the relevant evidence reaches stakeholders and decision-makers. An example is the communication strategy developed by the Sabin Vaccine Institute for the evidence base generated through PAHO's ProVac Initiative (see Box 3) [41].

Box 3

Guides for communication strategies targeted towards healthcare policy makers, the public, healthcare workers, community leaders and the media. Based on strategies developed by the Sabin Vaccine Institute for evidence generated through ProVac studies [41] and by the World Health Organization and PATH for the Meningitis Vaccine Project [85].

Target of communication strategies	Recommended approaches
Healthcare policy makers	<ul style="list-style-type: none"> Analyse the country's existing decision-making process for introducing new vaccines Identify stakeholders and their roles in the decision process Identify relevant evidence that should be used to properly inform the decision Address common questions about cost-effectiveness and its role in the decision-making on new vaccine introduction Create concise and effective technical presentations based on data from the economic analysis performed Construct key messages and provide supporting evidence to accompany the results of the economic analyses Draft policy briefs that include the national economic analysis and other relevant criteria for decision-making Draft technical reports, including more detailed information about the economic evaluation that was conducted
The public, healthcare workers, community leaders, the media	<ul style="list-style-type: none"> A culturally-appropriate approach Boost skills of healthcare teams in community dialogue and other interactive techniques Engage local and national media as well as social media, if appropriate Provide training in crisis communications Adapt strategy as appropriate, responding to evolving communication needs

To encourage acceptance of the new vaccine, communication strategies must be appropriate for the population to be vaccinated and developed on a local level. This was the aim of the Meningitis Vaccine Project (MVP) communication strategy in Africa [85]. Early in the project, a strategy was developed to engage the media, community leaders, populations to be targeted for vaccination (younger than 30 years) and healthcare professionals. The strategy was adapted as the project matured. For example, it became clear that many local journalists needed better scientific understanding of the project so regular media workshops and information updates were included in the communications plan. To address the challenge of convincing adolescents and young adults to take part in the vaccination campaigns, MVP employed peer education, targeted social mobilisation messages, participation of celebrities known by young people and launched vaccination campaigns in universities and schools. In other populations, community discussions with the aim of engaging tribal and administrative leaders improved outreach to desired targets. Training in crisis communications, including preparation of crisis management plans, was also an important component of the MVP strategy. The communication strategy proved to be key to the successful introduction of the meningococcal vaccine in Africa, due mainly to its early implementation, culturally-appropriate approach and emphasis on boosting the skills of healthcare teams in community dialogue.

It is important that communication strategies evolve over time, responding to any changes in vaccine coverage levels as well as populations' expectations and knowledge of immunisation services [85,86].

6. Conclusions

A well-functioning vaccination programme is a fundamental ingredient of successful public health interventions against infectious diseases. To optimise outcomes, an effective and efficient immunisation service requires careful planning, execution and monitoring. It is important to consider the viability of implementation strategies in terms of feasibility and cost of the proposed immunisation schedule, likely adherence to and acceptance of vaccination by the target population, the healthcare structure in place for vaccine delivery and compatibility with existing immunisation calendars. The capacity to make evidence-based vaccine policy decisions followed by the efficient introduction and management of immunisation programmes is also evaluated. Lack of appropriate infrastructure must be addressed in less developed countries, particularly for vaccines administered to age groups beyond early childhood.

Experience and research have shown which vaccine strategies work well and the factors that encourage success, which often include strong support from government and healthcare organisations, and tailored, culturally-appropriate approaches. There is no one-size-fits-all solution and vaccine strategies have to be adapted according to local conditions.

Contributorship

All authors were involved in the development of this manuscript and gave final approval before submission.

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KH, SK and SP are employees of the GSK group of companies, and report ownership of stock/restricted shares/shares in the GSK group of companies. PB has received grants and personal fees from Pfizer, and personal fees from GSK, Novartis, and Sanofi Pasteur MSD, unrelated to the present work. JIS reports no conflict of interest. MEI-H has received a speaking honorarium from the GSK group of companies, unrelated to the present work. GDZ is an investigator on investigator-initiated research funded by Merck and Roche.

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