Paediatric Infectious Diseases (PID) module

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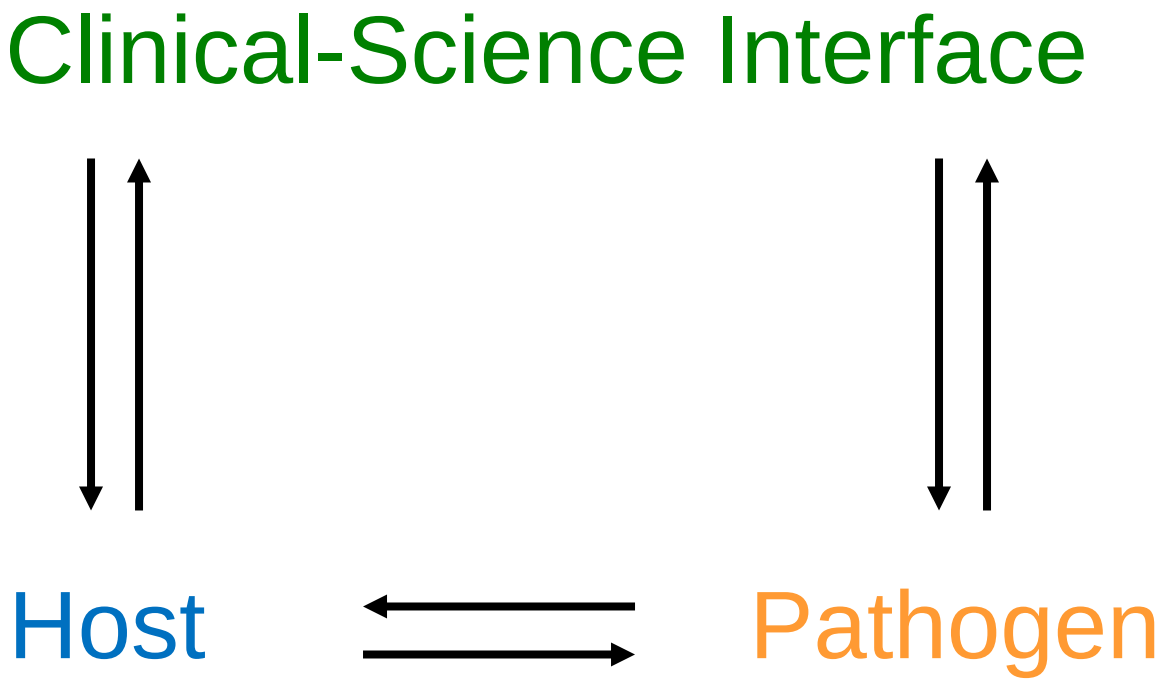
Aim

“To provide an understanding of how the interaction of host genetic predisposing factors and the virulence determinants of selected paediatric pathogens influences the outcome of infection.

There will be particular emphasis on the state of the art research methods used to identify host and pathogen factors and the impact of such knowledge on therapeutic intervention/prevention”


Clinical-Science Interface
Host
Pathogen

Host

- Host defence
- Immunity & inflammation
- Host genetic variability in immune response
- Genetic epidemiology
- Genetic polymorphisms
- Microarrays
- *In vitro/in vivo* models
- Proteomics
- Malnutrition
- Vaccines

Pathogen

- Virulence
- Identification of virulence factors
- Genomes & DNA arrays
- Epidemiology of infection
- Antibiotic resistance
- Intracellular pathogens
- Respiratory pathogens
- Tuberculosis
- Meningitis
- H1N1/influenza viruses
- Hepatitis C
- Gastrointestinal infections

Clinical-Science interface

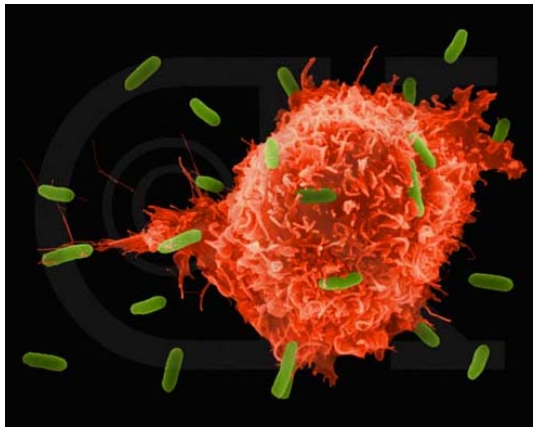
- Clinical science interface - examples
- Genetic polymorphisms and the clinic
- HIV pathogenesis
- Genetic susceptibility to mycobacterial disease
- Mycobacterial infections
- Sepsis and tissue injury
- Meningitis vaccines
- Necrotising enterocolitis
- Pneumococcal disease
- Genome wide screens
- Sequencing technologies
- Transcriptomic/proteomics approaches

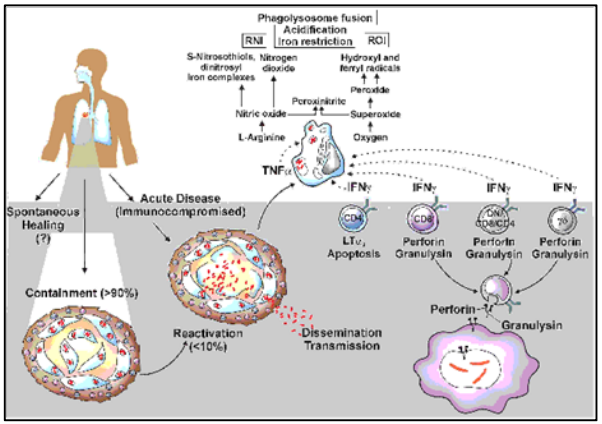
Human host response-host defence

- Physical barriers and routes of entry
- Immune defence
- Innate immunity
- Acquired immunity

Variability in the immune response

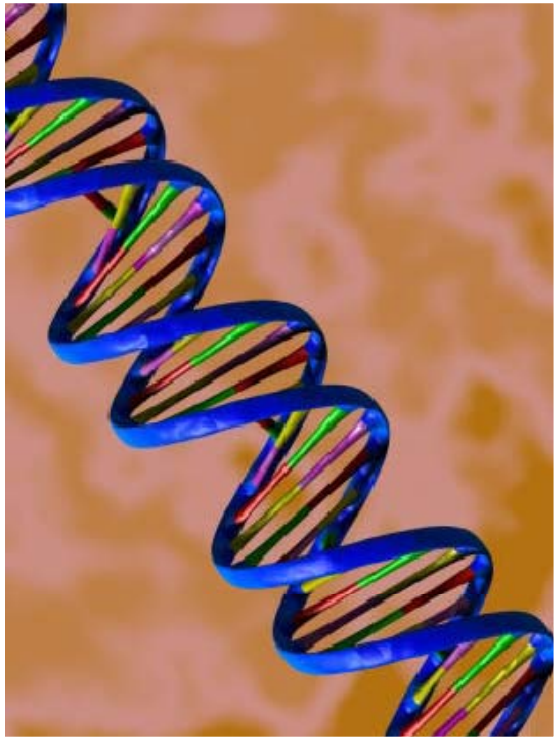
- Outline of specific and non-specific responses
- How responses are directed by immune system
- Manipulation of responses





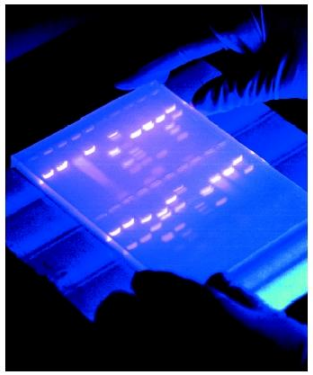
Human host response - genetic variation

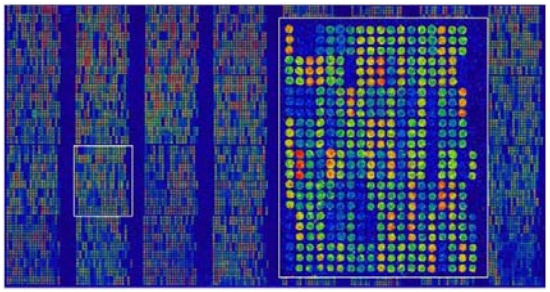
- What is a gene ?
- DNA structure + function
- Genetic variation
- Consequences of variation



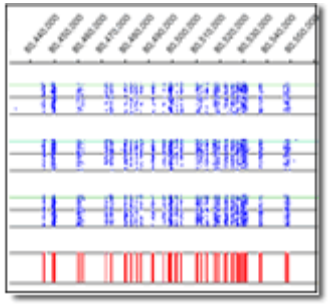
Detection of genetic polymorphisms

Current





Future



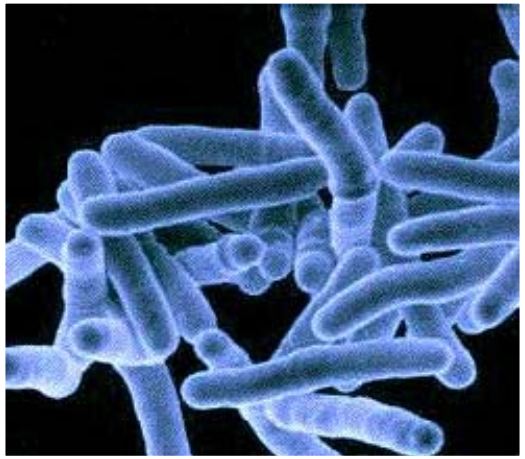
Population genetics

- Genetic causes of population variations
- Describing the populations
- Methods for analysis
- Selecting patients and controls

- Genetic susceptibility to infection
- Examples of paediatric host variation to infection
- Genome wide screens in infectious disease

Meningococcal disease

Tuberculosis



Pathogens - bacteria and viruses

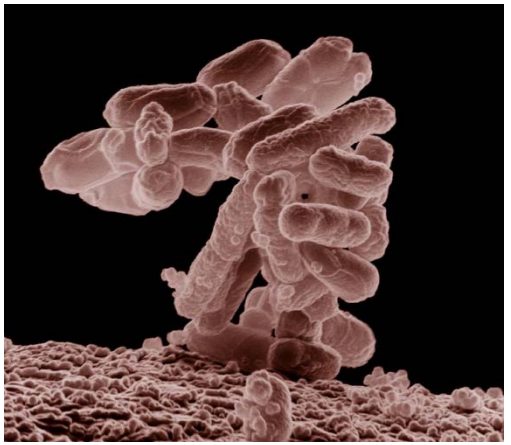
- Biology
  - Lifestyle of pathogens
  - Intracellular survival mechanisms
  - Evadasion of detection by the immune response

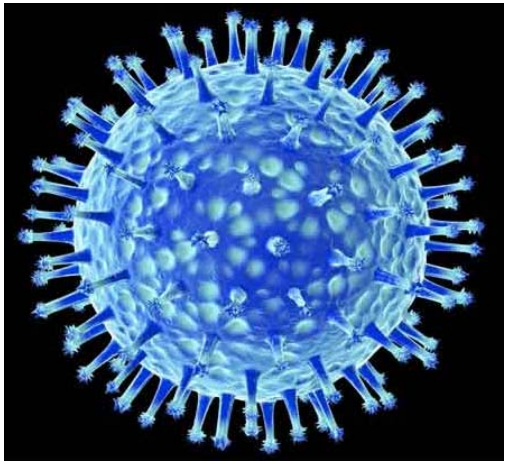
- Virulence
  - What is a virulence factor?
  - Methods to determine virulence factors

- Genomes
  - Genome analysis e.g. microarrays
  - Genotype-phenotype relationships

Pathogens - bacteria and viruses

- Epidemiology
- Pathogenesis
- Diagnostics
- Prevention of diseases
- Treatment





Clinical-Science Interface

Laboratory

Translational research

Bedside

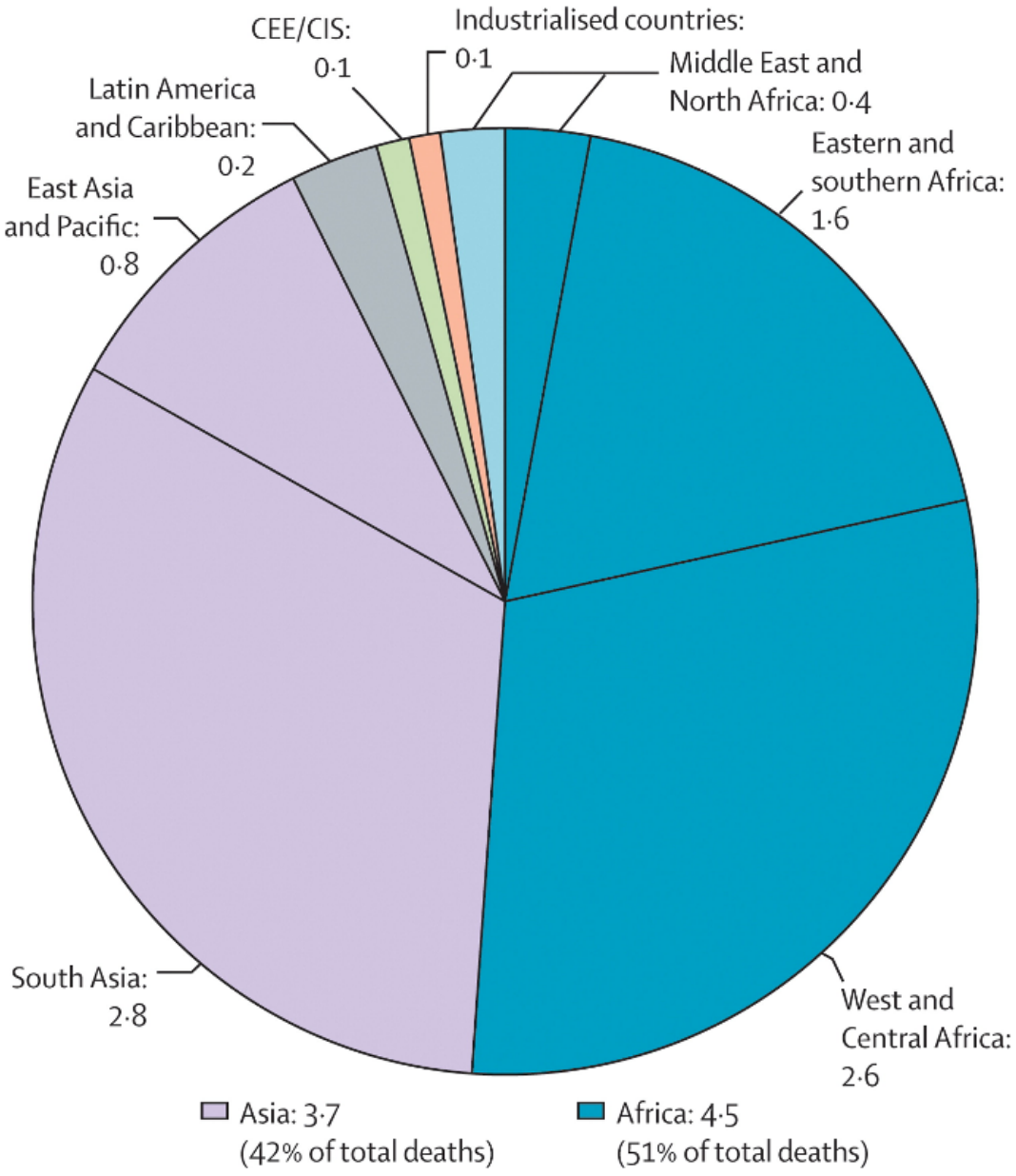
Coursework = essay + poster

Posters

- A1 size
- Send electronically to Mark as PPT or PDF for printing at HH
- Printed in pairs
- 5 mins talk + 5 mins question

Infectious Diseases

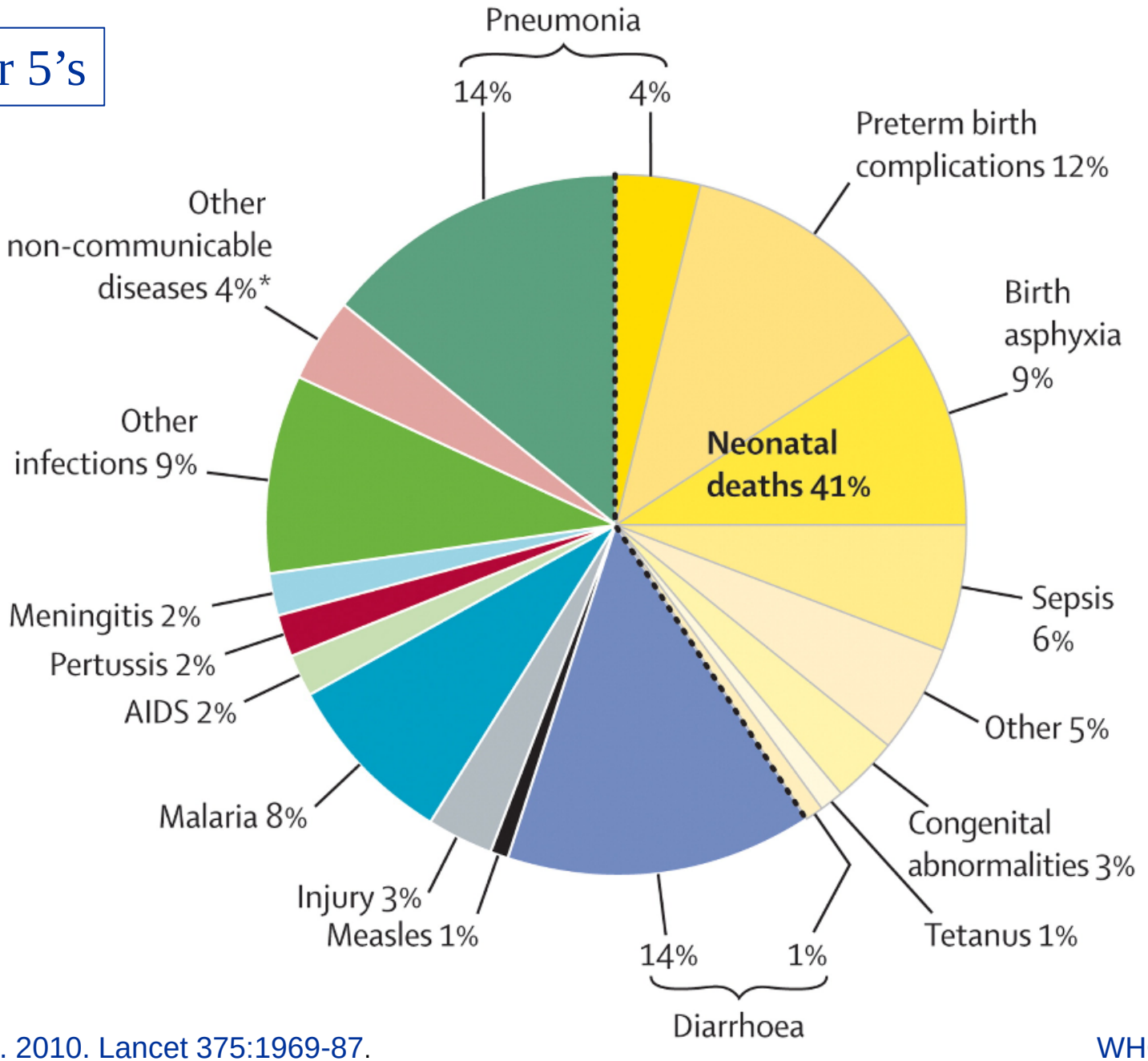
Under 5's



Black et al. 2010. Lancet 375:1969-87.

WHO 2008

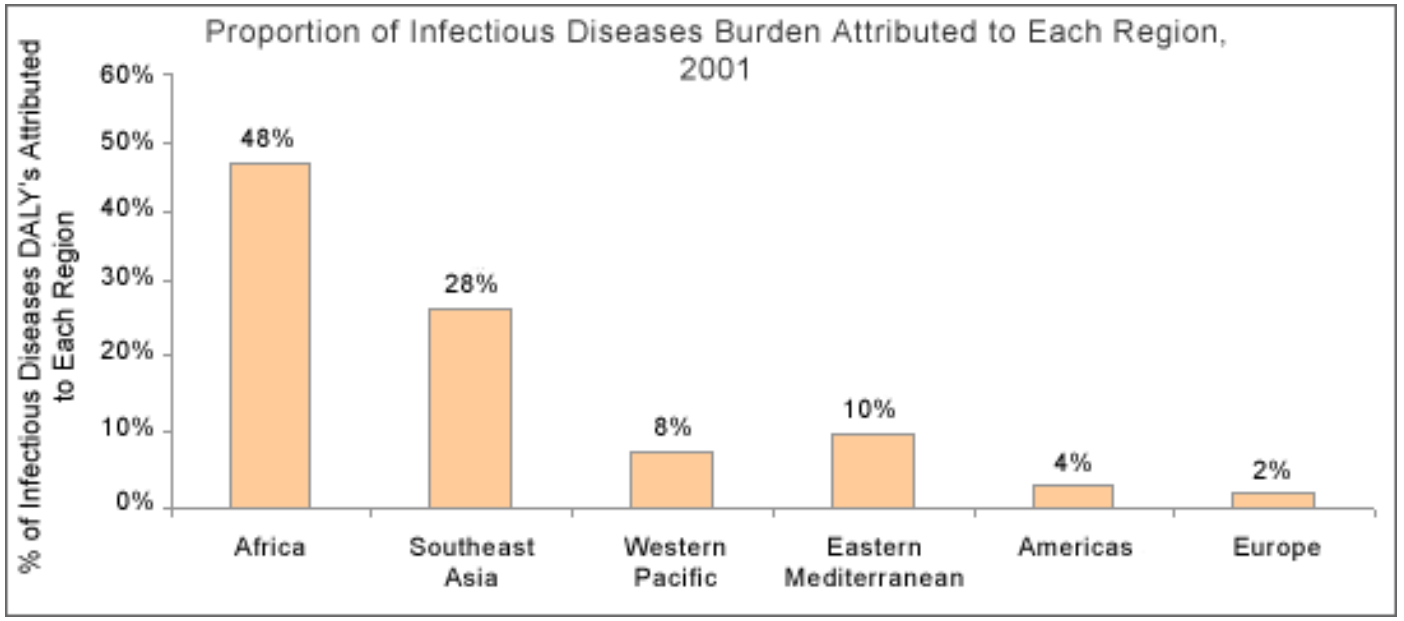
Under 5's



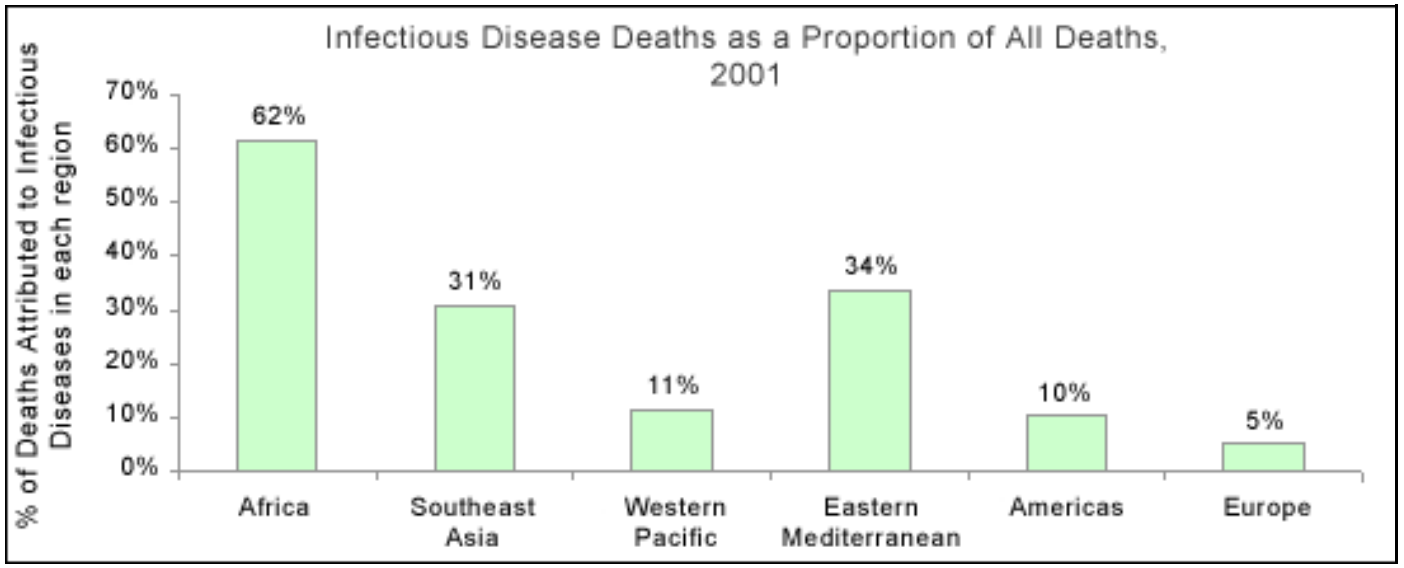
Black et al. 2010. Lancet 375:1969-87.

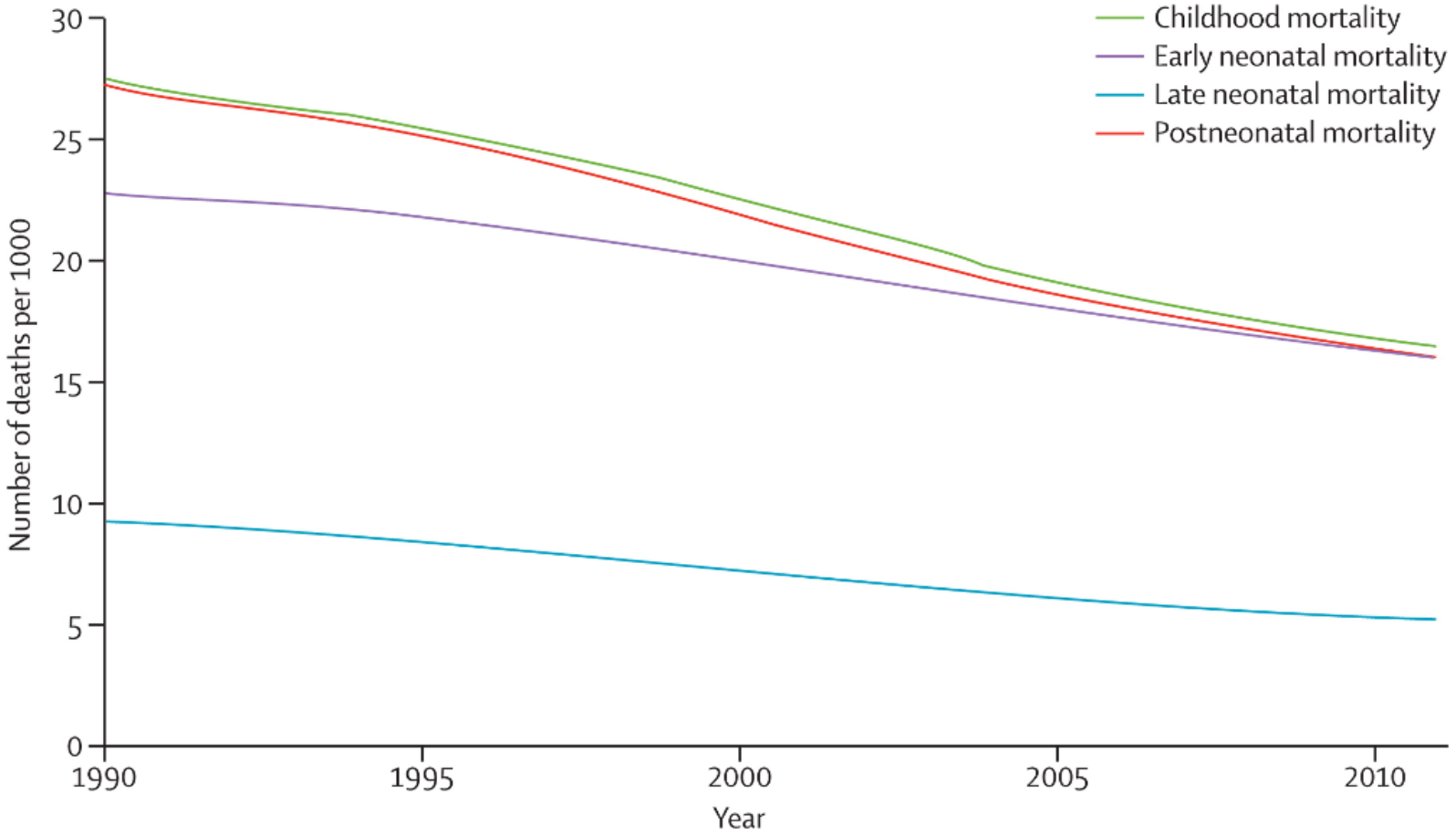
WHO 2008

Burden



Deaths





Lozano R et al. Lancet Volume 378:1139-1165

Infectious disease…

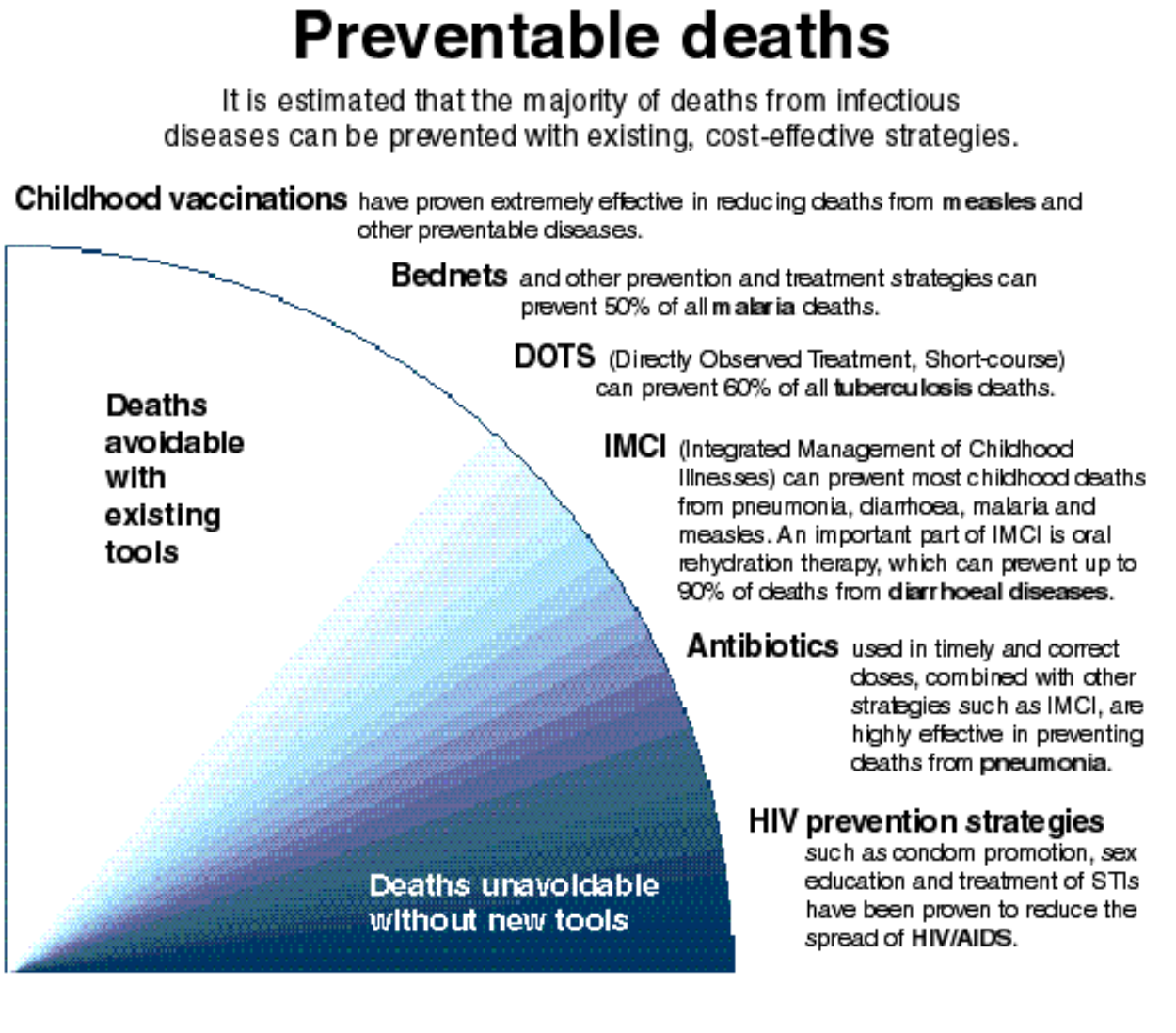
- Responsible for millions of deaths
- Disables millions of people
- Diminishes quality of life
- Decreases productivity
- Creates financial hardship

Lack of essential drugs and vaccines

Poverty and neglect

Prevention of death from infectious diseases

Low cost interventions exist…



Common Interventions for Malaria and Tuberculosis

	Intervention	Tuberculosis	Malaria
Diagnose	*Rapid diagnostic Tests (RDTs)*	Available for purchase but may not be affordable in many settings	More expensive and generally less-sensitive than microscopy; no lab required; may degrade in warm temperatures; requires training and quality assurance system; best for *P. falciparum*
	Microscopic examination	Sputum smear; limited availability of LED and fluorescent microscopy	Blood smear is standard; requires slides, reagents, microscope, well-trained technician and quality assurance plan
	Drug-resistant detection	Solid and liquid lab culture, requires special facilities and training; slow to provide results; some molecular methods in use	Standard in vivo field studies; lab in vitro assays; molecular methods to detect parasite mutations associated with resistance may be useful but are not yet validated for artemisinins
Prevent	*Vaccine*	BCG for children, unreliable for pulmonary TB	None yet available
	Vector control	---	IRS, ITNs (LLINs)
	Chemoprophylaxis	Isoniazid prevents progression to active disease	IPT for pregnant women
Treat	*First-line treatment*	DOTS	ACTs
	Second-line treatment	DOTS-plus	ACTs; quinine

*IPT: Intermittent preventive therapy. LLINS Long lasting insecticide nets, ITN Insecticide treated nets, IRS indoor residual spraying
ACT artemisinin-based combination therapies

Not always used due to…

- Inadequate funding of healthcare
- Government failure to prioritise
- Lack of cross-sectoral collaboration
- Inability of weak health science delivery systems to reach the entire population…
  - most vulnerable
  - difficult-to-reach

Medicines

- Few medicines exist in formulations developed specifically for children

- Worldwide many medicines for children are used "off-label", that is their effects on children have not been studied and they are not licensed for use in children

WHO initiatives

World Health Organization
Department of Child and Adolescent Health and Development (CAH)

unicef

Integrated Management of Childhood Illnesses

- pneumonia
- diarrhoeal diseases
- malaria
- measles
- malnutrition

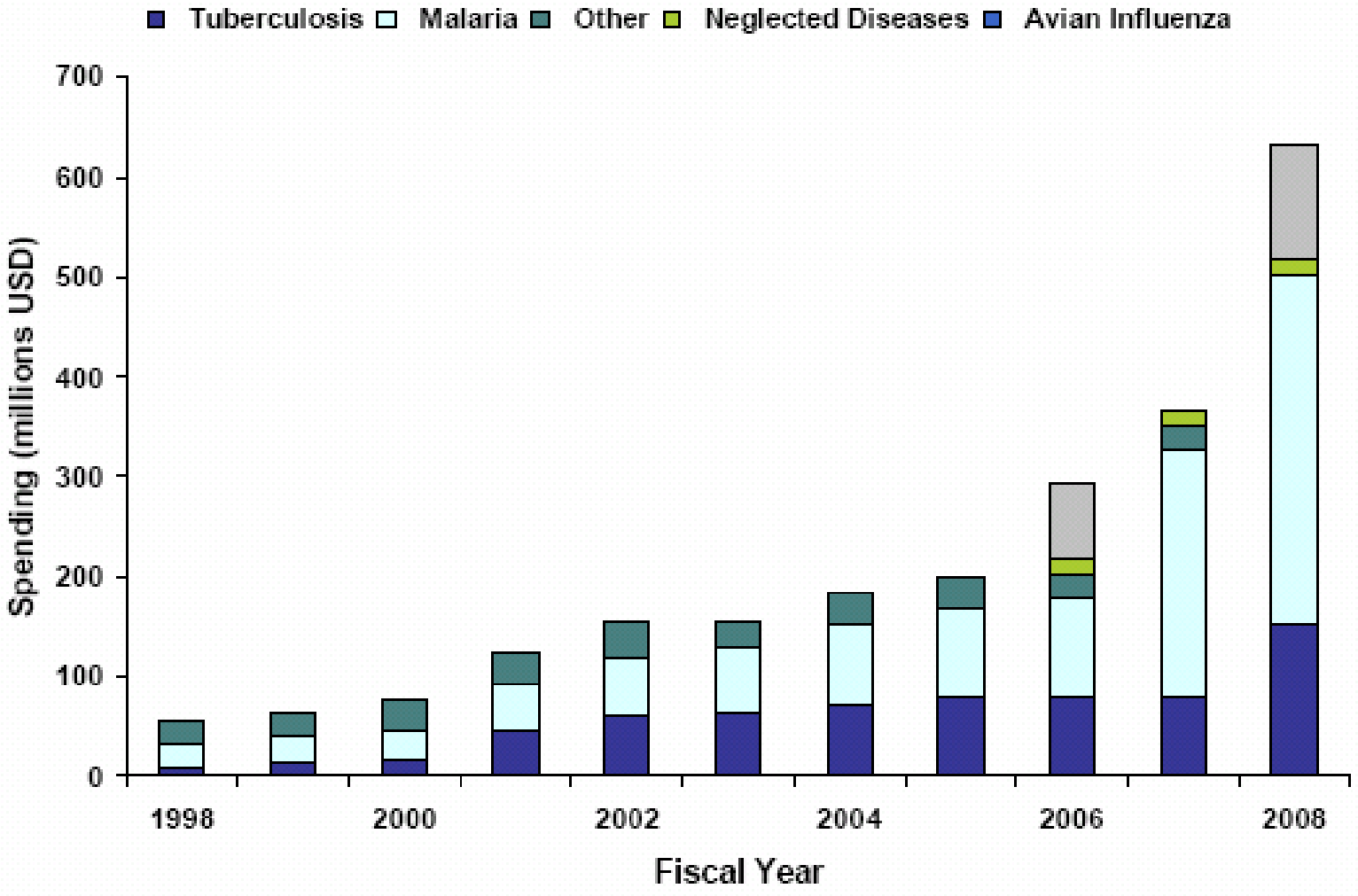
Investing in our future
The Global Fund
To Fight AIDS, Tuberculosis and Malaria

Strategy

- complementary interventions at health facilities in communities. Multi-country evaluation of effectiveness, cost and impact

- designed to determine whether IMCI has a significant impact on improving child health and is cost-effective

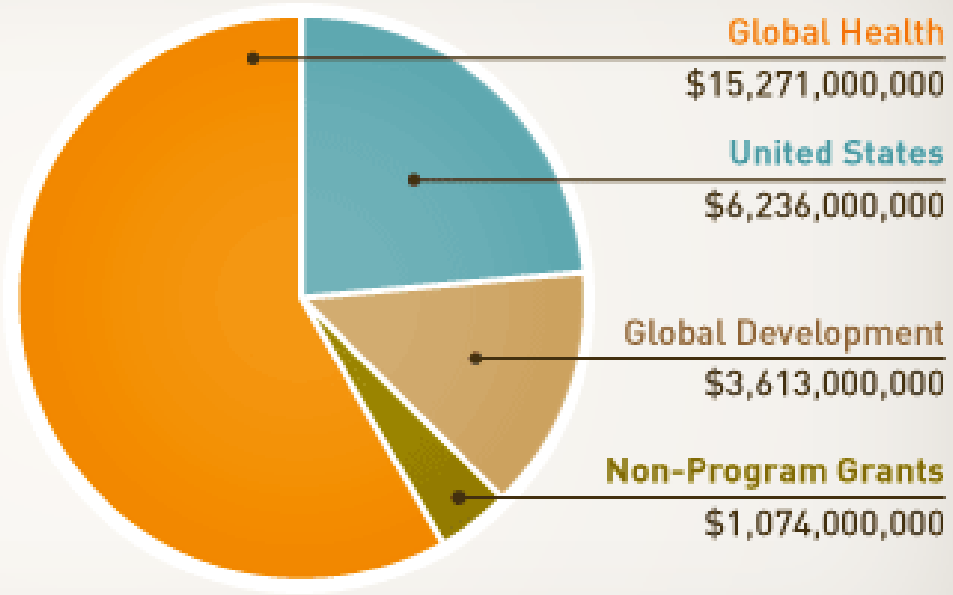
USAID Appropriations for Infectious Diseases, 1998-2008



BILL & MELINDA GATES foundation

Funding from 1994 to Present

Program Areas	
Global Development	$3,613,000,000
Global Health	$15,271,000,000
United States	$6,236,000,000
Non-Program Grants	
Charitable Sector Support	$71,000,000
Employee Matching Gifts & Sponsorships	$21,000,000
Family Interest Grants	$982,000,000
Total Grants	**$26,194,000,000**



This grant chart is updated quarterly and is based on funds committed from 1994 through September 2011
Dollars rounded to the nearest million.

unicef | BILL & MELINDA GATES foundation | World Health Organization | THE WORLD BANK

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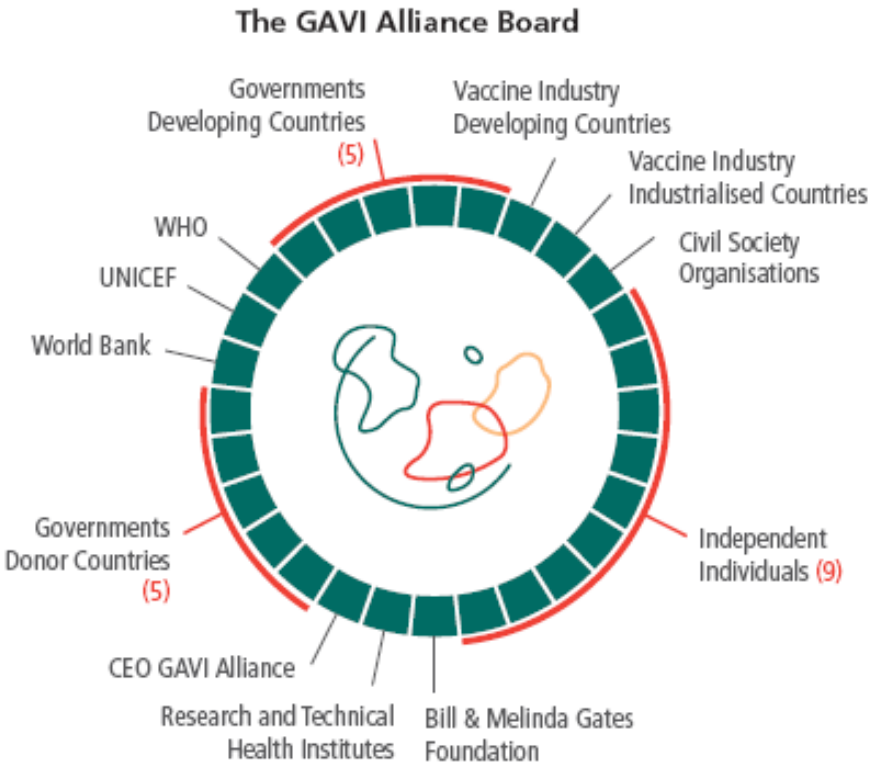
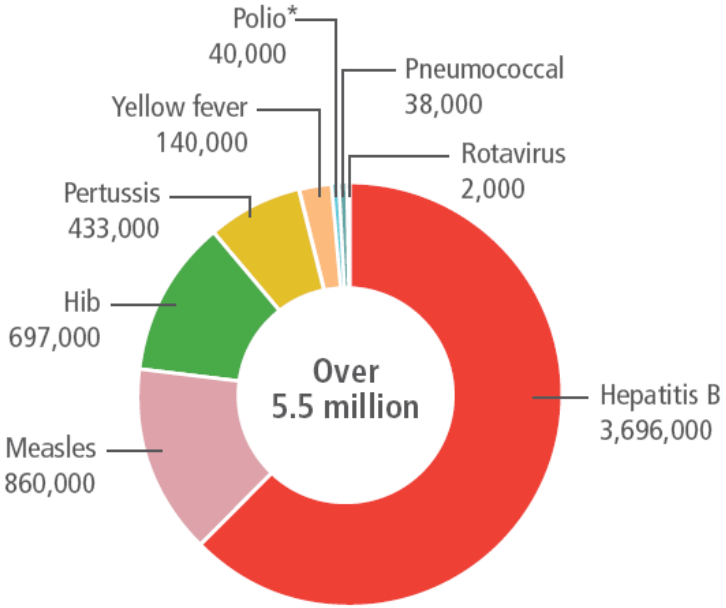
GAVI ALLIANCE





Research

- Develop new prevention, diagnostic and treatment options
- Study course and spread of disease
- Evaluate interventions to determine effectiveness

Surveillance

- Monitor disease occurrence to target
  - prevention
  - screening
  - treatment efforts

  to geographic areas and populations most in need

- Anticipate future needs so outbreaks can be quickly contained

Summary

- Infectious disease crisis - global proportions
- Infectious diseases world’s biggest killer of children
- 10 million deaths/yr, 1 in 2 deaths in developing countries
- Almost 1 in 3 children are malnourished
- 1 in 5 are not fully immunised by age of 1yr
- Lack of essential drugs, poverty and neglect
- Many diseases are preventable - low cost interventions
- WHO initiatives/global funding to reduce burden of disease

References

www.who.int/topics/child_health/en/

www.stoptb.org/

www.rbm.who.int/