Cost-effectiveness case studies

This document is intended to support immunization programme managers and staff in their efforts to secure sustainable funding for immunization.

Immunization is one of the most successful public health interventions in preventing suffering and death. Benefits go beyond health and encompass social and economic returns as well. Despite their success, immunization programmes are not always prioritized for continued or increased resources.

It is important therefore that decision-makers and partners appreciate the importance of immunization, not just as a public health intervention but as a national investment that yields socioeconomic returns and health care savings.

How to use this document
This document presents summaries and key findings from a range of cost-effectiveness analyses drawn mainly from evidence published in peer-reviewed journals and official documentation. The summaries can be drawn upon to support your country's efforts to raise the profile of immunization and ensure continued investment in it within the context of health care prioritization.

Use the summaries as inspiration, to prepare for a meeting or to hand out to stakeholders.

The case studies will help most when they are used to help paint a national picture and a strong country-specific case for continued support in immunization. Present the studies alongside descriptions of the national issues and challenges. If available, supplement them with your own national data. If the same data is not available, consider using other national data that can serve as a proxy.

Contents

Abbreviations

AOM	acute otitis media
CFR	case-fatality ratio
DALY	disability-adjusted life year
GAVI	Global Alliance for Vaccines and Immunisation
GBD	global burden of disease
GDP	gross domestic product
HBV	hepatitis B virus
Hib	Haemophilus Influenza type b vaccine
ICER	incremental cost–effectiveness ratio
IPV	inactivated polio vaccine
MCV	measles-containing vaccine
NPNM	non-pneumonia, non-meningitis
OPV	oral polio vaccine
PCV	pneumococcal conjugate vaccine
RVGE	rotavirus gastroenteritis
QALY	quality-adjusted life years

Glossary of Terms

Cost–effectiveness analysis
Analysis comparing the intervention cost, with the actual or expected health gains (effectiveness).

Cost–effectiveness ratio
Total cost per unit of health gain. It is the *outcome* of a cost–effectiveness analysis.

Cost-effective intervention
Provides an extra year of healthy life (equivalent to averting one DALY) for less than three times the Gross Domestic Product (GDP)[1]. A highly cost-effective intervention does so for less than the GDP.

Disability-Adjusted Life Years (DALYs)
Sum of the years of life lost due to mortality (premature death compared to life expectancy) plus the years of life lost due to disability (less than perfect health). DALYs averted is a measure of the *effectiveness* of an intervention.

Disability weight
Multiplier between 0 and 1 that describes the severity of a disease. For DALYs, 1 is equivalent to death and 0 is perfect health. For QALYs, 1 is a state of ideal health and 0 is a state comparable to death.

Discount rate
Multiplier applied to discount future years' cost and benefits. (Rationale: US$1 in the future is not worth as much as US$1 today – and people prefer to have benefits now rather than in the future).

Economic modelling
Trial simulation using estimated input parameters to predict cost–effectiveness of an intervention where a real-life trial is not possible or not feasible.

Incremental Cost–Effectiveness Ratio (ICER)
Additional cost per unit of health gain. It is the *outcome* of a cost–effectiveness analysis.

Quality-Adjusted Life Years (QALYs)
Product of life expectancy and a measure of the quality of the remaining life-years. One QALY is a year of perfect health. QALYs gained is a measure of the *effectiveness* of an intervention.

Sensitivity analysis
Test of the robustness of the cost-effectiveness analysis results. Parameters are changed within a plausible range either one at a time *(one-way sensitivity analysis)* or many at a time *(multiway sensitivity analysis)*.

TRIVAC
Tool for estimating the cost-effectiveness of vaccines.

[1] WHO criterion : Adams T, Baltussen R, Tan-Torres T, Evans D, Hutubessy R, Acharya A, Murray CJL. Making Choices in Health. In: WHO Guide to Cost-Effectiveness Analysis. Geneva: World Health Organization; 2003.

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Cost-effectiveness evidence for the introduction of a vaccine

Case study: Armenia – rotavirus[1]

KEY POINTS:
A cost-effectiveness study on the introduction of rotavirus was conducted in Armenia. Key findings included the following.

Vaccination will be cost-saving to the health service by 2025, if the cost of vaccine purchase decreases as expected. Once coverage reaches high levels, per birth cohort rotavirus vaccination is predicted to:

- prevent 8 deaths and 25,000 cases;
- prevent 3000 primary care consultations and 1000 hospitalizations;
- reduce health care expenditure by US$180,000 and societal costs by $470,000;
- cost US$257,000.

Methods

In Armenia, a cost-utility analysis was performed for time horizon 2012-2025. The analysis compared no vaccination with universal Rotarix vaccination. It used a decision simulation based on an age structured cohort model.

Input parameters

- demographics and disease burden
- vaccine efficacy and coverage
- vaccination costs
- medical and societal costs.

About rotavirus

Rotaviruses are the most common cause of severe diarrhoeal disease in young children worldwide. They are also the cause of gastroenteritis and dehydration.

Worldwide, it causes an estimated 453 000 deaths in children below 5 years of age annually.

In the European Region deaths are rare, but there are 87 000 hospitalizations annually, which result in high health care costs.

There are two available rotavirus vaccines, Rotarix and RotaTeq, which are both considered safe and effective at preventing gastrointestinal disease.

[1] Jit, M., R. Yuzbashyan,G. Sahakyan, T. Avagyan, and L. Mosina. 2011b. The Cost-Effectiveness of Rotavirus Vaccination in Armenia. Vaccine 29:9104–11.

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Results

Health i mpact

Once coverage has reached high levels, rotavirus vaccination – per birth cohort vaccinated – would prevent about

Deaths:	8
Cases:	25,000
Primary care consultations:	3,000
Hospitalizations:	1,000
DALYs lost:	600

Cost-effectiveness

For birth cohorts 2012 to 2025: incremental cost per DALY saved

From the Ministry of Health perspective	$650
From the total health care perspective	$850
From a direct societal perspective	$820
Including indirect societal costs	$44

Rotavirus vaccination in Armenia would be **very cost-effective** by WHO criterion.[2] (cost per DALY averted US$ 44 - US$ 850, GDP per capita US$ 3,800).

In the sensitivity analysis, even in the **most pessimistic scenario** (no decline in vaccine prices, low estimates of disease burden, age weighted DALYs), rotavirus vaccination was **still cost-effective** in Armenia (US$ 8300 per DALY averted).

Budget impact

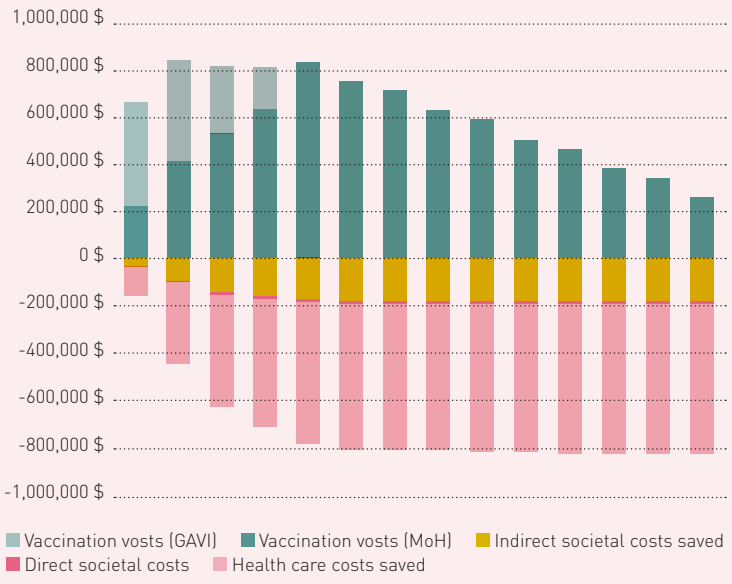
Undiscounted vaccination costs and costs saved

Over five years, for the 2025 birth cohort:

Cost
Total vaccination cost: $257,000

Cost reduction
Health care costs reduced by $182,000
Direct societal costs reduced by $13,800
Indirect societal costs reduced by $ 459,000

Budget impact 2012-2025



[2] WHO criterion : Adams T, Baltussen R, Tan-Torres T, Evans D, Hutubessy R, Acharya A, Murray CJL. Making Choices in Health. In: WHO Guide to Cost-Effectiveness Analysis. Geneva: World Health Organisation; 2003.

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Parameters and input values for the model

	PARAMETER	INPUT	SOURCE
DEMOGRAPHICS	BIRTH COHORT	1.2% OF POPULATION	WHO-UNICEF (1)
DISEASE BURDEN	HOSPITALIZATION	RATE 6.5 PER 1,000 CHILDREN	SENTINEL SURVEILLANCE
	AGE DISTRIBUTION (MONTHS)	6.9% <6; 28% 6-11; 36% 12-23; 29% 24-59	SENTINEL SURVEILLANCE
	UNDER 5 MORTALITY	RATE 16 PER 100,000	WHO (2), SENTINEL SURVEILLANCE
	PRIMARY CARE	8,829 UNDER-5 DIARRHOEA CONSULTATIONS, 51% ROTAVIRUS	EMAIL SURVEY
	SYMPTOMATIC ROTAVIRUS	INCIDENCE 0.24 A YEAR, DISABILITY WEIGHT OF 0.119 PER EPISODE	INCIDENCE (3, 4, 5), DISABILITY WEIGHT (6)
EFFECTIVENESS	VACCINE EFFICACY	E.G. TWO-DOSE EFFICACY PREVENTING HOSPITALIZATION 79%	EQUIVALENT TO LATIN AMERICAN TRIALS
	VACCINE COVERAGE	50% 2012, 90% 2013, 93% 2014, 95% 2015	WHO-UNICEF (1)
COSTS	VACCINATION COST	$0.72, $1.44, $2.16, $2.88 PER DOSE IN 2012, 2013, 2014, 2015.	MOH, GAVI (7)
		LIKELY $4 PER DOSE 2016	GAVI (7)
		LINEAR PRICE DROP TO $1 PER DOSE BY 2025 (PRICE MATURITY)	GAVI (7)
	PROGRAMME COSTS	COMMUNICATION ETC $30,000 (GAVI FUNDING $60,000 IN 2012)	WHO-UNICEF (1)
		TRAINING $20,000 EVERY TWO YEARS (GAVI FUNDING $40,000 IN 2012)	WHO-UNICEF (1)
		MONITORING $15,000 EVERY YEAR	WHO-UNICEF (1)
		COLD CHAIN $130,000	WHO-UNICEF (1)
	DIRECT MEDICAL COSTS	PAEDIATRIC HOSPITALIZATIONS $195 PER CASE RVGE	UNIT HEALTH CARE COSTS
		PRIMARY CARE CONSULTATION $5.95 PER CONSULTATION	EMAIL SURVEY, WHO-CHOICE STUDY (8)
	DIRECT SOCIETAL COSTS	CAREGIVERS' TRANSPORT, ACCOMMODATION $14.90 PER PATIENT	NATIONAL STATISTICAL SERVICE
	INDIRECT SOCIETAL COSTS	CAREGIVER PRODUCTIVITY LOSS $7.29 HOSPITALIZATION//$2.43 ANY EPISODE	NATIONAL STATISTICAL SERVICE
		PRODUCTIVITY LOSS DUE TO CHILD DEATH $53,112.73	NATIONAL STATISTICAL SERVICE

1. WHO-UNICEF Guidelines for Comprehensive Multi-Year Planning for Immunization (2013) Available from: http://www.who.int/immunization/programmes_systems/financing/tools/cmyp/en [accessed on 08.09.14]
2. World Health Organization (WHO). World health statistics. (2008) Available from http://www.who.int/whosis/whostat/2008/en/ [accessed on 08.09.14]
3. Parashar U D, Hummelman E G, Bresee J S, Miller M A, Glass R I. Global illness and deaths caused by rotavirus disease in children, Emerg Infect Dis 2003;9(May (5)):565-72.
4. Bilcke J, Van Damme P, Van Ranst M, Hens N, Aerts M, Beutels P. Estimating the incidence of symptomatic rotavirus infections: a systematic review with meta-analysis. PLoS One 2009;4(June(6)):e6060.
5. Armenia 2005: Results from the Demographic and Health Survey. Stud Fam Plann 2008; 39(September (3)):221-6.
6. Murray C J L, Lopez A D. The global burden of disease a comprehensive assessment of mortality and disability from disease, injuries and risk factors in 1990 and projected to 2020. WHO (1996).
7. PATH. Accelerating the introduction of rotavirus vaccines into GAVI-eligible countries (October, 2006) Available from: http://www.gavialliance.org/resources/Rotavirus_Investment_Case_Oct06.pdf [accessed on 08.09.14]
8. WHO. Choosing Interventions that are Cost-effective (WHO-CHOICE). Estimates of unit costs for patient services for Armenia (2010) Available at: http://www.who.int/choice/country/arm/cost/en/index.html [accessed on 08.09.2014]

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Cost-effectiveness evidence for the introduction of a vaccine

Case study: Belarus and Uzbekistan – *Haemophilus influenzae* type B[1]

KEY FINDINGS

A comparative economic evaluation of *Haemophilus influenzae* type b (Hib) vaccination in Belarus and Uzbekistan was conducted to guide decision-makers on whether:

- Belarus should expand current regional Hib vaccination countrywide;
- Uzbekistan should continue Hib vaccination following termination of funding from the GAVI Alliance in 2015.

Key findings included the following.

Hib vaccination for one birth cohort is predicted to:

- prevent about **350** deaths and **3000** Hib disease cases **annually** in children less than 5 years of age in Uzbekistan;
- prevent about **3** deaths and **500** Hib disease cases **annually** in children less than 5 years of age in Belarus;
- **reduce** by **80%** treatment costs for Hib (outpatient visits and inpatient admissions) in both countries;
- **reduce** by **80%** the number of children with long-term disabilities due to Hib meningitis.
- increase immunization costs per fully vaccinated child to **US$ 43** and **US$ 16** in Belarus and Uzbekistan respectively.

Methods

A decision analytic model was used to predict the impact of Hib vaccination for the 2009 birth cohort in Belarus and Uzbekistan.

Input parameters included:

- demography and disease burden
- health service utilization and costs
- vaccination coverage and efficacy
- vaccination cost.

About *Haemophilus influenzae* type B

Hib is the most common cause of serious infection and mortality in children under 5 years of age in industrialized countries that do not include Hib vaccination in their routine immunization schedules.

Hib often presents as meningitis, epiglottitis, pneumonia, septic arthritis or osteomyelitis.

Hib is frequently associated with severe neurologic sequelae, even if antibiotics are given promptly.

Vaccines are the only public health tool that can prevent most cases of serious Hib disease.

[1] Griffiths UK, Clark A, Shimanovich V, Glinskaya I, Tursunova D, Kim L, et al. (2011) Comparative Economic Evaluation of Haemophilus influenzae Type b Vaccination in Belarus and Uzbekistan. PLoS ONE 6(6): e21472. doi:10.1371/journal.pone.0021472.

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Results

Health impact

Hib vaccination is predicted to:

- prevent 3002 cases of Hib disease for the 2009 birth cohort in Uzbekistan and 467 cases in Belarus;
- reduce under-five mortality by 1.1% and 0.3% in Uzbekistan and Belarus respectively.

Table 1. Discounted health and economic impact for 2009 birth cohort (0-59 months)

	BELARUS	UZBEKISTAN
Hib disease cases averted	467	3.002
Hib deaths averted	3	334
Hib meningitis sequelae cases averted	4	33
DALYs averted	152	11 473
Annual incremental vaccine costs (US$)	1 764 322	4 241 611
Treatment costs averted (US$)	343 740	1 183 681
Annual net costs (US$)	1 420 582	3 057 930
Incremental costs per DALY averted (US$)	**9 323**	**267**

Cost-effectiveness

- The cost per discounted disability-adjusted life-year (DALY) averted was calculated to be US$ 9323 in Belarus and US$ 267 in Uzbekistan, making Hib vaccination cost-effective and highly cost-effective respectively.
- Hib vaccination is more cost-effective in Uzbekistan mainly due to the country's:
  - higher baseline Hib mortality burden
  - lower price of vaccine.

Table 2. Cost-effectiveness

	BELARUS	UZBEKISTAN
Cost per discounted DALY averted (US$)	$9 323	$267
GDP per capita (US$)	$5 560	$1 100
Cost-Effectiveness (WHO Criteria)	Cost-effective	Highly cost-effective

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Cost-effectiveness evidence for the introduction of a vaccine

Case Study: Croatia – PCV[1]

KEY FINDINGS

A cost-effectiveness study on the introduction of Pneumococcal Conjugate Vaccine (PCV) was conducted in Croatia. Key findings included the following.

Pneumococcal vaccination in children aged less than 5 years in Croatia in the period 2014-2033 was predicted to:

- prevent 36 000 episodes of pneumococcal illness;
- prevent 3650 outpatient visits, 100 hospital admissions and 1 death each year;
- reduce by 50-60% incidence of pneumococcal meningitis and the number of children with long term disabilities due to meningitis;
- reduce health service expenditure for treating pneumococcal illnesses by US$ 6–7 million;
- cost the government US$ 50–55 million to introduce;
- be potentially cost-effective at vaccine price less than US$ 20 per dose.

Methods

PCV10 and PCV13 were compared to a scenario assuming no vaccination for 20 birth cohorts of children over the period 2014–2033 using a static cohort model (TRIVAC).

Input parameters included:

- demography and disease burden
- health service utilization and costs
- vaccination coverage and efficacy
- vaccination cost.

About *Streptococcus pneumoniae*

These bacteria cause a wide range of diseases including meningitis, pneumonia, sinusitis and otitis media.

Worldwide, about 14.5 million episodes of serious pneumococcal disease occur each year, and it is the most important cause of vaccine-preventable deaths in children younger than 5 years.

The two available pneumococcal conjugate vaccines (PCV), PCV10 and PCV13, target either 10 or 13 of the most prevalent serotypes respectively, which cause over 70% of serious pneumococcal disease in children.

[1] Višekruna Vuđina V, KureĐiĐ FilipoviĐ S, Kožnjak N, StameniĐ V, Clark A, Mounaud B, Blau J, Hoestlandt C, KaiĐ B. Cost-effectiveness of pneumococcal conjugate vaccination in Croatia.

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Results

Health benefits

- Each year, in children less than 5 years of age either vaccine is estimated to prevent about:
  - 1800 pneumococcal cases
  - 100 hospital admissions
  - 1 death

Table 1. Discounted health benefits (20 cohorts vaccinated over the period 2014–2033)

HEALTH OUTCOME	NO VACCINE	NUMBER OF CASES AVERTED	
		PCV 10	PCV 13
Pneumococcal cases in children less than 5 years	680 474	36 348	36 931
Outpatient visits	1 360 359	72 381	73 497
Inpatient admissions	3 365	1 808	2 086
Deaths < 5 years	27	15	17
Children with permanent disability	15	8	9
DALYs Lost	1 297	559	643

Economic benefits

For the period 2014-2033, about 600 disability-adjusted life years (DALYs) would be prevented

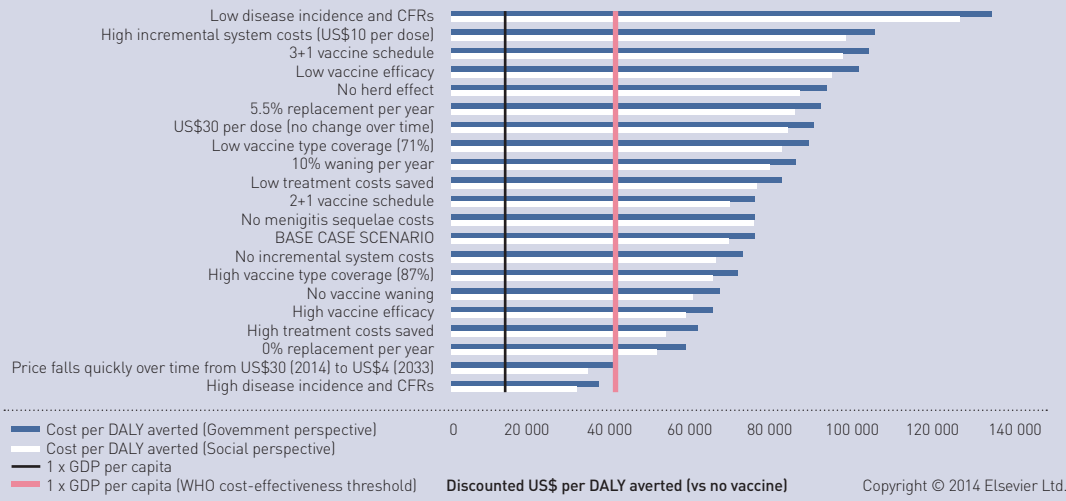
Over 20 years, either vaccine would avert costs amounting to approximately:

- US$ 6–7 million (government perspective)
- US$ 10–11 million (societal perspective).

The cost per DALY averted would be US$ 69 000–77 000. In Croatia, 3 x GDP per capita (i.e. the WHO-recommended cost-effectiveness threshold) is around US$ 40 000, therefore routine vaccination with PCV in Croatia is **unlikely to be cost-effective** unless:

- the vaccine is priced at US$ 20 per dose or less;
- the disease burden is higher than estimated;
- the burden of pneumococcal disease in older age groups is considered.

Figure 1. US$ per DALY averted for PCV10 with variable input parameters



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Evidence for strengthening an existing vaccine programme

Case study: Germany – measles[1]

KEY FINDINGS

A study of the costs of a measles outbreak in a region of Germany was conducted. Parental reasons in the case of non-vaccinated children were also explored. The key findings included the following.

- An accumulation of **non-immune individuals** led to an outbreak of 1749 cases in North Rhine-Westphalia in 2006.
- **Targeted efforts such as school-based catch-up campaigns for older age groups are needed to close immunity gaps to prevent outbreaks.**
- Most cases occurred in the city of Duisburg (614 cases), where
  - at least 80% of cases were reported as having received **no vaccinations**;
  - almost **3000 school days** and about **300 work days** were missed by patients with measles;
  - 95 patients were hospitalized for a total of **775 days**;
  - each measles case cost about **€520** (including the cost to the local public health office).

Methods

A school-based retrospective cohort study was conducted during the initial phase of the 2006 measles outbreak in North Rhine-Westphalia (NRW).

Overall coverage with two-dose measles-containing vaccine (MCV) in 2005 in NRW was 74.7%.

All cases notified in the worst-affected city, Duisburg, were invited to participate by interview or questionnaire. 81% of 614 cases in Duisburg were interviewed. The median age of interviewed measles cases was 11 years.

About measles

The measles virus is highly infectious. Measles can lead to serious complications such as death, blindness, encephalitis, pneumonia and severe diarrhoea.

Measles incidence increased by 348% in the WHO European Region between 2007 and 2013 due to immunity gaps.

[1] Wichmann O, Siedler A, Sagebiel D, Hellenbrand W, Santibanez S, Mankertz A, et al. Further efforts needed to achieve measles elimination in Germany: results of an outbreak investigation. Bull World Health Organ.

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Results

Coverage

- 94% were unvaccinated or had only received one dose of MCV.
- Among the key reasons for under-vaccination were that parents had forgotten, they rejected vaccination, or a doctor had advised against vaccination.

Health

- Complications reported:
  - 19% otitis media
  - 7% pneumonia
  - 0.6% encephalitis
  - 2 deaths.

Economy

- Measles patients missed 2 854 school days and 301 work days
- Healthcare provider costs for the 614 measles patients in Duisburg were estimated at € 229 000.

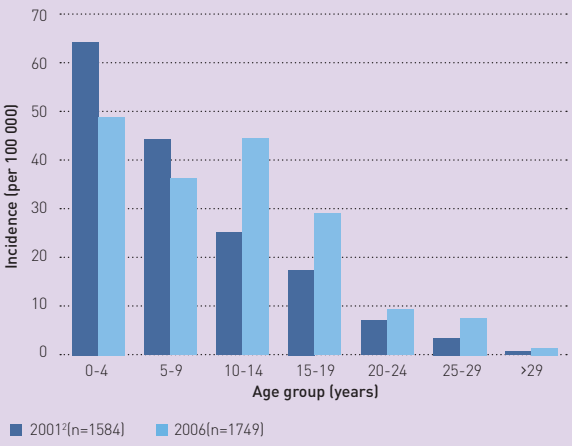
Table 1. Reasons for non-vaccination (reported by parents of measles patients in the Duisburg 2006 outbreak)

Reason for not being vaccinated	%
Parents forgot about the vaccination	36.4
Parents rejected the vaccination	27.8
Doctor recommended against vaccination (inappropriately)	16.5
Doctor recommended against vaccination (appropriately)	0.3
Child was less than 12 month	13
Vaccination was not offered	6

Table 2. Health care costs, Duisburg measles outbreak 2006

Total costs for hospitalization	€ 178 329
Outpatient consultations	€ 27 528
Laboratory tests	€ 20 826
Antibiotic treatment	€ 2 440
Total	**€ 229 123**

Figure 1. Reported measles cases by age group, North Rhine-Westphalia region, Germany, 2011 and 2006



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Cost-effectiveness evidence for introducing and sustaining a vaccine

Case study: Germany – rotavirus[1]

KEY FINDINGS

A study on the impact of rotavirus vaccine was conducted in Germany. Key findings included the following.

Rotavirus vaccination, with low-moderate vaccine uptake in Germany, was associated with:

- 36% reduction in rotavirus-related hospitalization for children less than 24 months in the eastern Federal States;
- 25% reduction in rotavirus-related hospitalization for children less than 24 months in the western Federal States;
- significantly lower incidence of rotavirus-related hospitalization when vaccine uptake is higher and earlier.

The greatest health impact was recorded for infants 6–11 months of age.

Method

Incidence rates of rotavirus-related hospitalizations were compared before (2004-2006) and in the seasons after (2008/09-2010/11) the vaccine was available on the German market.

A retrospective questionnaire survey was used to assess the **vaccine coverage.**

Rotavirus cases were identified through the national mandatory disease reporting system[2].

Results

A **low-moderate uptake** was observed (rotavirus vaccination was not introduced into the national immunization schedule in Germany until 2013).

The study population was stratified into eastern Federal States (EFS) and western Federal States (WFS) – because of the **remarkable difference in vaccine uptake.** (Rotavirus vaccine uptake was consistently higher in EFS).

About rotavirus

Rotaviruses are the most common cause of severe diarrhoeal disease in young children worldwide. They are also the cause of gastroenteritis and dehydration.

Worldwide, it causes an estimated 453 000 deaths in children below 5 years of age annually.

In the European Region deaths are rare, but there are 87 000 hospitalizations annually, which result in high health care costs.

There are two available rotavirus vaccines, Rotarix and RotaTeq, which are both considered safe and effective at preventing gastrointestinal disease.

[1] Dudareva-Vizule S, Koch J, an der Heiden M, Oberle D, Keller-Stanislawski B,Wichmann O. Impact of rotavirus vaccination in regions with low and moderate vaccine uptake in Germany. Human Vaccines & Immunotherapeutics 2012;8:1407–15.

[2] Robert Koch -Institut. Infektionsepidemiologisches Jahrbuch für 2010, Berlin, 2011

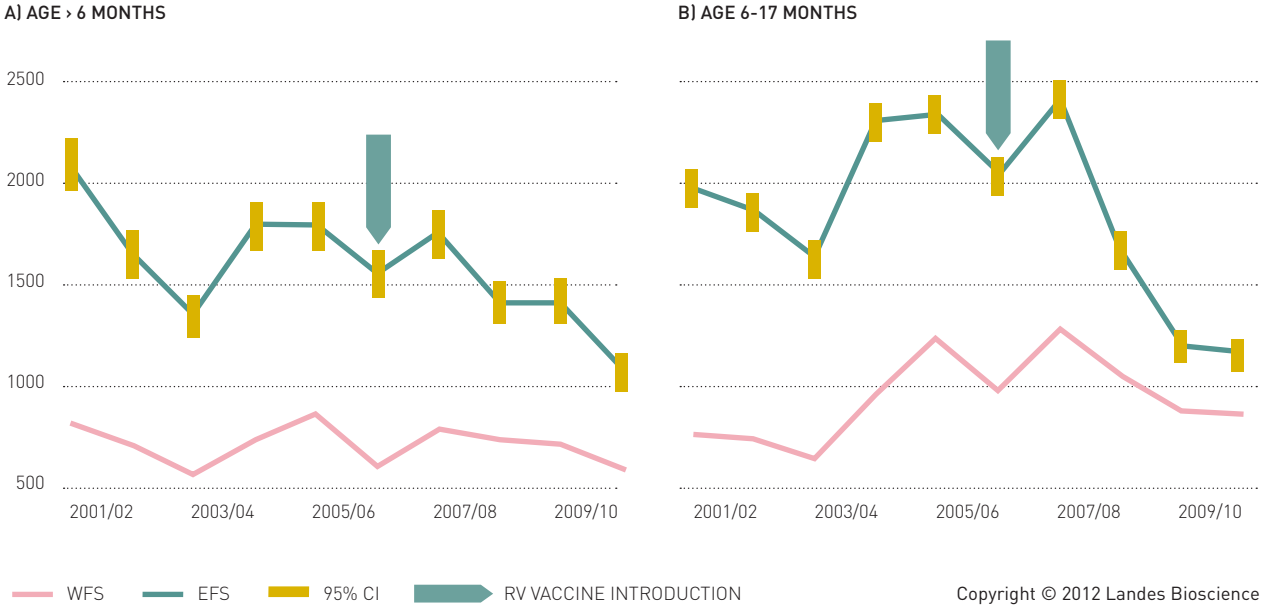
Table 2. Incidence of reported RV-related hospitalisations in EFS pre-vaccination (2004-6) and post-vaccination (2010/11)

	INCIDENCE PER 100,000		
AGE GROUP	2004-2006	2010-2011	% CHANCE
LESS THAN 6 MONTHS	1798	1075	-40
6-11 MONTHS	2585	1114	-57
12-17 MONTHS	2076	1226	-41
18-29 MONTHS	1525	1189	-22

Incidence of rotavirus-related hospitalization

- **decreased significantly** in children less than 24 months of age;
- did not decrease significantly in children aged 24 months or more;
- decreased more in EFS than WFS.

Fig. 1. Rotavirus-related hospitalization incidence 2001–2010 in age groups a) less than 6 months and b) 6–17 months demonstrate a steeper decline in EFS than WFS



Note: the incidence of rotavirus was also higher in EFS, however regression analysis demonstrated that the vaccination impact would be similar in both regions with similar coverage (that is, the difference in incidence of rotavirus-related hospitalization between the two regions is not accounted for by the difference in rotavirus incidence).

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Cost-effectiveness evidence for the introduction of a vaccine

Case study: Georgia – PCV[1]

KEY FINDINGS

A cost-effectiveness study of Pneumococcal Conjugate Vaccine (PCV) introduction in Georgia produced the following key findings.

- PCV introduction in Georgia is predicted to:
  - prevent 4 deaths and 717 cases of acute otitis media per year;
  - prevent 533 cases of pneumonia per year;
  - result in treatment cost savings of US$ 2.14 million;
  - have a net cost of US$ 2.3 million;
- Introduction of PCV10 vaccine in Georgia was estimated to be cost-effective based on WHO criteria[2] even in the worst-case scenario tested.

Methods

A cost-effectiveness analysis on the introduction of PCV10 in Georgia was conducted from the Government's perspective.

The analysis was conducted using a TRIVAC decision-analytic model time horizon of 10 years, 2014 to 2023. The introduction of PCV10 was compared to a scenario of no PCV vaccination.

Input parameters included:

- demographics and disease burden
- vaccine efficacy and coverage
- health services utilization and costs
- vaccine programme costs.

About *Streptococcus pneumoniae*

These bacteria cause a wide range of diseases including meningitis, pneumonia, sinusitis and otitis media.

Worldwide, about 14.5 million episodes of serious pneumococcal disease occur each year, and it is the most important cause of vaccine-preventable deaths in children younger than 5 years of age.

The two available PCVs target either 10 or 13 of the most prevalent serotypes, which cause over 70% of serious pneumococcal disease in children.

[1] Komakhidze T, Dolakidze T, Shakhnazarova M, Chlikadze R, Kopaleishvili N, Goginashvili K, Kherkheulidze M, Mosina L, Clark A, Blau J. Cost-effectiveness analysis of the introduction of the pneumococcal conjugate vaccine (PCV) in Georgia.

[2] Adams T, Baltussen R, Tan-Torres T, Evans D, Hutubessy R, Acharya A, Murray CJL. Making Choices in Health. In: WHO Guide to Cost-Effectiveness Analysis. Geneva: World Health Organization; 2003.

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Results

Health impact

Table 1: Aggregated outcomes prevented due to PCV programme for 10 cohorts

DEATHS	CASES AOM	ADMISSIONS (PNEUMONIA)	ADMISSIONS (SP. MENINGITIS)	ADMISSIONS (SP. NPNM SEPSIS)	MENINGITIS SEQUELAE	DALY (ALL DISEASES)
41	7 170	5 325	87	508	17	1 438

AOM: acute otitis media; NPNM: non-pneumonia non-meningitis; DALY: disability-adjusted life-years.

Economic Impact

Table 2. Costs of the PCV10 programme 2014 to 2023

TOTAL COSTS OF PCV PROGRAMME	TREATMENT COSTS	TOTAL NET COSTS
US$ 4.44 MILLION	US$ 2.14 MILLION	US$ 2.30 MILLION

Conclusion

PCV vaccination in Georgia would be **very cost-effective** by WHO criteria[2] in most scenarios modelled. The cost per DALY averted is US$ 1599 from the Government perspective.

In the **worst-case scenario modelled**, the introduction of PCV10 in Georgia would still be **cost-effective**.

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Cost-effectiveness evidence for introducing and sustaining a vaccine

Case study: Italy – Hepatitis B[1]

KEY FINDINGS

An economic evaluation of the clinical impact of hepatitis B immunization in the 20 years following its introduction in Italy in 1991 was conducted. Key findings included the following.

- The first 20 years of the hepatitis B vaccination programme resulted in:
  - **reduced burden** of hepatitis B virus (HBV) related diseases;
  - return on investment of 1.02 from the National Health Service (NHS) perspective;
  - clinical **savings exceeding** vaccination **costs** in 2010

Italy context

1980s

- 11 000 symptomatic cases of acute viral hepatitis per year (incidence rate 19/100 000).
- 64 000 affected by chronic viral hepatitis or cirrhosis.
- 3 400 affected by hepatocellular carcinoma.

1991

- Italy introduced a programme of routine immunization against HBV.
- Immunization of all newborns within their first years of life.
- Immunization of 12-year-olds during the first 12 years of the programme.
- HBV incidence rate declined to 5/100 000 due to behaviour changes and improved health care procedures.

2010

- HBV incidence rate decreased to 0.9/100 000.

About hepatitis B

Approximately 2 billion people worldwide have been infected with HBV. Of the 360 million people chronically infected, 600 000 die each year from HBV-associated liver cirrhosis or hepatocellular carcinoma.

In endemic areas, HBV transmission mainly occurs perinatally or during early childhood. However, in low endemic areas, transmission mainly occurs later in life through sexual contact or through the use of contaminated needles.

Methods

The authors used a mathematical simulation model to conduct an economic evaluation of the clinical impact of hepatitis B immunization in the 20 years following its introduction in Italy. The authors also projected future benefits that could be expected to be delivered by the programme.

[1] Boccalini S, Taddei C, Ceccherini V, Bechini A, Levi M, Bartolozzi D, Bonanni P. Economic analysis of the first 20 years of universal hepatitis B vaccination program in Italy: An a posteriori evaluation and forecast of future benefits. Human Vaccines & Immuno-therapeutics. May 2013, 9(5): 1119-1128.

Results

- The study found that hepatitis B incidence declined between 1990 and 2010 by:
  - 100% among children aged 0–14 years
  - 97% among teenagers and adults aged 15–24 years
  - 70% among adults older than 24 years of age
  - 82% in the total population.
- Benefit-to-cost ratio was 0.91 from the societal perspective for the period 1991-2010, and predicted to be 2.47 for the period 1991-2059.
- Projections for 2011–2059 estimated a 77% reduction of costs, from the both the NHS and societal perspectives.

From the NHS perspective, the break-even point was achieved in approximately 2010. Therefore, benefits of the immunization programme will continue to become more evident in the future.

The impact of the immunization programme was far reaching, affecting all age groups within the Italian population.

Figure 1. Cumulative clinical savings and vaccination costs from the NHS perspective during the period 1991–2010

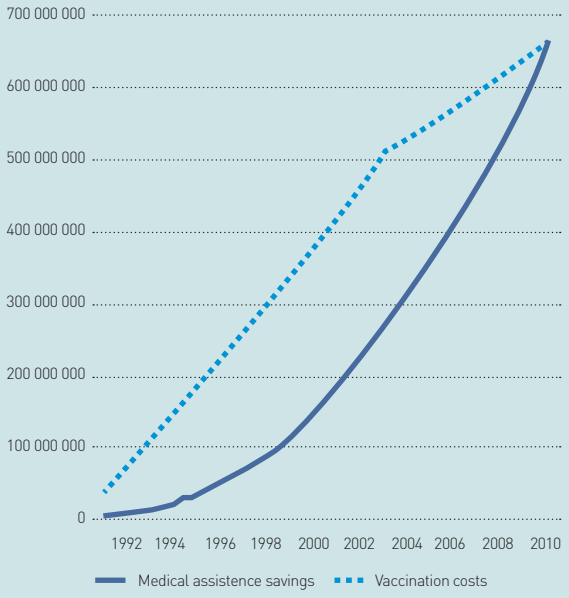

Table 1. Total number of cases related to HBV infection in Italy during the 1991-2010 period in the vaccination and no vaccination scenario

CLINICAL CASES	NO VACCINATION	VACCINATION	AVOIDED CASES	% REDUCTION
HBV infection	168 930	42 038	126 892	75
Symptomatic acute HBV infection	43 140	28 520	14 621	34
Chronic hepatitis B	5 465	1 360	4 105	75
Compensated cirrhosis	129	59	70	54
Decompensated cirrhosis	9	4	5	54
Hepatocellular carcinoma	86	22	64	74
Liver transplantation	24	7	17	72

Table 2. Clinical costs during the 1991–2010 period from the NHS perspective in the vaccination and no vaccination scenarios

	NHS PERSPECTIVE			
CLINICAL COSTS (1991–2010)	NO VACCINATION	VACCINATION	AVOIDED CASES	% REDUCTION
Symptomatic acute HBV infection	572 051 723	362 160 953	209 890 771	37
Chronic hepatitis B	649 157 949	210 059 569	439 098 380	68
Compensated cirrhosis	18 485 689	8 914 521	9 571 168	52
Decompensated cirrhosis	1 193 807	575 700	618 107	52
Hepatocellular carcinoma	8 330 359	2 830 361	5 499 999	66
Liver transplantation	3 135 545	1 117 773	2 017 771	64
Total	1 252 355 072	585 658 877	666 696 195	53

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Evidence for strengthening an existing vaccination programme

Case study: Italy – measles[1]

KEY FINDINGS

A study of two measles outbreaks in Lazio, Italy was conducted. Key findings included the following:

- Despite high overall coverage within the population, pockets of unvaccinated communities create a risk for disease outbreaks.
- The outbreaks started in groups with **low vaccine coverage** (Roma/Sinti community, secondary school students).
- **None** of the 102 Roma/Sinti cases were vaccinated against measles.**5.5%** of the 347 remaining cases had received one dose of measles containing vaccine.
- Four **health care professionals** developed measles.
- **About 60**% of the 449 cases required **hospitalization.**

Methods

Two measles outbreaks in the period June 2006 – August 2007 were investigated using data from the regional Public Health Agency and National Institute of Health.

Measles vaccine coverage has historically been low in Lazio, but after a national measles elimination plan, overall coverage had increased from 83.9% (2003) to 90.7% (2007).

About measles

The measles virus is highly infectious. Measles can lead to serious complications such as death, blindness, encephalitis, pneumonia and severe diarrhoea.

Measles incidence increased by 348% in the WHO European region between 2007 and 2013 due to immunity gaps.

[1] Curtale F, Perrelli F, Mantovani J, Cioffi Degli Atti M, Filia A, Nicoletti L, Magurano F, Borgia P, Di Lallo D. Description of two measles outbreaks in the Lazio Region, Italy (2006–2007). Importance of pockets of low vaccine coverage in sustaining the infection. BMC Infect Dis 2010, 10:62

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Results

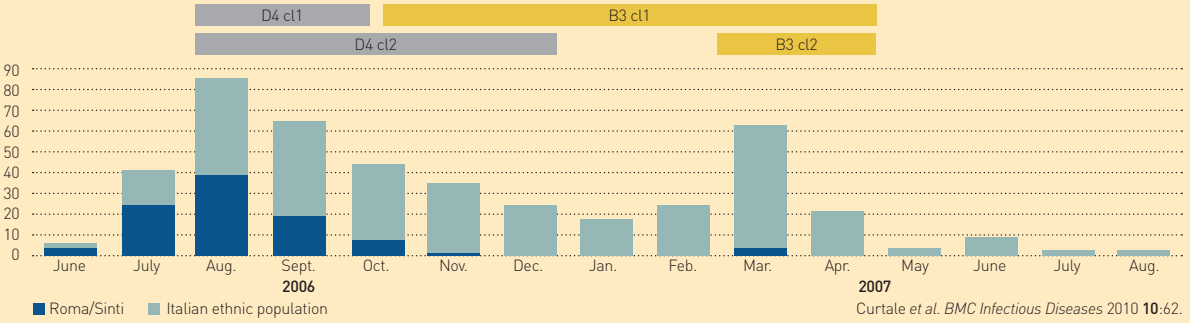
The first outbreak started in the Roma/Sinti population, and was transmitted to the general population.

The second outbreak started in a secondary school and affected mainly adolescents and adults in the general population.

Table 1. Sources of outbreaks

	FIRST OUTBREAK	SECOND OUTBREAK
Serotype	D4	B3
Dates reported	June-Dec 2006	Oct 2006-Aug 2007
First Reported cases	Roma/Sinti population	Secondary school

Figure 1. Number of reported measles cases by month in Lazio



Curtale *et al. BMC Infectious Diseases* 2010 **10**:62.

Vaccination status and age distribution

None of the Roma/Sinti cases were vaccinated against measles. Most cases in the Roma/Sinti group were aged 1-4 years. In the general population, most cases were aged 15-19 years and there was a higher percentage of vaccinated subjects, especially among young children.

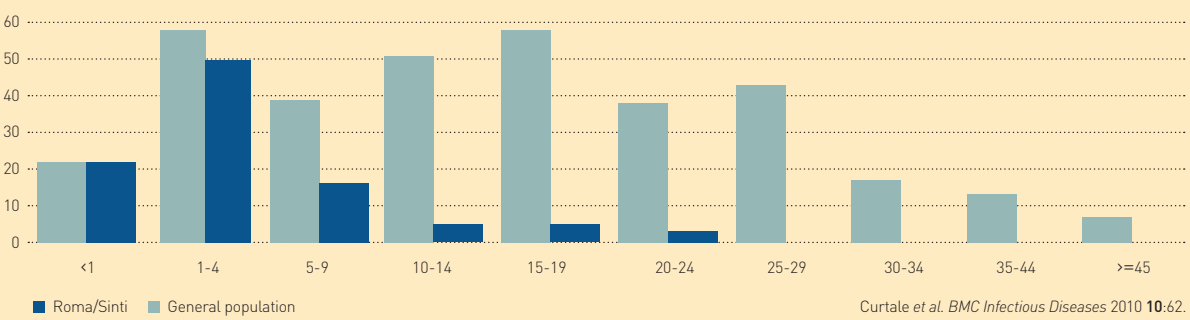
Table 2. Sources of outbreaks

	ROMA/SINTI	NON-ROMA/SINTI
Number of cases	102	347
% received one dose measles-containing vaccine	0 %	5.5 %
Median age of cases (years)	2	15
% cases aged 0-4 years	70 %	23 %
% cases aged less than 15 years	90 %	49 %

Conclusion

Despite high overall coverage within the population, pockets of unvaccinated communities create a risk for disease outbreaks.

Figure 2. Number of reported measles cases by age group



Curtale *et al. BMC Infectious Diseases* 2010 **10**:62.

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Evidence for sustaining a vaccine

Case Study: United Kingdom - measles[1]

KEY FINDINGS

A study of the short-term impact of measles infection on health-related quality of life was conducted in the United Kingdom during 2012 and 2013. Key findings included the following.

- 2366 cases of measles resulted in an estimated **23 110 age-adjusted days of lost productivity** during the 12 month period of the study.
- For each measles patient who fully recovered, on average, about:
  - **10 days** were taken off school or work and their carer took **7 days** off;
  - **4 nights** were spent in hospital (if hospitalized);
  - **4 contacts** with a health care professional were reported during the period of infection.

Method

All eligible confirmed cases of measles from 1 June 2012 to 31 May 2013 were invited to participate in a postal survey.

The survey included the **EuroQol EQ-5D-3L** questionnaire to assess the impact on **HRQoL (health-related quality of life)** and additional questions about **direct and indirect impact** of measles infection.

The EuroQol scoring algorithm produces a health utility specific to the individual's health state. These utilities are then used in combination with the duration of symptoms to generate **the Quality-Adjusted Life Years or Days lost** (QALYs or QALDs).

About measles

Measles is a highly contagious viral disease.

It can cause serious complications, including blindness, encephalitis and death.

Measles caused an estimated 2.6 million deaths globally each year before widespread vaccination was introduced.

Vaccination costs less than US$1 per child.

[1] The effect of measles on health-related quality of life: a patient-based survey. Thorrington D, Ramsay M, van Hoek AJ, Edmunds WJ, Vivancos R, Bukasa A, Eames K. PLoS One. 2014 Sep 9;9(9):e105153. doi: 10.1371/journal.pone.0105153. eCollection 2014.

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Results

Impact on health-related quality of life

About **80%** of measles cases reported either some or severe problems for each dimension of health assessed.

Measles resulted in **0.019 QALYs** lost per patient (95% confidence interval: 0.016 – 0.022) – which is equivalent to **6.9 QALDs.**

The overall burden of disease in the United Kingdom (2366 confirmed cases) in the 12 month period from 1 June 2012 was estimated to be:

- **44.2 QALYs lost**
- **23 110 days of lost productivity (including carers).**

Figure 1. Responses to each of five dimensions of health in EQ-5D-3L questionnaire for the worst day of infection for individuals with confirmed measles

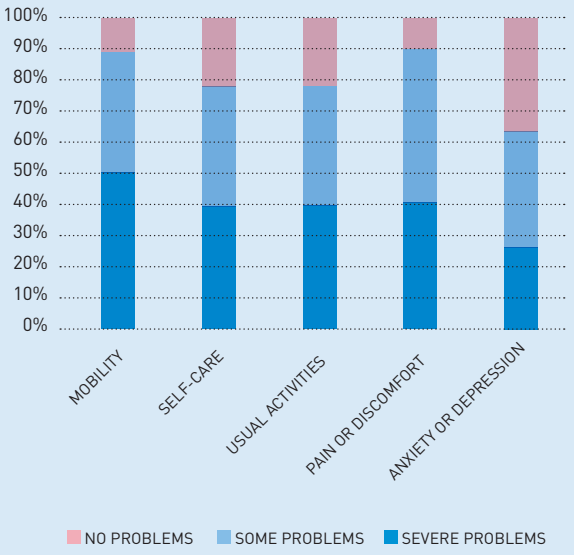

Table 1: Impact of measles infection on the duration of symptoms, time off school or work and hospitalization

	ALL CONFIRMED MEASLES CASES	AGED UNDER 7 YEARS	AGED 7-12 YEARS	AGED 13 YEARS AND OVER
Mean duration of perceived symptoms (days)	13.8	12.8	13.5	14.4
Individuals reporting time off work or school (%)	63.1 %	37.1 %	88.0 %	74.1 %
Mean time off work or school (days)	9.6	8.6	9.1	10.1
Individuals reporting time off work for primary caregivers (%)	39.6 %	44.3 %	40.0 %	31.5 %
Mean time off work for primary caregivers (days)	7.3	7	7.7	7.2
Individuals reporting at least one night in hospital (%)	36.5 %	32.9 %	8.0 %	45.4 %
Mean number of nights spent in hospital	4.2	4	4	4.4

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Cost-effectiveness evidence for sustaining a vaccine

Case study: United States – polio[1]

KEY FINDINGS:
A retrospective cost-effectiveness analysis for polio vaccination was conducted in the United States (U.S). Key findings included the following.

In retrospect, the U.S. polio vaccination programme is a cost-saving intervention.
In the period 1955-2015, the U.S. polio vaccination programme is estimated to have:

- prevented over 160 000 deaths;
- averted about 1.1 million cases of paralytic polio.

Due to treatment cost savings, the net economic benefit is approximately $180 billion (2002 US$).
If the time horizon is extended to 2099, polio vaccination is predicted to prevent 2.3 million more cases.

Methods

Estimated economic and health outcomes were calculated from the societal perspective comparing each new polio intervention with the existing polio intervention during four major periods in U.S. polio vaccination history - 1955, 1961, 1980 (mid-point of transition period) and 1997.

The total vaccination costs for a given year were calculated from the cost of vaccine doses distributed (plus wastage) minus the net treatment costs saved from prevented polio cases.

Predicted health and economic outcomes for status quo options were calculated using a dynamic disease transmission model.

The history of polio vaccination in the USA

1955 Salk inactivated poliovirus vaccine (IPV) was introduced and paralytic polio incidence dropped significantly

1961 Monovalent oral poliovirus vaccine (OPV) was introduced

1963 Monovalent OPV switched to trivalent OPV

1971 More cases of vaccine-associated paralytic polio (VAPP) than paralysis from wild polioviruses begin to be reported

1979 Circulating wild polioviruses were eliminated and the last indigenous case occurred in 1979

1997 Transition started from almost exclusive trivalent OPV to enhanced-potency IPV (eIPV)

2000 eIPV used exclusively assumed until 2015

[1] Thompson KM and Duintjer Tebbens RJ. (2006). Retrospective Cost-Effectiveness Analyses for Polio Vaccination in the United States. Risk Analysis, 26, 6,

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Results

Health impact 1955-2015

Polio cases prevented	1.1 million
Deaths averted	160 000

Economic impact 1955-2015

Discounted cost of vaccine (US$ 2002)	US$ 36.4 billion
Treatment costs saved (US$ 2002)	US$ 215 billion
Net costs saved (US$ 2002)	US$ 178 billion

Cost and effectiveness of the polio immunization programme in the United States 1955-2015

YEAR OF DECISION	**1955**	**1955**	**1961**	**1980**	**1997**
LAST YEAR IN MODEL	**2015**	**2015**	**2015**	**2015**	**2015**
INTERVENTION	ACTUAL PROGRAMME	IPV INDEFINITELY	OPV INDEFINITELY	IPV INDEFINITELY	IPV INDEFINITELY
COMPARATOR PROGRAM	NO PROGRAMME	NO PROGRAMME	IPV INDEFINITELY	OPV INDEFINITELY	OPV INDEFINITELY
CUMULATIVE DISCOUNTED BENEFITS					
COSTS (BILLIONS, US$ 2002)	-180	-110	-76	3.5	1.9
PARALYTIC CASES (INCLUDING DEATHS) PREVENTED*	480,000	340,000	160,000	200	130
DEATHS PREVENTED*	73,000	52,000	23,000	30	20
CUMULATIVE NET BENEFIT (BILLIONS US$ 2002)	840	580	290	-3.2	-1.7

*1955 NET PRESENT VALUE