

NTDs

- A group of bacterial and parasitic infections endemic in tropical climates
- Some of the most common infections among the world's poorest people
- Affect rural areas in the developing world
- More than 1 billion people infected
- Transmission cycles perpetuated by
 - environmental contamination
 - poor standards of living
 - lack of hygiene.



Core group of 17 tropical infections

- Helminths
 - Soil-transmitted helminths, tapeworms, foodborne trematodiasis, elephantitis, river blindness, Guinea worm disease, schistosomiasis
- Protozoan
 - Leishmaniasis, Chagas, sleeping sickness
- Bacterial
 - Leprosy, trachoma, Buruli ulcer, yaws
- Viruses
 - Rabies, Dengue, Chikungunya
- Others.

The diseases: worms

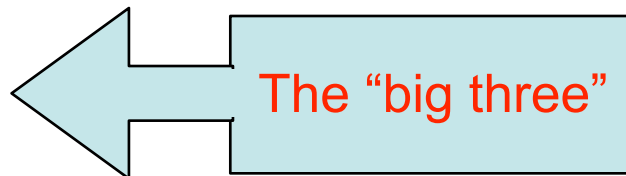
Infection		Global prevalence (millions)	Population at risk
<i>Soil-transmitted helminths</i>	Hookworm	807	4.2 billion
	Roundworm	604	3.2 billion
	Whipworm	576	3.2 billion
Foodborne trematodiasis		56	750 million
<i>Tapeworms</i>	Taeniasis	50	N/A
	Cysticercosis	40	N/A
	Echinococcosis	1	6 billion

The diseases: non-worms

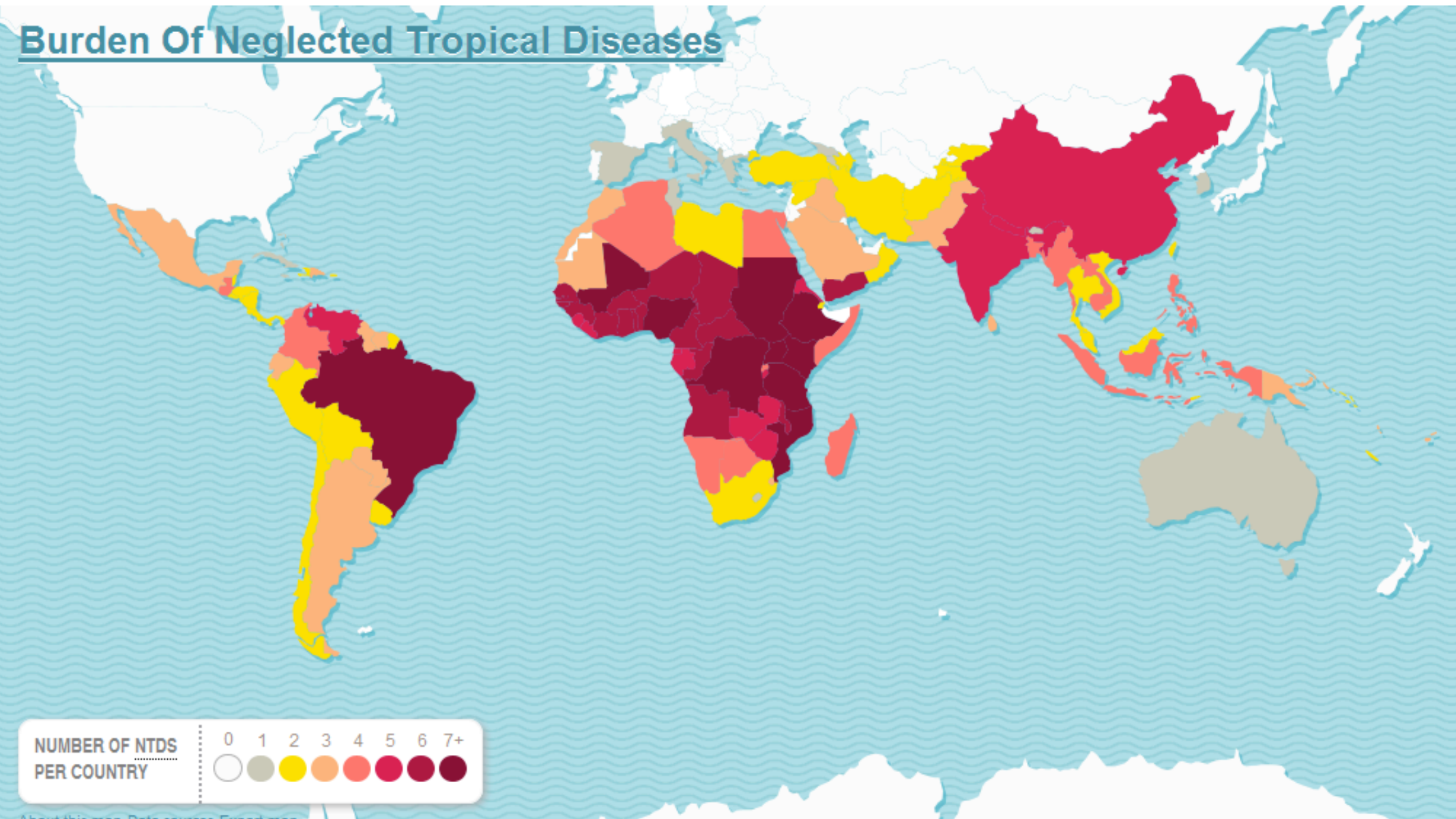
Infection	Prevalence (millions)	Population at risk
Dengue	528	2.5 billion
Schistosomiasis	207	779 million
Elephantitis	120	1.3 billion
Trachoma	84	590 million
River blindness	37	90 million
Leishmaniasis	12	350 million
Chagas' Disease	8–9	25 million
Yaws	2.5	434 million
Chikungunya	2	793 million
Leprosy	0.4	N/A
Sleeping sickness	0.3	60 million
Rabies	0.06	3 billion
Guinea Worm Disease	0.0001	N/A
Buruli ulcer	N/A	N/A.

Neglect

- These diseases are neglected at the
 - community
 - national
 - international levels
- Attention to disease in endemic areas usually focuses on
 - HIV/AIDS
 - malaria
 - TB
 - novel emerging infections.



Global NTD burden



Common features

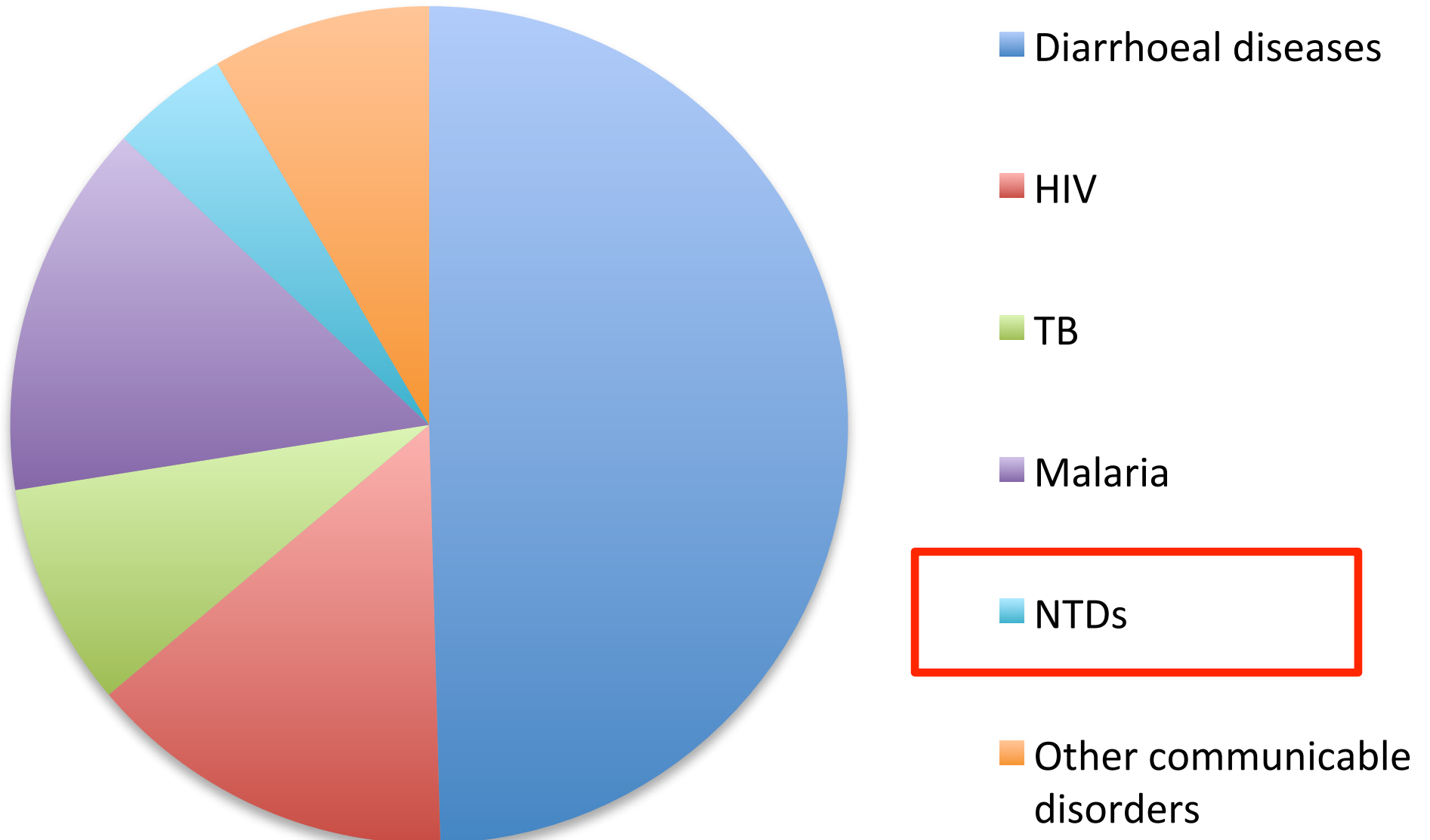
- Ancient
- Chronic
- Disfigurement and disability
- Impair growth and development in children
- Large socioeconomic effect
- Poverty promoting
- Reduce economic productivity
- Stigmatising
- High disease burden, low mortality (530,000 per year).

Measuring the impact




- DALYs (Disability-Adjusted Life Years)
 - measure the number years of life lost from premature death/disability
- These are likely underestimates, especially for NTDs.

Infection	# of DALYs/year (millions)
Malaria	82.6
HIV/AIDS	81.5
TB	49.4
NTDs	26.1





Proportion of disease DALYs



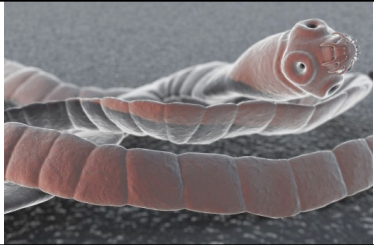
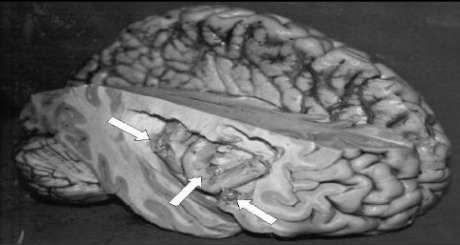


Soil-transmitted helminths (“the unholy trinity”)

Disease	Roundworm	Whipworm	Hookworm
Target	Small intestine	Large intestine (colon)	Small intestine
Transmission	Contact with soil contaminated by larva or eggs		
Clinical manifestation/impairment	Anemia: impairs growth and development in children		
	Intestinal obstruction	Inflammation, dystentry	Iron deficiency, malnutrition
	 <small>Ascaris lumbricoides roundworms - post-surgery in resected bowel _Image by Dr. Vikas Arora, India</small>		
Treatment	Benzimidazole anthelmintics		
Control	Mass dewormings, drugs.		





Other helminths

Disease	Elephantitis	River blindness	Guinea worm	Schistosomiasis
Target	Lymphatic system, genitals	Subcutaneous tissue	Subcutaneous tissue, legs	Urinary tract, liver, intestines
Transmission	Mosquitoes	Blackflies	Water fleas in drinking water	Larvae in freshwater
Clinical manifestation/impairment	Filarial fever, swelling, disfigurement	Malnutrition, developmental/educational impairment		
		Blindness, disfigurement, skin disease	Painful blister in foot, inflammation	Target organ damage, highest mortality
				
Treatment	Diethylcarbama-zine, ivermectin, albendazole	Ivermectin	Extract worm on stick	Praziquantel
Control	Interrupt transmission cycle, yearly mass drug admin	Vector control, yearly mass drug admin	Safe water, health education	Molluscicide, yearly mass drug admin.


Tapeworms, trematodes

Disease	Tapeworms			Foodborne trematodiasis
	Taeniasis	Cysticercosis	Echinococcosis	
Target	Intestines	Muscles, central nervous system	Liver, lungs	Liver, lungs
Transmission	Tapeworms in pork or beef	Tapeworm larvae in meat	Tapeworm eggs from dogs, foxes	Trematode worms in fish, crustaceans
Clinical manifestation/impairment	Abdominal pain, nausea, diarrhoea, constipation	Cysts in central nervous system, epilepsy	Weight loss, abdominal pain, liver failure, death	Abdominal and liver pain, jaundice, coughing blood
				
Treatment	Praziquantel, niclosamide	None	Albendazole, mebendazole	Praziquantel, triclabendazole
Control	Sanitation, vaccination and treatment of pigs, meat inspection	Case management, anti-epileptic drugs, surgery	Puncture and repair, surgery, anti-infective drug treatment	Case management, preventive chemotherapy




Protozoans

Disease	Leishmaniasis		Chagas' Disease	Sleeping sickness	
	Visceral	Cutaneous		T.b.g.	T.b.r.
Target	Liver, spleen, blood, bone marrow	Skin	Multiple	Blood, lymph, spinal fluid, central nervous system	
Transmission	Sandflies		Triatome bugs	Tsetse flies	
Clinical manifestation/impairment	Decreased red blood cell count, fever, weight loss	Disfigurement	Chronic heart disease, megacolon, megaesophagus	Coma & death	
				Anemia, enlarged lymph nodes, personality change, gait	Death within a year
				 <small>Mosca tse tse</small>	
Treatment	Amphotericin B, Pentamidine, Mitefosine		Nifurtimox, Benznidazole, Pacemakers/transplant	Pentadmine, Suramine, Melarsoprol, Eflornithine	
Control	Case detection & management, vector control		Case detection & management, vector control	Case detection & management.	

Bacterial

Disease	Buruli ulcer	Leprosy		Yaws	Trachoma
Transmission	Unknown	Unknown		Skin to skin	Direct contact with discharge
Clinical manifestation / impairment	Disfiguring skin infection, amputation	<i>Tuberculoid</i>	<i>Lepromatous</i>	Ulcers, painful joints, bones	Irreversible visual impairment, blindness
		Loss of sensation, skin lesions	Disfigurement, bone invasion		
Treatment	Rifamprin, streptomycin, debridement	Dapsone, rifamprin, clofazimime		Penicillin, azithromycin	Azithromycin
Control	Amputation	Multidrug treatment		Drug treatment	facial hygiene, surgery

Viruses

Disease	Dengue	Chikungunya	Rabies
Transmission	Mosquitos	Mosquitos	Saliva from dogs, bats
Clinical manifestation/ impairment	Haemorrhagic fever, flu-like illness, rash, headache, low blood pressure	Musculoskeletal pain, fever, rash, headache, fatigue	Violent movements, fear of water, uncontrolled shaking, death
			
Treatment	None	None	Post-exposure vaccination, rabies immunoglobulin
Control	Mosquito control	Mosquito control	Vaccination

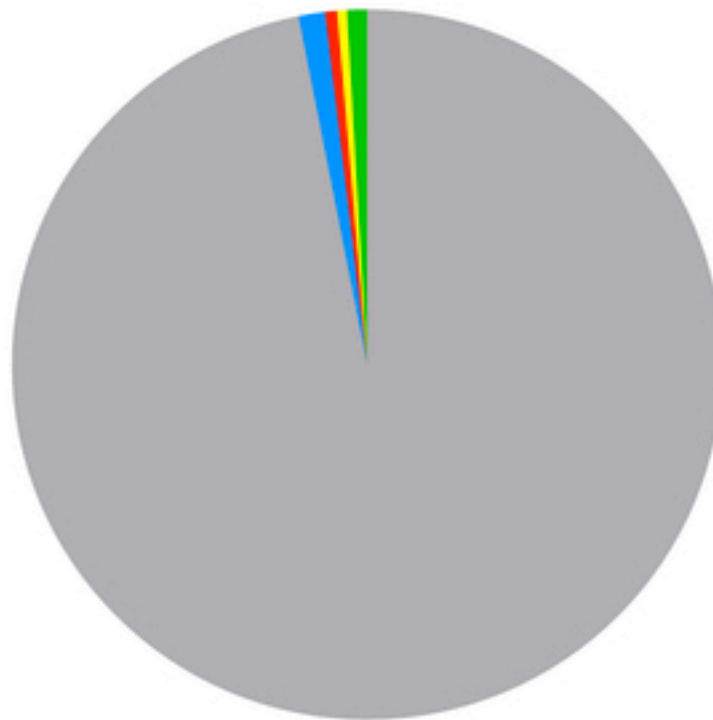
Management and control

- Prevention/treatment exists for most NTDs
 - cheap and effective chemical pharmaceuticals are available for some NTDs
- Not available to the people at risk
 - access and distribution difficulties
- Lack of healthcare infrastructure
 - lack of R&D for existing and novel pharmaceuticals
 - treatments may be toxic
- Inadequate funding.



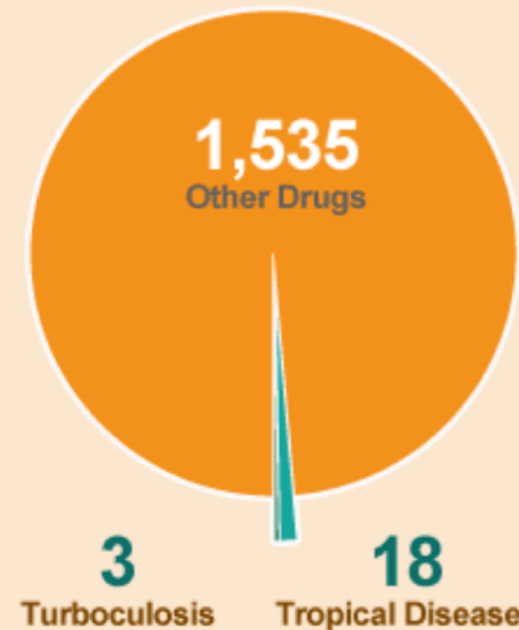
Pharmaceutical priorities

Global Spending on Pharmaceutical R&D



- Non-NTD (96.9%)
- HIV/AIDS (1.2%)
- Malaria (0.54%)
- Tuberculosis (0.44%)
- All Other NTDs (0.91%)

New drugs approved 1974-2004



What can help

- Availability and access to health care
- Clean living conditions
- Clean drinking water
- Adequate nutrition
- Education
- Gender equality
- Non-discrimination
- Pharmaceutical research and development
- Overhaul of drug patent systems
- Identification/targeting of vulnerable groups.

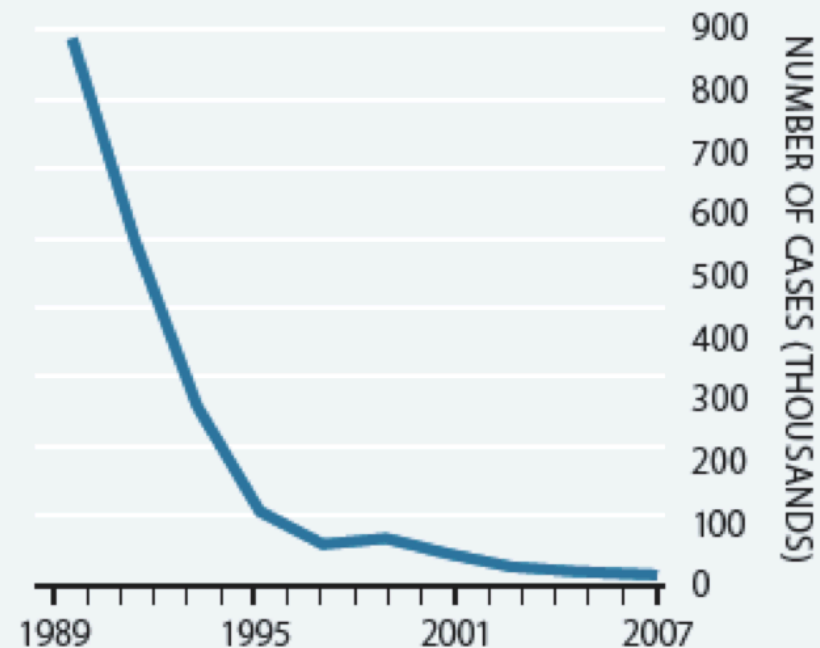


Organisation

- Public-private partnerships have had considerable success
- Eg Guinea worm disease has been almost entirely eradicated, despite no biomedical intervention
- These relationships need to be strengthened.

GUINEA WORM ERADICATION PROGRESS

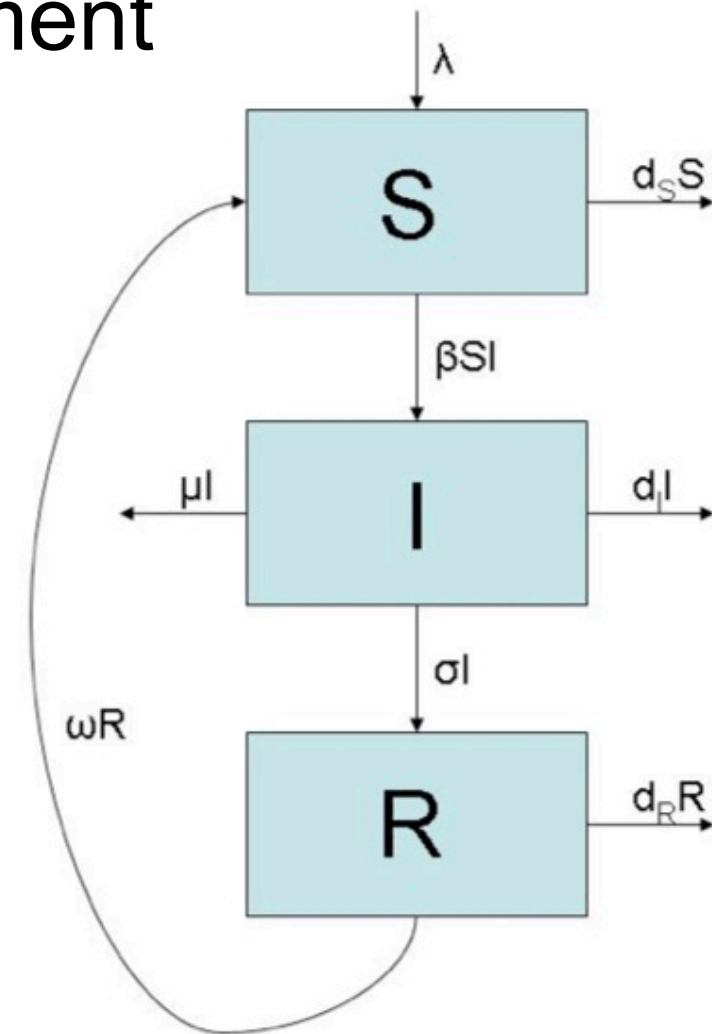
Declines in total number of cases since 1989



Source: World Health Organization

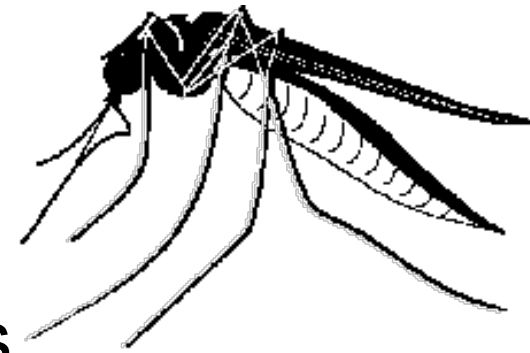
Mathematical models

- Have contributed to many advances in disease control and management
- Eg
 - malaria control
 - smallpox eradication
 - polio eradication
 - vaccine design
 - mosquito management
 - effects of climate change
 - emergency preparedness.



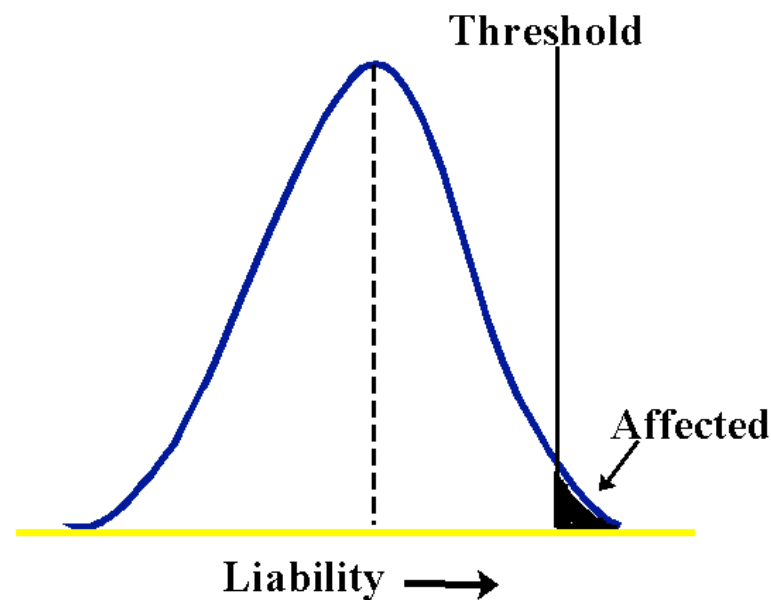
Advantages of models

- Can assess theoretical intervention methods in the absence of data
- Eg
 - optimal drug administration schedule
 - optimal allocation of limited resources
 - vector control
- However, models depend critically on the assumptions used to construct them
- Modellers need to be clear about limitations
- Policy analysts need to be better educated about the power of models.



Modelling

- Provides greater understanding of existing control strategies without costly experiments
- Can find control/eradication thresholds
- Limited by
 - lack of access to data
 - disinterest by funding bodies
 - insufficient communication between policy analysts and modellers
 - a reliance on a model's conclusion that does not consider its assumptions.



NTD modelling so far...

- Substantial theoretical modelling has been developed for
 - sleeping sickness, dengue, chikungunya, rabies
- No explicit models for
 - the Buruli ulcer, foodborne trematodiasis
- Only one for Guinea worm
- Models that do exist are often limited to one lab and its collaborators per NTD
- A diversity of voices is urgently needed.

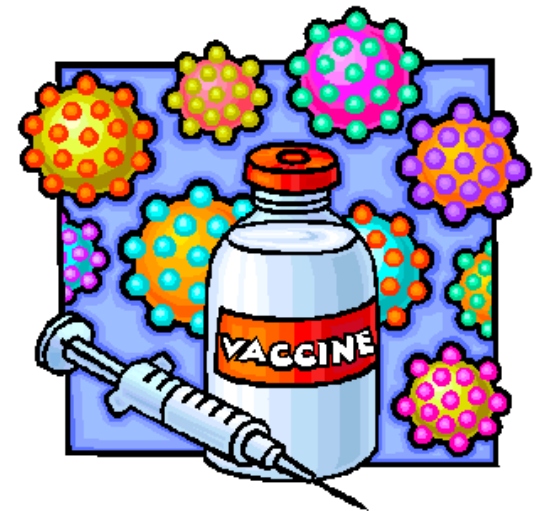


A modelling success story

- The West African River Blindness Control Program was hailed as a success due to integrated modelling and control efforts
- Modelling predicted that 14 years of vector control would reduce the risk to less than 1%
- Helped convince donors that control was feasible
- Models were refined using subsequent data to include treatment
- Modelling retained a prominent role in subsequent policy discussions.

Future directions for modelling

- More mathematical models are urgently needed
- Existing control efforts need to be optimised
- Theoretical interventions need to be examined
 - eg potential vaccines
- Spatial effects are crucial
- Urban/rural models
- Fill in potential gaps in knowledge
 - eg routes of transmission.



Specific problems

- Adapting malaria pesticide models for vector control in Chagas' Disease
- Modelling access to resources across geographically difficult terrains
 - eg distance to hospitals, swamps, mountains, road networks
- Categorise the cost to developing economies of disabling NTDs
- Model NTD research funding
- Co-infection models
 - with other NTDs and the big three.



Summary

- NTDs require immediate attention
- NTDs extract an enormous price in
 - suffering
 - lack of economic development
 - promotion of poverty
- Mathematical models can be used to inform policy at minimal cost.



Conclusions

- NTDs are the low-hanging fruit of disease modelling
- A great many problems could be solved, relatively easily, by harnessing the power of mathematical modelling
- The price — political and otherwise — for such a huge improvement in the quality of life for 1/6 of the world's population is tiny.

