

The Value of Vaccines

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International
Vaccine
Institute

IVI is a Vaccine R&D Center with a Global Health Mission

Vision: Developing countries free of suffering from infectious disease

Mission: Discover, develop and deliver safe, effective and affordable vaccines for global public health



Global Vaccine Research Institute

- HQ and labs at Seoul National University
- Field programs in 29 countries: Asia, Africa, Latin America
- 12 nationalities in workforce of ~130

OECD-recognized Nonprofit International Organization

- UNDP initiative
- First international organization in Korea (1997)
- 35 countries and WHO as state parties



Outline

- **Introduction: life expectancy and infectious mortality**
- **Why vaccines have value**
- **Vaccines as a work in progress**
- **Summary**

Disclaimers: None

Use of vaccine images does not imply endorsement of any product.

Human life expectancy has increased, especially after the 19th C

LIFE EXPECTANCY THROUGH THE AGES

Early humans did not generally live long enough to develop heart disease, cancer or loss of mental function. A snapshot of how life expectancy has changed, and the big killers of each era:

AVERAGE LIFE EXPECTANCY

30 years



Neanderthals (30,000 years ago): Died of injuries caused by rock falls, hunting accidents and conflicts. Food scarcity led to malnutrition. These hunter-gatherer groups contracted diseases that spread from animals. Rabies, tuberculosis, brucellosis, yellow fever and encephalitis were widespread.

38

Neolithic (8500 BC to 3500 BC): Agriculture, irrigation and urbanization brought problems associated with settled populations, such as fecal contamination of water and diseases such as cholera, smallpox, typhoid, polio and influenza. Malaria and other diseases carried by mosquitoes and insects, which fed on domesticated animals, appeared.



35 **Classical Greece and Rome** (500 BC to 500 AD): Tuberculosis, typhoid fever, smallpox and scarlet fever spread among the denser urban populations. Malnutrition, gastroenteritis and violence were also big killers.

48 EARLY MEDIEVAL



Medieval period (500 AD to 1500 AD): Life expectancy grew with urbanization, but famine caused by crop failures and bubonic plague were the big killers. The Black Death (1347-1351) wiped out 25 million people in Europe and 60 million in Asia, returning several times, culminating in the Great Plague of London (1664-1666). By 1500, life expectancy had dropped back to 38.

38 LATE MEDIEVAL

40

Victorian (1850s to 1900): Typhus, typhoid fever, rickets, diphtheria, tuberculosis, scarlet fever and cholera raged in crowded cities.



MEN **70** **WOMEN** **75**

1900s: Better health care, sanitation and living conditions boosted life expectancy to 70 for men and 75 for women by 1950.

CANADA: MEN **82** **WOMEN** **85**

Today: Cancer, heart disease and stroke are the biggest killers in the developed world. Our longer lifespan also comes with unprecedented loss of mental function and mobility problems.

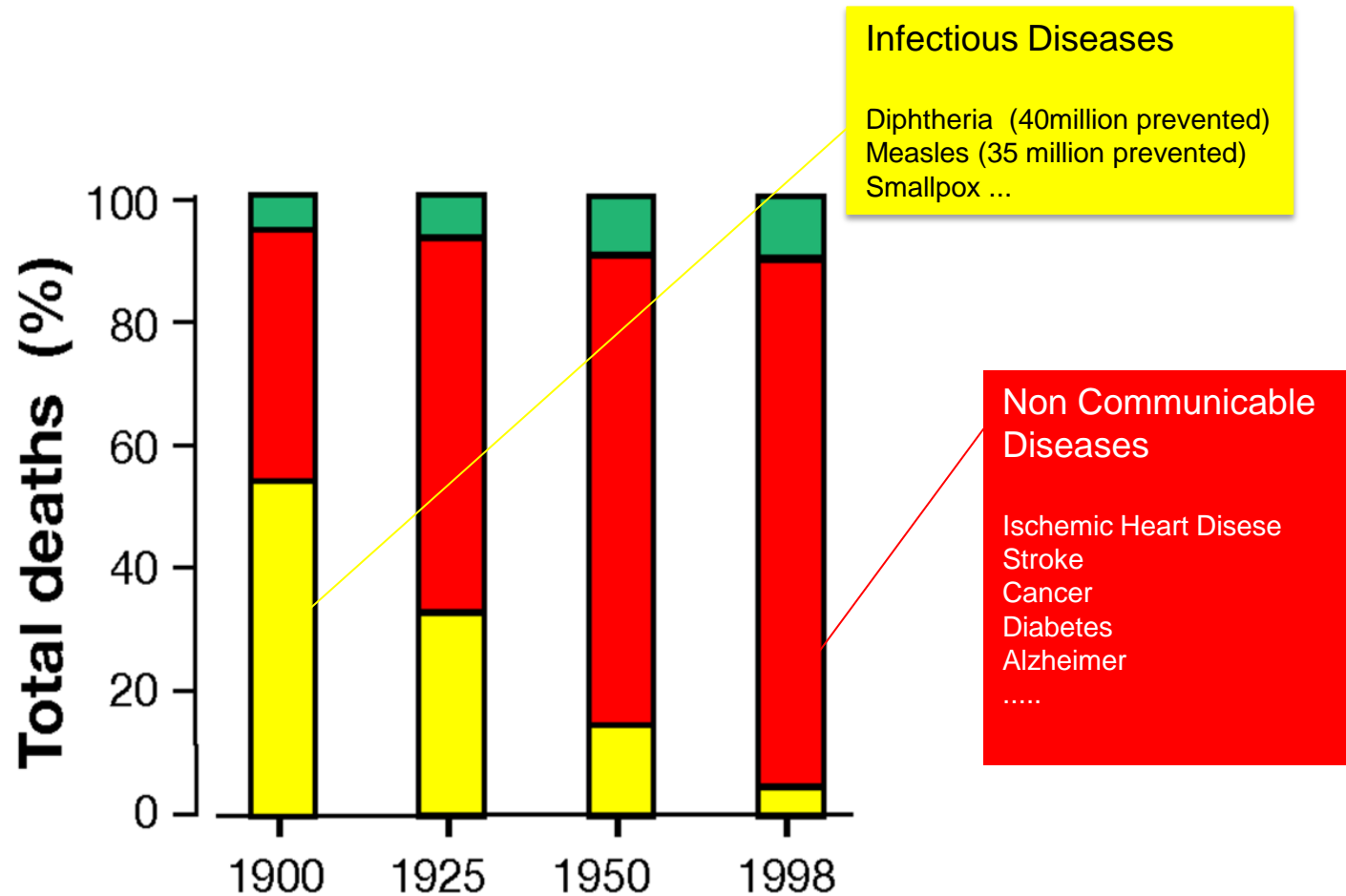
RESEARCH BY RICK SZNAJDER/TORONTO STAR LIBRARY

SOURCES: JOURNAL OF POPULATION RESEARCH, PRINCETON UNIVERSITY, STANFORD UNIVERSITY, WORLD HEALTH ORGANIZATION



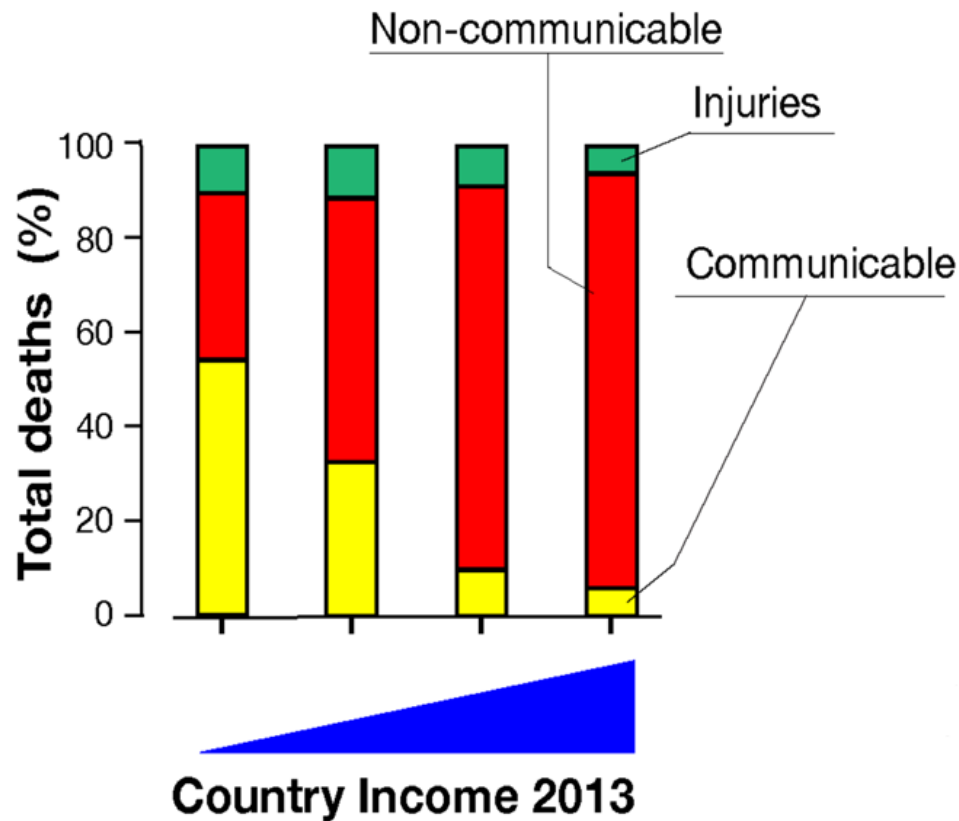
And the life of man, solitary, poor, nasty, brutish and short.

Infectious disease mortality has decreased with development



Vaccines may have greater effect in LDCs

As income levels fall, infectious diseases have a greater impact on mortality.

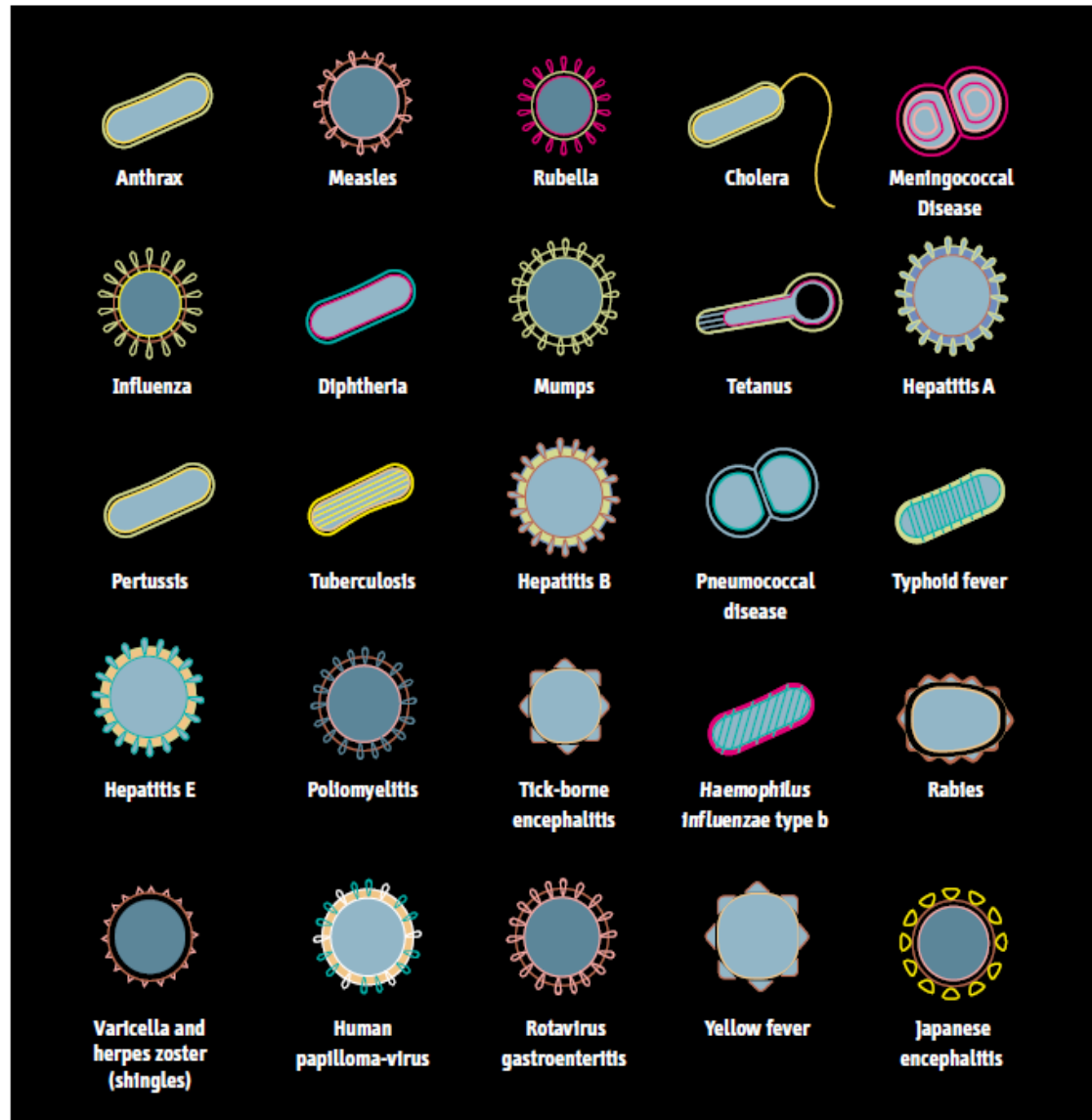


Vaccines work!



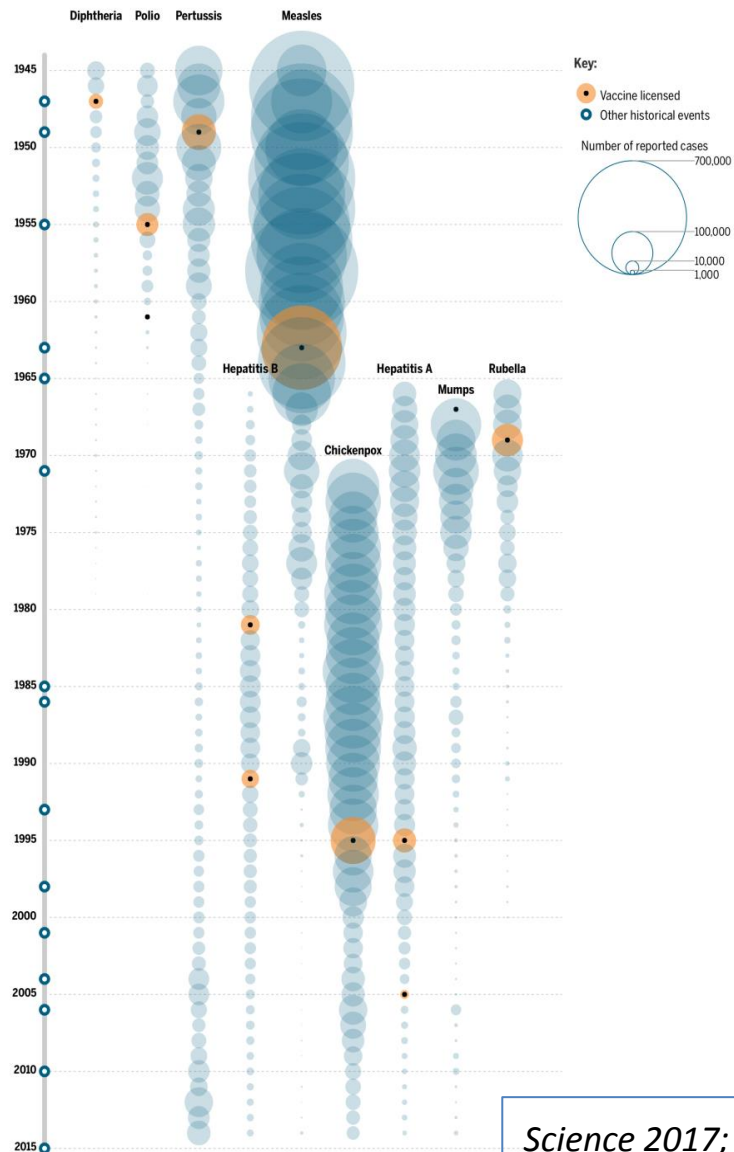
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The 25 vaccine preventable infectious diseases



**Global Vaccine Action
Plan: 2011-2020**

Impact of vaccine introduction on diseases in USA



Estimate of decline of disease morbidity due to vaccination

Disease	Reduction
Diphtheria	100%
Measles	99.9%
Paralytic poliomyelitis	100%
Rubella	99.9%
Congenital rubella syndrome	99.3%
Smallpox	100%
Mumps	95.9%
Tetanus	92.9%
Pertussis	92.2%

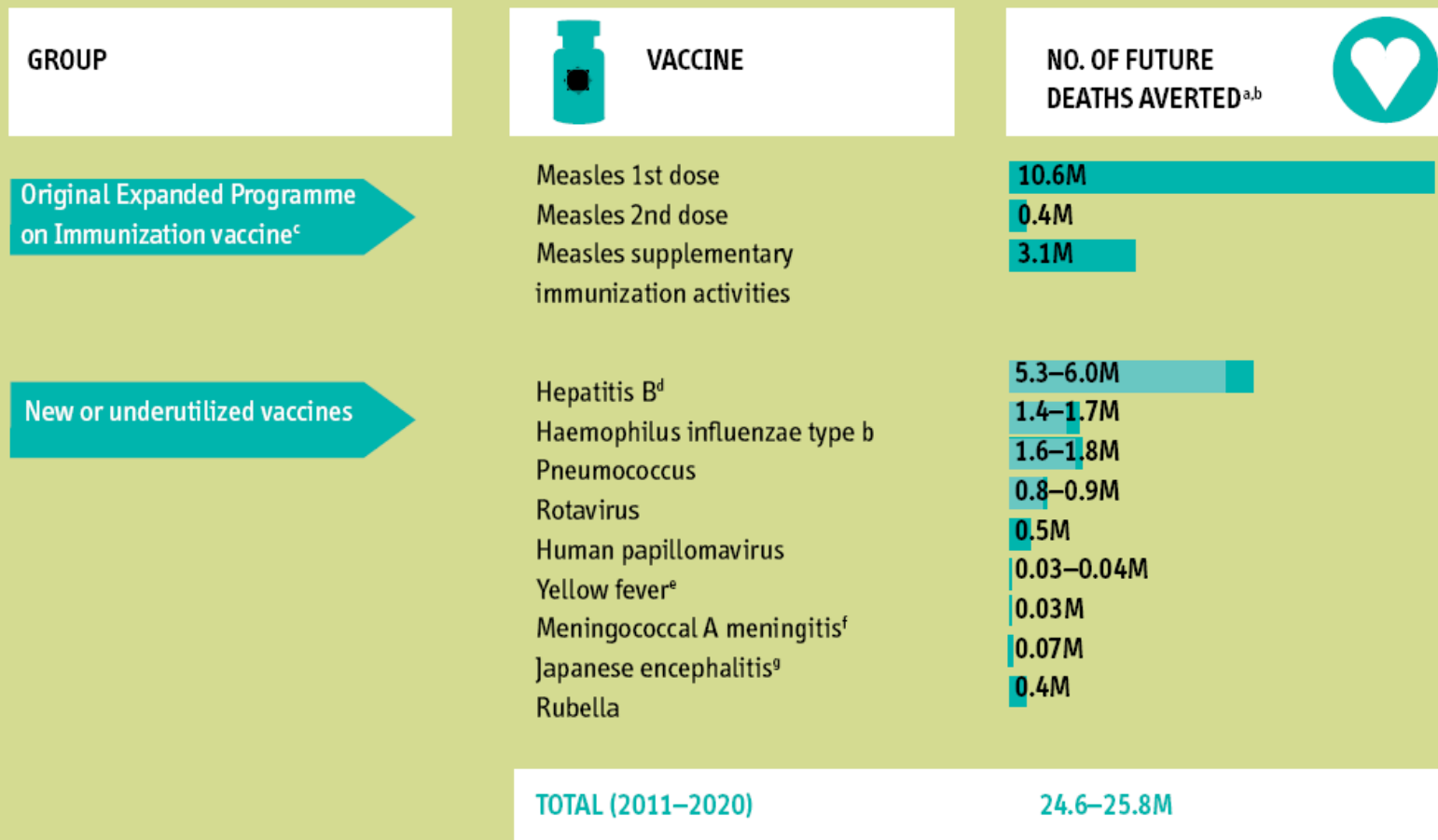
Ventola, P&T 2016, 41:426

Science 2017; 356:364



Vaccination prevents millions of cases of death and illness

Underutilized vaccines: 25M lives could be saved in 10 years



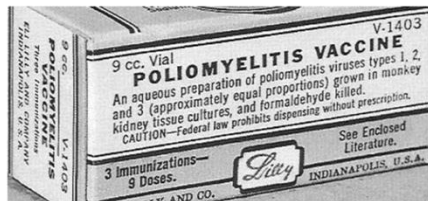
Diseases for which no vaccines exist: 4.8M deaths / year; 48M over 10 years (more later)

Vaccines wipe out deadly diseases

- 1695 first mention of variolation
Zhang Lu (or 1549, Wan Quan, Douzhen xifa)
 - Given by intranasal inoculation or by wearing the clothes of a smallpox infected child
- 1721 Lady Mary Montagu introduces the West to variolation
- 1798 Jenner's report published in the Proceedings of the Royal Society



in Caserta
 The more accurately to observe the progress of the infection, I selected a healthy Boy about eight years old, by the goodness of whose father for the Cause. He had been taken from a suppurated sore on the hand of a dying child, who was infected by her Mother's Scurvy and transmitted with it, at eight years old, into the hands of the King by means of the regular inoculation, such about three quarters of an inch long. On the 1st day he complained of uneasiness in his stomach, on the 4th of headache, little belly, little heat, little appetite, and had a slight head-ach. During the whole of this day he was perfectly insensible to heat either in a stuffy room, or in the shade following he was perfectly well. The appearance and progress of the infection is a little of redness, some pus, which made the same as if inoculated in a common manner, the infection matter, the only difference, I observed was that the edges appeared rather a darker hue, and that the effluvia coming from the incision, took on rather more greenish yellow, than in ordinary inoculation matter has been made use of for the same purpose.



Last case, variola minor, 1977, Somalia



SMALLPOX

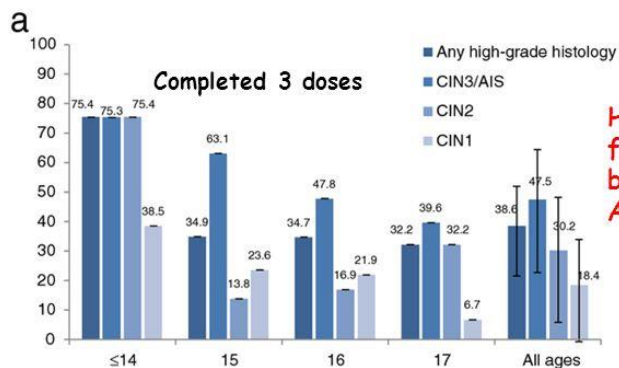
Last case, variola major, Bangladesh, 1975



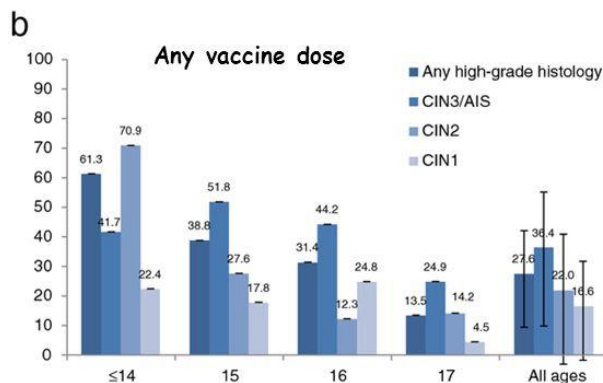
Vaccines can prevent cancer

Impact of Hepatitis B vaccination on Hepatocellular Carcinoma in Korea & Taiwan

LOCATION	BEFORE	AFTER	NOTES
Taiwan	0.70	0.36	Ages 6-14
"	0.52	0.13	Ages 6-9
Korea	18.1	1) Vaccinated 0.58 2) "natural" anti-HBs 0.34	Cohort 370,285 m. 30+ 35,934, vaccinated



HPV vaccine effectiveness for CIN outcome to end 2011 by age of vaccination in 2007 Australia



Gertig et al 2013 BMC Med Oct 22 epub

Note: use of images does not imply endorsement of any vaccine shown.

Vaccines are cost-effective



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Epidemics are expensive

- Healthy societies make better partners
 - UN Sustainable Development Goal 3
- The cost/burden of infectious diseases is enormous
 - MERS in Korea \$10 billion
 - SARS - \$40 billion
 - Ebola - \$6 billion
 - Global pandemic (1918 Spanish flu, 5% of global GDP ~3 trillion USD (World Bank)
 - Total cost for 21st century \$6 trillion
- How do we value the human cost?
- Global Health Security is National Security



Children with measles, Africa

An ounce of prevention is worth a pound of cure

Saving a life costs very, very little

Sample pricing in 2013 of vaccines contracted with suppliers by UNICEF, the world's largest vaccine buyer

Meningitis	\$0.58	\$0.07	BCG Fights tuberculosis
Measles	\$0.24	\$0.16	Hepatitis B
Measles, mumps and rubella	\$0.97	\$0.70	Yellow fever
Rotavirus Fights severe diarrhea	\$3.50	\$0.19	DTP Fights diphtheria, tetanus and pertussis

And it doesn't cost much

Usually...

Take the 2009 US birth cohort, 4.1M children

- The vaccines they receive will save \$13.5B in health treatment costs
- It will have a total savings of \$70B (when including other measures, such as productivity)
- Global costs saved by just pneumococcal, rotaviral and HiB vaccines could total \$63B 2011-2020.

Vaccination prevents deaths and saves money

- Vaccination programs have prevented >3.0 billion infections worldwide
 - >500 million deaths prevented
- Vaccines will save lives from 2011-2020:
 - 25 million deaths prevented



US CDC estimate

From 1994-2013 in USA

Vaccines prevented:

- 322 million illnesses
- 21 million hospitalizations
- 732,000 deaths

Vaccines saved:

- \$295 billion direct costs
- \$1.38 trillion in total societal costs

For every \$1 spent on vaccines, \$16 are saved in future healthcare costs, lost income, and lost productivity. If all indirect costs are included, the ROI is 44:1.

WHO Global Action Plan

http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/index.html

Example: Indirect effects of vaccination

Vaccine 33 (2015) 5020–5026



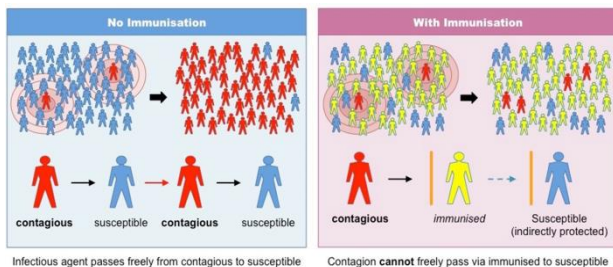
In RSA introduction of PCV result in an 80% decrease in non-susceptible *S. pneumoniae* infections (van Gottberg, NEJM 2014)

The causal effect of childhood measles vaccination on educational attainment: A mother fixed-effects study in rural South Africa

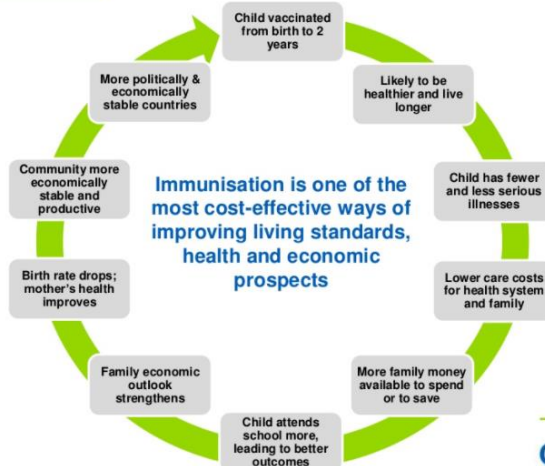
Tobenna D. Anekwe^{a,b,*}, Marie-Louise Newell^{b,c}, Frank Tanser^b, Deenan Pillay^{b,d}, Till Bärnighausen^{b,e}



- Education
- Herd immunity
- Antimicrobial resistance (direct & indirect)
- Improved health & economic prospects
- Improvements in GDP



A VIRTUOUS CYCLE



- 1) Improve IQ
- 2) Higher survival lower birth rate
- 3) Higher parental productivity
- 4) 30-50% of Asian growth from 2,3



Vaccines don't save lives,
vaccination does

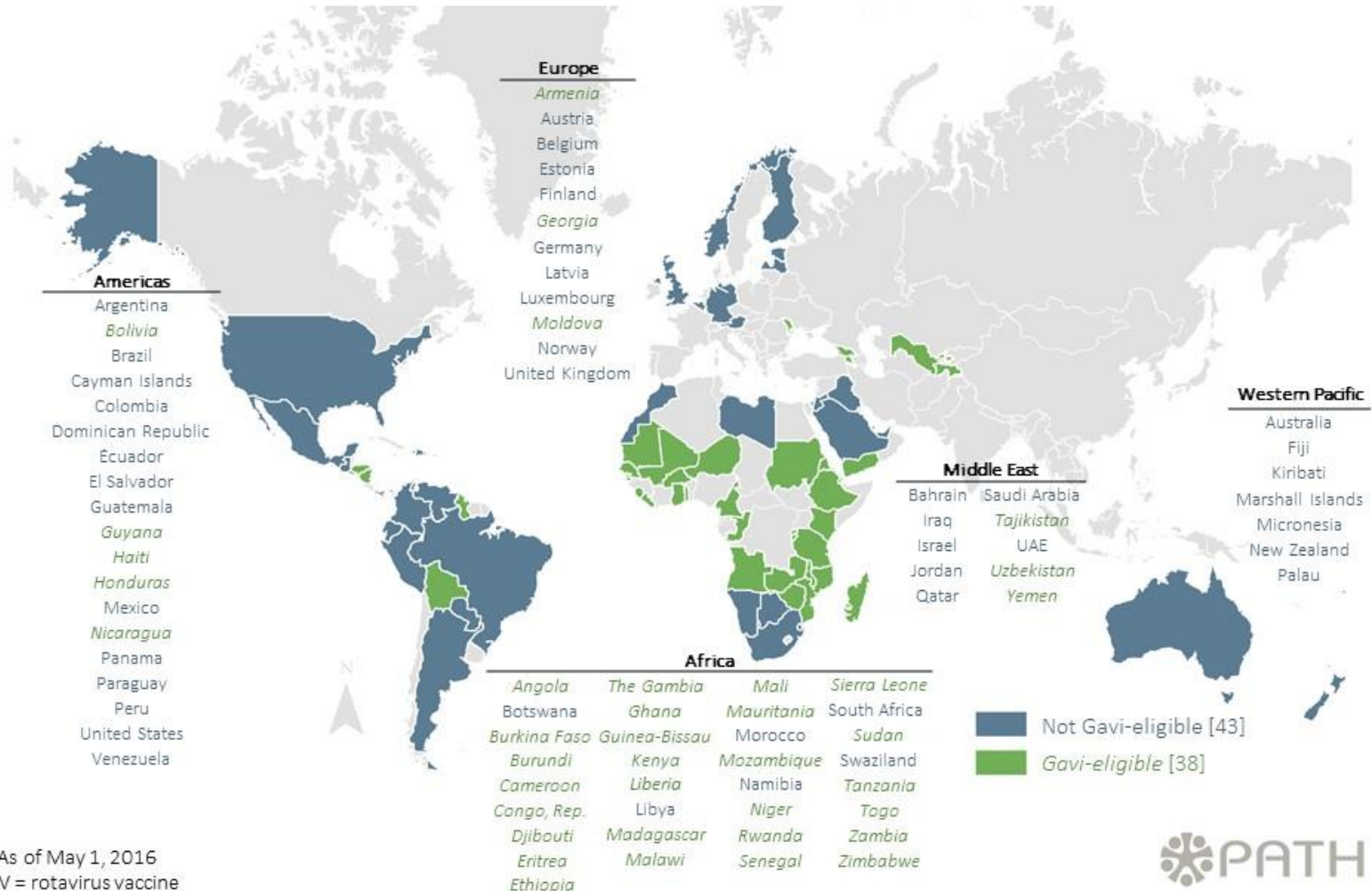


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Income is not the only driver of vaccination uptake

Rotavirus vaccine 2016

National RV introductions by geographic region: 81 countries*

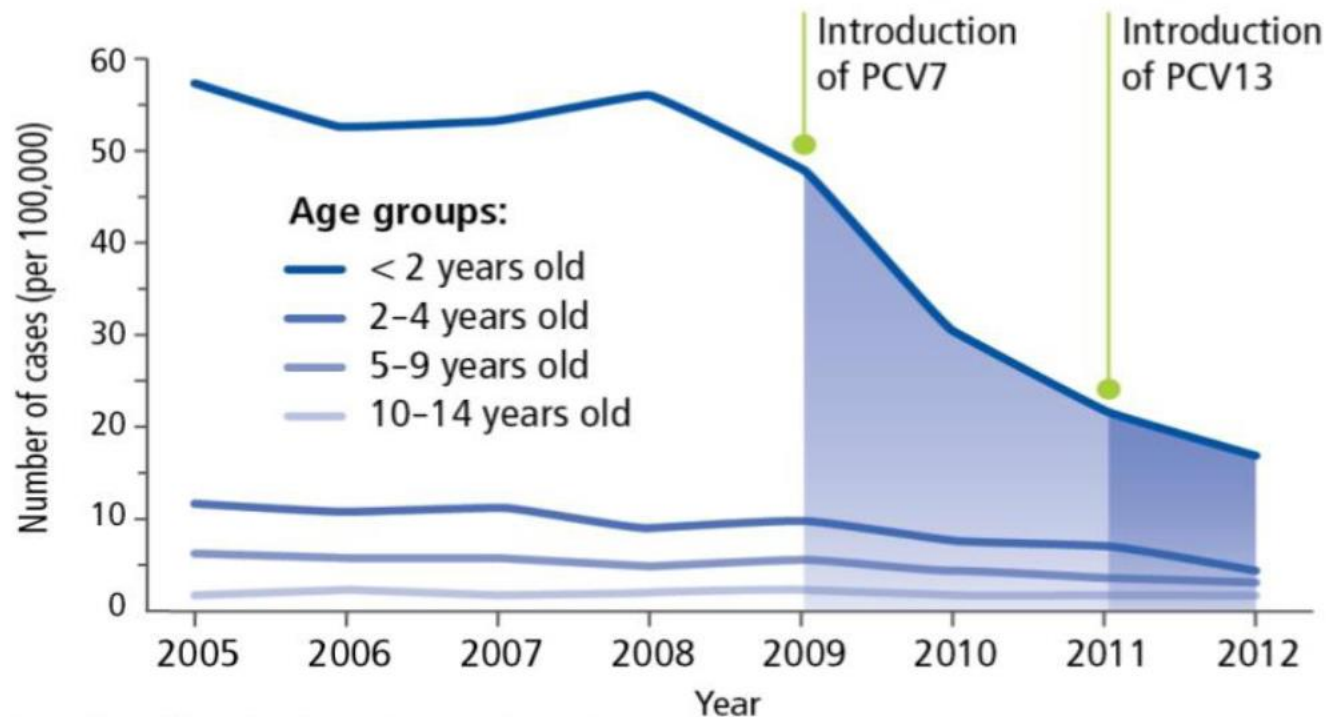


*As of May 1, 2016
RV = rotavirus vaccine

Impact of PCV: RSA

Substantial reduction in pneumococcal disease in South Africa thanks to vaccines

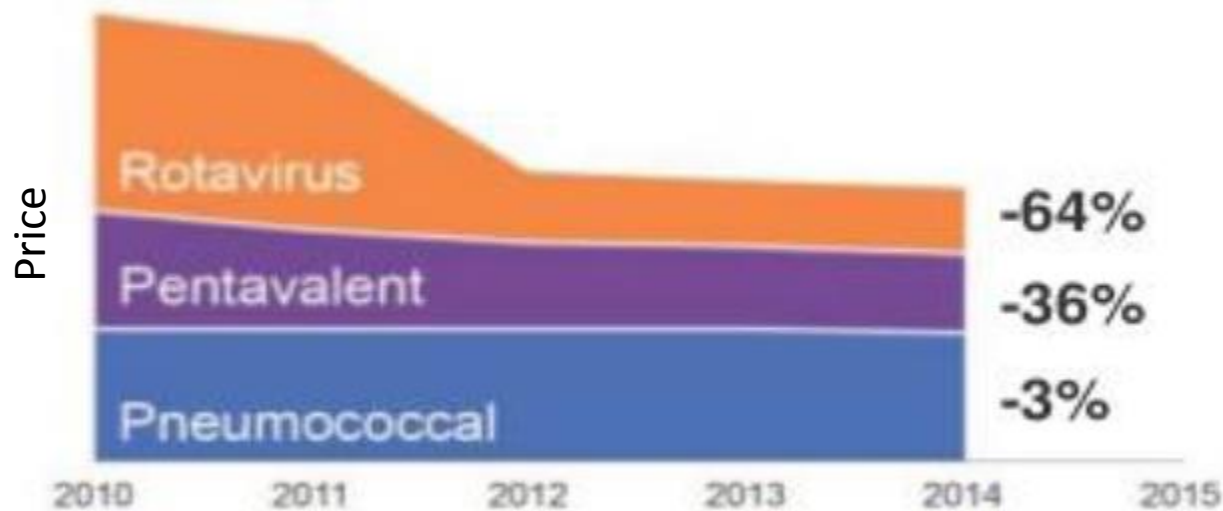
Invasive pneumococcal disease cases by age group



Source: Effects of Vaccination on Invasive Pneumococcal Disease in South Africa. *New England Journal of Medicine*, November 13, 2014.

Success has a price

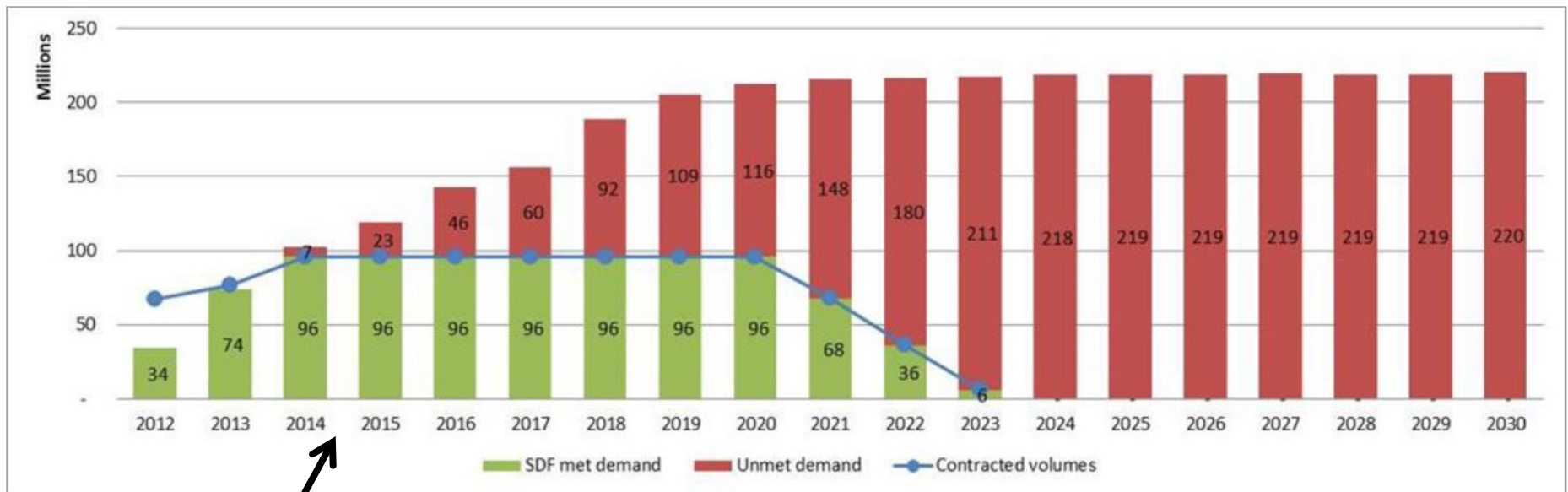
PCV accounts for a large % of spending



Unicef, 2015, Cost to fully immunize a child with rota, pentavalent, and pneumococcal vaccines

Unmet Demand for PCV – the challenge of supply

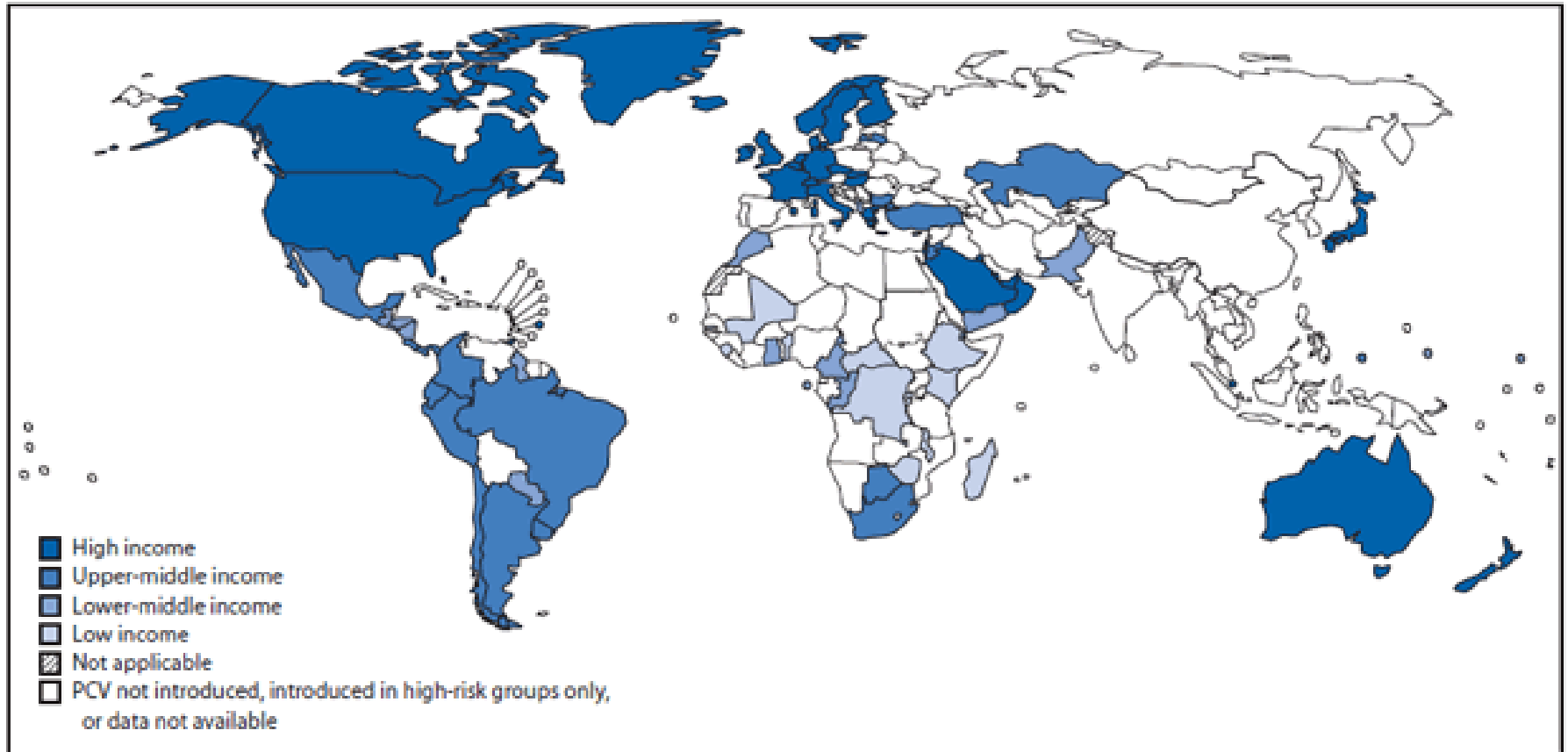
GAVI: Strategic demand forecast for PCV



Current Advanced Market Commitment

Income is not the only driver of vaccination uptake

PCV implementation by country income



Non-Gavi countries, primarily middle/lower middle band

Why is there a resurgence in measles in Europe?

Measles cases surge in Europe, 2017

20,000

people infected

35

patients died across Europe

15 countries had large outbreaks of measles last year

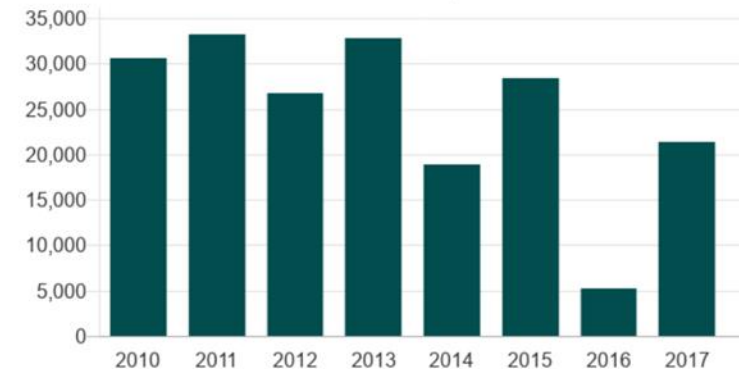
282 cases in the UK

5,562 cases in Romania - the worst-affected country

Source: WHO



Number of confirmed measles cases, 2010-17



Source: Centralised information system for infectious diseases, WHO Europe

BBC

BBC, 21 Feb 2018

ROMANIA

- Poorer European country
- Poorer public health infrastructure
- Weak disease surveillance
- Marginalized population (Roma)
- Vaccine shortage (!)

ITALY

- Anti-vaxer
- Laissez faire?

FRANCE

- Anti-vaxer

UK – measles eliminated, imported cases cause measles

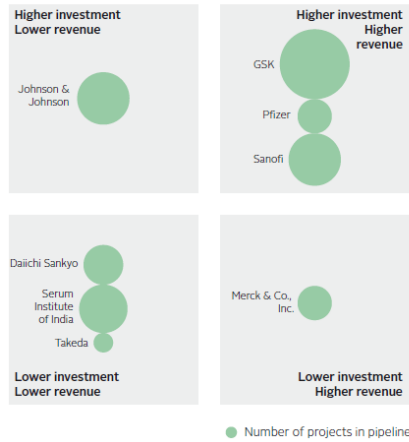
We need to invest in new
vaccines and in smarter
vaccines



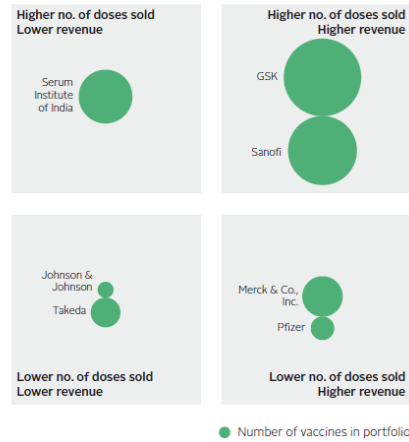
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Though operating models are different, the vaccine industry is highly consolidated

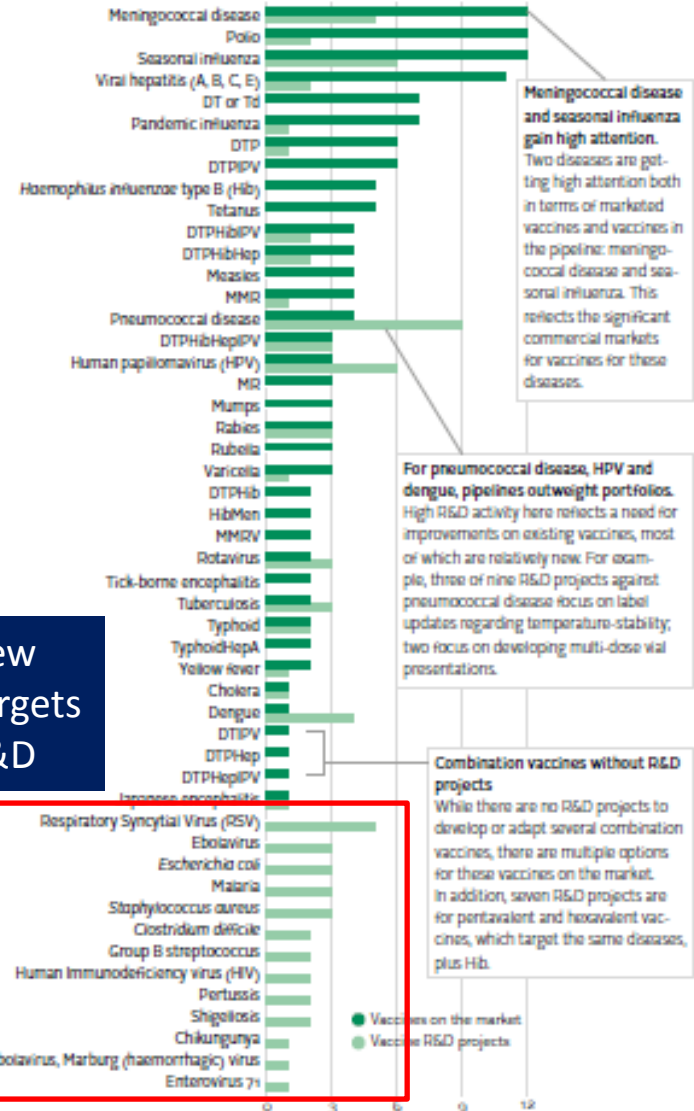
Company vaccine pipelines



Company vaccine portfolios



Vaccine Industry Focus: Products, Pipelines, Revenue

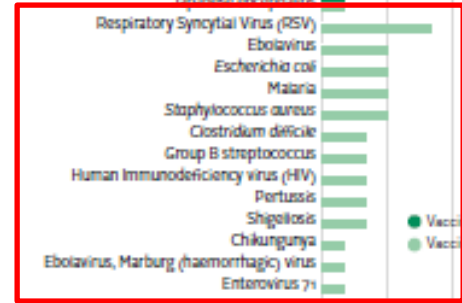


Meningococcal disease and seasonal influenza gain high attention. Two diseases are getting high attention both in terms of marketed vaccines and vaccines in the pipeline: meningococcal disease and seasonal influenza. This reflects the significant commercial markets for vaccines for these diseases.

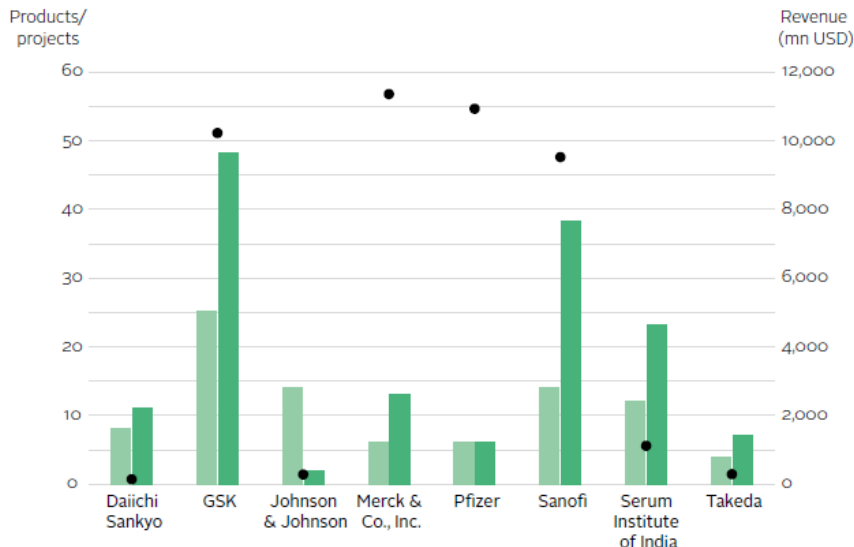
For pneumococcal disease, HPV and dengue, pipelines outweigh portfolios. High R&D activity here reflects a need for improvements on existing vaccines, most of which are relatively new. For example, three of nine R&D projects against pneumococcal disease focus on label updates regarding temperature-stability; two focus on developing multi-dose vial presentations.

Combination vaccines without R&D projects While there are no R&D projects to develop or adapt several combination vaccines, there are multiple options for these vaccines on the market. In addition, seven R&D projects are for pentavalent and hexavalent vaccines, which target the same diseases, plus Hib.

New Targets R&D



Vaccines on market, in pipeline, and revenues



light green: projects in pipeline; green: products in portfolio; dots: revenue



Vaccine R&D: Gaps

Newly Approved Vaccines

Vaccine	Company	Approval
Dengue (Dengvaxia®)	Sanofi	COFEPRIS, Dec 2015
DTPHibHepIPV (Vaxelis®)	Merck & Co., Inc., Sanofi	EMA, Feb 2016
HPV (Gardasil 9®)	Merck & Co., Inc.	FDA, Dec 2014
HPV (Gardasil®) Controlled Temperature Chain	Merck & Co., Inc.	EMA
Meningococcal A (MenAfriVac®) 5 µg dose for children under one year	Serum Institute of India	WHO, Dec 2014
Meningococcal B (Trumenba®)	Pfizer	FDA, Oct 2014
Pneumococcal (Prevenar 13®) four-dose vial	Pfizer	EMA, Apr 2016
Rabies	Serum Institute of India	CDSCO, Jun 2016
Seasonal influenza (VaxiGripTetra™)	Sanofi	UK, Jul 2016

- 1/3 of R&D covers new vaccine targets
- At least 32 diseases have no vaccines from companies in review
- Adaptations to existing vaccines cover 50% of R&D
- Cost
 - \$500M less complex vaccine
 - \$1 B more complex vaccine
- Failure rate
 - Only 7% of vaccines reaching preclinical development are licensed

Diseases without vaccine R&D


Adenovirus
 Amoebiasis
 Balantidiasis
 Buruli ulcer
 Campylobacter enteritis
 Chagas disease
 Cryptosporidiosis
 Cytomegalovirus (CMV)
 Dracunculiasis
 Echinococcosis
 Food-borne trematodiasis
 Giardiasis
 Hantavirus pneumonia
 Human African trypanosomiasis
 Human metapneumovirus
 Human monkeypox
 Isosporiasis
Klebsiella pneumoniae
 Lassa fever
 Leishmaniasis
 Leprosy
 Lymphatic filariasis
 Onchocerciasis
 Parainfluenza
Pneumocystis jiroveci
 Schistosomiasis
 Severe Acute Respiratory Syndrome (SARS)
 Soil-transmitted helminthiasis
 Taeniasis/cysticercosis
 Trachoma
 Yaws
Yersinia enterocolitica

Diseases that don't make the list of diseases without vaccine R&D

- Group A Strep?
- Hepatitis E?
- Non typhoidal Salmonella?
- Shigella?

SUMMARY

- **Vaccines work – to prevent morbidity, mortality, cancer and have numerous “additional benefits”**
- **Vaccines are cost-effective**
- **Vaccines only work when used**
- **We need to keep developing new vaccines – there are still diseases with high burden > new mechanisms for funding.**

The image shows a large, modern building with a glass facade and a sign that reads "IVI International Vaccine Institute". The building is surrounded by greenery and a large rock. A light blue text box is overlaid on the image, containing the text: "We thank our funders & donors: Korea, Sweden, India, the Bill and Melinda Gates Foundation, the Samsung Family Foundation, the Korea Support Committee, and many other corporate and individual donors".

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