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Overview of Vaccines and Global Vaccination Coverage

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Abstract

Worldwide, it has been estimated that immunisation programs prevent approximately 2.5 million deaths each year. An additional 1.5 million deaths could be avoided, however, if global vaccination coverage improves. Global vaccination coverage is generally holding steady. The Strategic Advisory Group of Experts on immunization identified 5 factors to achieving results in immunization coverage: quality and use of data, community involvement, better access to immunization services for marginalized and displaced populations, strong health systems, access to vaccines in all places at all times. Monitoring data at sub-national levels is critical to helping countries prioritize and tailor vaccination strategies and operational plans to address immunization gaps and reach every person with lifesaving vaccines. Countries are aiming to achieve vaccination coverage of at least 90% nationally and at least 80% in every district, introduction of one or more new or underutilized vaccines in all low-and middle-income countries, certification of polio eradication, measles and rubella eliminated in at least five World Health Organization regions by 2020.

By 2016, 130 countries had reached at least 90% coverage of third dose of Diphtheria-tetanus-pertussis vaccine. Haemophilus influenzae type b vaccine had been introduced in 191 countries and coverage with 3 doses of vaccine is estimated at 70%.Global coverage with 3 doses of hepatitis B vaccine is estimated at 84%.Human papillomavirus vaccine was introduced in 74 countries by the end of 2016.Of the children worldwide, 85% had received 1 dose of measles. Mumps vaccine had been introduced nationwide in 121 countries by the end of 2016.Pneumococcal vaccine had been introduced in 134 countries by the end of 2016, and global coverage was estimated at 42%. In 2016, 85% of infants around the world received 3 doses of polio vaccine. Rotavirus vaccine was introduced in 90 countries by the end of 2016, and global coverage was estimated at 25%. Rubella vaccine was introduced nationwide in 152 countries by the end of 2016 and global coverage was estimated at 47%.

Keywords: Vaccines; Vaccination coverage; Global

Abbreviations: SAGE: Strategic Advisory Group of Experts; GVAP: Global Vaccine Action Plan; UNCEF: United Nations Children's Fund; GNI: Gross National Income; EPI: Expanded Programme on Immunization; MNTE: Maternal Neonatal Tetanus Elimination; HPV: Human Papillomavirus; RCT: Randomized Controlled Trial; DTP:

Diphtheria Tetanus Pertussis; PCV: Pneumococcal Vaccine; MCV: Measles Containing Vaccine; IPV: Inactivated Polio Vaccine

Introduction

For more than 200 years, since Edward Jenner first demonstrated that vaccination offered protection against smallpox, the use of vaccines has continued to reduce the burden of many infectious diseases. Vaccination has been demonstrated to be one of the most effective and cost-effective public health interventions. Worldwide, it has been estimated that immunisation programs prevent approximately 2.5 million deaths each year [1]. An additional 1.5 million deaths could be avoided, however, if global vaccination coverage improves. An estimated 19.4 million infants worldwide are still missing out on basic vaccines [2].

Vaccination not only protects individuals, but also protects others in the community by increasing the overall level of immunity in the population and thus minimising the spread of infection [1]. The last week of April each year is marked by World Health Organization (WHO) and partners as World Immunization Week. It aims to accelerate action to increase awareness and demand for immunization and improve vaccination delivery services so that people everywhere can be protected against deadly diseases [2].

New knowledge about the functioning of the immune system and host pathogen interactions has stimulated the rational design of vaccines. The design toolbox includes vaccines made from whole pathogens, protein subunits, polysaccharides, pathogen-like particles, use of viral/bacterial vectors, plus adjuvants and conjugation technology to increase and broaden the immune response. Processes such as recombinant DNA technology can simplify the complexity of manufacturing and facilitate consistent production of large quantities of antigen. Any new vaccine development is greatly enhanced by, and requires integration of information concerning: knowledge of pathogen structure, route of entry, interaction with cellular receptors, subsequent replication sites and disease-causing mechanisms are all important to identify antigens suitable for disease prevention. The demographics of infection, specific risk groups and age-specific infection rates determine which population to immunise, and at what age. The candidate vaccine must be tested for immunogenicity, safety and efficacy in preclinical and appropriately designed clinical trials [3].

Vaccination Coverage

Global vaccination coverage is generally holding steady. Uptake of new and underused vaccines is increasing. The Strategic Advisory Group of Experts on immunization (SAGE) identified 5 factors to achieving results in immunization coverage: quality and use of data, community involvement, better access to immunization services for marginalized and displaced populations, strong health systems, access to vaccines in all places at all times. Monitoring data at sub-national levels is critical to helping countries prioritize and tailor vaccination strategies and operational plans to address immunization gaps and reach every person with lifesaving vaccines. Around 60% of children who were not reached with routine immunization services live in 10 countries: Angola, Brazil, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Iraq, Nigeria, Pakistan and South Africa [2].

The Global Vaccine Action Plan (GVAP) is a roadmap to prevent millions of deaths through more equitable access to vaccines by 2020. Countries are aiming to achieve vaccination coverage of at least 90% nationally and at least 80% in every district, introduction of one or more new or underutilized vaccines in all low- and middle-income countries, certification of polio eradication, measles and rubella eliminated in at least five WHO regions by 2020 [4]. In April 2016, WHO warned that 5 out of the 6 GVAP targets were off-track, with only 1 target on the introduction of underutilized vaccines showing sufficient progress. The GVAP recommends 3 key steps for closing the immunization gap: integrating immunization with other health services, such as postnatal care for mothers and babies; strengthening health systems so that vaccines continue to be given even in times of crisis; and ensuring that everyone can access vaccines and afford to pay for them [2]. According to African Regional report on progress towards GVAP goals; routine immunization coverage has increased considerably across Africa–average diphtheria-tetanus-pertussis (DTP3) coverage increased from 57% in 2000 to 80% in 2014. Cases of many vaccine-preventable diseases, such as measles and meningitis, have fallen in many African countries. However, in recent years, attempts to increase immunization coverage on the continent have slowed. Additional commitments are needed to increase coverage to levels high enough to interrupt transmission of diseases and introduce new vaccines into country immunization systems [4].

Based on 2015 WHO and United Nations Children's Fund (UNICEF) estimates, coverage varied widely by

WHO Region, country, and district; in addition, for the vaccines evaluated (MCV, DTP3, Pol3, HepB3, Hib3), wide disparities were found in coverage by country income classification(HepB3 = 3 doses of hepatitis B vaccine; Hib3 = 3 doses of Haemophilus influenzae type b vaccine; MCV1 = first dose of measles-containing vaccine (MCV); MCV2 = second dose of MCV; Pol3 = 3 doses of polio vaccine). Improvements in equity of access are necessary to reach and sustain higher coverage and increase protection from vaccine-preventable diseases for all persons. WHO and UNICEF derive national coverage estimates through an annual country-by-country review of all available data, including administrative and survey-based reviews. To analyze equity of vaccination coverage, countries were categorized by World Bank income classification (low, lower-middle, upper-middle, high) [5].

Gavi is an international organization that was created in 2000 to improve access to new and underused vaccines for children living in the world's poorest countries when global immunisation efforts were beginning to plateau [5]. Eligibility for Gavi support is typically based on a country's Gross National Income (GNI) per capita; the threshold for support started at US$1,000 per capita in 2000 and increased to US$1,580 by 2016 [6]. Despite the promising progress of the previous two decades, by the Expanded Programme on Immunization (EPI), there were still 30 million children living in poor countries who were not fully immunised. Coverage was stagnating and in some places even declining. And even though new life-saving vaccines were becoming available, beyond the original six EPI vaccines, virtually none were reaching children in developing countries, those who needed them most, because they were too expensive [5]. 54 countries are eligible to apply for Gavi support in 2016 based on a Gross National Income (GNI) [7].

Diphtheria-Tetanus-Pertussis

By 2016, 130 countries had reached at least 90% coverage of DTP3 vaccine. DTP1 to DTP3 dropout rates (the proportion of children who received DTP1 but did not receive DTP3) ranged from 0% to 61% [2]. DTP3 coverage by age 12 months is an indicator of immunization program performance and, is commonly used to measure the strength and reach of routine immunization programs [2,4].

Routine use of whole-cell pertussis vaccines was suspended in some countries in the 1970s and 1980s because of concerns about adverse effects. Following this action, there was a resurgence of whooping cough. Multi-component cellular vaccines are more effective than low-efficacy whole-cell vaccines, but may be less effective than the highest-efficacy whole-cell vaccines [8].

Tetanus Elimination: In 1989, the 42nd World Health Assembly called for the elimination of neonatal tetanus by 1995. The following year, the 1990 World Summit for Children listed neonatal tetanus elimination as one of its goals, and the goal was again endorsed by the 44th World Health Assembly in 1991 [9].

Tetanus vaccine to prevent maternal and neonatal tetanus had been introduced in 106 countries by the end of 2016. An estimated 84% of newborns were protected through immunization [2]. The world has made substantial progress toward maternal neonatal tetanus elimination (MNTE), defined as less than one case per 1,000 live births in every district [4]. While progress continues to be made, by en of 2016, 16 countries have still not reached the MNTE status, mainly in Africa and Asia [2,9]. Activities to achieve the goal are on-going in these countries, with many likely to achieve MNTE in the near future [9].

Haemophilus Influenzae Type B

Haemophilus influenzae type b (Hib) is a bacterium that can cause severe diseases such as pneumonia and meningitis among children [4]. Hib vaccine had been introduced in 191 countries by the end of 2016. Global coverage with 3 doses of Hib vaccine is estimated at 70%. In the WHO Region of the Americas, coverage is estimated at 90%, while it is only 28% in the WHO Western Pacific Region. The WHO South-East Asia Region raised coverage from 56% in 2015 to 80% in 2016 [2].

Hepatitis B

Hepatitis B vaccine for infants had been introduced nationwide in 186 countries by the end of 2016. Global coverage with 3 doses of hepatitis B vaccine is estimated at 84% and is as high as 92% in the Western Pacific. In addition, 101 countries introduced one dose of hepatitis B vaccine to newborns within the first 24 hours of life, and the global coverage is 39% [2].

Human Papillomavirus

Human papillomavirus vaccine was introduced in 74 countries by the end of 2016 [2]. Because of poor access to screening and treatment services, cervical cancer is a leading cause of cancer death among women in developing countries. However, high prices and delivery

challenges have been barriers to widespread routine use of HPV vaccines in many countries [4].

Since 2006, three vaccines against infections and disease caused by human papillomavirus (HPV) became available in Europe-in 2006a quadrivalent HPV 6/11/16/18 vaccine, in 2007 a bivalent HPV 16/18 vaccine and in 2015 a nonavalent HPV 6/11/16/18/31/33/45/52/58 vaccine. HPV 16 and 18 are the most oncogenic HPV strains, HPV 6 and 11 cause 85% of all genital warts [10]. The Advisory Committee on Immunization Practices recommends routine HPV vaccination starting at age 11 or 12 years, though the series can be started as early as 9 years of age. Vaccination is also recommended for females ages 13 through 26 years and for males ages 13 through 21 years who have not completed the three-dose series. Men up to age 26 should also be vaccinated if they have sex with men or are immunocompromised. According to data from the 2014 National Immunization Survey, only 39.7 % of girls ages 13-17 in the United States had completed the recommended three-dose HPV vaccination series; 60 % had received at least one dose. A new 9-valent HPV vaccine (9vHPV) was approved by the FDA in December 2014 for females ages 9-26 and males ages 9-15 [11].

According to studies examining efficacy and/or immunogenicity of 9vHPV; it was shown to have potential benefits as compared with 4vHPV, increasing the overall estimated rate of prevention to 90% for cervical cancer and up to 80% for precancerous cervical lesions with seroconversion rates close to 100.The 9vHPV vaccine shows clinical potential for the prevention of HPV-related diseases in both sexes [12,13]. According to a study by Pimenta and et al. the vaccines against human papillomavirus 16 and/or 18 in women older than 24 until 45 years have an important efficacy at reducing the risk of having persistent infection and/or to acquire cervix cancer precursor lesions. The relative risk reduction was 41% (95% CI: 29-50%) for the vaccinated group [14].

Measles

Because measles is a highly infectious virus, its control requires more than 95% coverage with two doses of MCV in all districts, administered through routine immunization or supplemental immunization activities [3]. Under the GVAP, measles and rubella are targeted for elimination in five WHO Regions by 2020 [15]. By the end of 2016, 85% of children had received 1 dose of measles vaccine by their second birthday, and 164 countries had included a second dose as part of routine immunization and 64% of children received 2 doses of measles vaccine according to national immunization schedules [2]. Despite the WHO's recommendation for a two-dose schedule, less than half (48%) of African countries have integrated MCV2 into their routine immunization programmes. In 2014 coverage of MCV1 and MCV2 in Africa were 75% and 19% respectively [4].

Meningitis A

By the end of 2016 –6 years after its introduction – more than 260 million people in African countries affected by the Meningitis A disease had been vaccinated with MenAfriVac, a vaccine developed by WHO and PATH (An international nonprofit organization, for saving lives and improving health, especially among women and children). Ghana and Sudan were the first two countries to include the MenAfriVac in their routine immunization schedule in 2016 [2].

According to a study that 8 randomized controlled trials (RCTs) were included; the protective effect of polysaccharide vaccines for preventing serogroup A meningococcal meningitis in the first year was consistent across RCTs- summary vaccine efficacy 95% (95% CI 87% to 99%). Protection extended to the second and third year after vaccination but the results did not attain statistical significance [16].

Mumps

Mumps vaccine had been introduced nationwide in 121 countries by the end of 2016 [2].

Pneumococcal Diseases

Pneumococcal vaccine (PCV) had been introduced in 134 countries by the end of 2016, and global coverage was estimated at 42% [2]. Diseases caused by Streptococcus pneumoniae continue to cause substantial morbidity and mortality globally [17]. PCV is effective in preventing invasive pneumococcal disease, X-ray defined pneumonia, and clinical pneumonia among HIV-1 negative and HIV-1 positive children under two years. An 11% reduction with a 95% CI of -1% to 21% and a P = 0.08 is compatible with reduction in all-cause mortality [17]. According to a meta-analysis by Moberley, et al. evidence supporting the recommendation for PPV to prevent IPD in adults is provided. The meta-analysis does not provide evidence to support the routine use of PPV to prevent all-cause pneumonia or mortality [18]. However, on the contrary, a review by Sheikh and et al. found very

limited evidence to support the routine use of pneumococcal vaccine in people with asthma [19].

Polio

In 2016, 85% of infants around the world received 3 doses of polio vaccine. Targeted for global eradication, polio has been stopped in all countries except for Afghanistan, Pakistan and Nigeria. Polio-free countries have been infected by imported virus, and all countries – especially those experiencing conflict and instability – remain at risk until polio is fully eradicated [2]. The world is on the brink of eradicating polio; however, several challenges remain, including conducting high quality immunization campaigns, improving routine immunization, introducing the inactivated polio vaccine (IPV), and addressing security challenges to reach every child. Africa has been free of wild polio since 11 August 2014, when the last case of wild poliovirus type 1 (WPV1) was identified in Somalia. However, major threats to the eradication of polio still exist in Africa. For instance, there is the risk of reintroduction of the virus if routine immunization coverage with three doses of polio vaccine-currently 79% across Africa–is not increased and sustained [4]. Other diseases targeted for elimination in the GVAP, including measles and neonatal tetanus, persist in Africa and efforts are needed to increase coverage for vaccines against them.

Rotaviruses

Rotavirus vaccine was introduced in 90 countries by the end of 2016, and global coverage was estimated at 25% [2]. Unlike other causes of diarrhea, it cannot be prevented with improvements in water and sanitation alone and cannot be treated with antibiotics. Rotavirus vaccines are now considered one of the most cost-effective interventions for preventing diarrheal death and disease [4]. Since 2009, the World Health Organization (WHO) has recommended that a rotavirus vaccine be included in all national immunization programmes. Currently licensed rotavirus vaccines include a monovalent rotavirus vaccine and a pentavalent rotavirus vaccine. Lanzhou lamb rotavirus vaccine is used in China only. According to a review by Weiser and et al. RV1 and RV5 prevent episodes of rotavirus diarrhoea. The vaccine efficacy is lower in high-mortality countries; however, due to the higher burden of disease, the absolute benefit is higher in these settings. Efficacy percentages are higher among children aged less than one year compared to children aged up to two years [20].

Rubella

Rubella is a contagious, generally mild viral infection that occurs most often in children and young adults. Rubella infection in pregnant women may cause fetal death or congenital defects known as congenital rubella syndrome. Worldwide, over 100 000 babies are born with this syndrome every year. There is no specific treatment for rubella but the disease is preventable by vaccination [21]. Rubella vaccine was introduced nationwide in 152 countries by the end of 2016 and global coverage was estimated at 47% [2].

Yellow Fever

Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes. Large epidemics of yellow fever occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination [22]. As of 2016, yellow fever vaccine had been introduced in routine infant immunization programmes in 35 of the 42 countries and territories at risk for yellow fever in Africa and the Americas. In these 42 countries and territories, coverage is estimated at 45% [2]. No outbreaks of yellow fever were reported in West Africa during 2015 [22].

Conclusion

While the introduction of new vaccines has been promising in recent years, efforts for routine immunization coverage should be increased, particularly among those most at risk of diseases. Wishing to save thousands of lives with the discovery of new vaccines without profit-oriented intent.

Conflict of interest: None

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