do more feel better live longer

The future of Vaccines and their impact

PDA Vaccines Conference

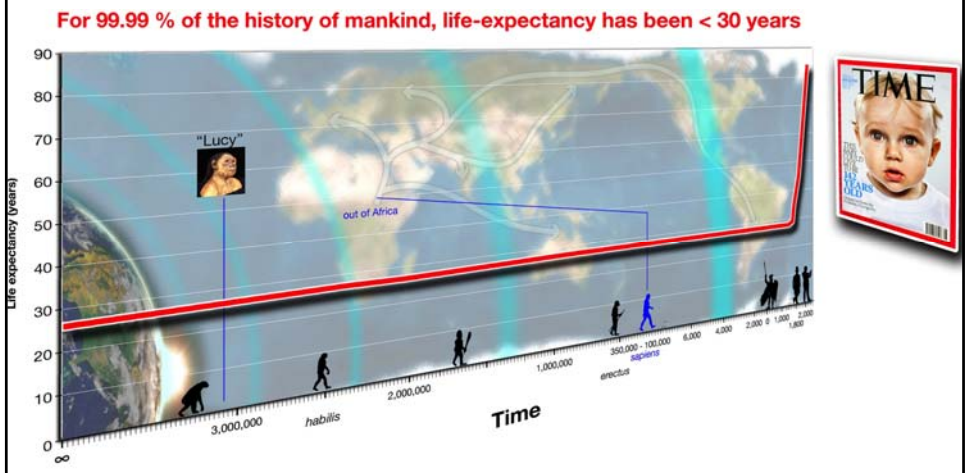
Rino Rappuoli

Berlin Dec 1st 2015

One Sentence Summary of this Lecture

Vaccines are the oldest medical intervention, and their utility is not yet fully realized. Vaccinology is one of the most vibrant and innovative fields of our times and vaccines will continue to have a great impact on the society for the next century

Some history of human evolution



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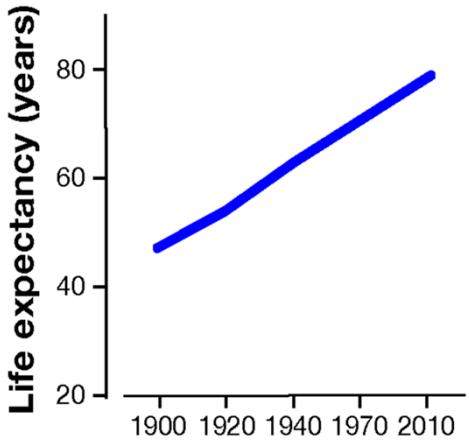
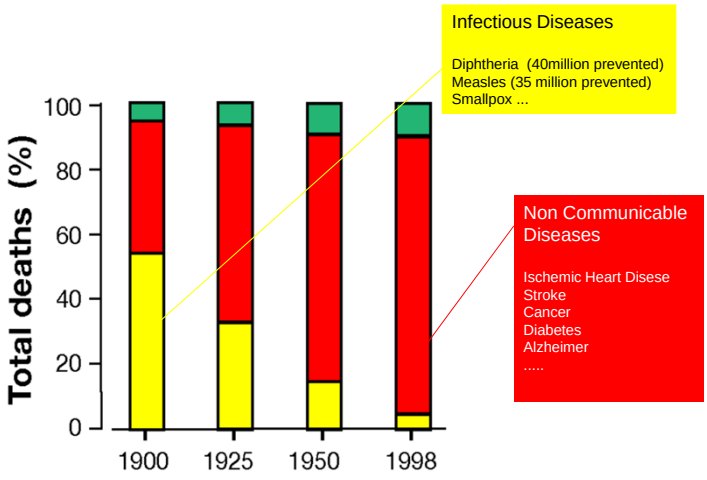
In 1900 in the USA life was short



In 1900 in the USA people died of infectious diseases



Vaccination, the most effective medical intervention ever introduced

- So far saved >3.0 billion disease cases
  >500 million deaths
- 2011-2020 vaccines will save
  - 25 million deaths
    - 2.5 million/year
    - 7000/day
    - 300/hour
    - 5/min

WHO Global Action Plan
http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/index.html)

Vaccination is the most cost-effective medical intervention ever introduced

The value of vaccines according to CDC

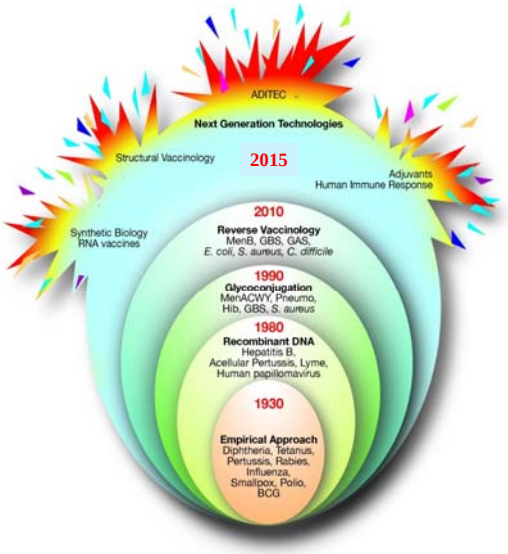
MMWR / April 25, 2014 / Vol. 63 / No. 16

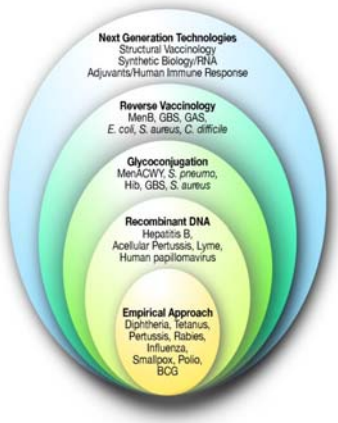
USA 1994-2013

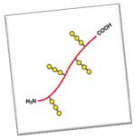
Vaccine prevented
- 322 million illnesses
- 21 million hospitalizations
- 732,000 deaths

Vaccines generated net savings of
- 295 Billion dollars direct costs
- 1.38 Trillion dollars in total societal costs

The evolution of Vaccines Vaccines from past 30 years,and the future



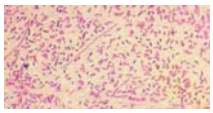




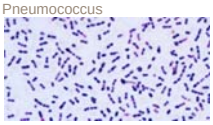
Conjugate vaccines

Capsular polysaccharides & Conjugates

Haemophilus influenzae type B (Hib)

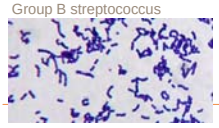


Pneumococcus

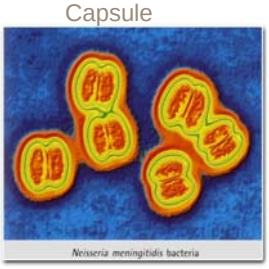


Meningococcus

Group B streptococcus

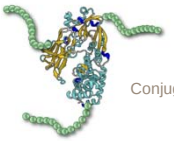


Capsule



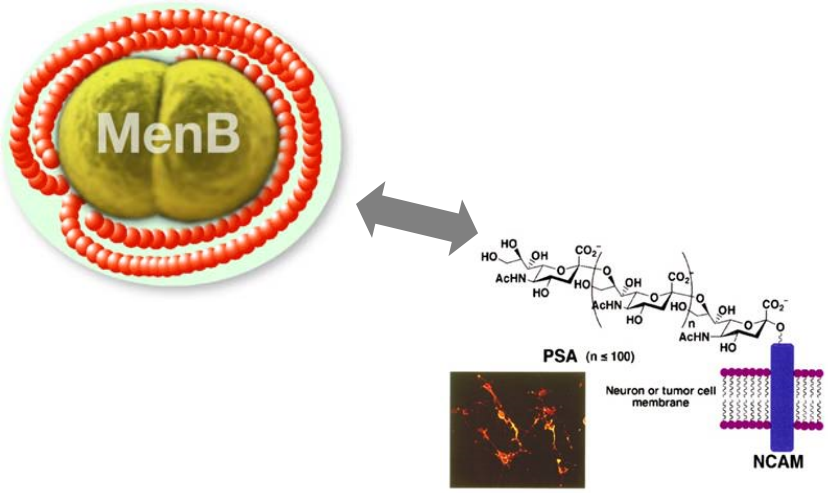
Capsule

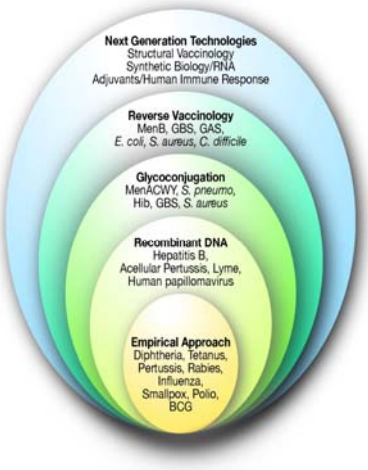
Polysaccharide



Conjugate

Meningococcus B capsule is a self antigen and cannot be used for vaccination

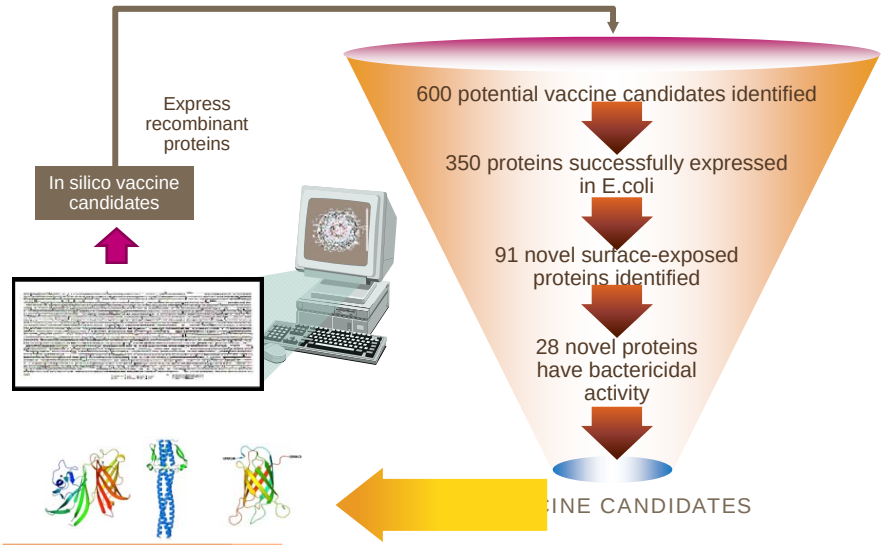




Reverse Vaccinology

and a vaccine for Meninigococcus B

Reverse Vaccinology A genomic approach for a Meningococcus B vaccine



Clinical Development

Immunogenicity, Persitance, Concomitant administration, Tolerability

Infants and children 2 months to <2 years of age

- **5850** received at least 1 dose of BEXSERO
- 3285 received booster dose in second year of life

Children 2 to 10 years of age

- **250** were included

Adolescents and adults ≥11 years of age

- **1703** were included

*Evaluated in 13 studies including 9 randomiz

MenB, first vaccine to receive **breakthrough therapy designation** by FDA

Princeton, USA

Meningitis B vaccine deal agreed - Jeremy Hunt

London, UK

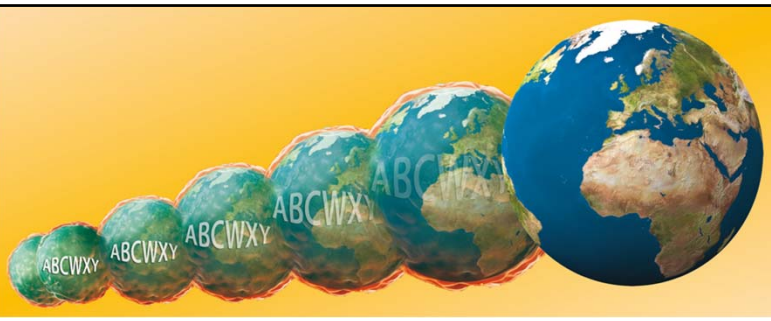
Since september 1st 2015 all newborns in the UK will be vaccinated with MenB vaccine

Seguenay-Lac-Saint-Jean

Vaccination of the entire population from 2 months to 20 years of age

- 43,740 people vaccinated between May 5 and 17 June 2014
- 12,332 followed with active surveillance
- 14-15 % fever in less than 2 years

Active surveillance has not identified any severe problem and confirmed significant frequency of local pain, fever (less than expected) and general malaise.

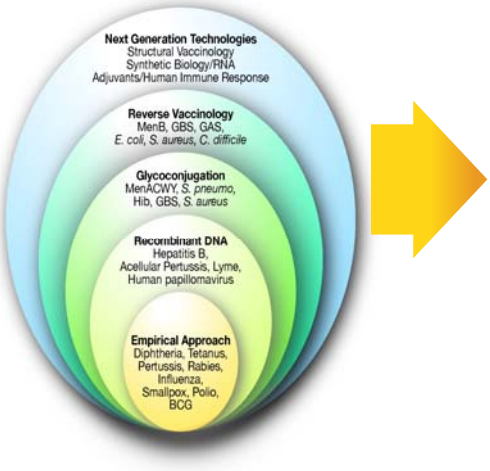


Working towards a meningitis free world

Now we can eliminate meningococcal meningitis

Reverse Vaccinology can also provide vaccines for Antibiotic Resistant bacteria (superbugs!!!)

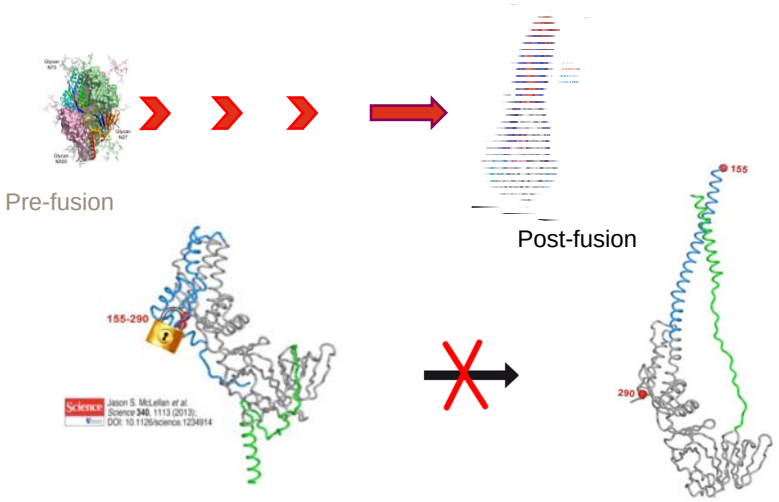
Staphylococcus
E. coli
C. difficile
Pseudomonas
Group A Streptococcus

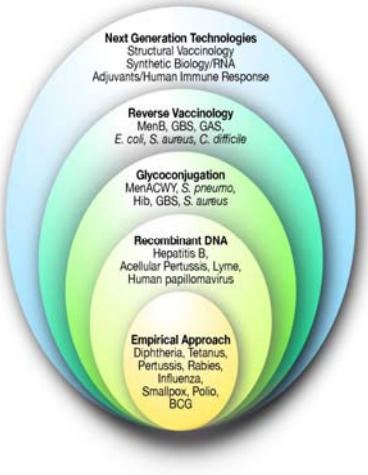


Structural Vaccinology

Structure-based antigen design

Structural Vaccinology
the RSV example



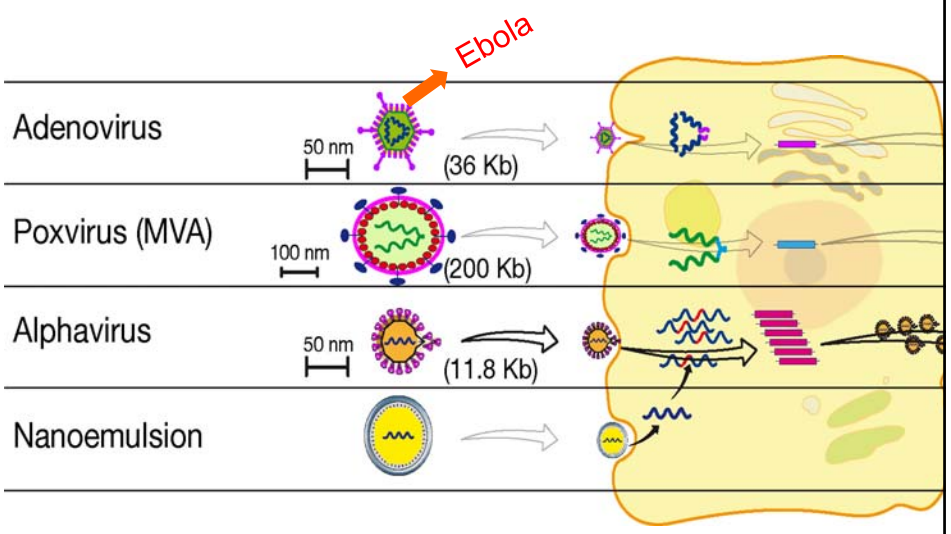


Synthetic biology

- Vectors
- Synthetic seeds
- Self Amplifying Messenger RNA **(SAM)**

From vectors to synthetic vaccines

replicating and non replicating viral vectors are used to transfer genes to cells



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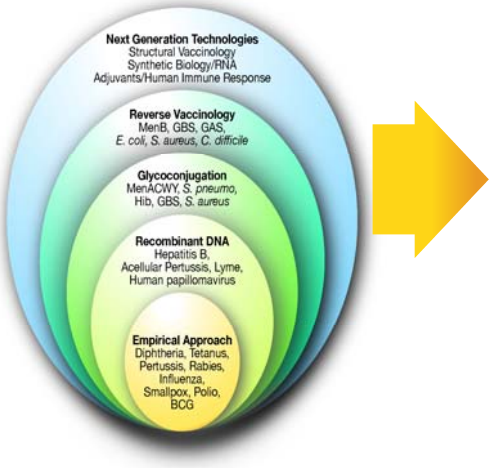
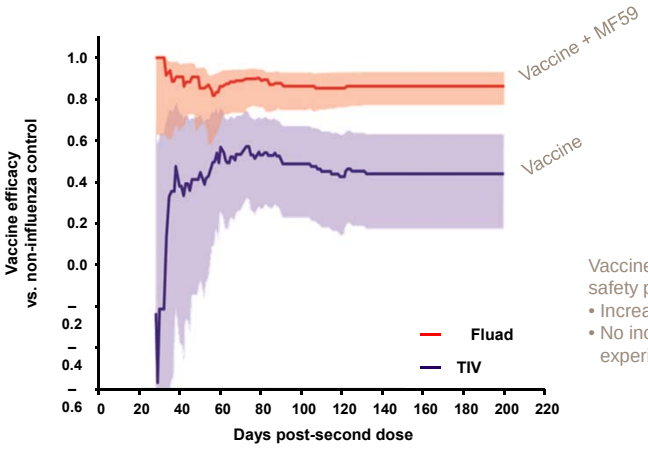


Adjuvants

MF59 increases efficacy of influenza vaccine in children from 43 to 86%



Vaccine also showed satisfactory safety profile:
- Increased local reactogenicity
- No increase in serious adverse experiences vs. control

Vesikari T, *et al.* NEJM.

Three breakthrough vaccines in 2015

Vaccines continue to serve our society

First Malaria vaccine licensed

Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial

RTS,S Clinical Trials Partnership*

www.thelancet.com Vol 386 July 4, 2015

Zoster vaccine 97% efficacy in the elderly

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

N ENGL J MED 372;22 NEJM.ORG MAY 28, 2015

Ebola vaccine 100% efficacy

Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial

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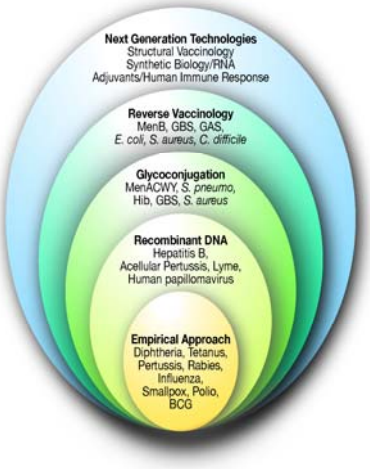
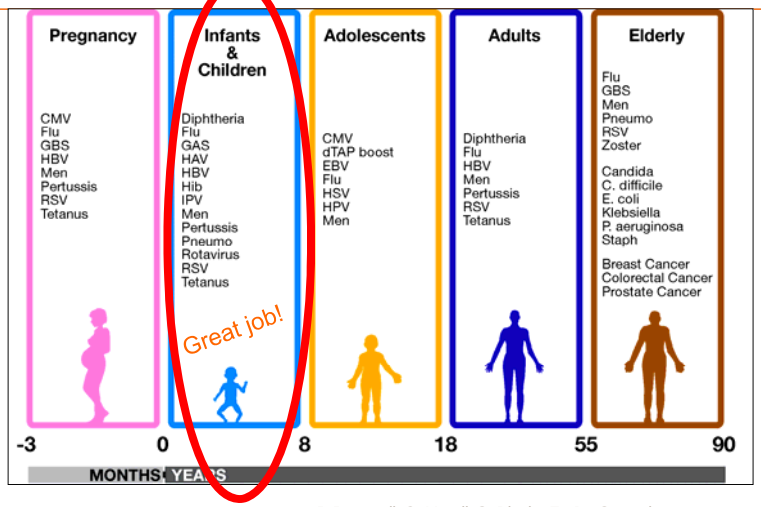
www.thelancet.com Published online July 31, 2015



How can these technologies help our society?

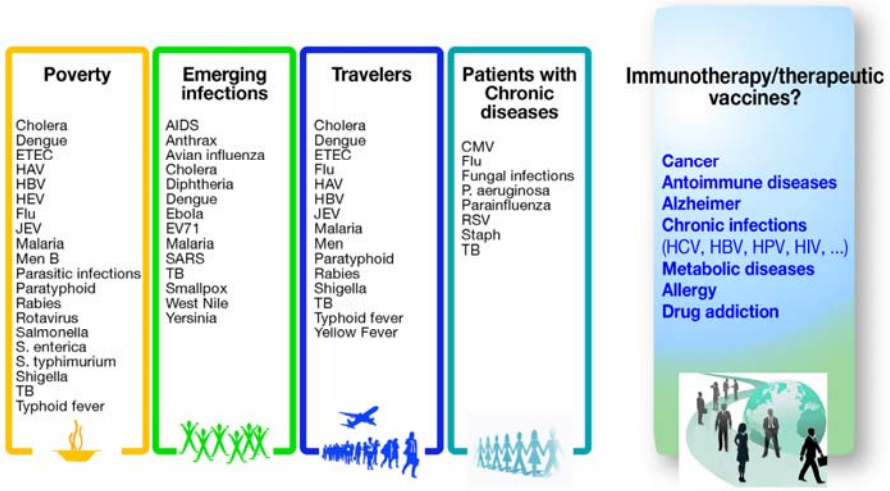
Vaccines for every age



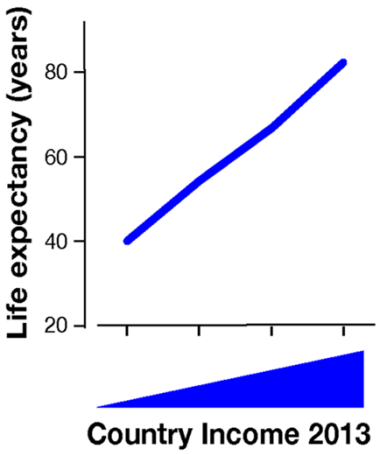
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

R.Rappuoli, C. Mandl, S: Black , E. De Gregorio
Nature Reviews Immunology | November 2011; doi:10.1038/nri3085

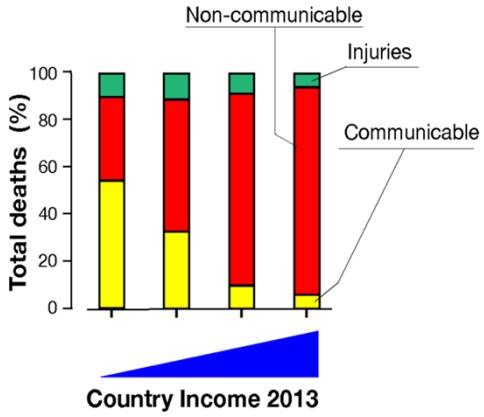
Vaccines for today's society



In low income countries life is still very short



In low income countries people die from Infectious Diseases. Vaccines can offer major improvements in reducing communicable and non communicable diseases.



Vaccines against poverty
An Institute to address the gaps in vaccine development

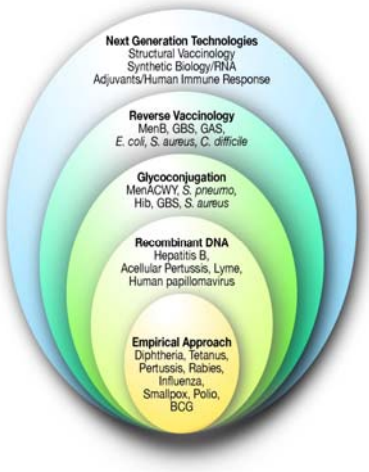
Previously, no mechanism was in place to develop vaccines needed only in developing countries

Novartis Vaccines Institute for Global Health (NVGH)

New name: **GSK Vaccine Institute for Global Health (GVGH)**

A new **non-profit initiative**
to develop effective and affordable vaccines for neglected infectious diseases of developing countries

- Located in Siena , Italy
- Legal entity started in Feb 2007
- Allan Saul hired as CEO Sept 2007
- Inauguration Feb 22, 2008
- **Typhoid vaccine licensed to BioE post phase II, June 2013**
- **Shighella vaccine Phase I 2014**



challenges for vaccine development

Fatigue, misperceptions, failure to assign the appropriate value to vaccines

- **Fatigue and misperceptions** Immunization typically prevents diseases, which have been nearly eradicated, so most people lack first-hand experience
- **Vaccine value** in a world of limited resources **cost-effectiveness** becomes important in decision making. Health economics not a to assign the appropriate value to vaccin
- Governments face difficult decisions. Many **conflicting priorities** vs vaccination programs

SMART VACCINES

Institute of Medicine (IOM) initiative SMART Vaccines multi-criteria decision making

http://www.nap.edu/smartvaccines

From → Cost/QALY

To → Cost/QALY + 27 attributes

Strategic Multi-Attribute Ranking- Toll (SMART) Vaccines

28 attributes 8 categories

Health Considerations	• Premature Deaths Averted per Year • Incident Cases Prevented per Year • QALYs Gained or DALYs Averted
Economic Considerations	• Net Direct Costs (Savings) of Vaccine Use per Year • Workforce Productivity Gained per Year • One-Time Costs • Cost-Effectiveness ($/QALY or $/DALY)
Demographic Considerations	• Benefits Infants and Children • Benefits Women • Benefits Socioeconomically Disadvantaged • Benefits Military Personnel • Benefits Other Priority Population
Public Concerns	• Availability of Alternative Public Health Measures • Potential Complications Due to Vaccines • Disease Raises Fear and Stigma in the Public • Serious Pandemic Potential
Scientific and Business Considerations	• Likelihood of Financial Profitability for the Manufacturer • Demonstrates New Production Platforms • Existing or Adaptable Manufacturing Techniques • Potential Litigation Barriers Beyond Usual • Interests from NGOs and Philanthropic Organizations
Programmatic Considerations	• Potential to Improve Delivery Methods • Fits into Existing Immunization Schedules • Reduces Challenges Relating to Cold-Chain Requirements
Intangible Values	• Eradication or Elimination of the Disease • Vaccine Raises Public Health Awareness
Policy Considerations	• Interest for National Security, Preparedness, and Response • Advances Nation's Foreign Policy Goals
User-Defined Attributes	• Up to Seven Attributes

Support for multi-criteria decision making

Cosensus on the core values for vaccines

1. Mortality/Severity of disease
2. Vaccine safety considerations
3. Economic evaluation method capturing the full benefits of vaccination

Overall Summary

- Vaccines are the oldest medical intervention, with the greatest impact on mankind
- Utility of vaccines are not over. They remain e one of the most vibrant and innovative field of our times and will continue to have a great impact on the society of our century
- Cost-effectiveness is not enough, Multi-criteria evaluation methods are needed to capture the full benefits of vaccination