

# NEGLECTED INFECTIOUS DISEASES

Key research questions  
and role of EDCTP2

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**DNDi**  
Drugs for Neglected Diseases *initiative*



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**Eighth EDCTP Forum**



Defeating poverty-related and neglected  
diseases in Africa: harnessing research for  
evidence-informed policies

# Neglected Tropical/Infectious Diseases

17 NTDs listed in WHO



18th added May 2016

The diagram consists of a vertical orange line with brackets at both ends. A diagonal orange line connects the text '17 NTDs listed in WHO' to the top bracket. Another diagonal orange line connects the text '18th added May 2016' to the bottom bracket. The list of diseases is positioned to the right of the vertical line.

- Buruli ulcer
- Dengue
- Dracunculiasis
- Endemic treponematoses (yaws/bejel)
- Human African trypanosomiasis
- Leishmaniasis (visceral and cutaneous)
- Leprosy
- Lymphatic filariasis
- Onchocerciasis
- Rabies
- Schistosomiasis
- STH
- Trachoma
- Cysticercosis
- Echinococcosis
- Fascioliasis
- (Chagas)
- Mycetoma

# Disease burden ... & the vicious cycle

>1 billion affected incl. 500 million children

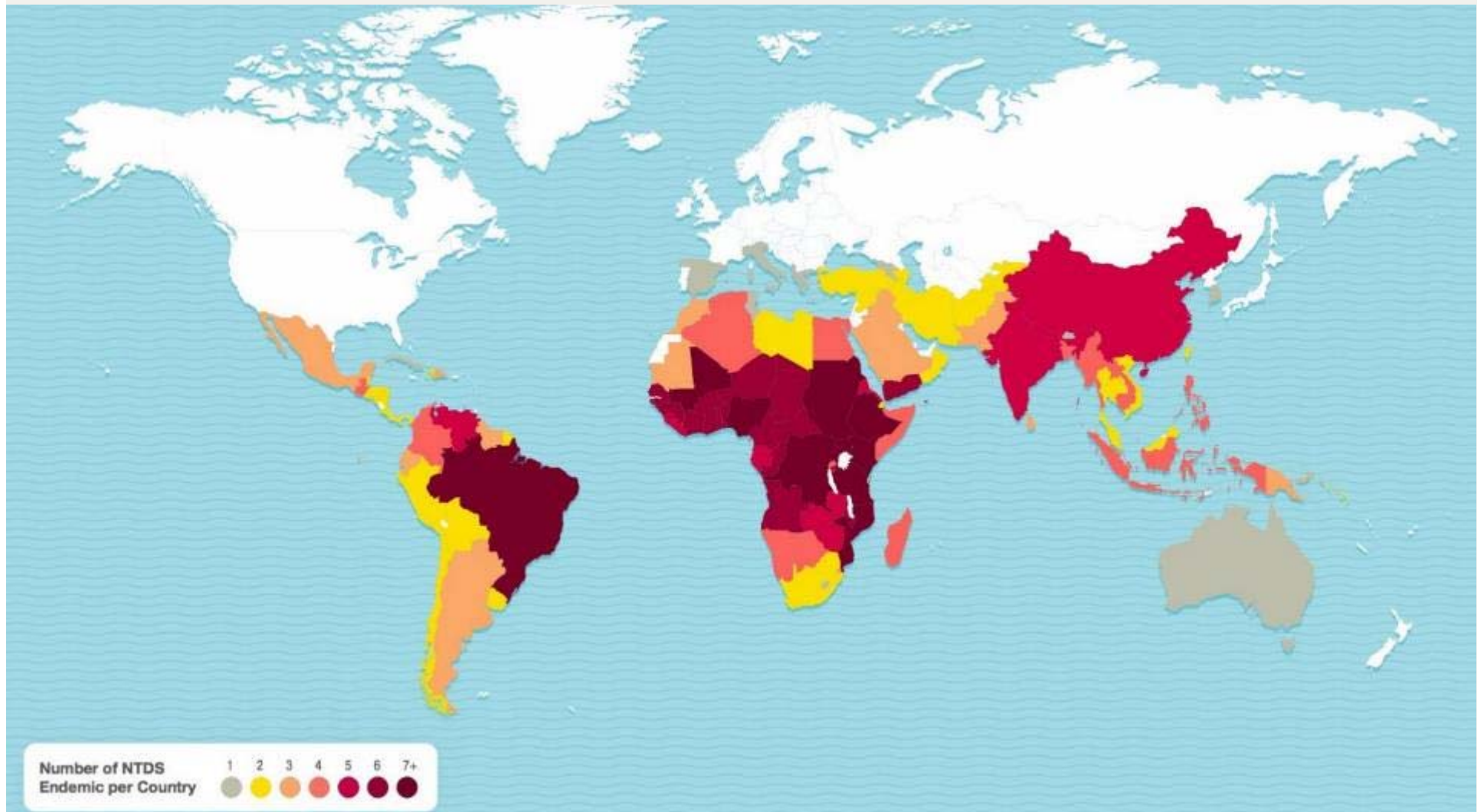
	Global Burden of Diseases (2010)	'Chronic pandemic' The Lancet (2016)
Deaths/year	150,000	350,000
DALYs	27 million	48 million

- Disease is both cause and consequence of poverty
- Poorest of the poor
- Living in remote areas
- Socioeconomic burden on family and community
- Marginalized & voiceless patients





# Africa concentrates over 90% of NTD burden



Source: Uniting to Combat NTDs, 2012

# Ranking of NTDs in SSA by prevalence and distribution

Disease	Estimated Population Infected in SSA	Estimated % of SSA Population Infected	Estimated % Global Disease Burden in SSA	Reference
Hookworm	198 million	29% <sup>a</sup>	34% <sup>b</sup>	[3,24]
Schistosomiasis	192 million	25%	93%	[21]
Ascariasis	173 million	25% <sup>a</sup>	21% <sup>2b</sup>	[3,24]
Trichuriasis	162 million	24% <sup>a</sup>	27% <sup>b</sup>	[3,24]
Lymphatic filariasis	46–51 million	6%–9%	37%–44% <sup>c</sup>	[25–28]
Onchocerciasis	37 million	5%	>99%	[15,29]
Active trachoma	30 million	3%	48%	[30]
Loiasis	≤13 million	1%–2%	100%	[31,32]
Yellow fever	180,000	0.02%	90%	[33,34]
Human African trypanosomiasis	50,000–70,000 (17,000 new cases annually)	<0.01%	100%	[39,40]
Leprosy	30,055 (registered prevalence); 21,037 new cases in 2007	<0.01%	14%	[35]
Leishmaniasis (visceral)	19,000–24,000 new cases annually in Sudan and Ethiopia	<0.01	ND	[41–44]
Dracunculiasis	9,585	<0.01%	100%	[36]
Buruli ulcer	>4,000	<0.01%	57%	[37,38]

<sup>a</sup>Based on reported 2003 population of 683,330,334 [24]. For all other estimated population prevalence, we use the 2005 value of 764,328,000 published by the United Nations, <http://esa.un.org/unpp/>, and querying sub-Saharan Africa and 2005, accessed July 29, 2009.

<sup>b</sup>Calculated from global burden data from [48].

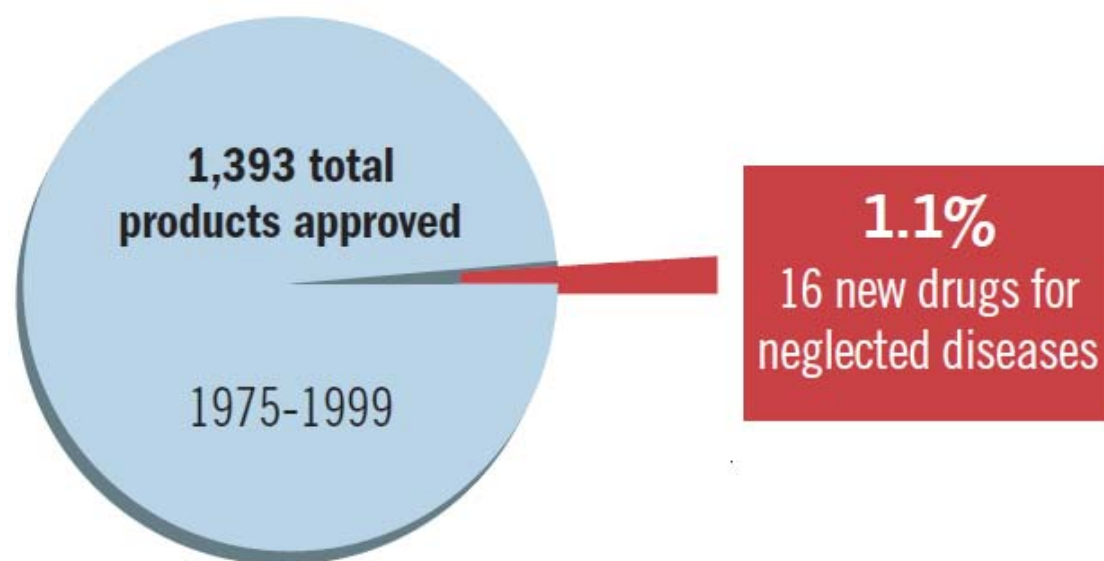
<sup>c</sup>The lower value is from [3,26,27]; the higher value from [25].

doi:10.1371/journal.pntd.0000412.t002

Hotez PJ, Kamath A (2009) Neglected Tropical Diseases in Sub-Saharan Africa: Review of Their Prevalence, Distribution, and Disease Burden. *PLoS Negl Trop Dis* 3(8): e412. doi:10.1371/journal.pntd.0000412



# A Decade Ago, Neglected Disease R&D at a Standstill: The 'Fatal Imbalance'

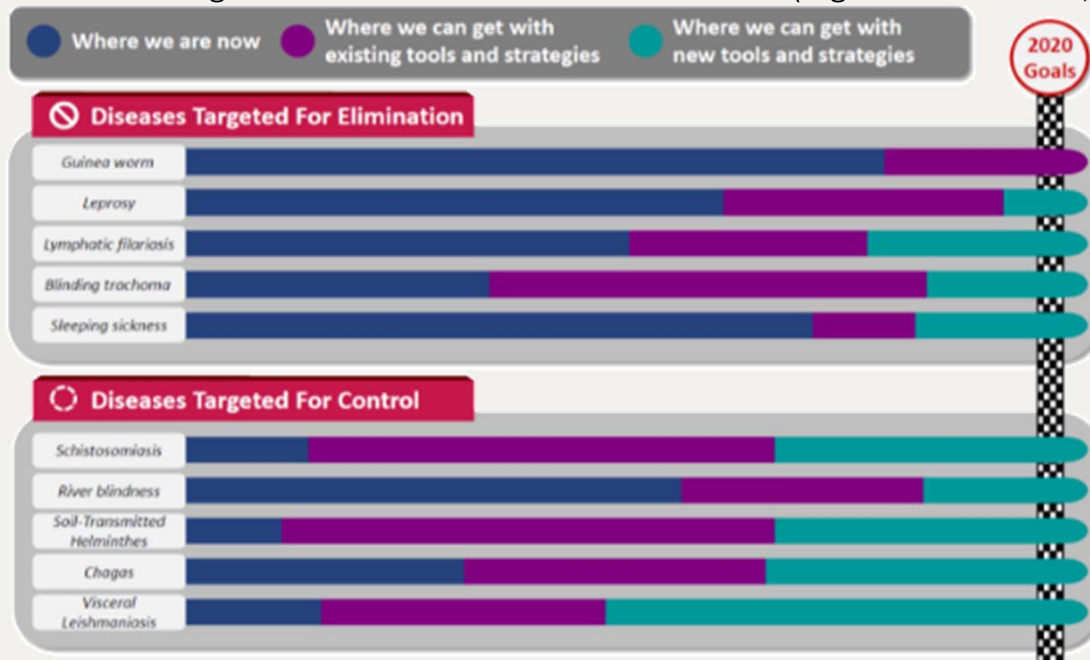


- 1.1% of 1393 new products for NTDs + malaria & TB () despite their global disease burden of 12%
- Illustration of the '10/90 Gap'

Source: Fatal Imbalance: The Crisis in Research and Development for Neglected Diseases, MSF, 2001

# Putting NTDs on the political agenda (1)

- 2005 creation of WHO Department of Control of Neglected Tropical Diseases
- 2011 WHO roadmap
- 2012 Endorsed at London Declaration including increased commitments for donations
- 2013 WHA Resolution 66.12, endorses Roadmap, strategies for NTDs with targets
  - eradication of dracunculiasis (2015) and yaws (2020)
  - global elimination of blinding trachoma, leprosy, HAT, and lymphatic filariasis by 2020;
  - regional elimination of selected diseases (e.g. onchocerciasis, schistosomiasis in several African



## London Declaration

- Pharmaceutical companies
- World Bank
- Donor countries (UK, USA, UAE)
- BMGF and other private donors
- Endemic country MoHs
- DNDi

Source: United to Combat NTDs

# Putting NTDs on the political agenda (2)

- 2015 GFATM Board opens funding for co-morbidities
- 2015 G7 Heads of State recognise NTDs as a major challenge emphasising need to support research and interventions
- 2014 EDCTP adds NTDs in its new business plan
- 2015 Inclusion in SDGs

## 3 GOOD HEALTH AND WELL-BEING



SDG 3.3: “By 2030, end the epidemics of AIDS, tuberculosis, malaria and **neglected tropical diseases** and combat hepatitis, water-borne diseases and other communicable diseases”

SDG 3.8: “Achieve universal health coverage, including financial risk protection, access to quality essential health care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all”

Coverage of NTD interventions are a tracer for universal health coverage



# Increased Investment in NTDs



EDCTP



Federal Ministry  
of Education  
and Research

# New partnerships



THE  
CARTER CENTER



Waging Peace • Fighting Disease • Building Hope



Because diagnosis matters



AFUTUREFREEOFLF  
GlobalAlliance



The International Podoconiosis Initiative



International Trachoma Initiative



GLOBAL SCHISTOSOMIASIS ALLIANCE



EXPANDED SPECIAL PROJECT  
FOR ELIMINATION OF  
NEGLECTED TROPICAL DISEASES

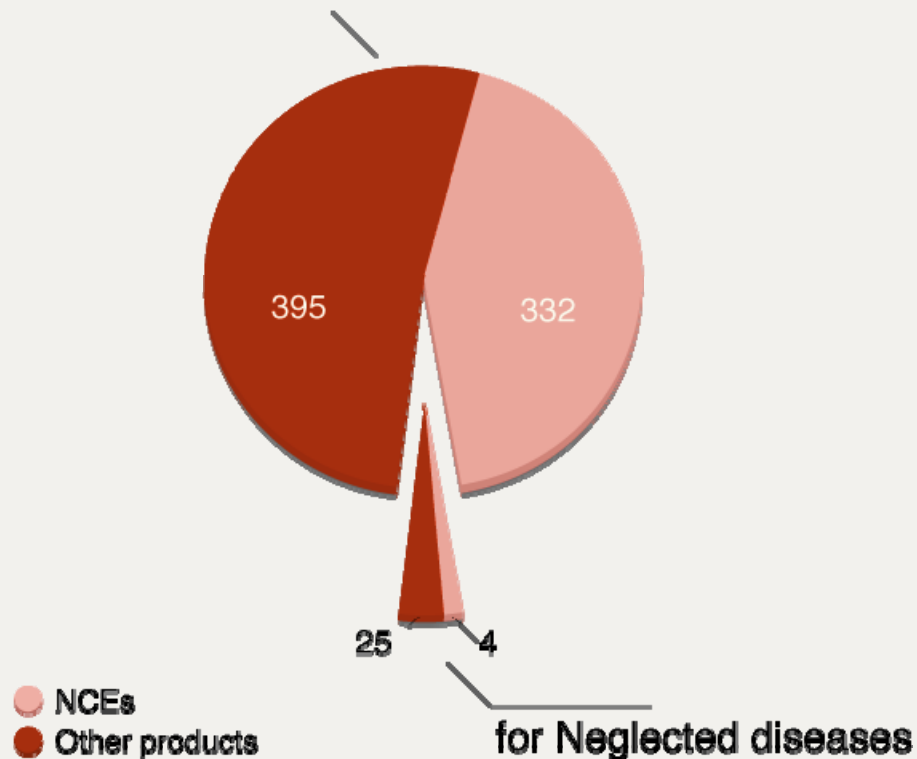


Drugs for Neglected Diseases *initiative*

# But Despite Progress, Fatal Imbalance Remains

756 products developed (excluding vaccines)  
(2000-2011)\*

**Other diseases**



\* Source: Pedrique B et al. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment. *Lancet Global Health*, Online Publication, 24 Oct 2013.

- 3.8% of new products (reformulations, combinations) for neglected diseases
- 1.2% of NCEs for neglected diseases
- 1.4% clinical trials (of nearly 150,000 trials) focus on neglected diseases
- Only 1% of global health investment for neglected diseases\*

\*Source: Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory? Rottingen et al. *Lancet*, May 2013

# Reality In The Field: Treatment Limitations for Neglected Diseases



- ❑ Ineffective (resistance)
- ❑ Toxic
- ❑ Expensive
- ❑ Painful when administered
- ❑ Difficult to use
- ❑ Not registered in endemic regions
- ❑ Restricted by patents

**We Need Safe, Effective, Affordable and Easy-to-Use Drugs**



# Identification of key gaps (awaiting R&D Observatory)

A proxy assessment for gaps

- 0 = no critical R&D gaps: existence of either:
  - interventions to prevent infection or
  - at least 2 field adapted treatments
- 1 = critical R&D gaps but some ongoing clinical research
- 2 = critical R&D gaps but no ongoing clinical research

Source: Pedrique B et al. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment. *Lancet Global Health*, Online Publication, **24 Oct 2013**.

Critical gaps but ongoing research (WHO-NTDs- AFRICA)	Critical gaps and NO ongoing research (ALL)
STHs	Food borne trematodes
Schistosomiasis	(Buruli ulcer)
LF	Leprosy
Onchocerciasis	Leptospirosis
Taeniasis-cysticercosis	Bartonellosis
Leishmaniasis	Bovine tuberculosis
Dengue Fever	Relapsing fever
Rabies	Mycetoma
	Paracoccidiomycosis
	Podoconiosis
	Loiasis
	Tungiasis
	Myiasis

## Research needs: Some examples

# Research needs

- 1 Regional response to treatment and specific medical needs
- 2 Co-morbidities
- 3 Diagnostic and treatment research approach
- 4 Responding to pediatric needs
- 5 Pregnant and breast feeding mothers
- 6 Conducting and running CTs effectively
- 7 Transitioning from clinical research to implementation
- 8 New category of NTDs
- 9 The development of resistance

# 1 Regional response to treatment and specific medical needs

## a) regional response to treatment

Drugs	SSG	Ampho B Liposomal	Ampho B deoxycholate	MIL	PM sulphate	SSG+PM	LAB+SSG	LAB+MIL	PM+MIL
Clinical efficacy									
Asia	35-95% (depending on areas)	> 97% all regions	> 97%; single dose: > 96%	94-97% (India)	94% (India)	Not documented	> 97%	> 97%	> 97%
Africa	93%	33 - >97% (depending on areas)	Not fully established	72%	84%	91%	87%	79%	Not documented
Resistance	As high as 60% (India)	Not documented	Not documented	20% (Nepal)	Lab isolates (easily)	Lab isolates (easily)	Lab isolates	Lab isolates	Lab isolates (easily)

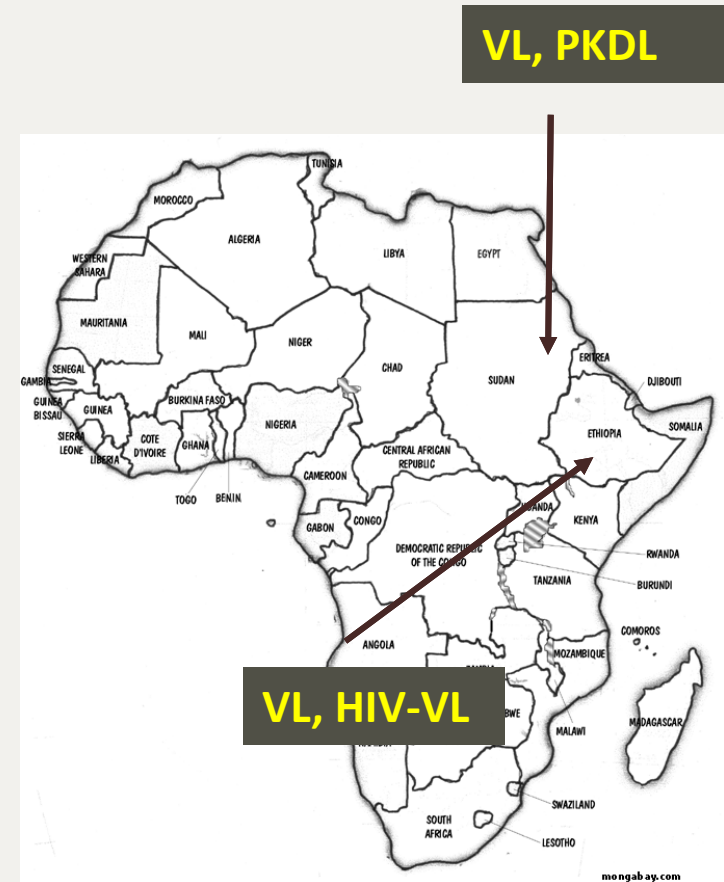
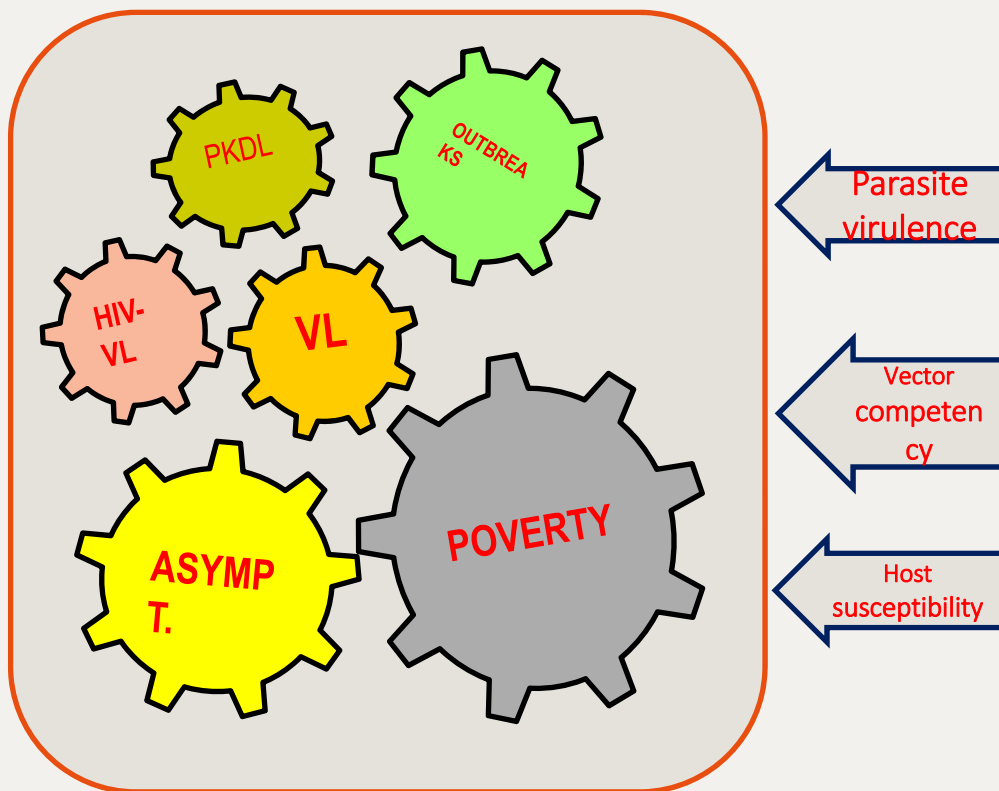
**Efficacy and resistance of different medicines by geographical areas (modified from van Griensven, 2010)**

**The treatment of African VL is far from optimal**



# 1 Regional response to treatment and specific medical needs

b) disease complexity and regional distribution



# 1 PKDL: reservoir of disease

Post Kala-azar Dermal Leishmaniasis (PKDL)  
An immune mediated process: VL (m2) - PKDL (m2/m1) - cure (m1)



macular

papular

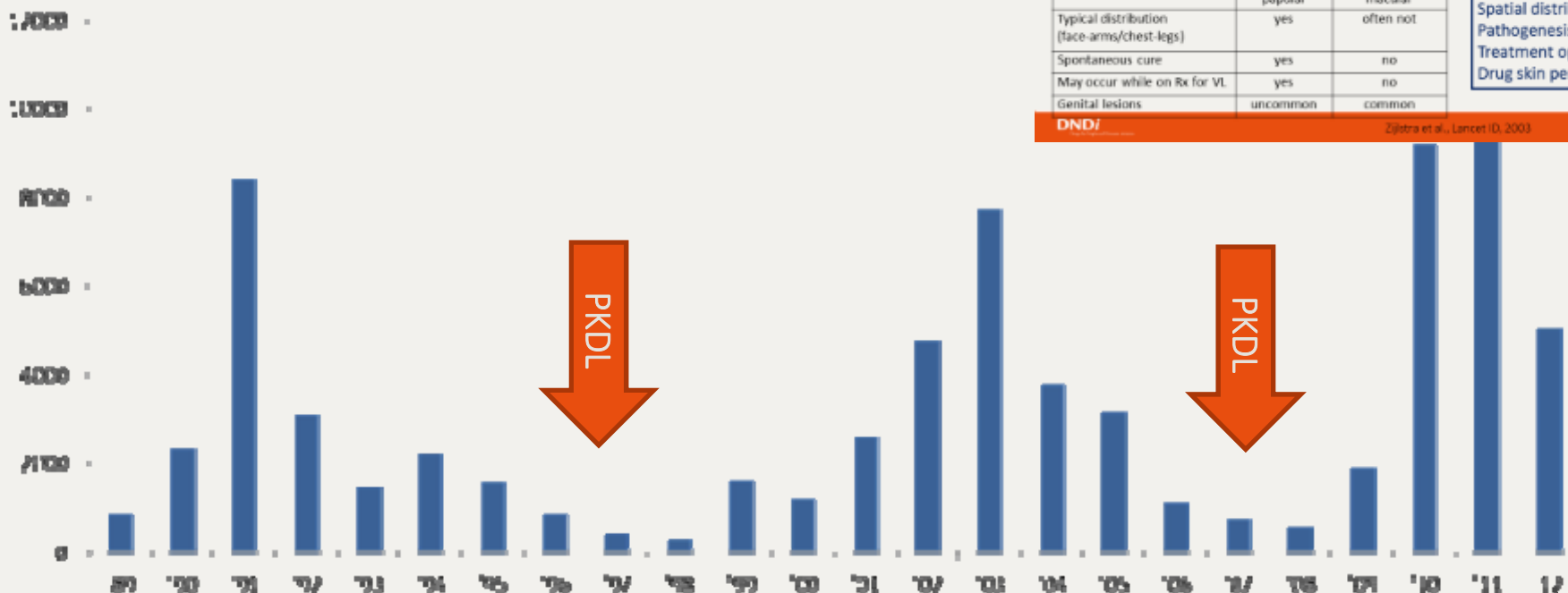
nodular

Main clinical differences	Sudan	India
Most common presentation	polymorphic, papular	monomorphic, macular
Typical distribution (face-arms/chest-legs)	yes	often not
Spontaneous cure	yes	no
May occur while on Rx for VL	yes	no
Genital lesions	uncommon	common

**Main gaps in knowledge**  
Infectivity  
Spatial distribution  
Pathogenesis  
Treatment optimization  
Drug skin penetration

DNDI

Zijlstra et al., Lancet iD, 2003



	Global incidence	Post-Rx estimates
INDIA (Bihar)	5:10,000	5-10%
BANG (Fulbaria/Trishal)	6-16:10,000	9,5%
Sudan	NA	50-60%

# 1 Regional response to treatment and specific medical needs

b) disease complexity and regional distribution  
tb rhodesiense vs gambiense

One disease: two strains



- *T.b. gambiense* is endemic in 24 countries of west and central Africa
- Less than 3,000 cases reported in 2015
- Transmission cycle:



- *T.b. rhodesiense* is endemic in 13 countries of eastern and southern Africa
- 117 cases reported in 2014
- Transmission cycle:



Source: Adapted from WHO

Geographic distribution of HAT cases



## 2 Co-morbidities are frequent

- Schistosomiasis & mycetoma

van Hellemond JJ, Vonk AG, de Vogel C, Koelewijn R, Vaessen N, et al. (2013) Association of eumycetoma and schistosomiasis. *PLOS Negl Trop Dis* 7: e2241

- HIV-VL: need for treatment and prophylaxis

WHO. Control of the Leishmaniasis: Report of the WHO expert committee on the Control of Leishmaniasis, Geneva, 22-26 March 2010. *WHO*, 2010.

- Onchocerciasis and nodding syndrome / epilepsy

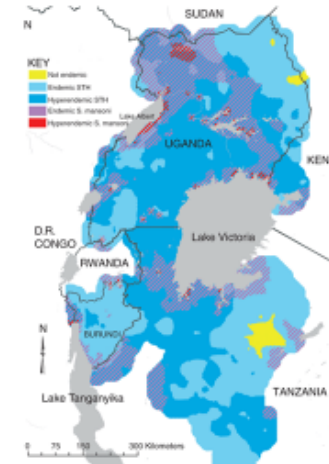
Winkler AS, Friedrich K, König R, et al. The head nodding syndrome - Clinical classification and possible causes. *Epilepsia*. 2008;49(12):2008-2015. doi:10.1111/j.1528-1167.2008.01671.x.

Kaiser C, Pion SDS, Boussinesq M. Case-control Studies on the Relationship between Onchocerciasis and Epilepsy: Systematic Review and Meta-analysis. *PLoS Negl Trop Dis*. 2013;7(3). doi:10.1371/journal.pntd.0002147.

- Helminths-HIV ...

Borkow G, Teicher C, Bentwich Z (2007) Helminth-HIV Coinfection: Should We Deworm? *PLoS Negl Trop Dis* 1(3): e160. doi:10.1371/journal.pntd.0000160

Spatial co-distribution of neglected tropical diseases in the East African Great Lakes region: revisiting the justification for integrated control



*Tropical Medicine & International Health*  
Volume 15, Issue 2, pages 198-207, 12 JAN 2010 DOI: 10.1111/j.1365-3156.2009.02440.x  
<http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3156.2009.02440.x#item>

### Research needs

Understanding morbidity impact

Assessing combined treatment needs

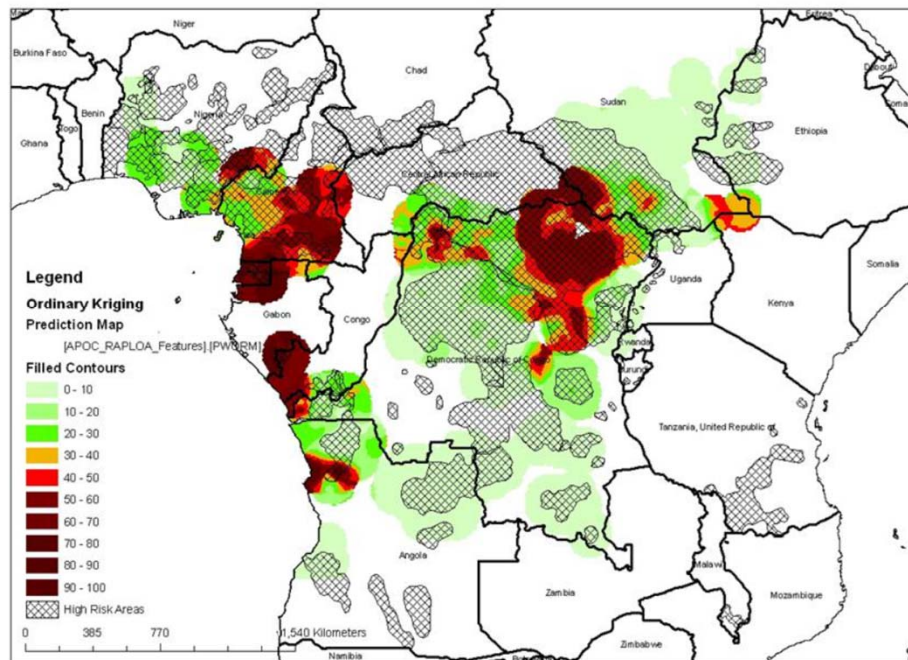
Testing field use



## 2 Co-morbidities

- Onchocerciasis and Loa-loa

*Onchocerciasis (grey) and Loa-loa (coloured) high risk areas (Source: APOC)*



LF and onchocerciasis co-endemic in 18% of endemic districts in Africa (28%).

Loiasis coendemic with onchocerciasis or LF.in 18%

In areas of *Loa loa* coinfection, **SAEs (encephalopathy) with high load of microfilariae (that can be fatal) limits MDA**

### 3 Diagnostic and treatment research approach: HAT





### 3 Diagnostic and treatment research approach: HAT



15 years ago:  
Eflornithine  
Melarsoprol

Since 2009:  
NECT & first  
generation  
RDTs

2018 and beyond:  
Oral treatment &  
second generation  
RDTs

3

# Diagnostic and treatment research approach: HAT

1. Passive case detection

2. Post elimination monitoring

3. Early test of cure

## Objectives DiTECT-HAT project



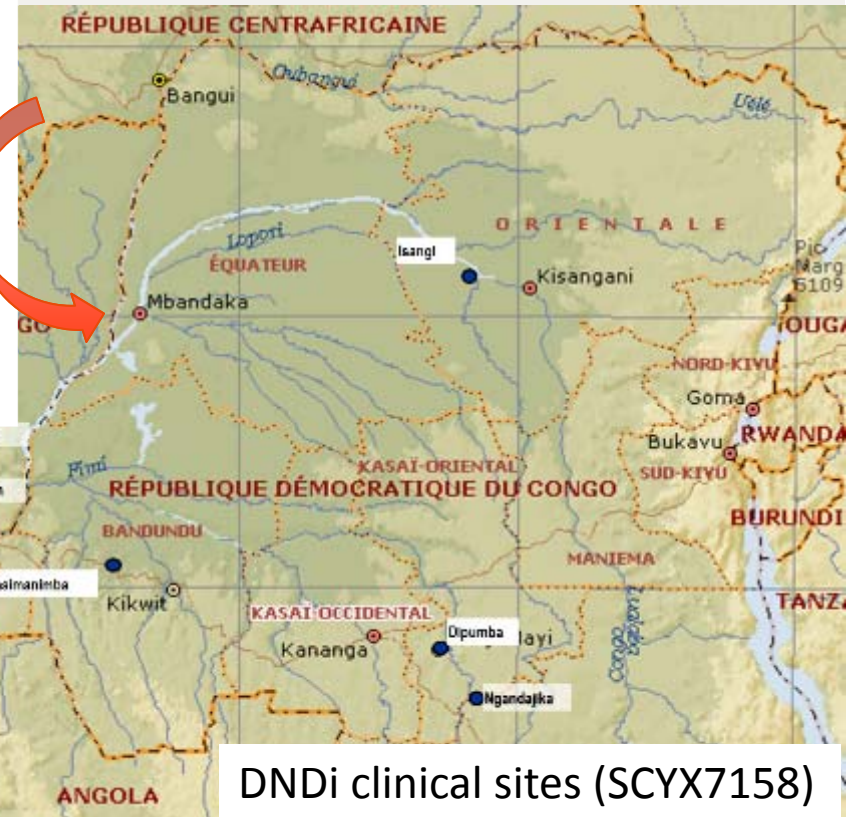
EDCTP

European & Developing Countries  
Clinical Trials Partnership

- To evaluate accuracy and feasibility of new, ready to implement diagnostic tools, and to propose algorithms for HAT diagnosis in 3 contexts :



1. Passive case detection in peripheral health centres
2. Post-elimination monitoring for detection of disease re-emergence
3. Early test of cure in therapeutic trials



DNDi clinical sites (SCYX7158)



## 4 Responding to pediatric needs

**Table 1.** Responses to questions of target population for mass drug administrations (MDAs).

	Lymphatic Filariasis	Onchocerciasis	Trachoma	Schistosomiasis	Soil-transmitted Helminths	P-value <sup>†</sup>
Elimination possible from indirect effects of MDAs, N (%)	8/26 (30.8%)	2/22 (9.1%)	12/22 (54.6%)	28/85 (32.9%)	16/48 (33.3%)	0.03
Elimination possible by targeting...*						
Pre-school children	2/22 (9.1%)	2/17 (11.8%)	9/17 (52.9%)	11/65 (16.9%)	7/38 (18.4%)	0.006
School children	5/22 (22.7%)	3/17 (17.7%)	6/17 (35.3%)	30/65 (46.2%)	11/38 (29.0%)	0.10
Those with clinical signs	7/22 (31.8%)	3/17 (17.7%)	3/17 (17.7%)	11/65 (16.9%)	6/38 (15.8%)	0.59
Targeting not effective	10/22 (45.5%)	12/17 (70.6%)	3/17 (17.7%)	26/65 (40.0%)	19/38 (50.0%)	0.03
Other	4/22 (18.2%)	2/17 (11.8%)	5/17 (29.4%)	9/65 (13.9%)	5/38 (13.1%)	0.55

\*Respondents were allowed to provide more than 1 response; therefore, percentages within an NTD do not sum to 100%.

<sup>†</sup>Chi square test.

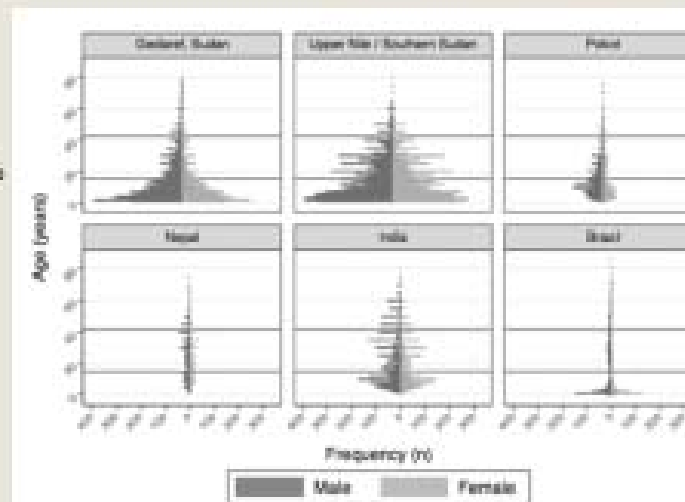
doi:10.1371/journal.pntd.0002562.t001

Source: Keenan JD, Hotez PJ, Amza A, Stoller NE, Gaynor BD, et al. (2013) Elimination and Eradication of Neglected Tropical Diseases with Mass Drug Administrations: A Survey of Experts. *PLoS Negl Trop Dis* 7(12): e2562. doi:10.1371/journal.pntd.0002562

## 4 Responding to pediatric needs: the case of VL

Strong Epidemiological Data:  
Visceral Leishmaniasis: 50% of cases are below the age of 12

Age distribution of leishmaniasis patients




Source: Who is a Typical Patient with Visceral Leishmaniasis? Characterizing the Demographic and Nutritional Profile of Patients in Brazil, East Africa, and South Asia by Harhay M.O., Ollaro P.L., Vaillant M., Chappuis F., Lima M.A., Ritmeijer K., Costa C.H., Costa D.L., Røjal S., Sundar S., Balasegaram M. Am. J. Trop. Med. Hyg. 84(4), 2011, pp. 543-550

**DNDi**  
Drugs for Neglected Diseases initiative

# Responding to pediatric needs

## Ulcère de Buruli



© Médecins Sans Frontières  
Health education is a tool to achieving elimination

- Au moins **33 pays** ont signalé l'ulcère de Buruli en Afrique, en Amérique du Sud et dans le Pacifique occidental.
- Environ **6000 nouveaux cas** rapportés chaque année dans 12 des 33 pays.
- La plupart des patients sont des enfants de **moins de 15 ans**.
- Une association d'antibiotiques permet de **guérir 80%** des cas détectés à un stade précoce.

Burden	Disability risk	Treatment
<b>~6000</b>	<b>25%</b>	<b>80%</b>
<small>Between 5000–6000 cases are reported annually from 15 of the 33 countries</small>	<small>late reporting results in high percentage of disability</small>	<small>of cases detected early can be cured with a combination of antibiotics</small>

In **onchocerciasis** IVM is not registered < 5 years and doxycycline contra-indicated < 8 years

**Schistosomiasis:** children under five could also be vulnerable to schistosomiasis and in the absence preventive chemotherapy they could be at risk of severe morbidities

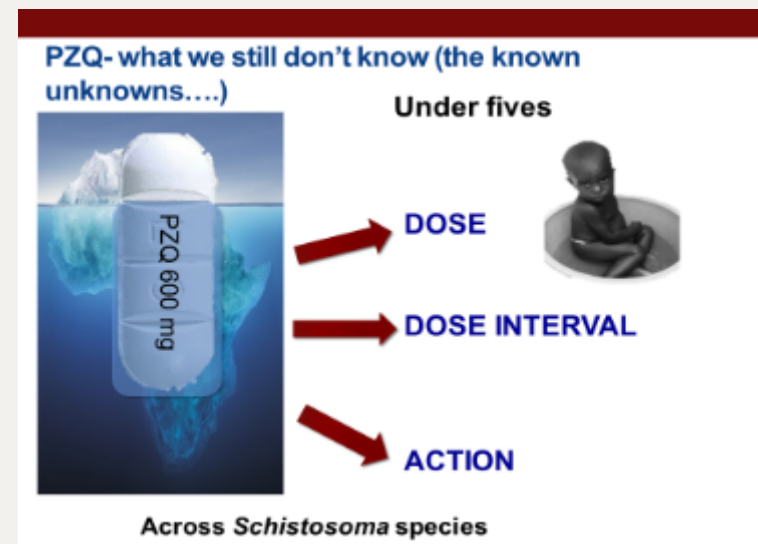
## Pian



- Actuellement **13 pays** endémiques (contre 88 en 1950)
- **Peut être éradiqué:** les êtres humains sont le seul réservoir
- Découverte en 2012: une dose unique d'**azithromycine p.o.** permet de guérir
- Environ **75%** des personnes atteintes sont **des enfants** de moins de 15 ans
- L'absence ou la présence de la **maladie doit être confirmée** dans **73 pays** où elle était endémique

Réunion de lancement du réseau francophone sur les maladies tropicales négligées, Montpellier, 7-8 avril 2016

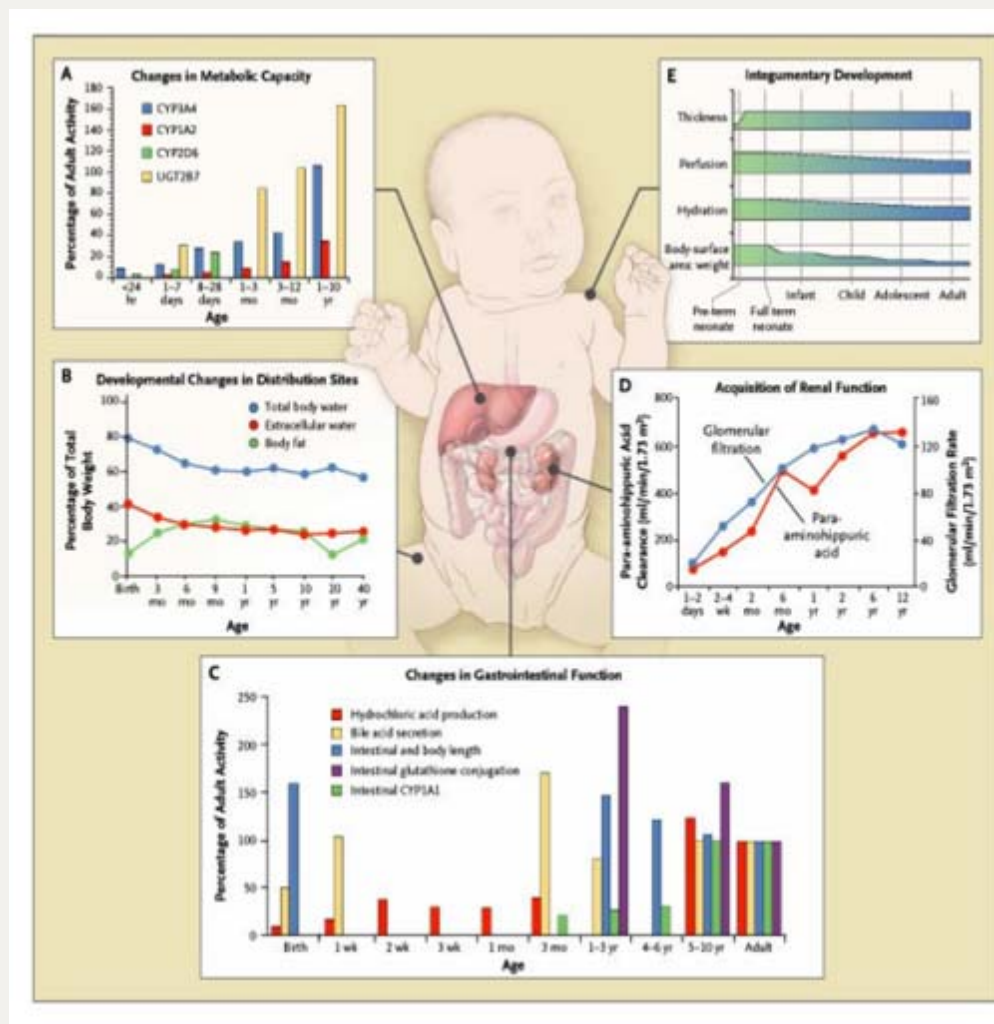
 World Health Organization



## 4 Responding to pediatric needs

Children and adults differ in:

- ✓ Absorption
- ✓ Distribution
- ✓ Renal function (excretion)
- ✓ Hepatic function (metabolism)
- ✓ Pharmacodynamics:
  - ✓ therapeutic response
  - ✓ adverse reactions
  - ✓ mechanisms of disease



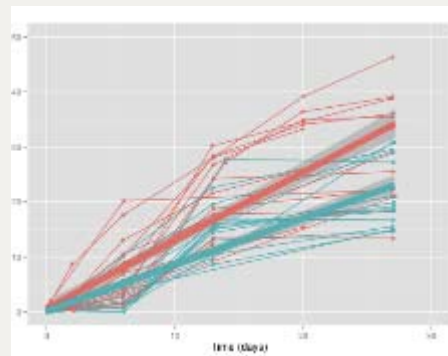
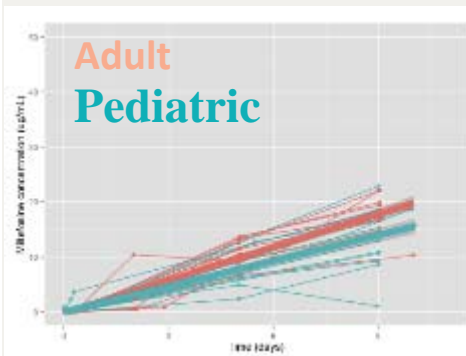
Kearns et al. NEJM 2003. 349:1157-1167

4

# Responding to pediatric needs in VL

LEAP 0208 – Miltefosine PK and clinical outcome

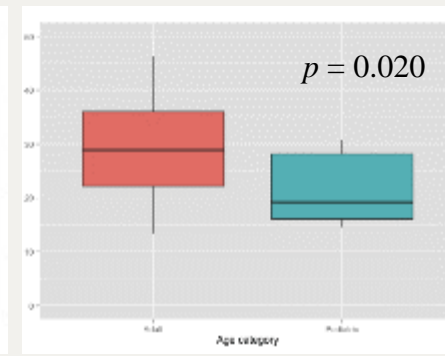
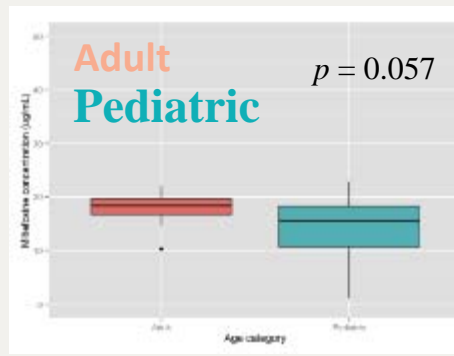
Miltefosine concentration over time



Ambisome + Miltefosine

Miltefosine alone

Miltefosine concentration at end of treatment



Ambisome + Miltefosine

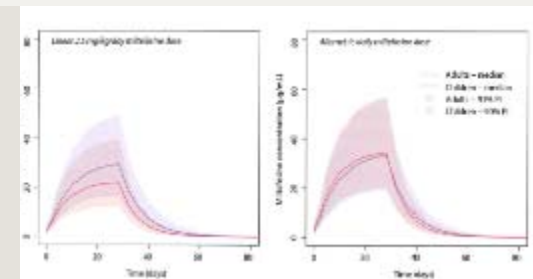
Miltefosine alone

## D210 Efficacy by age group

	AmBisome® + Miltefosine	Miltefosine monotherapy
Final number of patients		
7-12	27	22
13-60	22	29
Final number cured, n (%)		
7-12	20 (74.1%)	13 (59.1%)
13-60	20 (90%)	25 (86.2%)
Fisher's exact test p-value	0.25	0.061

Children had poorer clinical response as compared to adults, which can be explained by the underexposure to the drug.

Allometric dose to be assessed in children



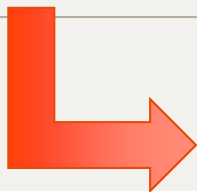
Study was not powered for sub-group analysis.

## 5 Pregnant and breast-feeding mothers

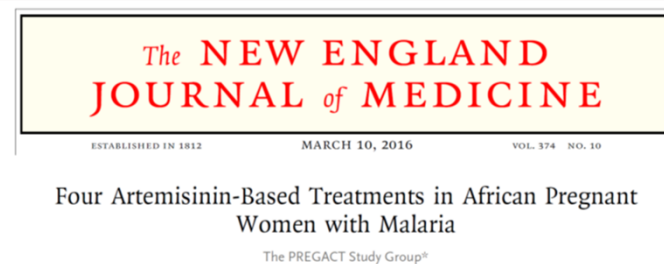
1. Females historically less included in CTs, and generally exclude pregnancy, but ....

*... Pregnant women get sick and sick women can become pregnant ...*

1. Drug PK is modified by pregnancy (higher acidity, lower GI motility, lower pulmonary exposure, slower renal clearance. Modified immune response....)
2. Pregnancy rates are high (from 3.95–63.9 pregnancies / 100 women-years in HIV)
3. Vertical transmission documented / suspected for some NTDs
4. Some of the current treatments options are contra-indicated during pregnancy:
  1. Antimonials and miltefosine for VL, PKDL, HIV-VL
  2. Melarsoprol for tb rhodesiense HAT



Research needs: prospective efficacy





## 6 Conducting and running trials effectively

Approval timelines for clinical trials remains a challenge

From submission  
to import license:

**Mean: 8 months**

**Median: 6 months**

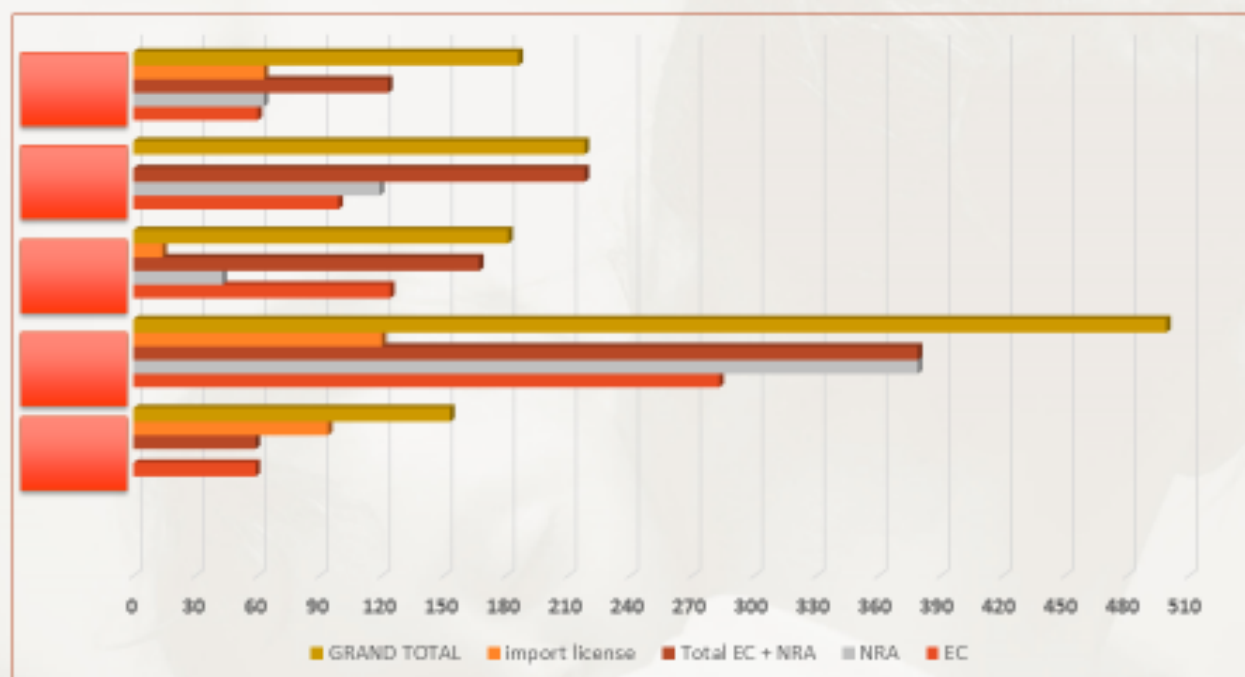
+

Lack of  
expertise/experience



**Capacity strengthening  
AVAREF ...  
Joint reviews ...**

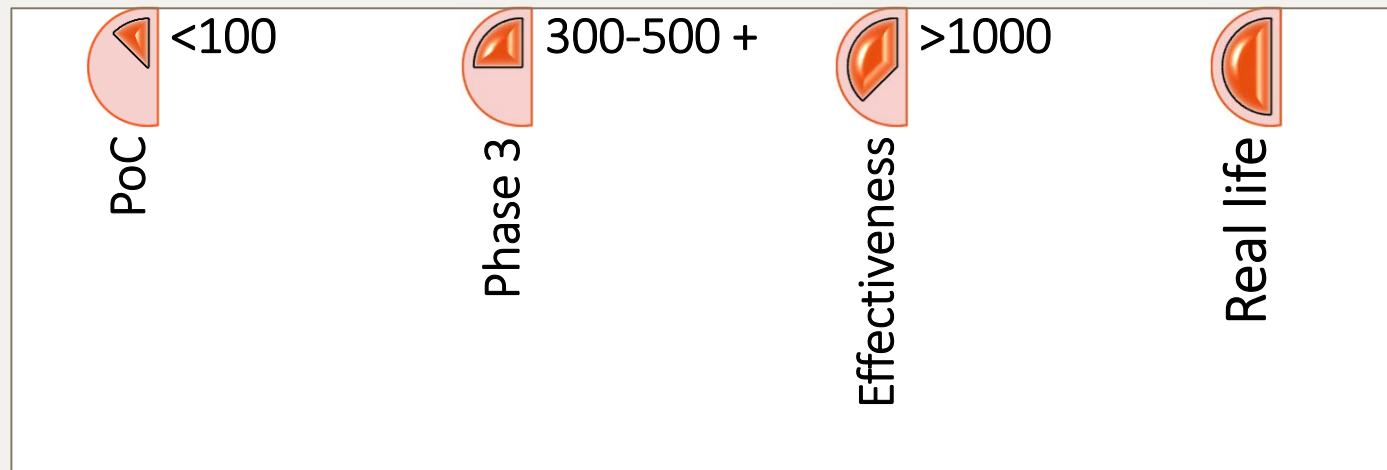
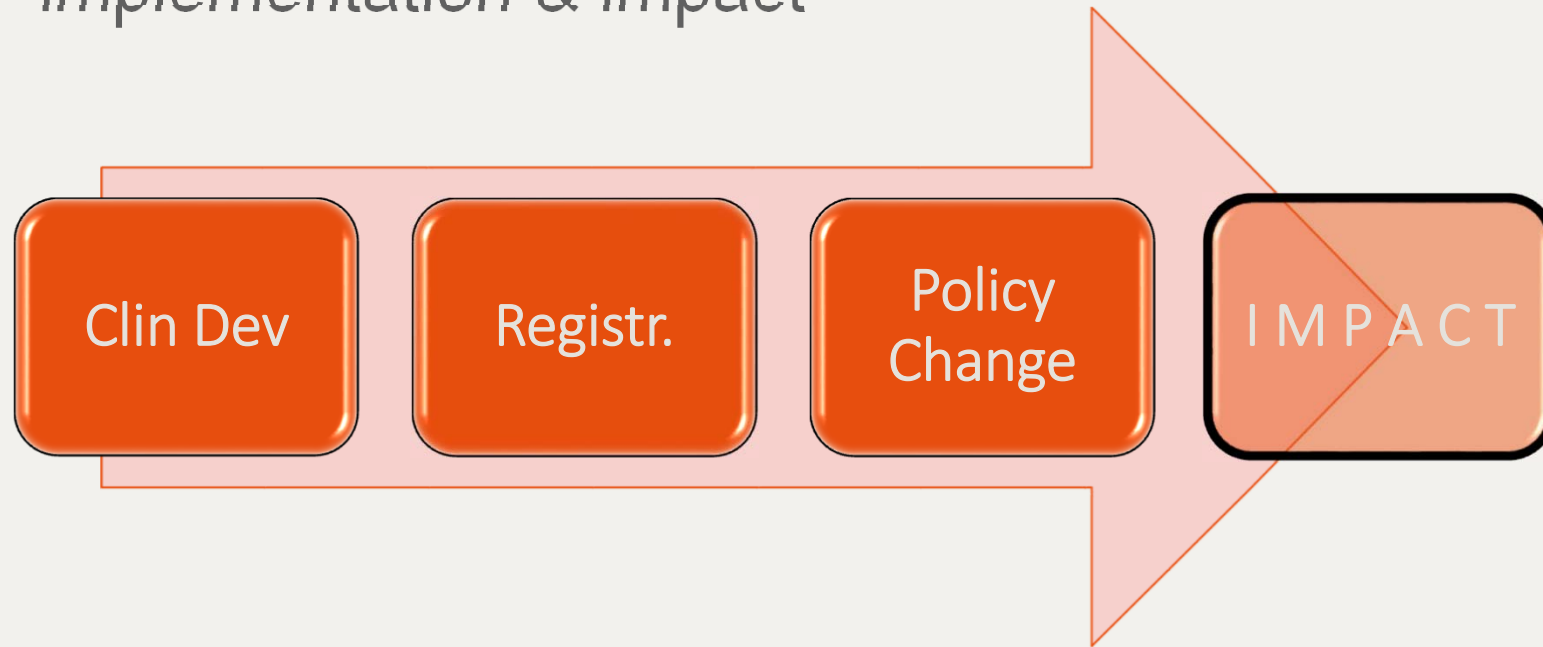
Updated timelines EC/NRA (new DNDi studies)



	EC	NRA	EC + NRA	TOTAL with import license
median	99	91	167	186
mean	125	151	189.2	247.4

7

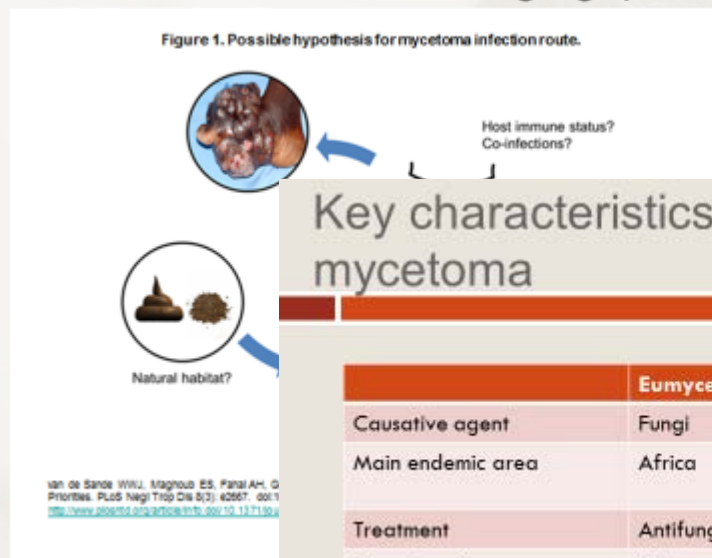
## Transitioning from clinical research to implementation & impact



## 8 New category of NTDs: example of mycetoma



### Transmission – knowledge gaps



DNDi  
Drugs for Neglected Diseases Initiative

### Key characteristics of eu- and actinomycetoma

	Eumycetoma	Actinomycetoma
Causative agent	Fungi	bacteria
Main endemic area	Africa	Middle- and South America
Treatment	Antifungal + surgery	antibiotics
Current regimen	Ketoconazole	amikacin (IV) + cotrim (PO)
<p>FDA Drug Safety Communication: FDA limits usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems</p> <p>or itraconazole 12 Months + mass removal</p>		
Rate	37% → 25.9%	> 90% (in Mexico)

**Very low efficacy of treatment in fungal form**

8

## New category of NTDs: example of mycetoma

Drug	Organism	N	Dose	Outcome	Country	Reference
Ketoconazole	M. mycetomatis	13	200 mg OD, 12 months	5 cured; 4 improved, 4 failed	Sudan	Mahgoub ES, 1984
	M. mycetomatis	50	200 mg OD, 12 months	15 cured; 10 improved, 25 failed; 10 with surgery in some cases	Sudan	Hay RJ, 1992
	M. mycetomatis (4) Other (4)	8	400 mg OD, 8-24 months	4 cured; 2 improved, 2 failed	India	Porte L, 2006
Itraconazole	M. mycetomatis	13	400 mg OD 3 months, then 200 mg OD 9 months	1 cured; 11 improved, 1 failed after surgery; 1 recurrence	Sudan	Fahal AH
Terbinafine	M. mycetomatis (10) L. senegalensis (4) Other (3) Not known (7)	23	500 mg BD, 24-48 weeks	4 cured; 11 improved, 7 failed	Senegal	N'Diaye B, 2006
Voriconazole	S. apiospermium	1	400 mg OD, 18 months	Cured	Ivory Coast	Porte L, 2006
	S. apiospermium	1	Dose not specified, 6 months	Cured	India	Gulati, 2012
	M. grisea	1	Dose not specified, 6 months	Little change	India	Gulati, 2012
	M. mycetomatis	1	200 mg, 3 months, then 300 mg, 13 months	Cured	Mali	Lacroix C, 2005
	Madurella spp	1	200 mg, 12 months	Cured	Senegal	Loulergue P, 2006
	S. apiospermum	1	200 mg BD, unknown duration	Cured, after 3 years follow-up	Brazil	Oliveira F de M, 2013
Posaconazole	M. mycetomatis (1) M. grisea (3) S. apiospermum (1)	6	800 mg OD	Initially: 5 cured, 1 no improvement; 2 successfully retreated after interval of >10 months	Brazil	Negrone R, 2005
Liposomal amphotericin B	M. grisea (2) Fusarium (1)	3	Total dose 3.4, 2.8, 4.2 grams; max. daily dose 3 mg/kg	All showed temporary improvement but relapsed within 6 months	Not specified	Hay RJ, 2005

Small Ns – need for RCTs

## 8 New category of NTDs: example of mycetoma

THE WHO STRATEGIC AND TECHNICAL ADVISORY GROUP FOR NEGLECTED TROPICAL DISEASES (WHO STAG)

RECOMMENDATIONS FOR THE ADOPTION OF ADDITIONAL DISEASES AS NEGLECTED TROPICAL DISEASES

28 MAY 2016 / GENEVA - The Sixty-ninth World Health Assembly closed today after approving new resolutions on ..... mycetoma; .....

### 3. Proposed criteria for classifying a condition as an NTD

Disease conditions that

1. disproportionately affect populations living in poverty; and cause important morbidity and mortality – including stigma and discrimination - in such populations, justifying a global response
2. primarily affect populations living in tropical and sub-tropical areas
3. are immediately amenable to broad control, elimination or eradication by applying one or more of the five public health strategies adopted by the Department for Control of NTDs, and/or
4. are relatively neglected by research – i.e., resource allocation is not commensurate with the magnitude of the problem - when it comes to developing new diagnostics, medicines and other control tools



# New category of NTDs: Loa Loa ?

THE WHO STRATEGIC AND TECHNICAL ADVISORY GROUP FOR NEGLECTED TROPICAL DISEASES (WHO STAG)

RECOMMENDATIONS FOR THE ADOPTION OF ADDITIONAL DISEASES AS NEGLECTED TROPICAL DISEASES

## 3. Proposed criteria for classifying

Disease conditions that

1. disproportionate burden in low-income countries; and cause
2. significant morbidity and disability; and cause
3. significant mortality; and cause
4. are relatively neglected by research and development, and/or

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**Excess mortality associated with loiasis: a retrospective population-based cohort study**

Cédric B Chesnais, Innocent Takougang, Marius Paguele, Sébastien D Pion, Michel Boussinesq

**Lancet Infect Dis 2016**  
Published Online  
**October 21, 2016**

[http://dx.doi.org/10.1016/S1473-3099\(16\)30405-4](http://dx.doi.org/10.1016/S1473-3099(16)30405-4)

## 9 Preparing for drug resistance? ...

- Melarsoprol resistance reports in *tb rhodesiense*

*R. Brun et al. Treatment failures in HAT Tropical Medicine and International Health volume 6 no 11 pp 906±914 november 2001*

- Ivermectin in onchocerciasis

*Prevalence and intensity of Onchocerca volvulus infection and efficacy of ivermectin in endemic communities in Ghana: a two-phase epidemiological study Mike Y Osei-Atweneboana, Lancet 2007; 369: 2021–29)*

**Table 2.** Responses to questions about drug resistance.

	Lymphatic Filariasis	Onchocerciasis	Trachoma	Schistosomiasis	Soil-transmitted Helminths	P-value*
Is drug resistance a problem...						
For the NTD?	14/27 (51.9%)	13/20 (65.0%)	4/22 (18.2%)	53/87 (60.9%)	28/46 (60.9%)	0.005
For another infection?	17/24 (70.8%)	11/17 (64.7%)	16/22 (72.7%)	58/82 (70.7%)	32/41 (78.1%)	0.87
Best strategy to minimize resistance						0.14
(1) Annual mass treatment	9/24 (37.5%)	6/16 (37.5%)	14/21 (66.7%)	29/78 (37.2%)	21/42 (50.0%)	
(2) Treatment scattered throughout year	3/24 (12.5%)	1/16 (6.3%)	1/21 (4.8%)	3/78 (3.9%)	5/42 (11.9%)	
No difference between (1) and (2)	12/24 (50.0%)	9/16 (56.3%)	6/21 (28.6%)	46/78 (59.0%)	16/42 (38.1%)	

\*Chi square test.

doi:10.1371/journal.pntd.0002562.t002

Source: Keenan JD, Hotez PJ, Amza A, Stoller NE, Gaynor BD, et al. (2013) Elimination and Eradication of Neglected Tropical Diseases with Mass Drug Administrations: A Survey of Experts. *PLoS Negl Trop Dis* 7(12): e2562. doi:10.1371/journal.pntd.0002562

# EDCTP critical role to support WHO road map for elimination

Despite many groups involved, R&D for **NTDs** is largely unfunded ... EDCTP can play a critical role to contribute to WHO elimination goals by supporting:

- **Capacities:** Reinforce/strengthen scientific collaboration btw European and African networks (and existing African networks)
- **Priorities for Innovation:** Support R&D gaps through Disease specific approaches and transversal approaches
- **Regulatory :** Continuation of contribution to AVAREF / AMRH initiatives
- **Clinical Implementation / effectiveness / PV trials**
- **Funding:** increase the available funding given the low success rate and huge demand & leveraging programs funding with other mechanisms/donors
- **African leadership :** Increase African participation (priorities, funding)
- **Process :** improve transparency, decrease time between calls and review
- ***Selection criteria : more focus on scientific excellence and originality, whilst disregarding product development impact (PDPs opinion)***



Thank you  
EDCTP 2  
!!!





# THANK YOU

TO ALL OUR

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## DONORS

**DNDi**  
Drugs for Neglected Diseases initiative

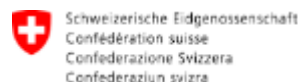


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