Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

Department of Medicine

Clinical Research Unit

Swiss TPH Summer Symposium 2018

Clinical Research in Resource Limited Settings:
Mission Impossible or Role Model for Future Drug Development?

Conducting Investigator Initiated Trials in Low Resource Settings – the Northern Perspective

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Head of Clinical Research Unit

Outline

- Clinical trial landscape in Africa vs. high-income countries
- Clinical trials categories
- Capacity development
- Case: Clinical TB trials in low resource settings

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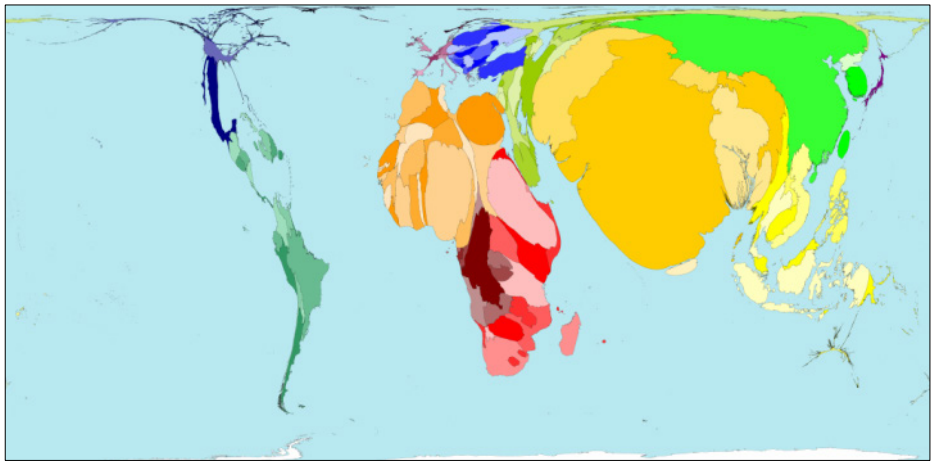
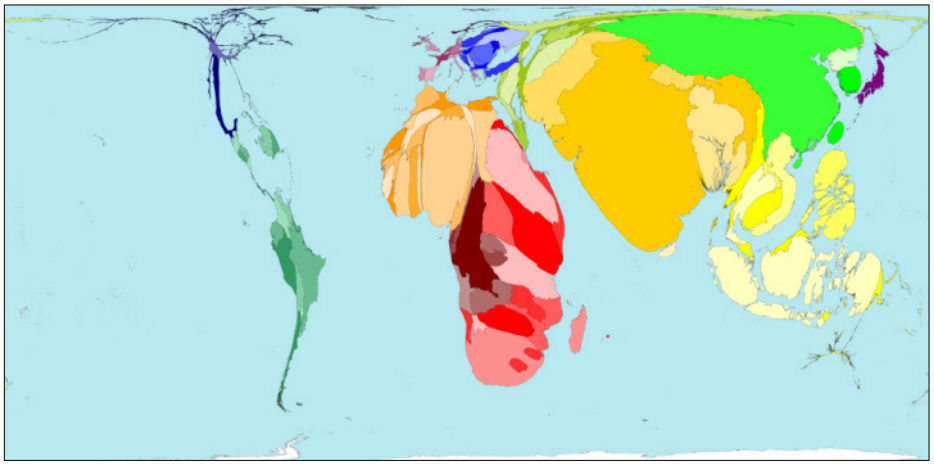
Poverty



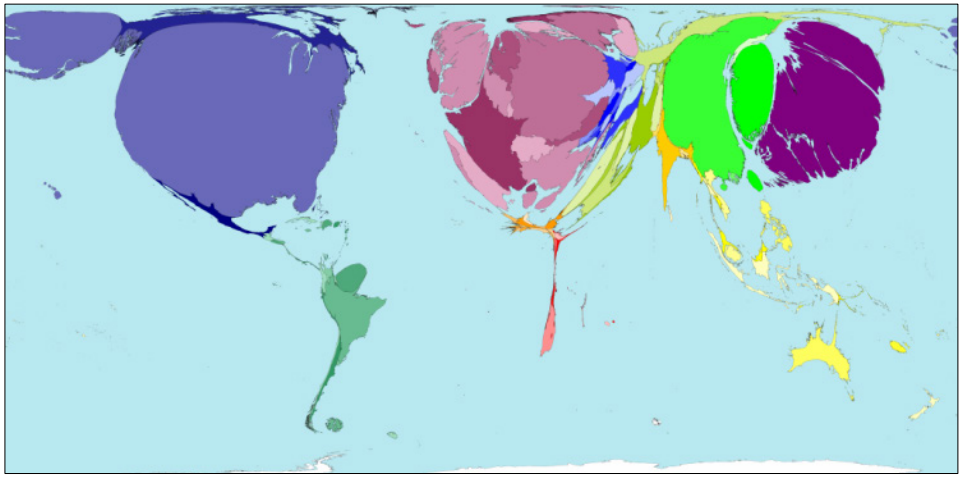
2002

Disease burden; e.g. Tuberculosis cases



2003

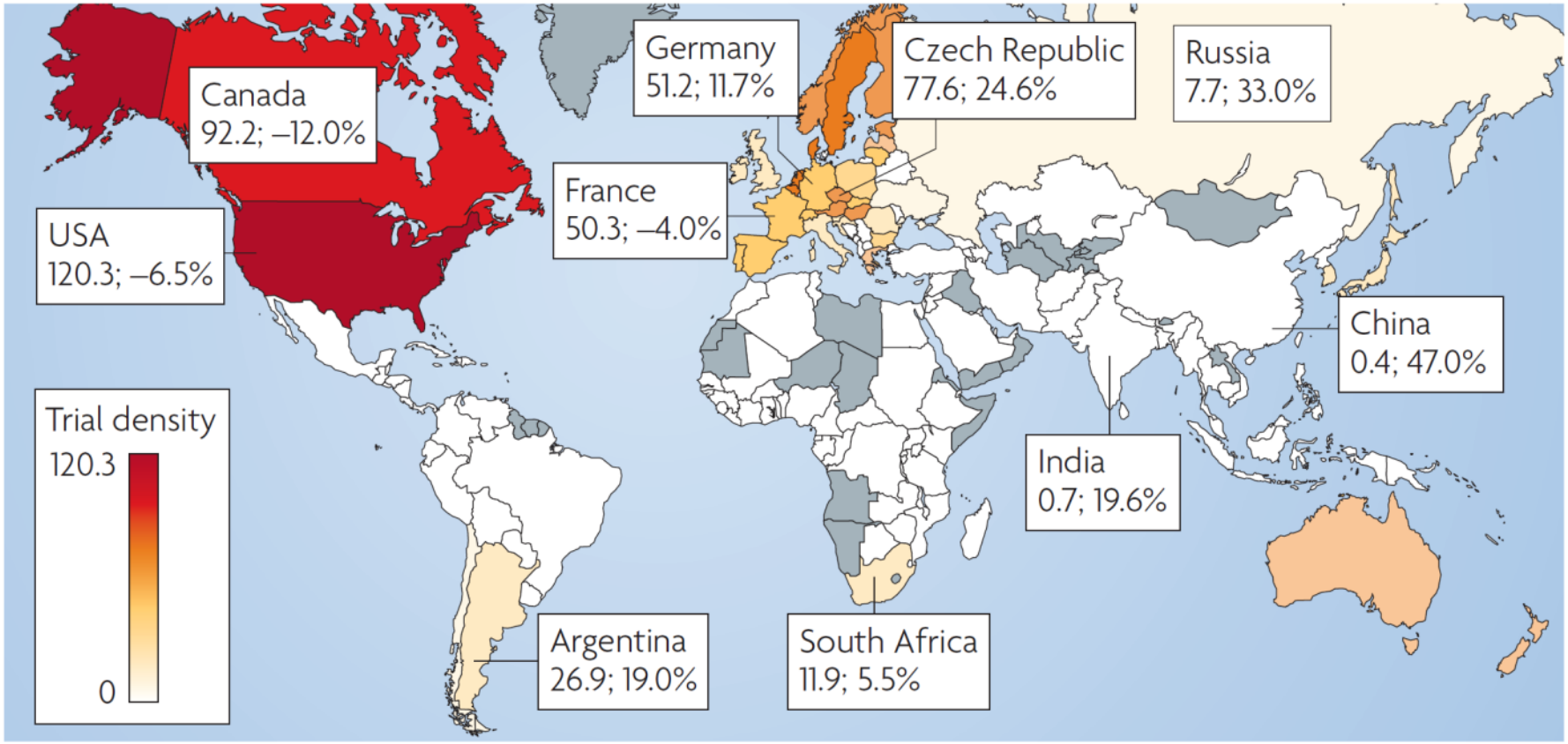
Research and Development Expenditure



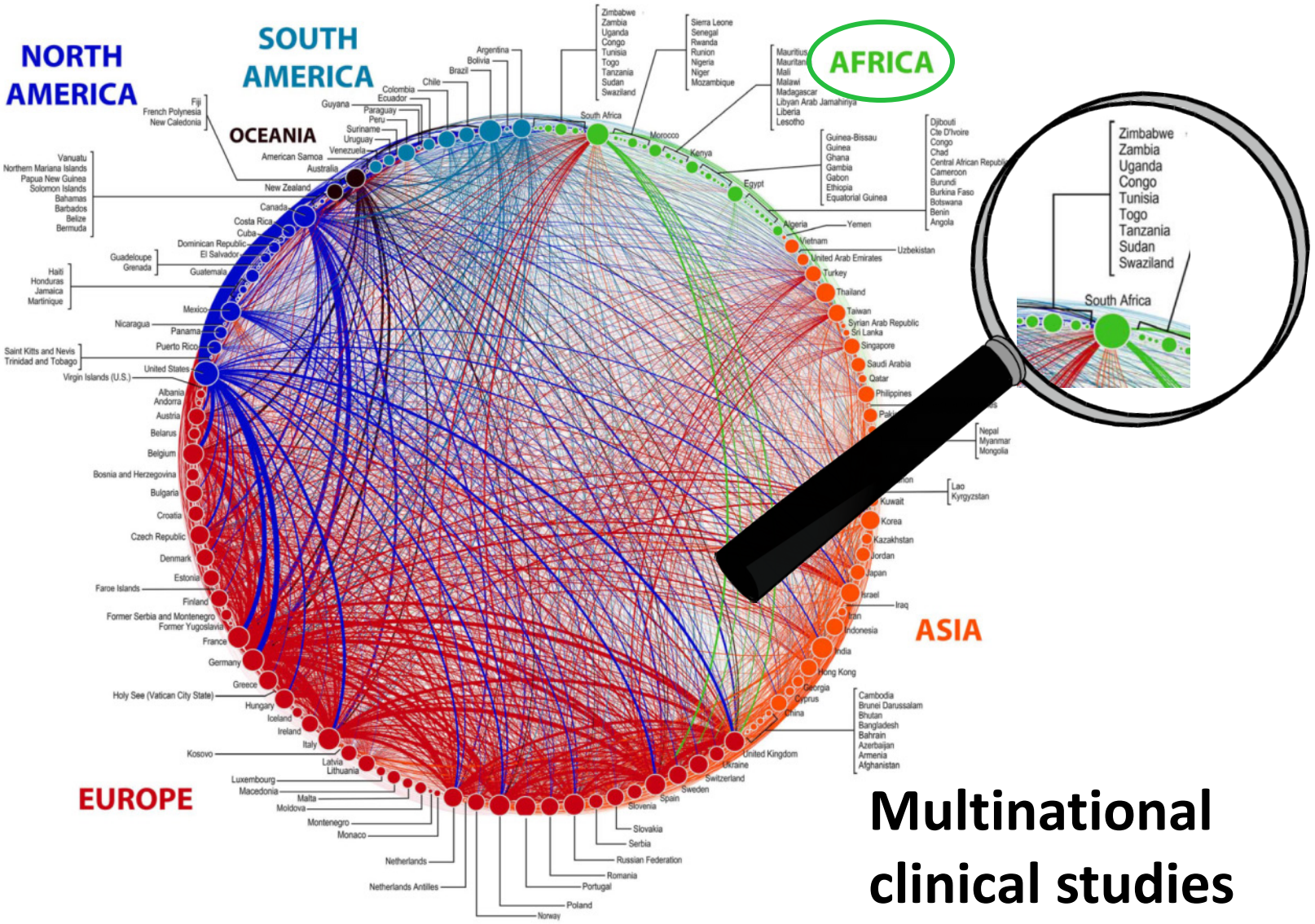
2002

Source: **http://www.worldmapper.org/**

Actively recruiting clinical sites of clinical trials worldwide (2007)



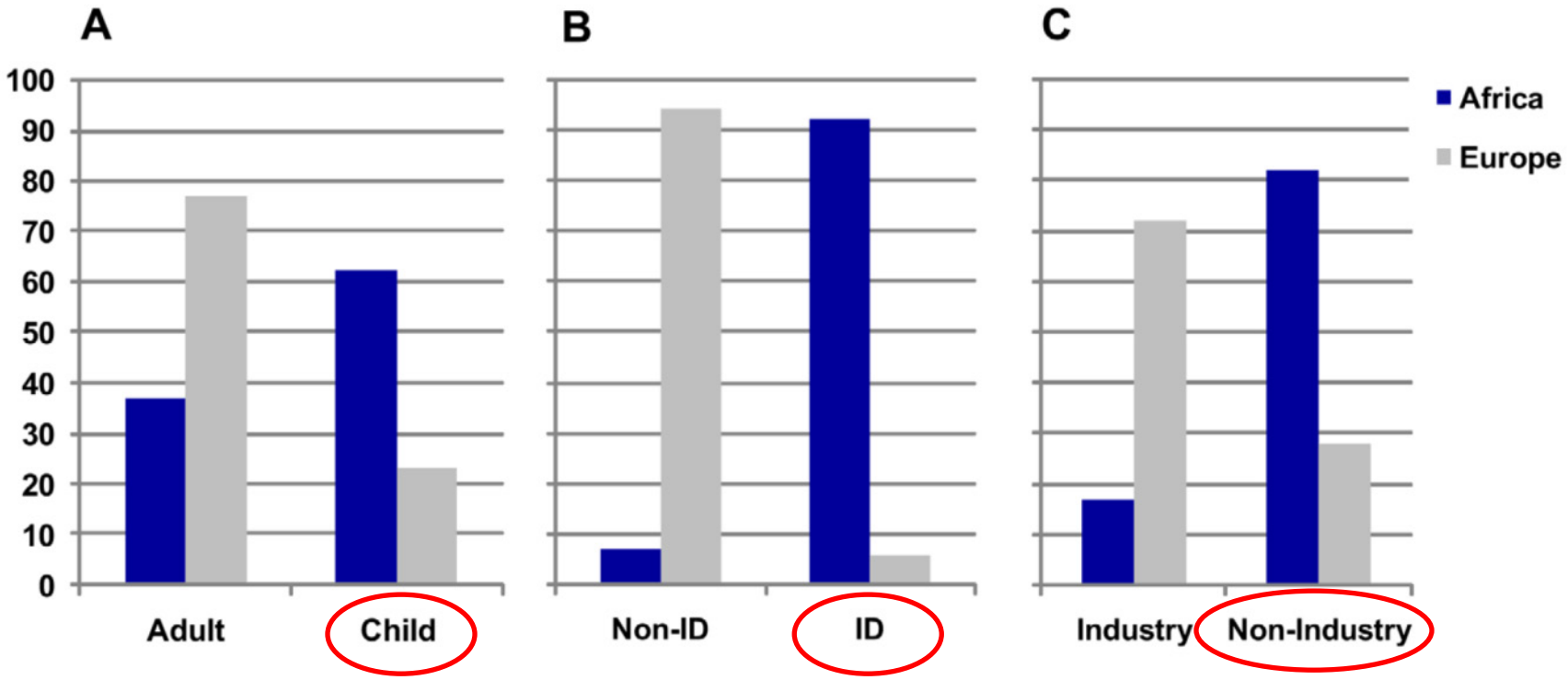
Source: Thiers FA et al., Nature Drug Discovery, 2008



Multinational clinical studies

Source: Richter TA, PlosOne, 2014

Clinical Trials: Africa vs. Europe



100 trials randomly chosen from France, Germany, Italy, Spain, and UK versus Kenya, Mali, Tanzania, Uganda, and Zambia

endpoints: more **often severe disease outcomes and mortality** in low resource settings

Source: Lang TA et al., PLoS Negl Trop Dis, 2010

High-tech clinical study site
(Example: Klinikum Aachen, Germany)

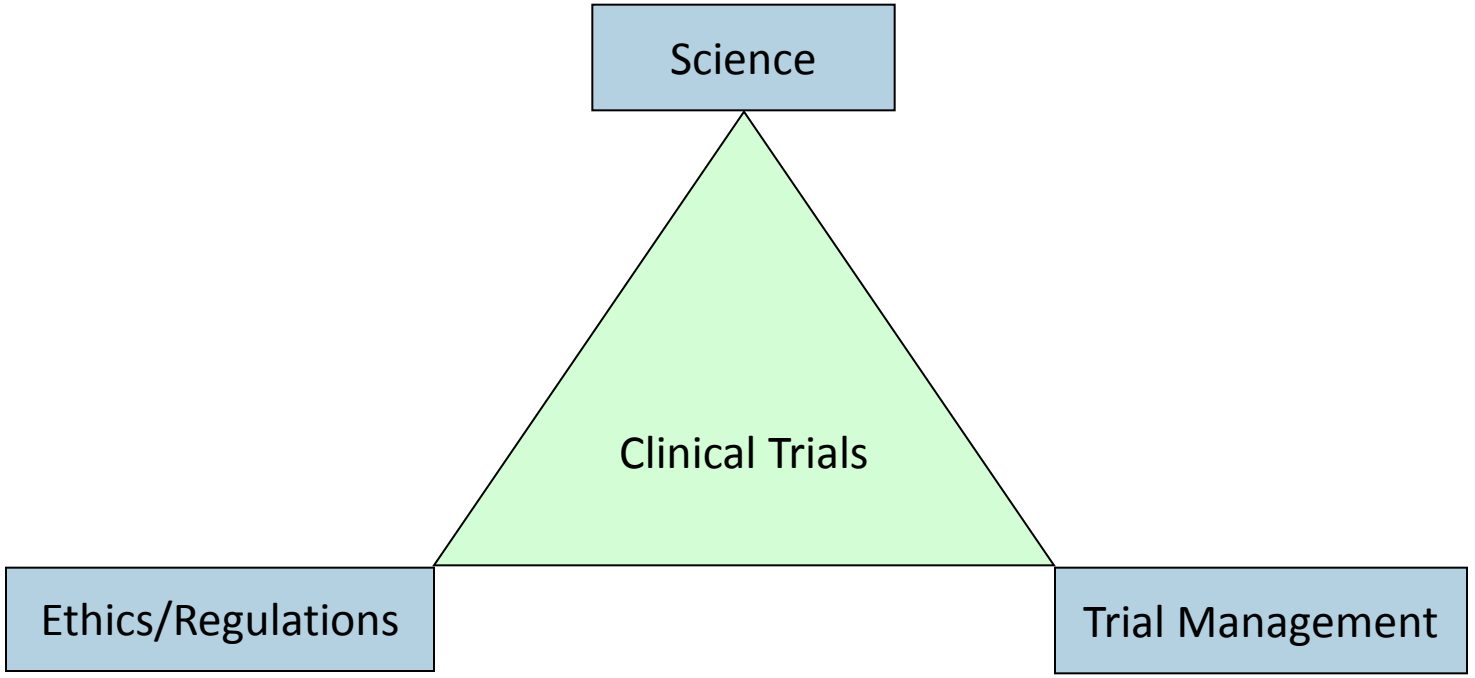
Clinical study site in DRC

Where are trials conducted?

Clinical study site in Kingani, Tanzania

… very variable settings in Sub-Saharan Africa.

Clinical trials – simple principles



Thanks to Marc Urich

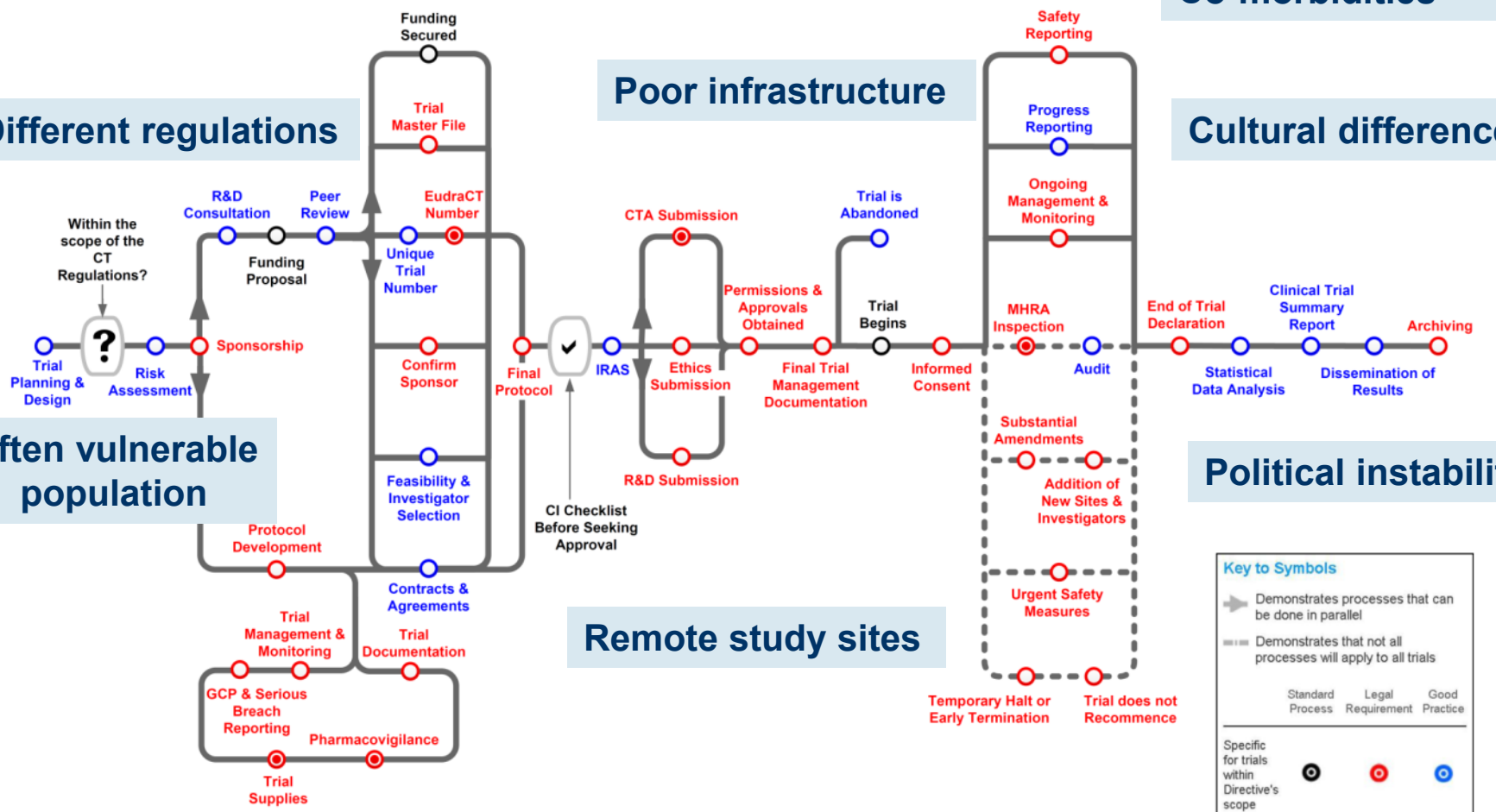
Clinical trials – complex processes

Co-morbidities

Poor infrastructure

Different regulations

Cultural differences



Often vulnerable population

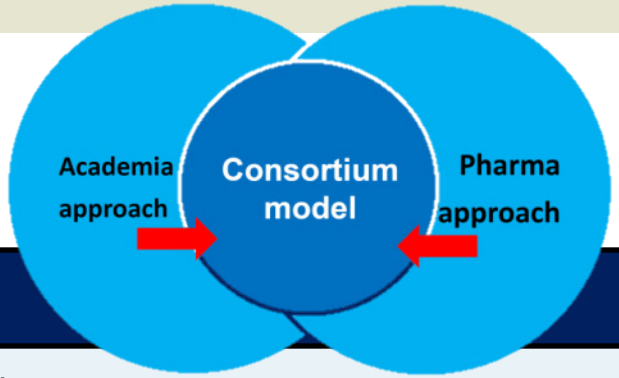
Political instability

Remote study sites

Difficult patient recruitment

http://www.ct-toolkit.ac.uk/routemap/

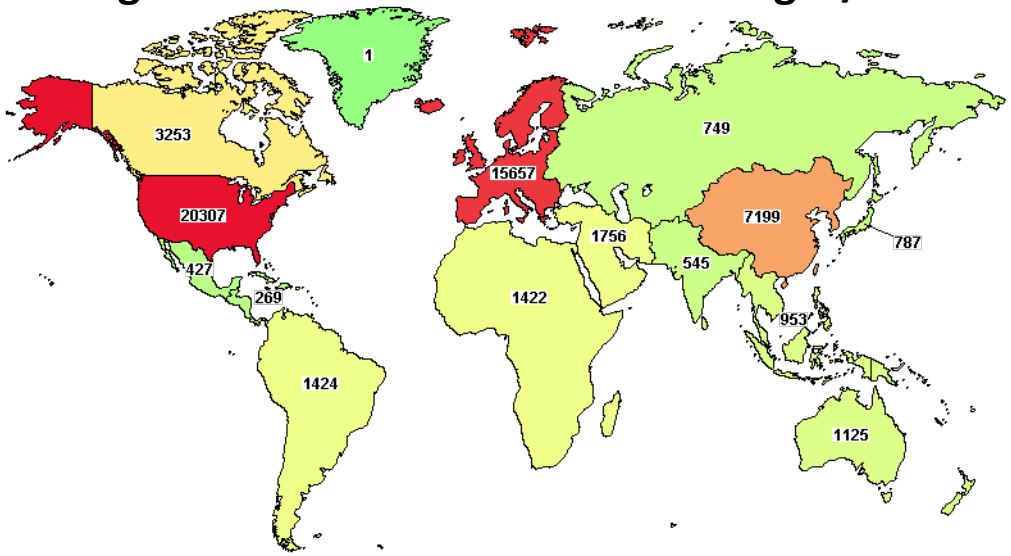
Types of trials

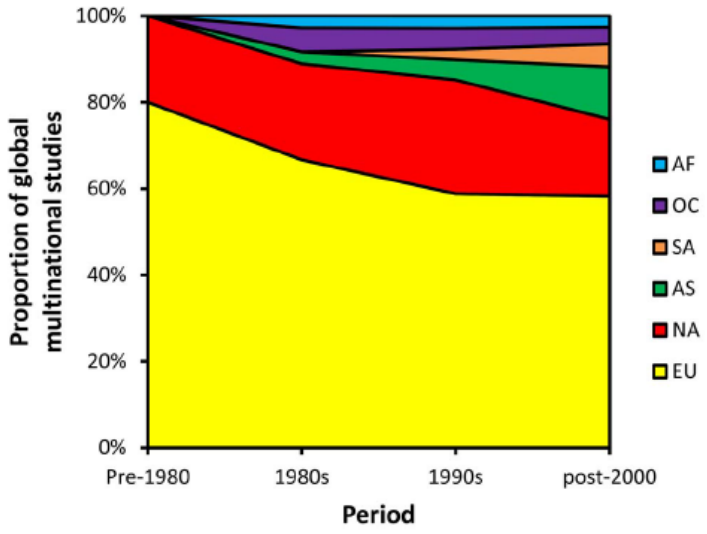


Investigator initiated		Sponsor initiated
Generating knowledge; locally relevant questions; “niche”	**Mission**	Commercialization of a product
Sponsor-investigator	**Oversight**	Sponsor
+	**Rules / Structures**	+++
+ (++)	**Experience**	+++
ICH-GCP	**Guidelines**	ICH-GCP
+++	**Empowerment of investigators**	+
+++	**Local ownership**	+
++	**Cost-effectiveness**	+
+	**Bias in favour of industry ***	++

*** In 1140 trials, statistically significant association between industry sponsorship and pro-industry conclusions ; Bekelman JE et al., JAMA 2003**

Registered clinical trials* – recruiting 6/2018





- Need for intensified **clinical trial site development** in resource limited settings
- Capacity development is a necessity, not a favour
- Many blind spots, e.g. in Central Africa
- Direct investments in building capacity rather than product-by-product approach

Source: *https://clinicaltrials.gov/ct2/results/map/image; Richter TA, PlosOne, 2014

Source: adapted from *www.undp.org*

Long-term partnership is key for successful capacity building

Das Schweizerische Tropeninsitut

Marcel Tanner:

"Mutual Learning for Change"

Swiss TPH

IFAKARA HEALTH INSTITUTE
research | training | services

Field Laboratory, STIFL Ifakara

> 60 years

Source: **www.unigeschichte.unibas.ch ; www.ihi.or.tz**

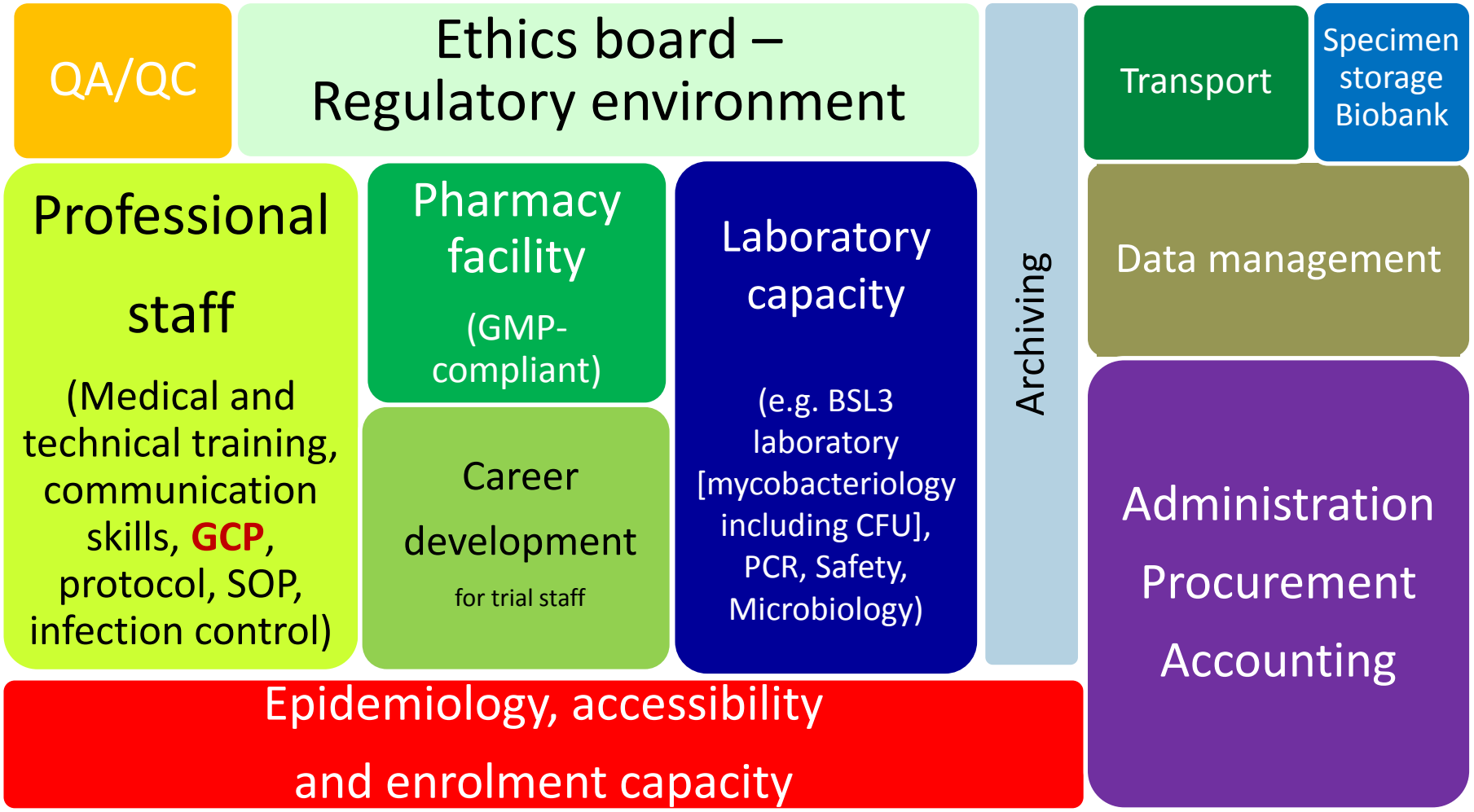






Physical infrastructure is an important aspect in trial site development…

… but there is much more to be considered for clinical trials:



& care outside of clinical trials

Challenges (personal 'top 5')

Sustainability	• **Staff fluctuation: 'brain drain' (partially self-made through MSc and PhD programmes) and lack of institutional funding for scientists**
Empowerment	• **Lack of leadership opportunities for African scientist in international consortia dominated by scientists from high income countries**
Supply chain management	• **Complicated procurement and importation of equipment and consumables**
Ethical boards Regulatory authorities	• **Unpredictable and delayed approval process**
Informed consent	• **Guidelines for the informed consent are often too restrictive**

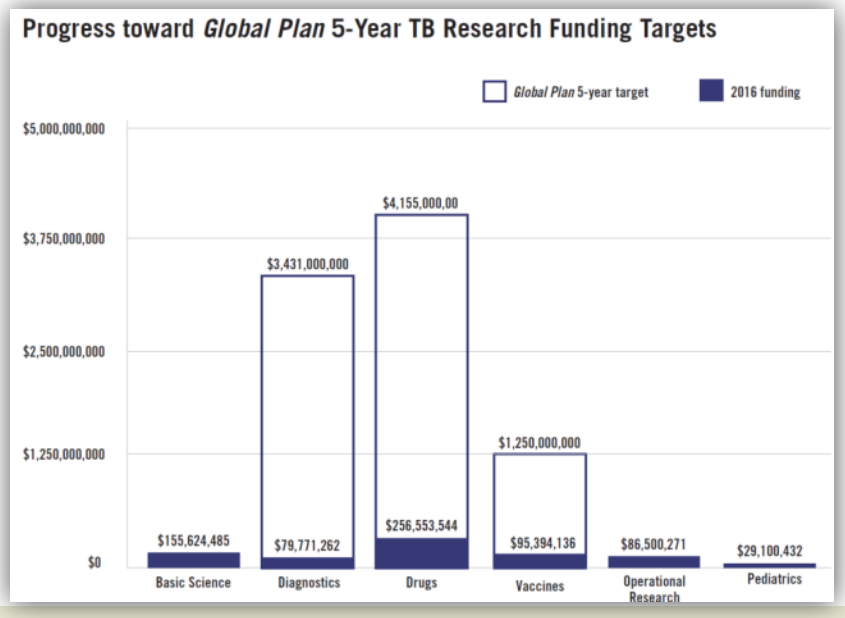
See also: publications of N. Vischer, Swiss TPH

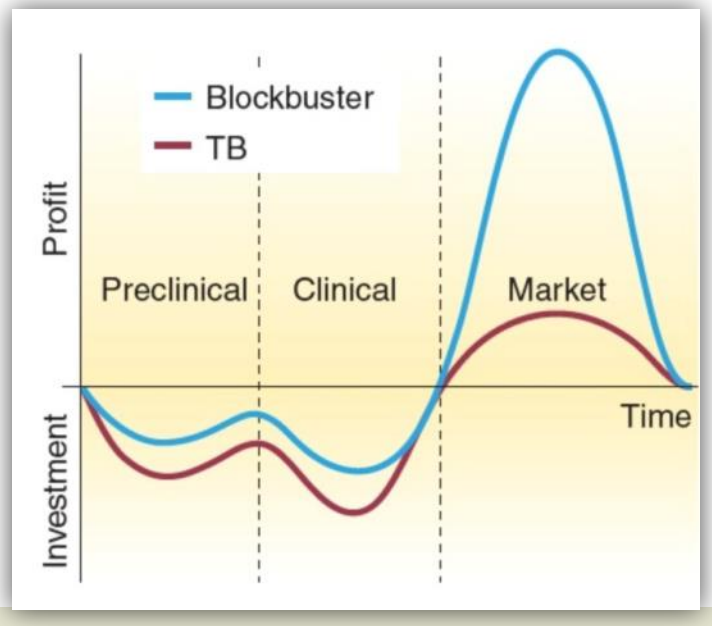
Case: Tuberculosis R&D

Tuberculosis *kills more people every year than any other infectious disease.*

Current funding: Not enough to close innovation gaps and to reach the global goals to end the TB epidemic by 2030.

Steady erosion of private spending (2016: 11%). TB research is not prioritized by **industry**: too complex, high costs, little incentives





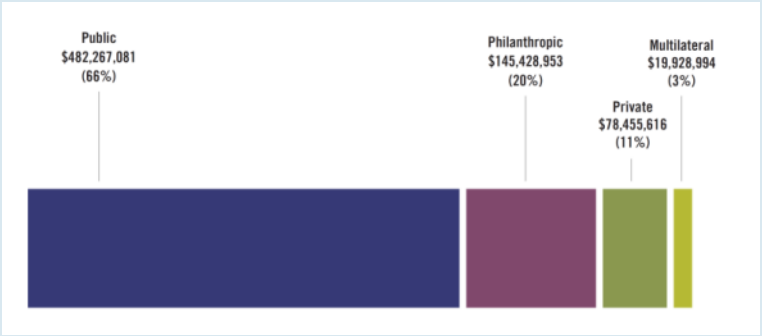
Source: http://www.treatmentactiongroup.org/tb

Source: Kaufmann SHE & Parida SK, Nature Medicine 2007

Tuberculosis clinical research in low resource settings

- Clinical TB research depends on non-commercial / investigator-initiated trials in low- and middle income countries with high burden of disease.

- Funding mainly comes from public and philanthropic sources:



→ **Major drivers of medical innovations and clinical trials are:**

- **Non-Profit Product Development Partnerships (PDP)**

TB ALLIANCE

FIND
Because diagnosis matters

AERAS

- **Academia / Scientific Consortia** (two examples of many)

PanACEA

TB CHILD
EDCTP PROJECT
New Diagnostics for Childhood TB

Source: http://www.treatmentactiongroup.org/tb

Tuberculosis clinical trials

Portfolio: Ifakara Health Institute – Swiss TPH (start 2009)

Achievements:

TB CHILD - diagnostics	IIT /consortium
HIGHRIF - phase II - drug	IIT/consortium
H1/IC31® - phase II - vaccine	IIT/consortium
MAMS - phase II - drug	IIT/consortium
NC002 - phase II SSCC - drug	PDP
NC005 - phase II SSCC - drug	PDP
[NC006 - phase III -drug	PDP]
NC008 - phase IIc - drug	PDP

Main challenge:
Large trials and 'commercial' funding approaches make site vulnerable, if the trial is prematurely terminated.

Conclusions

- It is possible to conduct **both sponsor- and investigator initiated trials** in resource limited setting. These trials are indispensable to improve global health.

- Clinical product development can only be successful in combination with intensified **capacity development** in high-burden countries.

- PDPs, academia and scientific consortia are the key partners in clinical TB research. Industry needs to be motivated to increase research efforts.

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Thank you very much!