





# Investing in immunisation through the GAVI Alliance

The evidence base

# The GAVI Alliance mission:

To save children's lives and protect people's health by increasing access to immunisation in poor countries

Every year, millions of children in poor countries die from preventable diseases because they do not have access to life-saving vaccines. There are many reasons for this, including existing vaccines being too expensive or not optimal for developing country use. Vaccine development and production have high fixed costs, and manufacturers have historically not seen value in investing in new products for developing country needs.

The Global Alliance for Vaccines and Immunisation (GAVI) was launched in 2000 with a bold ambition to save children's lives and protect people's health by increasing access to immunisation in the world's poorest countries.

The Alliance has achieved extraordinary success by bringing together the specialist skills and credentials of all the key stakeholders in immunisation, including the World Health Organization (WHO), UNICEF and the World Bank, and by being country-led.

By raising significant additional new resources for immunisation and focusing on the world's poorest countries, GAVI has changed the way vaccine manufacturers view developing world markets. By pooling demand from over 70 developing countries – representing more than 70 million surviving infants (over half of the world's annual birth cohort)<sup>1</sup> – and using UNICEF's global procurement system, the Alliance has helped to change the global vaccine market dynamic.

New manufacturers, including those based in emerging market economies, are entering the market. Vaccine products are becoming more appropriate to developing country needs, and increased competition has helped to put downward pressure on prices.

GAVI's market-shaping approach is underpinned by a unique public-private partnership model. Drawing on the particular strengths of each sector makes for a fertile environment for innovation. GAVI has demonstrated new ways of approaching development financing and programming.

Globally, immunisation rates are climbing, and more children are being immunised: 107 million children were vaccinated with basic childhood vaccines in 2011.<sup>2</sup> According to the WHO report, *State of the World's Vaccine and Immunization*, the reversal of what a decade ago was a downward global trend is attributable to the efforts of developing countries, making good use of support provided by GAVI and its partners.

This paper brings together the evidence around the rationale for GAVI's mission, the achievements to date and the potential for the future. It draws on available published data and analyses in the belief that policy and financing decisions should be rooted firmly in evidence.

As new evidence becomes available, it will be included. Feedback and advice are welcome. There are gaps in knowledge, which researchers and scientists are encouraged to help fill. However, there is already substantial evidence to assert that the power of vaccines as a cost-effective public health intervention in poor countries, and the development approach of the Alliance, are worthy of increased investment.

In simple terms, countries have averted more than 5.5 million future deaths with support from GAVI. Based on rigorous country demand projections, there is the potential to immunise an additional 245 million children between 2011 and 2015, thus saving approximately 4 million lives. But as evidence gathered in this report demonstrates, the impact extends beyond numbers of lives saved. Ensuring good health is a critical ingredient in the fight against poverty.

None of these results could have been achieved without the commitment of all of the partners in the GAVI Alliance. WHO's expert recommendations on appropriate vaccine use and its rigorous appraisal of new vaccine products, the World Bank's strategic advice on capital market dynamics that has helped to raise billions of dollars in new finance, and UNICEF's wide presence in developing countries and global vaccine procurement facility are all examples of the Alliance in action. Civil society helps to ensure that vaccines are delivered to the children who need them the most, and the vaccine industry has the research and production capacity to provide appropriate vaccines for developing countries. The generosity of donor governments, the Bill & Melinda Gates Foundation and other philanthropists has made this success possible. But most importantly, it is the commitment of developing countries themselves that ensures that every day hundreds of thousands of infants are reached and their health is protected by powerful new vaccines.

In many countries, expanding immunisation services has been the backbone for extending the reach of other critical public health interventions, such as maternal and child health programmes. This is GAVI's vision: to remain focused on the extraordinary power of vaccines but also, critically, to ensure that support is provided in a way that empowers national health systems to deliver comprehensive and appropriate services to those who need them most – the women and children of the developing world.

# **Executive summary**

#### Investing in health and immunisation

Investment in public health is a necessary building block for socioeconomic development. Death, illness and disability from often preventable, communicable diseases create some of the major inequities in health outcomes between poor countries and the rest of the world. Immunisation can help address this inequity. Governments all over the world implement immunisation programmes as a key strategy to **control disease**. The impact of vaccination is amplified through so-called herd immunity effects, which spread protection across the population and prevent disease even in non-vaccinated individuals. Immunisation also brings important longterm, broad economic benefits, including increased educational attainment and productivity gains, as vaccination reduces the time parents need to spend taking care of a sick child. While there is a strong **moral imperative** to increase access to global public goods such as life-saving vaccines, there is also an important value for money argument. The cost of vaccines is low relative to the overall public health impact achieved, and the investment can save costs through reductions in clinical visits, hospitalisations and permanent disability. While new vaccines are more expensive than traditional vaccines, all GAVI-supported vaccines are cost-effective according to standard classifications when compared with many other interventions.

#### Need and demand for immunisation support

GAVI programmes support the world's poorest countries: those with a Gross National Income (GNI) per capita of less than US\$ 1,520 per year. Globally, GAVI-eligible countries suffer the highest burden of vaccine-preventable diseases. Governments are aware of the potential of immunisation to prevent these diseases and their commitment to address this problem has translated into **strong demand** for GAVI support. With **immunisation coverage rates around 80%** in many of the poorest countries, few other public health programmes have the capacity to reach more children. Where coverage rates are high, the immunisation delivery system is **a strong platform** for the rapid introduction of prioritised new vaccines and other maternal and child health interventions.

#### GAVI Alliance – results and efficiency

In its first decade, the GAVI Alliance has achieved remarkable results. Significant **new resources** for immunisation have been mobilised. The delay that has historically characterised new vaccine introduction in low-versus high-income countries is being reduced. **Hepatitis B vaccine is now used in** the routine immunisation programmes of virtually all of the world's poorest countries and the **use of Hib vaccine is increasing rapidly**. Within the next few years, many developing countries will have introduced **new vaccines against pneumococcal disease and rotavirus diarrhoea**. These interventions are having a visible impact on disease prevalence and have resulted in impressive reductions in vaccine-preventable mortality. Across all GAVI-supported countries, more than 5.5 million future deaths have been prevented. Through health system strengthening support, the Alliance is building the workforce and improving peripheral healthcare facilities, helping countries to break through bottlenecks in immunisation and the delivery of other health services. The growth in predictable demand from low-income countries, together with new funds mobilised for immunisation, has created the sustainable market required to attract new manufacturers, stimulate competition and lower vaccine prices over time.

#### **GAVI Alliance – innovation**

Promoting innovation is a core GAVI value. As a new **public-private partnership**, the Alliance has played a catalytic role in instigating new approaches directly within its core operations, and more broadly in development financing and programming. **New models of innovative financing** have been pioneered, attracting donor commitments of approximately **US\$ 8 billion** and engaging new private sector partners.

### The potential impact of new vaccines

For the first time, low-income countries are introducing new vaccines at virtually the same time as high-income countries. The Alliance aims to help countries immunise an additional 245 million children between 2011 and 2015, thus preventing approximately 4 million future deaths. This is almost twice the impact made in GAVI's first decade, and will make a significant contribution to reaching the Millennium Development Goals.

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# 1 Investing in health and immunisation

This section starts with a brief review of the connection between good health and economic and social development, and the continuing inequity in health between low- and high-income countries. It then focuses on the particular value of vaccines in protecting health and presents evidence of their cost-effectiveness.

# 1.1. Why invest in health?

The burden of disease in low-income countries is a stark barrier to poverty reduction and long-term economic growth. The importance of health for development is clearly reflected in the Millennium Development Goals: three out of the eight goals are directly related to improving health. The Commission for Macroeconomics and Health<sup>a</sup>, established in 2000 by then WHO Director-General Dr Gro Harlem Brundtland, confirmed that "improving the health... of the poor is an end in itself, a fundamental goal of economic development. But it is also a *means* to achieving the other development goals relating to poverty reduction."<sup>3</sup>

Good health leads to social and economic development, enabling people to reach their full potential as active and productive members of society. It also encourages investment in human capital as investors shun environments in which the labour force suffers a heavy disease burden and where they may themselves be at risk.<sup>4</sup>

The relationship between health and wealth is bidirectional. To some extent wealth can buy health; similarly, poor health is costly. In low-income countries large "out-of-pocket" expenditures for healthcare can have catastrophic effects and drive people further into poverty.<sup>5</sup>

"...health of a population has been identified as one of the most robust drivers of economic growth – among such well-established influences as the initial income per capita, geographic location, and institutional and economic policy environment."

Copenhagen Consensus Challenge Paper: Disease Control<sup>6</sup>

a. The Commission on Macroeconomics and Health (CMH) was made up of 18 of the world's leading economists, public health experts, development professionals and policy-makers under the Chairmanship of Professor Jeffrey Sachs, then Director of the Center for International Development at Harvard University.

# 1.2. Global health inequity

# **Burden of disease**

The global burden of communicable diseases in particular is spread unequally between high- and low-income countries.<sup>b</sup> Table 1 compares death rates for a number of diseases in these income groups. For example, a child in a low-income country is 171 times more likely to die from rotavirus diarrhoea than a child in a high-income country.

## Table 1: Inequitable burden of communicable diseases (2008)

Disease	Average death rate per 100,000		LIC/ HIC	
	Low-income countries <sup>b</sup>	High-income countries <sup>•</sup>	ratio	
<b>1. Hib disease</b> (in children under 5) <sup>7</sup>	71	0.3	237	
<b>2. HIV/AIDS</b> (in children under 5) <sup>8</sup>	90	0.4	225	
<b>3. Rotavirus disease</b> (in children under 5) <sup>9</sup>	171	1	171	
<b>4. Pneumococcal disease</b> (in children under 5) <sup>10</sup>	202	3	67	
5. Tuberculosis (all ages) <sup>11</sup>	37	1	37	

# Life expectancy

Life expectancy in low-income countries lags far behind; on average, life is 23 years shorter compared to high-income countries. Although life-expectancy has increased in all income groups, the 23-year gap between poor and rich countries has been constant since 1990. The gap between Africa and all other regions has widened; an individual born in the Americas today lives almost a quarter century longer on average than an individual born in Africa,<sup>12</sup> in part reflecting the significant impact of HIV on the continent.<sup>13</sup>

# **Child mortality**

The UNICEF 2012 Progress Report, *Committing to Child Survival: A Promise Renewed*, reported 6.9 million annual deaths in children under the age of five, more than 80% of which were in sub-Saharan Africa and South Asia.<sup>14</sup> A child in a low-income country is approximately 18 times more likely to die before reaching the age of 5 compared to a child in a high-income country<sup>15</sup> (see Table 2 for countries with highest and lowest child mortality rates).

#### Table 2: Highest and lowest child mortality rates

Countries with highest under 5 mortality rates (2010)		Countries with lowest under 5 mortality rates (2010)	
Country	Deaths per 1,000 live births	Country	Deaths per 1,000 live births
1. Somalia	180	1. Iceland	2
2. Mali	178	2. Finland	3
3. Burkina Faso	176	3. Japan	3
4. Sierra Leone	174	4. Luxembourg	3
5. Chad	173	5. Norway	3

Source: UNICEF, The State of the World's Children 2012.<sup>16</sup> Note: Only countries with a population greater than 100,000 have been included.

Newborn or neonatal deaths – occurring in the first 28 days of life – account for over one third of all deaths in children under 5 years in low-income countries. Causes include prematurity and low birth-weight, infections (including pneumonia and diarrhoea), asphyxia (lack of oxygen at birth) and birth trauma.<sup>17</sup> After the first month of life, the leading killers of children are pneumonia and diarrhoea (see Figure 1).

b. Income groups: World Bank, 2011 GNI per capita

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Figure 1: Causes of under-5 child deaths in low-income countries



Source: The Child Health Epidemiology Reference Group (CHERG) of WHO and UNICEF 2012<sup>18</sup>

**Pneumonia**, or severe infection of the lungs, is the leading cause of child mortality. It kills an estimated 1.4 million children under 5 each year across the world, representing 1 in 5 child deaths.<sup>19</sup> The disease is characterised by high fevers, coughing and fast or difficult breathing. The **pneumococcal** bacterium is the main cause of serious pneumonia. *Haemophilus influenzae* type b (Hib) is another common cause. Both diseases are preventable with currently available vaccines.

The second most important cause of post-neonatal deaths in children is severe **diarrhoea**, or severe gastroenteritis. The most common cause of severe diarrhoea in both high- and low-income countries is **rotavirus**.

"The availability of new vaccines against pneumococcal disease and rotavirus is expected to have a rapid and major impact in global efforts to reduce child deaths (MDG 4), prevent sickness, and, for pneumococcal disease, prevent disability. At the same time, vaccination against these diseases provides a key opportunity to actively promote the prevention and treatment of pneumonia and diarrhoea, which together account for over one third of all deaths among children under five years old."

State of the World's Vaccines and Immunization<sup>20</sup>

# **Health spending**

Spending on health reflects a striking imbalance between high- and low-income countries (as shown in Table 3). High-income countries spend almost US\$ 4,700 per capita on health compared to US\$ 25 in low-income countries. Half of health spending in low-income countries is classified as "out-of-pocket", meaning that people pay directly for healthcare. When illness strikes, it can be financially catastrophic for the individual or the household.

In 2001, African countries pledged to set a target of allocating at least 15% of their respective annual budgets to the improvement of the health sector.<sup>21</sup> Spending on health in African countries rose from 8.6% of the national budget in 2001 to 9.4% in 2009.

#### Table 3: Average per capita health spending (2009)

Expenditure category	High-income countries	Low-income countries
Total health expenditure	US\$ 4,692	US\$ 25
Government health expenditure	US\$ 2,946	US\$ 10
Out of pocket health expenditure	US\$ 646	US\$ 12
Government health expenditures as a percentage of total government expenditure	17%	9%

Source: WHO, World Health Statistics. 2012<sup>22</sup>

# Immunisation inequity

WHO recommends the routine use of vaccines against the following diseases.<sup>23</sup>

High-risk populations:

Meningococcus

For immunisation programmes

with certain characteristics (eq

coverage rates >80%):

Typhoid

Cholera

Mumps

Influenza

Hepatitis A

Global:

- Tuberculosis (BCG)<sup>c</sup>
- Hepatitis B
- Polio
- Diphtheria, tetanus, pertussis (DTP)
- Haemophilus influenzae type b (Hib)
   Rabies
- Pneumococcal disease
- Rotavirus diarrhoea
- Measles
- Rubella
- Human papillomavirus (HPV)<sup>d</sup>

#### Specific regions:

- Japanese encephalitis
- Yellow fever
- Tick-borne encephalitis

c. Bacille Calmette–Guérin; recommended for children living in countries with a high-disease burden and for high-risk children living in countries with low-disease burden.

d. The primary target population is females before the onset of sexual activity.

Most high-income countries have rapidly made new vaccines part of their national routine immunisation programmes in line with WHO recommendations (see box). In low-income countries, vaccine introduction has been significantly delayed. For decades, most children in poor countries only had access to six vaccine antigens<sup>e</sup>: DTP, BCG, measles and polio. In recent years, with the support of the GAVI Alliance, low-income countries have begun to fill some of the critical gaps in their immunisation schedules. Nevertheless, millions of children still lack access to essential life-saving vaccines (see Figure 2). Lack of access remains particularly profound for newer vaccines, such as those protecting against pneumococcal and rotavirus disease.

#### Figure 2: Surviving infants vaccinated (2011)



Sources: WHO/UNICEF; UN DESA, Population Division<sup>24</sup>

Of the 2011 global cohort of 130 million surviving newborn children:

- 34 million children (26%) were not immunised with hepatitis B vaccines
- 74 million children (57%) were not immunised with Hib vaccines<sup>f</sup>
- 116 million children (89%) were not immunised with pneumococcal conjugate vaccines
- 118 million children (91%) were not immunised with rotavirus vaccines

e. An antigen (from antibody generator) is a substance that stimulates an immune response in the body.

f. Hib vaccine introduction has recently been accelerated in low-income countries, and coverage is expected to increase quickly.

# 1.3. The value of vaccination

#### Vaccine successes

Vaccines are powerful tools that help control disease. Unlike many other health interventions, they help people *stay* healthy, and in doing so they help to remove a major obstacle to human development.<sup>25</sup> Today, more than 30 common infectious diseases are preventable with vaccines.<sup>26</sup>

In addition to their impact on mortality, vaccines contribute significantly to the reduction of illness and long-term disability in children and adults, and generate savings by reducing clinic visits and hospitalisation.<sup>27</sup> Importantly, vaccines can also protect vulnerable (eg HIV-positive) people in poor health from further deterioration or secondary disease.

A global effort to extend vaccination coverage to all children began in 1974, when WHO founded the Expanded Program on Immunization (EPI). This initiative helped countries establish the infrastructure needed to deliver a package of recommended vaccines, which at the time included six vaccine antigens against tuberculosis, diphtheria, tetanus, pertussis, measles and polio.<sup>28</sup> Today, all countries have national immunisation programmes and in most developing countries children are immunised with at least these vaccines. By 2001, vaccination against these diseases was averting 61% of measles deaths, 69% of tetanus deaths, 78% of pertussis deaths, 94% of diphtheria deaths, and 98% of polio deaths that would otherwise have occurred.<sup>29</sup>

The impact of vaccines on global public health has been impressive. Smallpox was declared eradicated by WHO in 1979, after a global vaccination effort. In 1988, polio was endemic in 125 countries, paralysing an estimated 350,000 children every year. In 2012, the poliovirus remained endemic only in parts of three countries – the smallest geographic area in history<sup>9</sup>.<sup>30</sup> Measles is another success story: between 1990 and 2008, estimated measles-related mortality among children under 5 decreased by 86%.<sup>31</sup>

Since the launch of GAVI in 2000, an increasing number of developing countries have introduced hepatitis B, Hib, pneumococcal and rotavirus vaccines into their routine vaccination programmes, in line with WHO recommendations. Together, the original EPI vaccines plus hepatitis B and Hib vaccines are preventing more than 2.5 million future deaths each year.<sup>32</sup>

# Herd immunity

An increasing body of evidence demonstrates that for many vaccines there are important immunological benefits that extend beyond the immunised individual. The phenomenon whereby protection spreads to those not vaccinated is called herd immunity.

The effect has been demonstrated powerfully in relation to the use of hepatitis A vaccines in Israel<sup>33</sup> and the United States of America (USA)<sup>34</sup> and for typhoid vaccine in Chile.<sup>35</sup> In the Gambia, vaccination with Hib vaccines led to substantial indirect effects on the non-vaccinated population, including adults, probably because carriage of the bacteria by children was significantly reduced.<sup>36</sup>

More recently, herd immunity effects have also been observed following the introduction of newer vaccines such as pneumococcal and rotavirus vaccines.

The introduction of pneumococcal vaccines in the USA has had a dramatic impact on the incidence of the disease, which greatly exceeded what was expected based on the coverage in the population. Within a year after the vaccine was introduced, disease rates fell sharply in both vaccinated children *and* nonvaccinated adults.<sup>37</sup> Reduced colonisation in the nasal passages and membranes in vaccinated children reduces the transmission of pneumococcal bacteria to (nonvaccinated) adults and elderly people, thereby reducing disease in these groups. Four years after the introduction of pneumococcal vaccines in the USA, there was an estimated drop of approximately 70% in invasive pneumococcal disease in *non*-vaccinated children (which is nearly the same as the average *direct* effect of the vaccine in that cohort). This had a profound effect on the estimated costeffectiveness of the vaccine. After incorporating the reduction in disease burden for non-vaccinated individuals, the cost was estimated to be US\$ 5,500 per case averted (down from US\$ 33,000) and US\$ 7,500 per life-year saved (down from US\$ 112,000).<sup>38</sup> <sup>39</sup>

Similar herd immunity effects have been observed following the introduction of rotavirus vaccines. In many countries, declines in rotavirus disease have been greater than expected based on estimated vaccine coverage. The reduction in rotavirus disease in the USA exceeded 60–70 % a few years after the vaccine was introduced, despite the fact that only one third of children under the age of 2 were immunised.<sup>40</sup> In Sao Paolo, Brazil, there was a 29% reduction in rotavirus hospitalisations in children between 3 and 5 years, an age group too old to be vaccinated.<sup>41</sup> Similarly, in El Salvador there was a 65% decline in rotavirus hospitalisations in 2-year-olds who were not vaccinated.<sup>42</sup>

g. Afghanistan, Nigeria and Pakistan

## Societal and longer-term benefits

While immunisation brings direct health benefits in terms of reduced mortality and morbidity, there are also important long-term individual- and population-level gains.<sup>43</sup> Health economists have argued that the benefits of vaccination include:<sup>44</sup>

- Health gains (reduction in morbidity and mortality)
- Healthcare cost savings (savings of medical expenditures because vaccination prevents illness episodes)
- Care-related productivity gains (increased parental productivity by decreasing the need for taking care of a sick child)
- Outcome-related productivity gains (increased productivity because vaccination improves cognition, physical strength and educational attainment)
- Behaviour-related productivity gains (benefits accruing because vaccination improves child health and survival and thereby changes household behaviour)
- Community externalities (benefits accruing due to herd immunity in unvaccinated community members)

According to a Lives Saved Tool analysis developed by Johns Hopkins Bloomberg School of Public Health, WHO and the Futures Institute, scaling up the delivery of five life-saving vaccines and introducing malaria vaccine in 72 of the world's poorest countries would lead to substantial treatment savings and productivity gains – saving 6.4 million lives and averting 426.4 million cases of illness, resulting in savings of US\$ 6.2 billion in treatment costs and preventing US\$ 145 billion in productivity losses.<sup>45</sup>

Researchers have warned that a narrow cost-benefit analysis perspective can lead to an underestimation of the benefits of vaccination and to an overestimation of its costs, resulting in inappropriate decisions on vaccine adoption.<sup>46</sup> Taking into account the broader benefits of immunisation, Harvard University scientists calculated the expected return on investment of GAVI's programme to expand coverage of new and underused vaccines. In 2005, they estimated a return on investment of 18% by 2020, higher than most other health interventions, and similar to primary education.<sup>47</sup>

# Immunisation and women

Vaccination of children impacts on the lives of women in developing countries as they are often the principal providers of care to children. Preventing illness in children through vaccination liberates the mother's time, energy and resources and has the indirect benefit of increasing her productivity.<sup>48</sup>

In many societies, women are the primary point of contact between the family and the health system. Taking her child to be immunised presents an opportunity to address women's health as it brings the mother herself into contact with health providers.

There is some evidence that child survival has the long-term effect of lowering birth rates.<sup>49</sup> The explanation would be that when child mortality rates are high, couples choose to have more children in order to ensure the survival of a sufficient number who can work to support the family. When mortality rates fall, parents become more confident that their children will survive to adulthood and birth rates decline.

GAVI supports two new vaccines that specifically address women's health: human papillomavirus (HPV) vaccines, which help to protect against cervical cancer; and rubella vaccines. Cervical cancer is the biggest cancer killer of women in the developing world. Eighty-five percent of the estimated 275,000 women who die of cervical cancer each year live in developing countries.<sup>50</sup> Two safe and effective vaccines exist that protect against HPV types 16 and 18, which cause approximately 70% of cervical cancer cases.

Infection with rubella just prior to conception or during pregnancy can lead to serious consequences including miscarriages, stillbirths, and infants born with birth defects known as Congenital Rubella Syndrome (CRS). The most common congenital defects include lifelong heart problems, deafness, or blindness. An estimated 112,000 cases of CRS occur each year, mostly in developing countries in Africa and Asia.<sup>51</sup>

GAVI estimates that tens of millions of girls will be immunised with HPV vaccines by 2020.<sup>52</sup> By 2018, GAVI expects to have supported over 40 countries with large-scale measles-rubella vaccine campaigns and that these countries will simultaneously have introduced self-funded measles-rubella vaccine into their routine immunisation programmes.

# Gender equity in immunisation

In 2010, GAVI funded a comprehensive review by WHO which showed that globally there are no significant differences in immunisation coverage between girls and boys.<sup>53</sup> However, differences in coverage favouring either girls or boys are found in some countries and groups. In countries with high levels of gender inequity and "son preference", meaning that many families prefer having sons over daughters, more boys than girls are immunised. In other groups, such as among children in the poorest households, girls are more often immunised than boys.<sup>54</sup>

In societies where women have low status and therefore lack access to immunisation and other health services, both girls and boys are less likely to be immunised.<sup>55</sup> Countries with a high level of gender equity, as measured through the Gender Development Index, have higher immunisation coverage<sup>56</sup>, and the mother's education is strongly related to the vaccination and health of her children.<sup>57</sup>

GAVI requests that countries applying for support conduct gender analyses to identify gender-related barriers that hinder access to immunisation services. Countries are encouraged to apply for health system strengthening funding to address such barriers, and to disaggregate data based on sex, income and geographic location to help identify areas of low immunisation coverage.

# Vaccine affordability

While the effectiveness of vaccines is a key argument for their use, the value of vaccination also depends on cost and long-term affordability. All low-income countries are largely dependent on external support to finance routine immunisation, with one third still entirely donor dependent. However, governments are gradually allocating more of their own funds to national immunisation programmes.

All GAVI-supported countries contribute to the cost of new vaccines through co-financing. Low-income countries contribute the least (US\$ 0.20 per dose), while intermediate countries increase co-payments by 15% per year. Graduating countries are expected to take over the full cost of their vaccines after five years of gradually increasing their contributions.

A 2008 analysis found that, on average, the share of government financing of routine immunisation in low-income countries increased from 35% to 39% between 2000 and 2008.<sup>58</sup> During the same period there was a significant increase in the overall cost of vaccines (eg as a result of the widespread introduction of pentavalent vaccines). Consequently, even a small increase in the government's share of immunisation financing represents a substantial increase in government funding.

An important measure associated with increased budget allocations and longterm political commitment to immunisation is a separate line item for vaccines within the national budget. In 2000, 63% of low-income countries had a line item in their national budget for the purchase of vaccines. By 2010, this had increased to 83%. Six low-income countries did not have a specific budget line for financing vaccines.<sup>59</sup>

# **Cost-effectiveness**

Immunisation is considered to be one of public health's "best buys", often costsaving in the long run through reductions in healthcare and treatment expenses.<sup>60</sup> For example, eradicating smallpox at a one-time cost of about US\$ 100 million saved the world approximately US\$ 1.35 billion per year.<sup>61</sup> In the USA, for every US\$ 1 spent on Hib vaccines, more than US\$ 2 is saved.<sup>62</sup>

In 2012, some of the leading experts on health economics ranked childhood immunisation as one of the three most cost-effective solutions to advance global welfare. They estimated that spending approximately US\$ 1 billion annually on expanded immunisation coverage would prevent 1 million child deaths per year. Put into economic terms, the benefits would be 20 times greater than the costs.<sup>63</sup>

Although new vaccines supported by GAVI cost more than those that have long been included in national immunisation programmes, they are still cost-effective compared with many other interventions.<sup>64</sup> Table 4 presents evidence for the cost-effectiveness of a number of vaccines prioritised for GAVI support.

#### **Cost-effectiveness and DALYs**

Low-income countries have both higher rates of mortality and morbidity than high-income countries, meaning that life expectancy is shorter and more lifetime is spent in poor health. In order to account for the lost value of a healthy life year free of illness and disability, the measure commonly used in public health is disability-adjusted life year (DALY). DALYs combine the years of life lost due to premature death (mortality) and loss of full health due to illness and disability (morbidity).

For example, a 5-year-old contracts Hib meningitis and suffers long-term deafness as a result; 8 DALYs would have been averted if the disease had been prevented by vaccinating the child with Hib vaccine. Similarly, if the child died from the disease at age 5, 36 DALYs would have been averted had the child been vaccinated.<sup>h 65 66</sup>

The Commission on Macroeconomics and Health has classified interventions that gain a year of healthy life (ie a DALY averted) at a cost that is less than the GDP per capita as very cost-effective. Those averting each DALY at a cost between one and three times the GDP per capita are cost effective. The remainder are not cost effective.<sup>67</sup> WHO endorsed this recommendation.<sup>68</sup>

A 2006 study estimated the cost per DALY averted with the traditional EPI vaccines ranges from US\$ 7 to US\$ 438. The cost per *death* averted ranges from US\$ 205 in South Asia and Sub-Saharan Africa to US\$ 3,540 in Europe and Central Asia.<sup>69</sup>

#### Table 4: Vaccine cost-effectiveness

Vaccine	Research findings on cost-effectiveness
Hepatitis B	A review of economic evaluations found clear evidence that universal immunisation against <b>hepatitis B</b> in intermediate and high-endemic countries is cost-effective or even cost-saving in comparison to no vaccination. <sup>70</sup>
Haemophilus influenzae type b and Pneumococcal	The majority of economic evaluations of <i>Haemophilus influenzae</i> type b (Hib) vaccines conclude that the vaccine is a cost-effective intervention. <sup>71</sup> A 2007 study estimated that at a price of US\$ 5 per dose, <b>pneumococcal</b> vaccines are a very cost-effective intervention in 68 of the poorest countries. <sup>72</sup> A comparative study of child pneumonia interventions found cost-effectiveness ratios of <b>Hib</b> and <b>pneumococcal</b> immunisation <sup>1</sup> in low- and middle-income countries comparable to nutritional interventions and community-based treatment, and more cost-effective than environmental interventions (eg cleaner fuels or solid fuel stoves) or facility-based pneumonia treatment. <sup>73</sup>
Rotavirus	A 2009 study estimated that, at an initial price of US\$ 7 per dose which gradually decreases over time to US\$ 1.25 per dose by 2017, vaccination with <b>rotavirus</b> vaccines would be very cost-effective in all GAVI-eligible countries. <sup>174</sup>
Human papillomavirus	The 2009 WHO recommendation on <b>human papillomavirus (HPV)</b> vaccines cites that nationwide introduction of the vaccine would be cost- effective <sup>75</sup> in low-income and middle-income countries if the cost per vaccinated girl is less than US\$ 10–25. <sup>76</sup> At US\$ 10 per vaccinated girl, vaccination would be cost-effective in all GAVI-eligible <b>countries</b> . <sup>k</sup> <sup>77</sup>
Japanese encephalitis	A 2008 study in Indonesia found <b>Japanese encephalitis (JE)</b> vaccines to be very cost-effective. <sup>1</sup> <sup>78</sup> A 2003 study in Shanghai, China, where JE incidence was estimated to be higher, the vaccines were found to be cost- saving compared to a scenario without immunisation. <sup>79</sup>
Typhoid	Vaccination of school-aged and pre-school children with <b>typhoid</b> vaccines in high-incidence slums of several major cities in Asia has been classified as very cost-effective. <sup>m 80</sup>
Rubella	In both industrialised and less industrialised countries in Latin America and the Caribbean, where immunisation coverage is above 80%, cost-benefit studies of rubella vaccination have demonstrated that the benefits outweigh the costs, particularly when combined with measles vaccination. <sup>81</sup> However, no such studies have yet been conducted in low-income countries in Africa and Asia.

i. Cost-effectiveness ratios between US\$ 10-120 per DALY averted.

h. Based on assumptions of 3% discounting, non-uniform age weighting and a life expectancy of 68.

j. The cost per DALY averted decreases over time, from US\$ 450 per DALY averted to a sustained low of US\$ 30 per DALY averted during 2017–2025.

k. For 49 countries, the cost per DALY averted was less than US\$ 100 and for 59 countries, it was less than US\$ 200.

I. US\$ 31 per DALY averted.

m. The cost per DALY averted ranging between US\$ 177-674.

#### A country example: cost-effectiveness of Hib vaccines in Kenya

In Kenya, Hib disease incidence in children fell by 88% within three years after Hib vaccine introduction (Figure 3).<sup>82</sup> With a pentavalent vaccine price of US\$ 3.65 per dose (2004), the costs of vaccination were US\$ 1,197 per death averted and US\$ 268 per case averted. The intervention was classified as very cost-effective<sup>n</sup> and would have been cost-saving (ie vaccination costs would have been less than treatment costs averted from Hib disease) if the price of the vaccine had been US\$ 1.82 per dose.<sup>83</sup>

Figure 3: Impact of Hib vaccine on Hib invasive disease in children under 5 years, Kilifi District Hospital, Kenya



Source: Cowgill et al. 2006<sup>84</sup>

# "Immunization – even with the addition of the new, more costly vaccines – remains one of the most cost-effective health interventions."

State of the World's Vaccines and Immunization<sup>85</sup>

n. The cost of US\$ 38 per DALY averted was well below the classification of a very cost-effective intervention (Kenya's per capita GDP was US\$ 481 in 2004).

# **Hepatitis B**

- Hepatitis B can cause both acute and chronic disease, and puts people at high risk of death from cirrhosis of the liver and liver cancer. Worldwide, two billion people have been infected with the hepatitis B virus, which kills approximately 600,000 people every year.<sup>86</sup>
- Hepatitis B vaccine is 95% effective in preventing infection and its chronic consequences,<sup>87</sup> and it is the first vaccine against a major cancer.<sup>88</sup>
- In 1992, WHO recommended global vaccination against hepatitis B.<sup>89</sup>
- Immunisation beginning at birth and other vaccination strategies have resulted in a dramatic reduction of transmission of the hepatitis B virus in many countries.<sup>90</sup>

- A 2009 peer-reviewed study found clear evidence that universal immunisation against hepatitis B in intermediate and highendemic countries is cost-effective or even cost-saving in comparison to no vaccination.<sup>91</sup>
- With GAVI support, developing countries have immunised more than 300 million children against hepatitis B.

Figure 4: Global burden of liver cancer



Source: GLOBOCAN 2008 (International Agency for Research on Cancer)<sup>92</sup>

# **Hib disease**

- Haemophilus influenzae type b (Hib) is a bacterium that causes serious, often life-threatening, illnesses in young children. Hib can cause meningitis (inflammation of the membranes covering the brain and spinal cord) and severe pneumonia. It is spread through sneezing and coughing. Hib can be treated with antibiotics, but lack of access to adequate medical facilities and increasing levels of antibiotic resistance lead to high mortality rates.
- Hib caused approximately 200,000 child deaths in 2008, most of them in low-income countries.<sup>93</sup> Ten countries<sup>o</sup> in Asia and Africa account for 61% of all Hib-related deaths.<sup>94</sup>
- Clinical trials and national programmes in various (low-income) countries have shown a dramatic reduction in disease as a result of vaccination, similar to the experience in the USA and other industrialised countries. A large 1997 trial in the Gambia demonstrated 95% vaccine efficacy against invasive Hib disease.<sup>95</sup>

- In 2006, WHO issued a strengthened recommendation for Hib vaccines, stating that it should be included in all routine immunisation programmes.<sup>96</sup>
- Through GAVI support, low-income countries are increasingly making Hib vaccines part of their national immunisation programmes. Where introduced, routine use of the vaccine has led to the virtual elimination of Hib disease.<sup>97 98</sup>

o. India, Nigeria, Ethiopia, the Democratic Republic of the Congo, China, Afghanistan, Pakistan, Bangladesh, Angola and Niger

Figure 5: Global burden of Hib disease



Source: WHO, Estimated Hib and pneumococcal deaths for children under 5 years of age, 2000

# **Pneumococcal disease**

- Every year, more than half a million children under the age of five die of pneumococcal disease.<sup>99</sup> While the bacterium can also cause serious meningitis and sepsis, the majority of pneumococcal deaths in Africa (90%) are from pneumonia.<sup>100</sup>
- Pneumococcal disease results in high rates of disability among children who survive, including mental retardation, seizures and deafness.
- The vast majority (95%) of pneumococcal deaths occur in Africa and Asia<sup>101</sup> (see Figure 6). Ten countries<sup>p</sup> account for 66% of all pneumococcal deaths.
- Children with HIV/AIDS are up to 40 times more likely to contract pneumococcal disease than HIV-negative children.<sup>102</sup>
- Children often do not receive appropriate antibiotic treatment for pneumonia. According to a recent study, only 30% of children in sub-Saharan Africa receive appropriate antibiotic treatment for an episode of pneumonia.<sup>103</sup> The lack of access to prompt treatment of pneumonia in Africa emphasises the importance of prevention by immunisation, which reaches more than 80% of the world's children.<sup>104</sup>
- In 2007, WHO recommended the introduction of pneumococcal vaccines into all national immunisation programmes, particularly in countries with high child mortality.<sup>q 105</sup>

- Studies have shown high efficacy of pneumococcal vaccines in low-income countries. In the Gambia, a 9-valent vaccine was 77% effective against pneumococcal disease caused by the serotypes targeted by the vaccine and 37% effective against all types of severe pneumonia, which is often fatal. Efficacy against mortality from all causes was 16%.<sup>106</sup>
- A trial in Malawi found that a 7-valent pneumococcal vaccine prevented three out of four cases of pneumococcal disease in HIV-infected adults (74% efficacy against vaccine serotypes). This is remarkable given that the immune system of HIV-infected patients is often severely weakened and confirms that the vaccine is an important therapeutic intervention for HIV-infected adults.<sup>107</sup>
- WHO and UNICEF recommend an approach for addressing child pneumonia that includes measures of protection, including exclusive breastfeeding and improved nutrition; prevention, such as the routine use of Hib and pneumococcal vaccines; and treatment with appropriate antibiotics and oxygen.<sup>108</sup>

p. India (27%), China (12%), Nigeria (5%), Pakistan (5%), Bangladesh (4%), Indonesia (3%), Ethiopia (3%), the Democratic Republic of the Congo (3%), Kenya (2%) and the Philippines (2%).

q. Serotype replacement (an increase in the incidence of pneumococcal disease caused by non-vaccine serotypes) has been observed in Alaskan children following vaccination with the 7-valent pneumococcal conjugate vaccine (Singleton et al. *Journal of the American Medical Association*. 2007). This experience emphasises the importance of ongoing surveillance following pneumococcal vaccine introduction and development of expanded valency vaccines.

Figure 6: Global burden of pneumococcal disease



Source: WHO, Estimated Hib and pneumococcal deaths for children under 5 years of age, 2000

# **Rotavirus diarrhoeal disease**

- Rotavirus causes vomiting and diarrhoea, and often includes fever and abdominal pain. A person with rotavirus diarrhoea excretes large amounts of virus, which can spread readily through contaminated hands, objects, water or food.<sup>109</sup>
- Rotavirus diarrhoea causes more than 450,000 deaths each year in children under 5 years of age, and is responsible for millions of hospitalisations and clinic visits every year. The majority (95%) of rotavirus deaths in children are in low-income countries in Africa and Asia.<sup>110</sup>
- While other types of diarrhoea, such as those caused by bacteria and parasites, can be prevented through improvements in sanitation and hygiene, these measures do not prevent the transmission of rotavirus. The virus is so contagious and resilient that improving water and hygiene does not significantly impact incidence or mortality.<sup>111</sup>
- Rotavirus cannot be treated with antibiotics or other drugs. Immunisation is the only way to prevent severe episodes of the disease. Ensuring access to interventions such as oral rehydration therapy (ORT), zinc and exclusive breast feeding, together with improving hygiene and water quality, remains important for the prevention and treatment of other causes of diarrhoea.
- Clinical trials in high-income countries have demonstrated high efficacy (85–98%) against severe rotavirus disease.<sup>112</sup>113 In developing countries, efficacy ranging from 51% to 64% in the first year of life has been shown.<sup>114</sup>115116 In Nicaragua, a lower-middle-income country, which introduced the vaccine in 2006, a 45–49% reduction in risk of rotavirus diarrhoea requiring hospitalisation in young children was observed. The vaccine was 77% effective against very severe diarrhoea.<sup>117</sup> Following the nationwide introduction of rotavirus vaccine in Mexico in 2007, a 41% reduction in diarrhoea-related mortality was observed in young children. A 29% reduction was seen in older children, few of whom were age-eligible for vaccination, suggesting herd immunity effects.<sup>118</sup>
- In 2007, WHO recommended the inclusion of rotavirus vaccines into national immunisation programmes in the Americas and Europe. Based on the positive results of trials in Africa and Asia (eg the vaccine was 61% effective in trials in South Africa and Malawi),<sup>119</sup> WHO recommended in 2009 that infants worldwide be vaccinated against rotavirus.<sup>120</sup>

Figure 7: Global burden of rotavirus diarrhoeal disease



Source: WHO, Estimated rotavirus deaths for children under 5 years of age, 2008

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# 2 Need and demand for immunisation support

As the maps on the previous pages illustrate, GAVI-supported countries suffer the highest burden of vaccine-preventable diseases. Governments are aware of the potential of immunisation to prevent these diseases and their commitment to address this problem has translated into strong demand for GAVI support. The exceptionally high coverage of routine immunisation programmes provides a strong platform for the rapid introduction of new vaccines as well as other maternal and child health interventions.

# Public health need

GAVI funding is being put to work in the countries where it is most needed. Countries applying for support experience serious morbidity and mortality related to the diseases targeted by GAVI-supported vaccines. As illustrated in the maps showing disease burden for Hib, liver cancer, pneumococcal and rotavirus disease (see pages 14–21) the vast majority of countries with the highest burden are recipients of GAVI support. Not surprisingly, the public health need to reduce this burden is translating into strong demand for GAVI's programmes.

# **Country-led demand**

Following the launch of GAVI in 2000, eligible countries were invited to submit applications for vaccine support. Within three years, 43 countries had successfully applied for hepatitis B vaccine support and made it a part of their routine immunisation programmes. Demand for GAVI's vaccine support increased significantly with a peak of 55 approved applications in 2011. Figure 8 shows the annual number of approved country applications for new vaccine support from 2000 to 2011.

# Figure 8: Approved applications for new vaccine support, 2000–2011



Source: GAVI Alliance Secretariat data as of 31 December 2011

# A strong platform

The power of immunisation to prevent disease is well understood. Immunisation programmes in both high- and low-income countries have been in place for many years with well-established rules for planning, management and monitoring. As a result, immunisation comes closer to achieving universal coverage than many other health interventions (Table 5).<sup>121</sup> The percentage of children in the annual birth cohort receiving three doses of the combined diphtheria, tetanus and pertussis vaccine (DTP3) is an indicator of the reach of the immunisation programme. By 2011, global DTP3 coverage had climbed to 83%.<sup>122</sup> This provides a strong platform for rolling out other life-saving vaccines with the opportunity to reach the largest possible numbers of children. It also provides an important opportunity to deliver other health interventions, such as maternal health services.

# Table 5: Coverage rates for different health interventions

Indicator	Global coverage
Population using improved drinking water sources (2010)	89%
Surviving infants receiving 3 doses of DTP vaccine (2011)	83%
Under-fives receiving Vitamin A supplementation (2010)	66%***
Population using improved sanitation facilities (2010)	63%
Under-fives with suspected pneumonia taken to an appropriate healthcare provider (2006–10)**	61%
HIV-positive pregnant women who received antiretroviral drugs (2009)	53%*
Under-fives with diarrhoea who had oral rehydration and continued feeding (2006–10)**	39%***
Under-fives with suspected pneumonia receiving antibiotics (2006–10)**	30%***

\* Coverage aggregated for low- and middle-income countries only.

\*\* Data refer to the most recent year available during this period.

\*\*\* Excludes China.

Sources: UNICEF, Childinfo.org; 123 The State of the World's Children 2012 124

# **GAVI Alliance – results** and efficiency

GAVI has a track record as an effective, efficient and innovative model for development. Significant results have been achieved since the inception of the GAVI Alliance: additional resources have been mobilised for immunisation, previously underused vaccines are now part of routine immunisation programmes in low-income countries, and more than 5.5 million future deaths have been prevented. At the country level there is an increasing body of evidence showing that the vaccines are making a difference. At the global level, the dynamics of the vaccine market are changing in favour of low-income countries. The entry of new suppliers, including those based in emerging economies, is increasing competition and starting to drive down prices.

# 3.1. Results

# **Mobilising resources**

Significant new financial resources to support immunisation in low-income countries have been raised. By the end of 2011, the GAVI Alliance Secretariat had received US\$ 4.1 billion in direct contributions from government donors, the European Commission, the Bill & Melinda Gates Foundation, the "la Caixa" Foundation and other private donors. In addition, based on current donor commitments, over US\$ 5 billion will be generated for GAVI Alliance programmes through innovative finance instruments.

# Driving public health impact

Since 2000, GAVI has supported 67 countries in the introduction of pentavalent vaccines into their routine immunisation programmes, 46 countries have been approved for funding for pneumococcal vaccines, 28 for rotavirus vaccines, and 17 countries at high risk of outbreaks have received support for routine yellow fever immunisation.

A projected 370 million children have been immunised with GAVI-supported vaccines. WHO projects that GAVI support to routine immunisation programmes and one-off tactical campaign investments has helped to prevent more than 5.5 million future deaths caused by hepatitis B, *Haemophilus influenzae* type b (Hib), measles, pertussis, pneumococcal disease, polio, rotavirus diarrhoea and yellow fever.<sup>125</sup>

Figure 9: Number of additional children immunised with GAVI support

Source: WHO-UNICEF 2012. World Population Prospects, United Nations, 2010<sup>126</sup>

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# **Rolling out hepatitis B and Hib vaccines**

#### Hepatitis B vaccine introduction

Even though vaccines to prevent hepatitis B disease have been available since 1981, most low-income countries – where the burden of hepatitis B is highest – did not introduce the vaccine until the advent of GAVI in 2000. The dotted line in Figure 10 shows the proportion of high-income countries introducing hepatitis B vaccines. In 1982, Italy was the first to introduce the vaccine. By 1998, 50% of high-income countries had added the vaccine to their routine immunisation programmes. The first low-income country to introduce hepatitis B vaccine was Zimbabwe in 1994, 12 years after Italy.

With GAVI support for hepatitis B vaccines starting in 2000, lowincome countries were able to implement this long overdue public health priority intervention. Many low-income countries quickly introduced the vaccine, spurring a spectacular acceleration of vaccine introductions. By 2004, 50% of low-income countries had included hepatitis B vaccines in their immunisation programmes. This occurred 22 years after the very first introduction in Italy, but only 6 years after introduction in 50% of the high-income countries. In 2006, lowincome countries surpassed high-income countries in terms of the proportion using hepatitis B vaccine. By 2010, Haiti and Somalia were the only low-income countries that had not yet introduced hepatitis B vaccines in their national routine immunisation programmes. Haiti introduced the vaccine in 2012.

China suffers a large burden of hepatitis B infection, which constitutes a leading cause of death. From 2002 to 2006, GAVI collaborated with the Chinese Ministry of Health to provide hepatitis B vaccines to China's poorest provinces, covering 36% of China's children. Coverage increased dramatically and approximately 15 million children were immunised between 2003 and 2006, preventing more than 260,000 deaths from chronic liver disease.<sup>127</sup> GAVI's support helped to catalyse the Chinese Government's decision to introduce hepatitis B vaccines nationwide and to waive user fees.



#### Figure 10: Hepatitis B vaccine introduction in highand low-income countries

Source: WHO, Vaccine introduction database<sup>128</sup>

Equity between high- and low-income countries in terms of access to hepatitis B vaccines increased significantly as a result of GAVI support. Figure 11 shows the leap made by low-income countries between 2000 and 2011.

#### Figure 11: Routine use of hepatitis B vaccines in highand low-income countries



Source: WHO, Vaccine introduction database<sup>129</sup>

#### Hib vaccine introduction

Canada was the first high-income country to introduce Hib vaccines in 1986. Uptake was fast and by 1998, 50% of high-income countries had introduced the vaccine into their routine immunisation programmes. Similar to the situation with hepatitis B vaccines, low-income countries had no access to the vaccine for reasons of cost, with one exception: thanks to a donation by a vaccine manufacturer, the Gambia was the first low-income country to introduce Hib vaccine in 1997.

By 2000, Hib vaccines had been introduced in the majority of high-income countries, where routine vaccine use consistently led to dramatic declines in Hib disease. Among low-income countries, the Gambia was still the only country using this highly effective vaccine. When GAVI introduced support for Hib vaccines, initial uptake by GAVI-eligible countries was not as rapid as it was for hepatitis B vaccines, despite consistent evidence of substantial Hib disease burden in low-income countries. Barriers to vaccine introduction in these regions were thought to be limited awareness and communication about the disease, uncertainty about Hib disease burden and concerns about the cost of the vaccines. GAVI created the *Hib Initiative* in 2005 to help countries make informed decisions regarding the introduction of Hib vaccines. This work, coupled with the recommendation by WHO in 2006 that Hib vaccines should be included in every national immunisation programme, led to a surge in demand. By 2008 – 10 years after high-income countries crossed the 50% line – the vaccine had been introduced in half of all low-income countries. By 2011, all except four low-income countries had introduced Hib vaccine. Three of these introduced the vaccine in 2012

Equity between high- and low-income countries in terms of access to Hib vaccines increased significantly as a result of GAVI support. Figure 13 shows the leap made by low-income countries between 2000 and 2011.



Figure 12: Hib vaccine introduction in high- and low-income countries

Source: WHO, Vaccine introduction database<sup>130</sup>



WHO global recommendation

for Hib vaccines



Source: WHO, Vaccine introduction database<sup>131</sup>

#### Country examples of the impact of Hib vaccine introduction

Hib disease was a serious public health problem in **the Gambia** before the vaccine was introduced. Thirty percent of those who contracted Hib meningitis, mostly children, died of the disease, and survivors often suffered from long-term disabilities such as mental retardation. Less than half of patients recovered fully from Hib disease.<sup>132</sup> After a successful trial, the vaccine was routinely introduced in 1997 as part of a donation agreement with the vaccine supplier.

The efficacy of the vaccine was 94% against all Hib disease and incidence fell sharply immediately after introduction. Figure 14 shows the decline in incidence of Hib meningitis in the western region of the Gambia. The country was able to continue routine Hib vaccination with GAVI support from 2002. It is important to note that the remarkable effect of the Hib vaccination programme on the incidence of Hib disease in the Gambia was achieved despite an erratic supply of vaccine, and thus probably resulted largely from herd immunity effects. This indicates that virtual elimination of Hib disease can be accomplished even in sub-optimal circumstances.<sup>133</sup>

#### Figure 14: Impact of Hib vaccines in the western region of the Gambia



Source: Abegbola et al. 2005<sup>134</sup>

A 2008 study in **Uganda** estimated that within four years of the introduction of the Hib vaccine into the national vaccination programme, the incidence of Hib meningitis declined by 85%. By the fifth year following introduction, the number of cases fell to nearly zero.<sup>135</sup>

Figure 15: Impact of Hib vaccines in three sentinel hospitals in Uganda



The impact of Hib vaccine introduction has also been demonstrated in other GAVI-eligible countries including Kenya, <sup>137</sup> Malawi<sup>138</sup> and Senegal.<sup>139</sup>

# Rolling out pneumococcal and rotavirus vaccines

#### Pneumococcal vaccine introduction

In 2007, WHO recommended that pneumococcal vaccines – which protect against the main cause of pneumonia, as well as meningitis and sepsis – be included in the immunisation programmes of all countries, particularly in those where child mortality is high.<sup>140</sup>

The United States of America was the first country to introduce pneumococcal vaccines in its routine immunisation programme in 2001. The first low-income countries to introduce the vaccines were the Gambia and Rwanda in 2009. New vaccines that protect against more serotypes, and are thus expected to prevent more than 70% of childhood pneumococcal disease in Africa, were developed in 2009 and 2010. Nicaragua was the first country to introduce these new vaccines with GAVI support in 2010, within a year after they first came on the market. By the end of 2012, 15 low-income countries (42%) are expected to have introduced the vaccine (see Figure 17).<sup>141</sup>

#### Figure 16: Pneumococcal vaccine introduction in highand low-income countries



Source: World Health Organization Department of Immunization, Vaccines and Biologicals<sup>142</sup>

#### Figure 17: Routine use of pneumococcal vaccines in highand low-income countries



<sup>\*</sup>Planned 2012 introductions as of July 2012.

#### **Rotavirus vaccine introduction**

Austria and Luxembourg were the first high-income countries to include rotavirus vaccines in their routine immunisation programmes in 2006. In 2009, WHO recommended that infants worldwide be vaccinated against rotavirus.<sup>144</sup> Bolivia was the first to introduce the vaccine with GAVI support in 2008, followed by Guyana, Honduras and Nicaragua in 2009.

The Sudan became the first country in Africa to introduce the vaccine in 2011. In 2012, five low-income countries are introducing rotavirus vaccines.<sup>145</sup>

## Catalysing new injection safety standards

Recognising that expanding vaccine coverage in the age of highly transmissible diseases (such as HIV) risked spreading infection, GAVI successfully instituted a catalytic programme of injection safety support, which accelerated the adoption of new standards for safe injection in developing countries. Autodisable (AD) syringes, which lock and cannot be re-used, and safe disposal boxes were the core of GAVI's injection safety support.

Of 58 countries that received the three-year, time-limited support, 56 were able to sustain the use of AD syringes and safety boxes after GAVI support ended. In 2008, some countries drew to varying degrees on other donor financing, but more than half were fully financing their own commodities. Importantly, countries have indicated that GAVI support was influential in the decision to introduce safe injection policies or practices to the broader health sector.

# Scaling up DTP3 coverage

Figure 18 shows that DTP3 coverage was very low in poor countries in the early 1980s. Following a concerted effort by UNICEF and WHO to extend vaccination coverage to all children through the Expanded Programme on Immunization, rates climbed from less than 10% to 56% in just 10 years. In the 1990s, the rise in coverage stagnated as global attention turned to other pressing health problems such as the HIV/AIDS epidemic. From 1990 to 1999, coverage rates floated between 50% and 60% in low-income countries.





Source: Country income categories (World Bank) as of July 2012 (2011 GNI per capita); annual coverage estimates (WHO/UNICEF) weighted by annual number of surviving infants (UNDP)<sup>146 147</sup>

With the launch of GAVI in 2000, Alliance partners put immunisation back on political agendas. Although GAVI was set up, first and foremost, to help countries introduce new and underused vaccines, its programmes helped to accelerate increases in DTP3 coverage. It did so firstly by providing sustainable finance for the introduction of new and more efficient combination vaccines, adding hepatitis B to DTP in the so-called "tetravalent" vaccine, and by adding hepatitis B and Hib to DTP in "pentavalent" vaccines. Secondly, GAVI provided cash-based support for strengthening immunisation services (ISS). An independent assessment in 2006 showed that GAVI's ISS programme contributed to increases in DTP3 coverage, in particular in countries starting with the lowest levels of coverage.<sup>148</sup> The ISS programme is described in more detail on page 37.

Coverage in low-income countries increased from 66% to 79% between 2000 and 2011. By 2011, scaled-up coverage in low-income countries had driven global DTP3 vaccine coverage to 83%, meaning that 83% of children below one year of age were receiving the full three-dose schedule of the DTP vaccine.<sup>149</sup>

# Investing in health system strengthening

Effective health interventions, such as vaccines, are only useful if they reach the children and people who need them. WHO identifies six building blocks that underpin a functioning health system: service delivery; health workforce; information; medical products, vaccines and technologies; financing; and leadership and governance.<sup>150</sup> While the robustness and quality of these health systems building blocks vary from country to country, there are clear disparities between low- and high-income countries. For example, countries in Africa account for 24% of the global disease burden but have only 3% of the world's health workers.<sup>151</sup>

Health systems in many developing countries suffer from chronic underresourcing. The Taskforce on Innovative International Financing for Health Systems estimated health systems costs would account for between 62% and 74% of required resources for addressing basic health needs in low income countries. Human resources and infrastructure needs comprised the vast majority of the identified required investment.<sup>152</sup>

While weak health systems represent a major constraint on delivering vaccines to the children who need them, immunisation programmes also offer synergies for health system strengthening efforts. For example, surveillance data on coverage and drop-out rates can be used as an indicator of the equity of health system performance – a measure of its ability to provide health services to difficult-to-reach populations.<sup>153</sup>

Recognising that immunisation coverage is often constrained by health systems issues, GAVI has committed US\$ 800 million to support countries to strengthen their health systems in order to improve immunisation and other health service delivery. Countries are encouraged to use GAVI health system strengthening (HSS) funding to target "bottlenecks" or barriers in the health system that impede progress in improving the performance of immunisation services. The design of HSS programmes is fully owned and led by countries and is based on their needs and overall health system development priorities. Fifty-five countries have been supported with HSS grants. The duration of HSS support is aligned with the national health plan, and funding levels are determined by the size of the country's birth cohort and the national income per capita.

Countries are applying most GAVI HSS support to strengthening peripheral health service delivery. For example, HSS support to Armenia aims at improving the quality and accessibility of health services by training health workers and establishing outreach teams in remote, mountainous and near-border areas. In Vietnam, GAVI-supported activities include training courses and performance-based allowances for village health workers. Activities in Ghana have focused on strengthening maternal and child health interventions, especially immunisation of mothers and children, at district and sub-district levels. Typically, peripheral health workers are multi-purposed and provide a wide range of basic services: vaccinating children, delivering babies, treatment services and more.

# **Shaping markets**

Underlying the GAVI Alliance business model is the intention to ensure a lasting impact on the vaccine market to the benefit of the developing world. There is evidence of initial impact in the changing production and supply base, price declines for some vaccines and the consolidation of a tiered pricing approach that means the lowest-income countries pay significantly less for vaccines.

## **Changing supply base**

GAVI's marshalling of significant and long-term financing for vaccines, coupled with improved demand forecasting, provided an important signal to vaccine manufacturers that there is a large and viable market for vaccines in low-income countries. In 2011, UNICEF procured 2.5 billion vaccine doses worth over US\$ 1 billion on behalf of developing countries, with GAVI-funded vaccines representing nearly two thirds of this amount.<sup>154</sup> The emergence of a new market in low-income countries financially backed by GAVI has encouraged new market entry, particularly from vaccine manufacturers based in emerging economies. Figure 19 shows that the number of vaccines has increased significantly since 2001. These producers have strengthened their industrial capability and become credible players in the global vaccine market.<sup>155</sup>

Figure 19: GAVI vaccine suppliers, 2001–2011



Source: UNICEF Supply Division, 2012

#### Vaccine price declines

The affordability of a vaccine is a primary determinant of its sustainable use in low-income countries. Price declines have been observed in a number of GAVI-supported vaccines:

Prices of **hepatitis B** monovalent vaccines began to decline in the early 1990s. The technology for producing the vaccine had become relatively simple and efficient, and increasingly, manufacturers from emerging economies started producing the vaccine at low cost. With increased competition and the launch of GAVI in 2000, prices continued to decline.<sup>156</sup> Between 2000 and 2010 the price of the vaccine dropped from US\$ 0.56 to US\$ 0.18 per dose; a 68% reduction as shown in Figure 20.





Source: UNICEF Supply Division, 2010

In 2007, when most GAVI-eligible countries switched to the combination **pentavalent vaccine (DTP-hep B-Hib)**, the average price per dose of this vaccine was US\$ 3.61. In 2011, the weighted average price paid by GAVI was US\$ 2.49 per dose, <sup>157</sup> a 31% drop. In 2001, GAVI procured pentavalent vaccines from just one manufacturer. By 2011, this had increased to four, two of which were based in emerging market economies.

In 2010 and 2011, pentavalent vaccines produced by two Indian manufacturers were removed from the WHO list of prequalified vaccines due to concerns over quality control procedures. This highlighted the difficulty of producing large quantities of high-quality vaccines, given the complexity of the technologies involved. However, thanks to careful planning and efforts by the remaining manufacturers and procurement partners, supply disruptions were avoided or kept to a minimum. By procuring vaccines that have been prequalified by WHO, GAVI aims to ensure that the vaccines it supports are safe and effective, and meet the specific needs of each country.

# Figure 21: Number of manufacturers and price decline of pentavalent vaccine



Source: UNICEF Supply Division, 2012

In early 2012, GAVI established long-term agreements with two rotavirus vaccine manufacturers. The bulk of the volume will be procured at a cost of US\$ 5 per course, a two-thirds reduction on the previous lowest price paid by GAVI. The year before, one manufacturer offered its human papillomavirus (HPV) vaccine at US\$ 5 per dose, a 64% reduction on the lowest public price at the time. As countries start to apply for HPV vaccine support for the first time, GAVI is actively pursuing further price reductions from manufacturers.

# The Advance Market Commitment for pneumococcal vaccine – accelerating production of more appropriate and affordable vaccines

Pneumococcal conjugate vaccines have been sold in high-income markets such as the USA and Europe since 2000. The technology to produce these vaccines is significantly more complex than other vaccines that GAVI supports. In the US public market, the price of these vaccines was over US\$ 100 per dose in 2012.<sup>158</sup>

To accelerate low-income country access to a more appropriate and more affordable pneumococcal vaccine, GAVI launched the Advance Market Commitment (AMC) for pneumococcal vaccines in 2009. The AMC facilitates the conclusion of long-term contracts between GAVI and manufacturers to create incentives for the production of large volumes of vaccine at lower unit costs. Through the two-stage price model of the AMC, GAVI pays a price of US\$ 7 per dose for the initial vaccines procured and US\$ 3.50 or lower for the majority of doses procured thereafter. This represents a reduction of more than 90% on the price of pneumococcal vaccines in industrialised countries.<sup>159</sup> As emerging manufacturers enter the pneumococcal vaccine market with prequalified vaccines and competition increases, the price is expected to decline further.

Most GAVI-eligible countries have different circulating strains of the pneumococcal bacteria from those found in more affluent societies. The AMC has the additional benefit of having encouraged the development of more appropriate pneumococcal vaccines than those previously available, with additional serotypes against the most common and fatal strains of pneumococcus in GAVI countries. GAVI, through the AMC, only funds pneumococcal vaccines that are suitable for low-income countries, and that meet a product specification standard developed by WHO.

#### **Tiered pricing**

By aggregating demand from eligible countries and raising resources to finance this demand, GAVI has created predictability of funding for a tier of countries that together represent significant volume and value. This has led to sufficient incentives for the pharmaceutical industry to establish an accepted low-income pricing tier. Tiered pricing is a policy whereby low-income countries are charged a reduced price for the same product compared to prices charged in higher-income countries.

Figure 22 highlights the difference in price for the same or equivalent vaccines between the low-income UNICEF/GAVI market and the public sector US market.

In 2011, GAVI paid an average price of US\$ 2.49 per dose for pentavalent vaccine – less than 10% of the price in the US public market. For pneumococcal, rotavirus and HPV vaccines, prices are dropping to, at most, 5% of the current US prices.

#### Figure 22: Tiered pricing: vaccine prices in different markets



<sup>1</sup> The combination procured by UNICEF is not provided in the US markets; US prices refer to the sum of a DTaP (diphtheria-tetanus-acellular pertussis) vaccine, a HepB monovalent vaccine and a Hib vaccine.

- <sup>2</sup> 13-valent vaccine (US markets) and tail price cap under the AMC agreement (UNICEF/GAVI market).
- <sup>3</sup> Refers to GlaxoSmithKline product procured by GAVI as of 2012.
- <sup>4</sup> Refers to price offer to GAVI in 2011.

Source: UNICEF Supply Division, CDC Vaccine Price List<sup>160</sup>

The GAVI Alliance uses existing organisations and the infrastructure of partners with field presence to deliver its programmes, enabling administrative costs to remain small relative to the size of its operations. GAVI's overhead expenses (the aggregate of fundraising, management and general expenses') amounted to 3.7% of total expenditures in 2010 and 2.9% in 2011.<sup>161</sup>

GAVI has also brought more efficient technologies to the poorest countries. As Hib-containing combination vaccines became part of GAVI's portfolio, countries gradually started switching from separate hepatitis B vaccines and (in some cases) separate Hib vaccines to the pentavalent vaccine, which combines these two vaccines with DTP vaccines. By 2007, GAVI stopped making new commitments for hepatitis B monovalent vaccines to encourage the switch to combination vaccines. That year saw a surge in new applications (36) for pentavalent vaccines.

Bundling the five vaccines into one injection dramatically improves the experience of the baby, the mother and the health worker. It also introduces logistical benefits and cost-savings. The combined 2007 prices of hepatitis B monovalent vaccine<sup>5</sup> and Hib monovalent vaccine was US\$ 3.23. The price of tetravalent (DTP-hep B) vaccine added to the price of Hib monovalent vaccine amounted to US\$ 4.10 per dose. In 2011, the same five antigens (DTP-hep B-Hib) combined in the pentavalent vaccine cost an average of just US\$ 2.49 per dose.<sup>162</sup>

<sup>3.2.</sup> Maximising efficiency

r. Overhead expenses exclude indirect programme expenses such as those related to programme implementation and performance monitoring.

s. 10-dose vial
## **GAVI Alliance – innovation**

The coming together of public and private partners in the GAVI Alliance has catalysed new approaches directly within the core business of immunisation, and more broadly in development financing and programming.

#### 4.1. Development financing

#### **Pioneering innovative finance**

The GAVI Alliance has been credited with pioneering new approaches to development financing. A study on emerging good practices in improving the long-term sustainability of health aid commended GAVI for having a strategic goal specifically focussed on predictable financing. It also recommended that other agencies follow the example of aligning grants to the duration of the country health or immunisation plan.<sup>163</sup>

The testing of new models of innovative financing for development has attracted widespread interest, specifically the success of the International Finance Facility for Immunisation (IFFIm) and the Advance Market Commitment (AMC).

IFFIm uses long-term government commitments to raise funds on the international capital markets, making large volumes of funding immediately available for GAVI programmes. It has broken new ground in long-term international development financing, with donor governments making legally binding commitments of up to 20 years.

Between 2006 and 2011, IFFIm raised over US\$ 3.6 billion in additional financing for GAVI programmes. A 2011 independent evaluation of IFFIm concluded that it had yielded extremely good development returns. It found that IFFIm had performed much better than expected, with borrowing costs turning out to be considerably lower than originally anticipated.<sup>164</sup>

An early analysis that modelled the costs and benefits of the key features of the IFFIm model – long-term predictable financing and frontloading – found that IFFIm's approach could increase the impact of vaccine coverage by 22%, taking into account the costs of borrowing. The authors reported that this was because "stable and long-term financing allows vaccine manufacturers and countries to plan for long periods of time, knowing that resources will be available. Frontloading helps to reduce the spread of disease and to immunise large groups of people faster."<sup>165</sup>

IFFIm bond issuances in a number of different markets have demonstrated the attractiveness of the investment to both retail and institutional investors. In addition to delivering significant volumes of new finance, it has an additional advocacy value by introducing private investors to the health and immunisation needs of the developing world.

Private capital investors both secure a market rate of return for their investment and contribute to a life-saving development initiative. With the guidance of the World Bank and the IFFIm Board in selecting the timing and markets for bond issues, competitive rates of borrowing have been achieved, proving IFFIm as an efficient vehicle for bringing forward large volumes of finance. IFFIm has enabled the rapid scale-up of GAVI support for countries as well as demonstrated the viability of donors tapping the capital markets to finance development assistance just as they do for domestic public expenditures.

The pneumococcal AMC (see page 33) stimulates the supply of appropriate and affordable pneumococcal vaccines tailored to the needs of developing countries. In June 2009, the AMC became operational with five government donors and the Bill & Melinda Gates Foundation signing legal agreements amounting to a total commitment of US\$ 1.5 billion.

Donors commit funds to guarantee a fixed low price for vaccines once they have been developed, giving manufacturers an incentive to invest in vaccine development and manufacturing capacity. Other development sectors are monitoring GAVI's progress with the AMC and see it as a potential model for addressing market failures in delivering other appropriate product solutions for developing countries.

In March 2010, the first long-term AMC supply agreements were concluded, and in December the same year Nicaragua became the first developing country to introduce the new pneumococcal vaccine into its routine immunisation programme. By October 2012, 20 countries had introduced the vaccine and another 26 had been approved for GAVI-supported introductions.

#### **Promoting financial sustainability**

From inception, GAVI made financial sustainability a priority within the design of its programmes. The GAVI Alliance Board approved the following definition of financial sustainability in 2001: "Although self-sufficiency is the ultimate goal, in the nearer term, sustainable financing is the ability of a country to mobilise and efficiently use domestic and supplementary external resources on a reliable basis to achieve target levels of immunisation performance."<sup>166</sup>

GAVI's initiative to help countries develop financial sustainability plans (FSPs) was an early effort in global development to address the need to build national capacity in this area. The FSP described how the responsibility of vaccine financing would transition to government and other donor financing, and it had to be signed by both Ministries of Health and Finance. By 2006, more than 50 countries receiving GAVI support had developed FSPs.

Building on the lessons learned from this initiative, countries were assisted to develop comprehensive multi-year plans (cMYPs), which integrate vaccine financing into national plans and budgets. cMYPs combine the costing and financing elements of FSPs with programme planning into one strategic plan for immunisation, which forms part of the national health sector plan. Since 2006, countries are required to present their applications for support in the context of their cMYPs for immunisation and broader health sector planning.<sup>167</sup>

To support sustainability of financing for immunisation and promote country ownership, GAVI has pioneered a co-financing model which requires all countries to fund a portion of the vaccines themselves. The contributions are determined by the countries' ability to pay for each new vaccine. Countries with a GNI above US\$ 1,520 increase their co-payments annually to ease their transition to independent financing of their vaccines.

#### 4.2. Development programming

### Reinforcing country ownership and evidence-based decision-making

The GAVI business model represented a significant departure from traditional ways of programming development assistance. The idea of empowering developing countries to take the lead in managing external development grants is broadly accepted today as a tenet of effective aid.<sup>168</sup> However, when GAVI instituted a model of taking country-initiated proposals as the starting point for considering support, it was far from the norm. A similar approach was subsequently adopted by other development financing instruments. A focus on setting appropriate incentives, such as matching grant duration to the duration of country plans, has helped to inspire longer-term planning approaches.

The advent of GAVI's co-financing policy in 2006, which required the inclusion of the Ministry of Finance in decisions to adopt new vaccines, contributed to more rigorous decision-making. By requiring a contribution from domestic budgets, Ministries of Health now had a domestic counterpart demanding evidence of the value of a proposal to broaden immunisation programmes. The co-financing policy also provided the incentive to ensure GAVI-supported programmes were reflected in the national budgets, another accepted principle of effective aid.<sup>169</sup>

#### Strengthening service delivery

Health system strengthening (HSS) support, introduced in 2005 to provide flexible funding to enable countries to address bottlenecks in service delivery (see page 30), has contributed to the international momentum to ensure health systems needs are addressed comprehensively.<sup>170</sup>

GAVI also pioneered a programme of flexible cash grants employing a performance-based incentive approach to assist governments to overcome challenges when scaling up routine immunisation programmes. The immunisation services support programme encouraged better country-level coordination and planning by providing technical support and offering initial investment payments and subsequent reward payments based on the number of additional children targeted. The reward payments were conditional on achieving the targets and good quality coverage data. The funds were made available for the countries to invest in activities that they deemed appropriate to expand coverage. A 2006 study concluded that the performance-based approach had a positive effect on routine immunisation coverage rates.<sup>171</sup>

A 2007 study identified the potential for some countries to misreport coverage rates in order to qualify for performance payments, and this was also highlighted in a subsequent study.<sup>172</sup> Ensuring robust data collection systems, particularly in poor countries, is a challenge. GAVI's approach is to use and seek to strengthen country data systems, with appropriate checks and balances, but avoid creating parallel monitoring approaches.<sup>173</sup> A GAVI Transparency and Accountability Policy, introduced in June 2008, has established a risk-based approach to fiduciary management of cash grants while striking a balance with country ownership.

#### Learning through public-private partnership

The essential character of GAVI's public-private partnership is reflected in its decision-making bodies. The critical multilateral partners of the Alliance – WHO, UNICEF and the World Bank – and the Bill & Melinda Gates Foundation have permanent membership. Together with representatives of constituencies that reflect the key stakeholders, including developing and donor governments (in equal numbers), industry, research institutes and civil society, they comprise two thirds of the Board membership. One third of the Board consists of unaffiliated members who are appointed by a Governance Committee, based on their individual skills and attributes. This introduces an independent challenge function to GAVI decision-making and complements the value of the legitimacy, credibility and technical expertise of the public sector with a strong, unaffiliated and private sector voice.

A ground-breaking public-private fundraising partnership with the Spanish bank "Ia Caixa" combined an outreach campaign to the bank's 26,000 employees to contribute to GAVI through payroll reductions with a campaign to engage "Ia Caixa's" 400,000 corporate depositors. The bank's associated foundation, Fundación "Ia Caixa", delivered a  $\in$ 4 million grant to GAVI in 2008. Further contributions have brought the total "Ia Caixa" contribution to GAVI to over US\$ 21 million.

Not all of GAVI's innovations in development approaches may be replicable but the new approaches have garnered significant attention and continue to be referenced in other development sectors.<sup>174</sup> GAVI has sought to share its lessons, and learn from initiatives in other quarters, through active participation in the Global Programs Learning Group<sup>175</sup> and in other fora, such as those related to advancing the policy agendas on innovative financing and on aid effectiveness.

# t of new vaccines

# **5** The potential impact of new vaccines

There is strong country demand for new vaccines, which translates into the potential to save millions more lives. Through the rapid introduction of these vaccines between 2011 and 2015, countries can prevent an additional 4 million future deaths. In just five years this will nearly double the impact made in GAVI's first decade, representing a major acceleration of impact and contributing significantly to the achievement of the Millennium Development Goals.

#### 5.1. Country demand in 2010–2015

GAVI's mandate remains focused on catalysing the adoption of new vaccines and influencing vaccine markets to the benefit of the poor. Support continues to target those vaccines that, on the one hand, hold great potential to achieve progress on the Millennium Development Goals and, on the other, require external financial assistance to reach the world's poorest countries. GAVI's ambition is to complete the introduction of pentavalent vaccines and to roll out pneumococcal, rotavirus, human papillomavirus (HPV) and measles-rubella vaccines in line with country demand. GAVI will also continue to support routine immunisation and campaigns against yellow fever, and campaigns against meningitis A. In addition, there is anticipated demand for the other vaccines that have been prioritised as part of GAVI's Vaccine Investment Strategy – Japanese encephalitis and typhoid. GAVI is also monitoring the development of vaccines against dengue and malaria.

By the end of 2012, virtually all GAVI-eligible countries will have introduced **pentavalent vaccines**. The sustained support for routine use of this vaccine will continue to be a significant driver of impact on public health.

The introduction of **pneumococcal and rotavirus vaccines** has already started making an important further contribution to public health, with a rapid impact on global efforts to reduce child deaths (MDG 4), prevent sickness and, for pneumococcal disease, prevent disability. At the same time, vaccination against these diseases also provides a key opportunity to actively promote broader treatment and prevention of pneumonia and diarrhoea, which together account for almost one third of all deaths among children under five.<sup>176</sup> By mid-2012, 74 country applications for pneumococcal and rotavirus vaccines had been approved, and more are expected in the next few years. Financing this demand is, for the first time, resulting in the introduction of new vaccines with only minor delays compared to their introduction in high-income countries.

Forecasts<sup>t</sup> of future demand for the vaccines in the GAVI portfolio project that between 2011 and 2015:

- An additional 180 million children will be immunised with **pentavalent** vaccine.
- More than 80 million children will be immunised with pneumococcal vaccines with GAVI support.
- More than 30 million children will be immunised with rotavirus vaccines.
- Almost 230 million people will be protected against meningitis A and close to 125 million are expected to be immunised against yellow fever through vaccine campaigns and routine immunisation.
- In addition, by 2020 more than 30 million girls will have been immunised with HPV vaccines, protecting them against cervical cancer later in life.

Introducing the GAVI portfolio of vaccines into routine immunisation programmes between 2011 and 2015, based on country demand forecasts, can result in an additional **3.9 million future deaths** being prevented. In just five years this would double the rate of impact made in GAVI's first decade, contributing significantly to the achievement of the MDGs and helping to fulfil the GAVI Alliance's promise to save children's lives and protect people's health by increasing access to immunisation in poor countries.

#### Figure 23: Target future deaths averted with GAVI vaccine support



Source: AVI (Accelerated Vaccine Introduction) forecast February 2010<sup>u</sup>

t. AVI (Accelerated Vaccine Introduction) forecast September 2012 developed as per AVI forecasting Standard Operating Procedure using 2012 WHO/UNICEF estimates of national immunisation coverage (WUENIC) data; demographic data from United Nations Population Division, World Population Prospects: The 2010 Revision, medium variant; coverage projections using standard AVI rules; country eligibility from November 2009 GAVI Board decision.

u. Developed as per AVI forecasting Standard Operating Procedure using historical coverage data from WHO/UNICEF estimates, historical shipments from UNICEF SD, demographic data from UNPD 2008, coverage projections from standard AVI rules, eligibility from Nov. 2009 GAVI Board decision.

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