Neglected Tropical Diseases:
Best options for control and how to reach the scale required.

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Box 2. Common Features of the Neglected Tropical Diseases

- Ancient afflictions that have burdened humanity for centuries
- Poverty-promoting conditions
- Associated with stigma
- Rural areas of low-income countries and fragile states
- No commercial markets for products that target these diseases
- Interventions, when applied, have a history of success

Molyneux et al PLoS Med 2005

Why are they neglected?

- compete with more visible diseases like HIV/AID, tuberculosis, and malaria
- no explosive outbreaks - chronic problems
- do not travel internationally so don't affect wealthy nations
- affect the poorest of the poor - no incentive for the development of new diagnostic tools, drugs and vaccines
- cause enormous misery but do not kill large numbers of people.
- Endemic countries have limited resources to invest in health and competition for funds is fierce.
- The stigma associated with debilitating and deforming diseases makes the afflicted reluctant to seek care.

Adapted from http://www3.imperial.ac.uk/schisto/whatwedo/whatarentds

Key questions

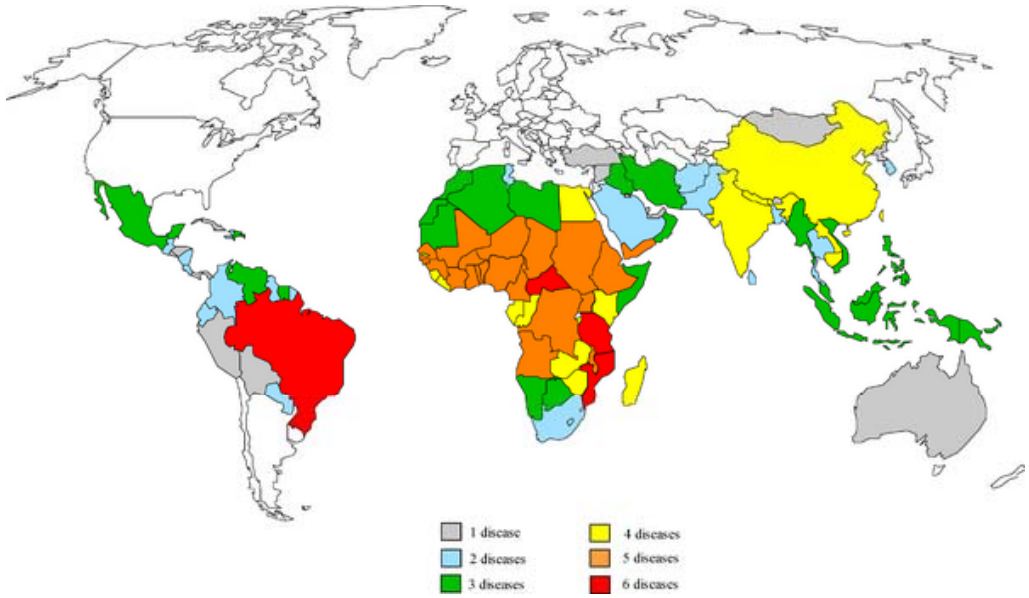
- What is the public health benefit of treating neglected tropical infections?
- Are new treatment and prevention tools needed, or is it merely a question of delivery of existing tools?
- What is the existing coverage?
- What are barriers to effective delivery and/or development of new drugs/vaccines?
- How best to implement control programs?

NTD Control could have huge Impact

- impair childhood growth, physical fitness, development, and school attendance
- impair worker productivity
- often disfiguring, painful
- major cause of anemia
  - hookworm alone accounts for 35% and 73% of anemia and severe anemia
- 500,000 deaths and 56M DALYs

Overlap of Neglected Tropical Diseases

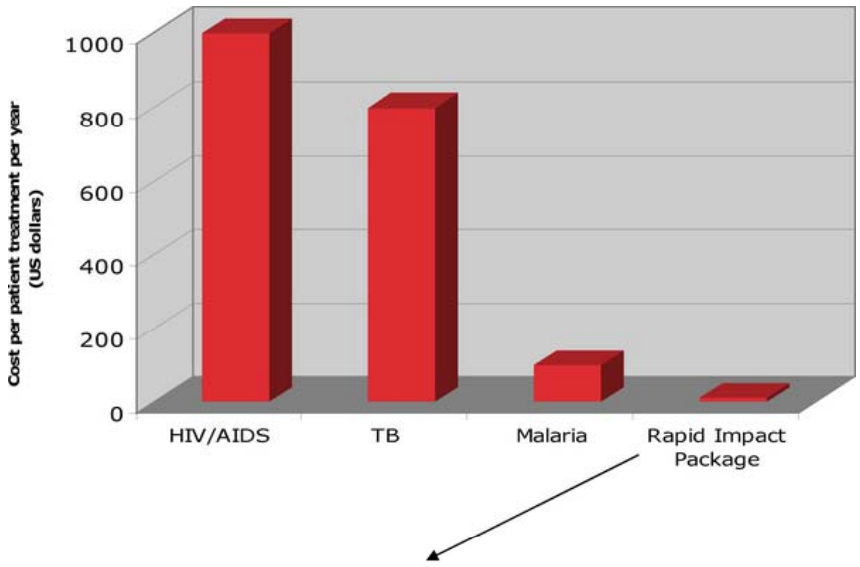
- geographically,
- same age groups,
- require same drugs
- Can treat 7 NTDs for $0.40/person/year using 4 drugs,
  - Ivermectin [Merck]; Azithromycin [Pfizer]; Albendazole [GlaxoSmithKline]; Praziquantel



Most individuals are 'polyparasitized'

Focus is often on the Big 3

- *HIV, malaria, and TB*
- NTDs cause sig. DALYs (below)
- major difference is cost-effectiveness of interventions



Lower respiratory tract infections (91.3M), HIV/AIDS (84.5M), diarrheal diseases (62M), NTDs (56.6M), Malaria (46.5M), Tuberculosis (34.7M), Measles (21.4M)

Minimal cost of interventions

Disease	Target Population	Numbers to Be Treated in Target Population	Drug, Source, and Cost If Not Donated	Delivery Strategy	Distribution Costs[a] (Ex Drug)	Annual Cost Required
Lymphatic filariasis	Total eligible[b] population in endemic areas	300 million	Mectizan donated by Merck and albendazole by GlaxoSmithKline	MDA for five years	$0.10 per person treated = $30 million	$30 million + donated drug
Schistosomiasis	School-aged children plus other high risk groups	200 million	Praziquantel at $0.25 per treatment = $50 million	MDA in high risk area plus school health programmes	$0.15 per person treated = $30 million	$30 million + $50 million = $80 million
Intestinal helminths	Pre-school-aged and school-aged children	400 million	Albendazole at $0.02 per treatment = $12 million	Health days and school health programmes	$0.10 per person treated = $40 million	$40 million + $12 million = $52 million
Onchocerciasis	Total eligible[b] population in hyper/mezzo endemic areas	80 million	Mectizan donated by Merck	MDA via community directed treatment	$0.10 per person treated = $8 million	$8 million + donated drug
Trachoma	Total population in endemic areas	168 million	Zithromax donated by Pfizer	MDA for five years	$0.20 per person treated = $34 million	$34 million + donated drug
Summary	The population of sub-Saharan Africa is an estimated 700 million	Up to 500 million individuals will receive treatment for one or more of these infections	$62 million + drug donations		$142 million	$142 million + $62 million for drugs + donated drugs
		500 million	$62 million		$142 million	= $204 million for five years

Table modified from [23], with permission from Elsevier.

Assumptions for Table 3 are as follows. (1) An estimated 500 million people will be reached and treated as appropriate for five diseases at a total cost of $204 million. (2) The per-person cost will therefore be [illegible] integrating treatments there could be substantial savings on delivery costs. (3) Cost saving by combining delivery could reach an estimated 25%. (4) After five years' intervention, it is expected that mass chemotherapy of some of these infections will no longer be necessary, but monitoring will be recommended on a longer-term basis to confirm this hypothesis. (5) Delivery could be combined with vaccinations (polio, measles-mumps-rubella, measles) and vitamin A capsules.

[a]The distribution costs are estimates derived from experience with vertical programmes. Schistosomiasis is very focal and therefore requires more extensive mapping data to determine the target population. Trachoma delivery costs include some allowance for surgical intervention in extreme cases.

[b]The following are not eligible: children less than 90 cm in height, severely ill patients, and pregnant women.

MDA, mass drug administration.

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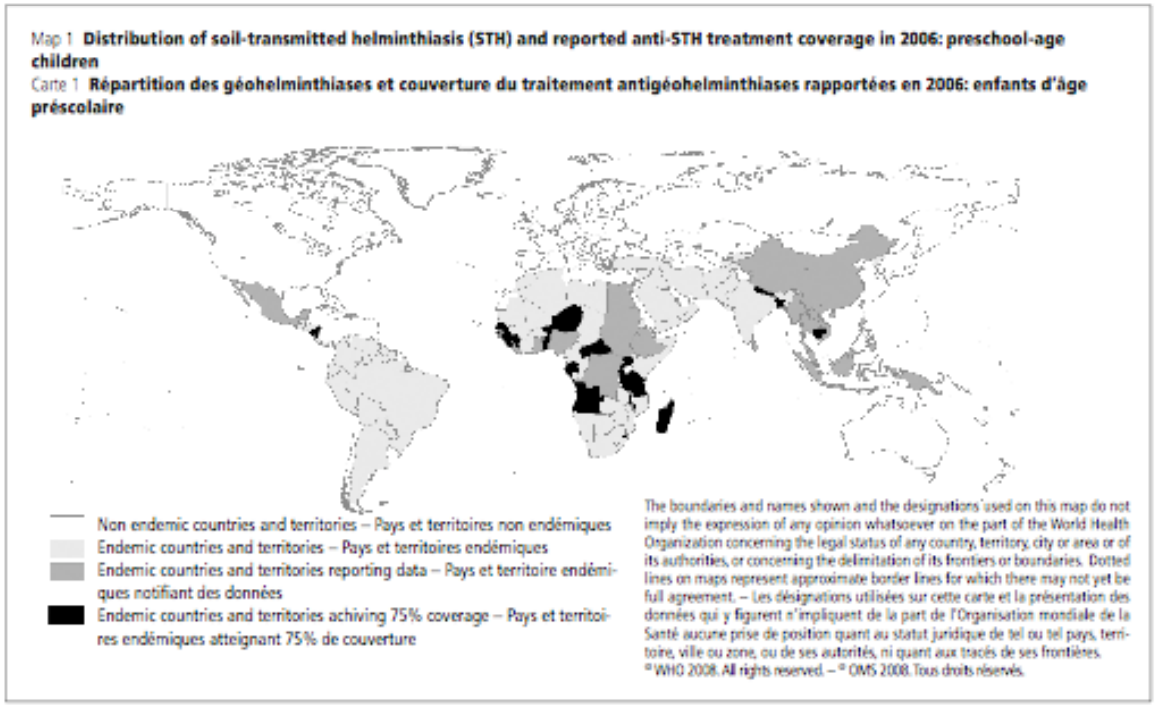
Immunological impact

- Many NTDs, helminths in particular, are powerful immunogens and chronic infections
  - suppressive, Th2 -skewing
- Some evidence these can impact childhood vaccines, immunity/susceptibility to HIV, TB, and malaria

- Impetus for ‘Big 3’ programs to include NTDs

Global coverage of STH deworming



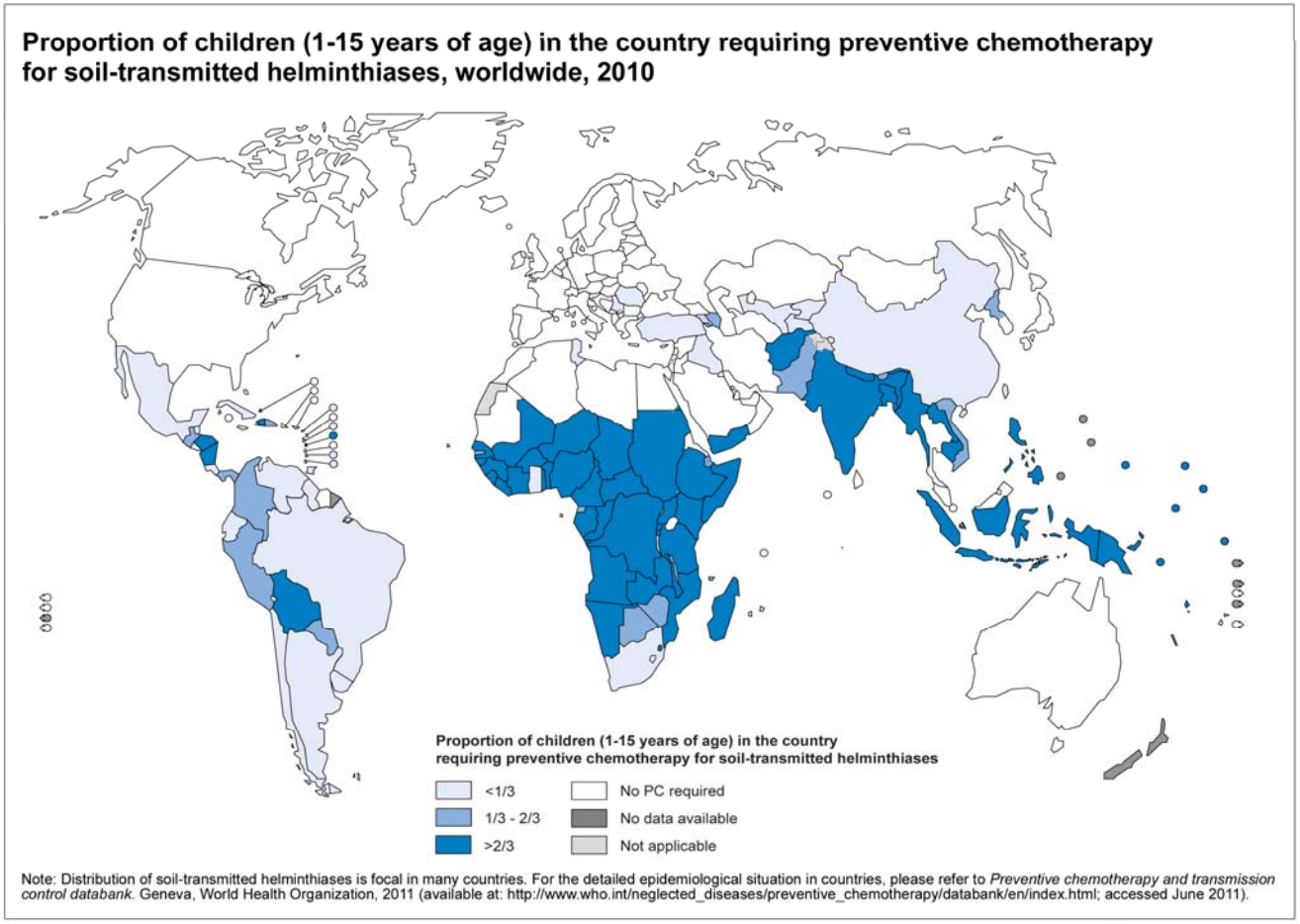
Good news >160m kids treated. Bad news is >1,2B at risk.

Issues:

- poor reporting (only 50% of countries with reliable data)
- poor implementation (26% of SAC-Africa)
- range = 0-144%

2006 Data. **Black** indicates countries with >75% coverage of pre-school children
Source: http://www.who.int/neglected_diseases/en/

Global Need


Proportion of children (1-15 years of age) in the country requiring preventive chemotherapy for soil-transmitted helminthiases, worldwide, 2010
Proportion of children (1-15 years of age) in the country requiring preventive chemotherapy for soil-transmitted helminthiases
<1/3
1/3 - 2/3
>2/3
No PC required
No data available
Not applicable
Note: Distribution of soil-transmitted helminthiases is focal in many countries. For the detailed epidemiological situation in countries, please refer to Preventive chemotherapy and transmission control databank. Geneva, World Health Organization, 2011 (available at: http://www.who.int/neglected_diseases/preventive_chemotherapy/databank/en/index.html; accessed June 2011).
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2011. All rights reserved
Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization
World Health Organization

Challenges

- Financing
- Reach remote areas
- Research and monitoring questions
  - compliance, drug interactions, resistance, sustainability,
- Target kids the same age,
- Human resources
  - a midwife and nurse to cover 30,000
  - incentive system
- Integrate into existing programs to achieve coverage

Gyapong et al Lancet 2010

Integration: What Why How Who

- Horizontal - vertical debate rages on
- Elimination programs - vertical by definition
- Vertical programmes have a track record, measurable outcomes
- Some nations spend $10/person/year on health
- Can vertical NTD programs be used to build health care system capacity?

Gyapong et al Lancet 2010

Poor market for New Drug and Vaccine development

- Main market is the global, rural poor
- Philanthropy - “creative capitalism”
- Government - particularly of affected countries
- NIH/FDA fast track for development of orphan drugs

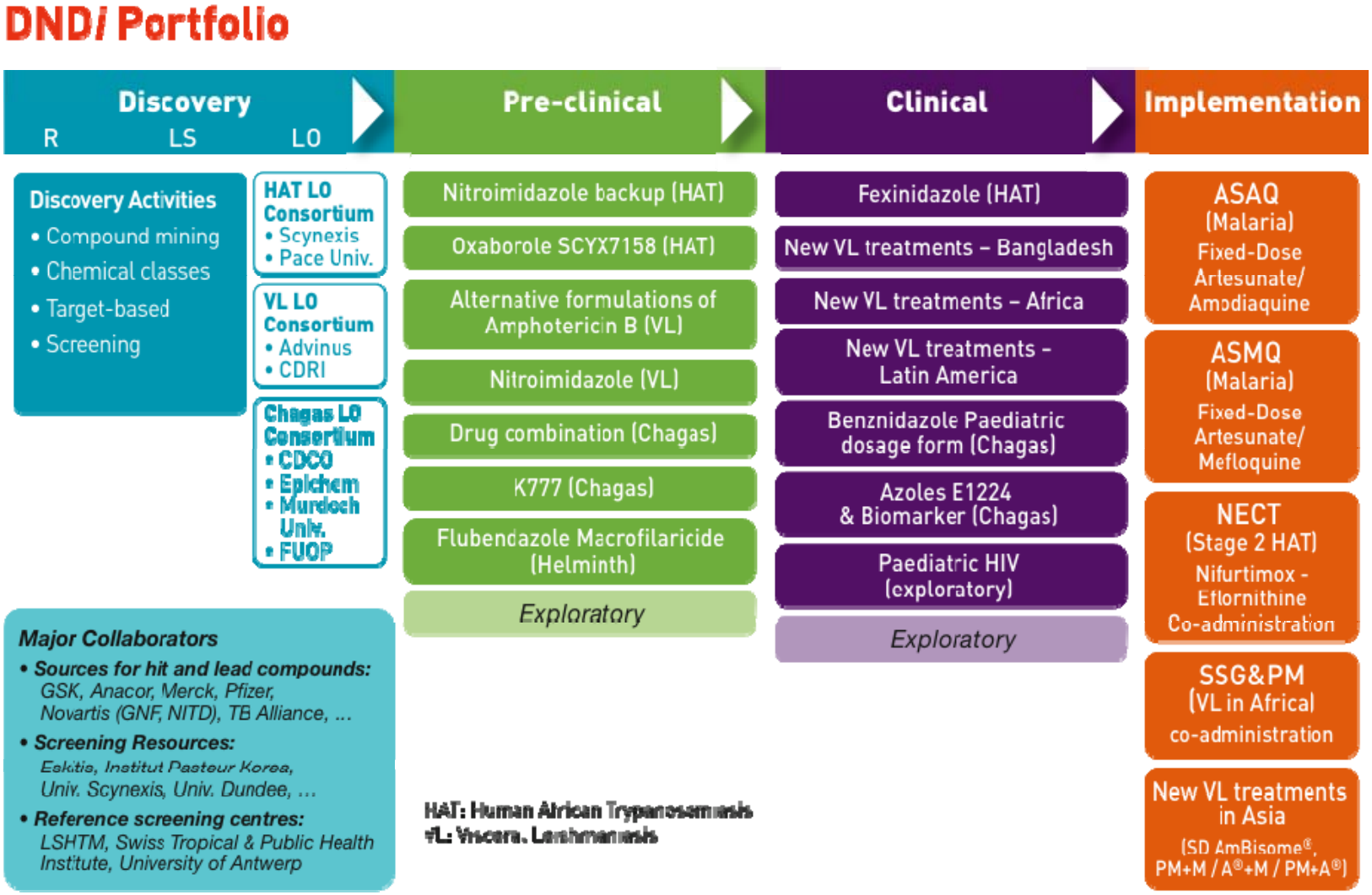
- Balance between R&D vs. implementing current, effective strategies

Private -Public Partnerships

Schistosomiasis Control Initiative
Partnership for Parasite Control (STH)
Human Hookworm Vaccine Initiative
International Trachoma Initiative
Global Alliance to Eliminate Lymphatic Filariasis
African Programme for Onchocerciasis Control
Drugs for Neglected Tropical Diseases initiative
WHO Programme to Eliminate Sleeping Sickness

- cover a wide range of NTD
- Some focus more on implementation, others on R&D, some both

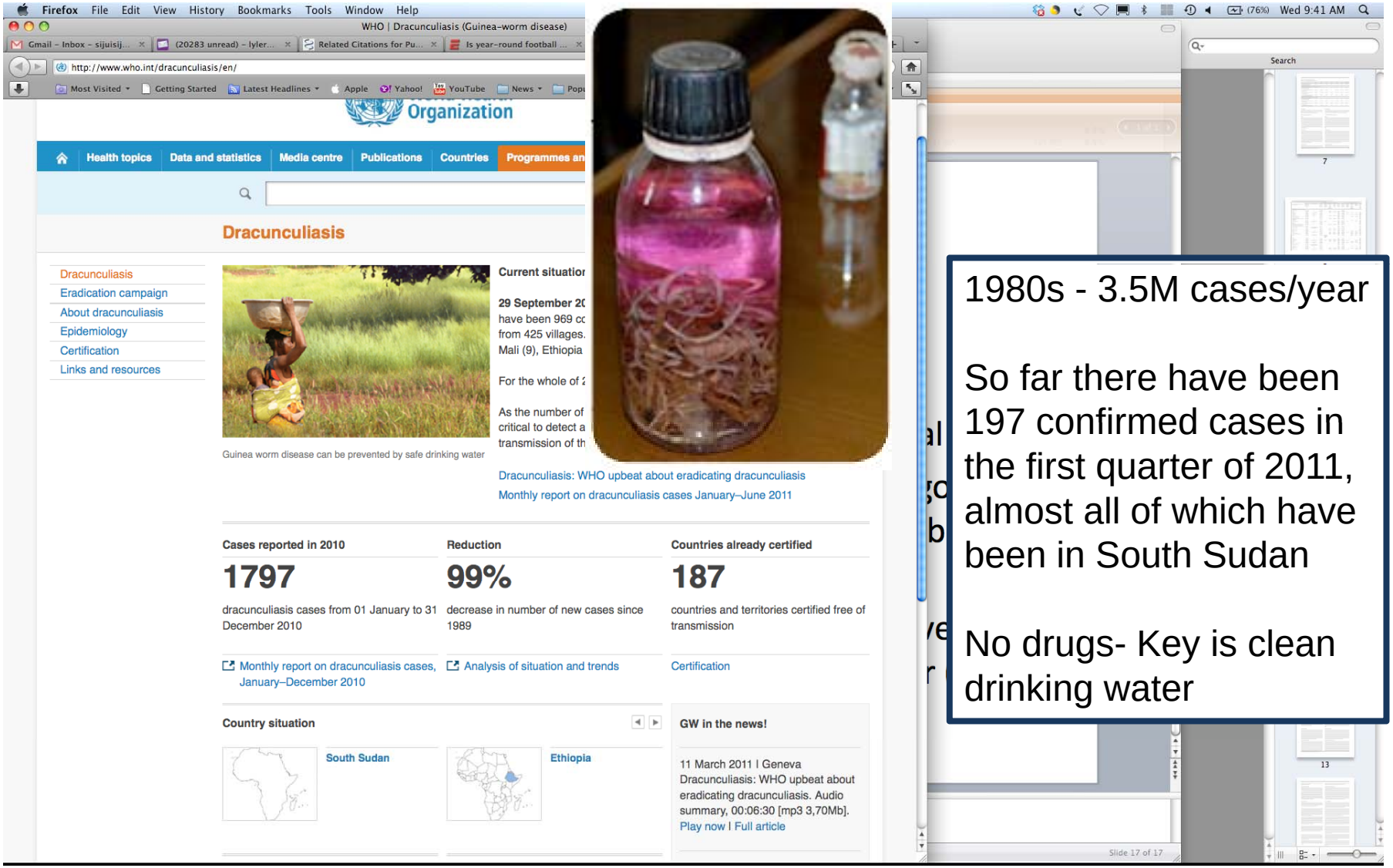
Drugs for Neglected Diseases initiative



Schistosomiasis Control Initiative

- created in 2002 at Imperial College London - 20M GBP from Gates Foundation
- by 2007, 40M Schisto treatments
- further funding from USAID and Geneva Global
- Currently targeting 7 NTDs in an integrated approach

Campaign to eradicate Guinea worm



1980s - 3.5M cases/year

So far there have been 197 confirmed cases in the first quarter of 2011, almost all of which have been in South Sudan

No drugs- Key is clean drinking water

Summary points

- Relatively small expenditure for major potential impact
- Way to improve the health of the global poor
- NTDs not in millennium development goals, but their effective control would contribute towards meeting 7 / 8 MDGs
- NTD programs among the most effective development investments in any sector (World Bank)

- Maybe one day, they will be known as the *'diseases formerly known as neglected'…*

Before surgery

After surgery

It is clear that elephantitis is a problem