

# Better Medicines for Children

## A McGill story with worldwide impact: 40 years on



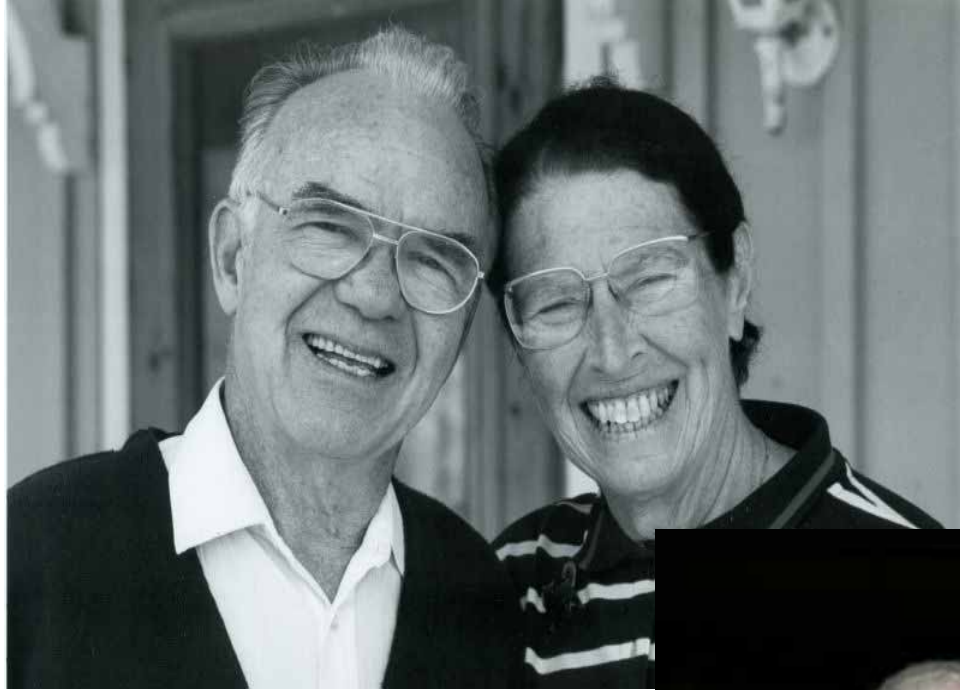
### Hillman Lectureship

McGill University ⊕ Department of Pediatrics ⊕ Medical Grand Rounds  
April 27, 2011

Stuart MacLeod, MD, PhD, FRCPC  
Vice President, Research Coordination and Academic Development,  
Provincial Health Services Authority, Vancouver  
Professor (Pediatrics), University of British Columbia









***My first message to younger colleagues is simple, nothing ever turns out as you expect, and you must enjoy every minute together as we did while we learned together and widened our vision of this strange, needy and wonderful world in which we live, where there is always more to be done and never enough time to do it all – which is why we must teach others”.....***

***Dr. Elizabeth Hillman Feb 2011***

# PRIMARY HEALTH CARE

A MANUAL FOR MEDICAL STUDENTS  
AND  
OTHER HEALTH WORKERS



EDITED BY  
PROF. KOPANO MUKELABAI  
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PROF. RACHEL N. MUSOKE

THIRD EDITION



爱护文物 您的美德

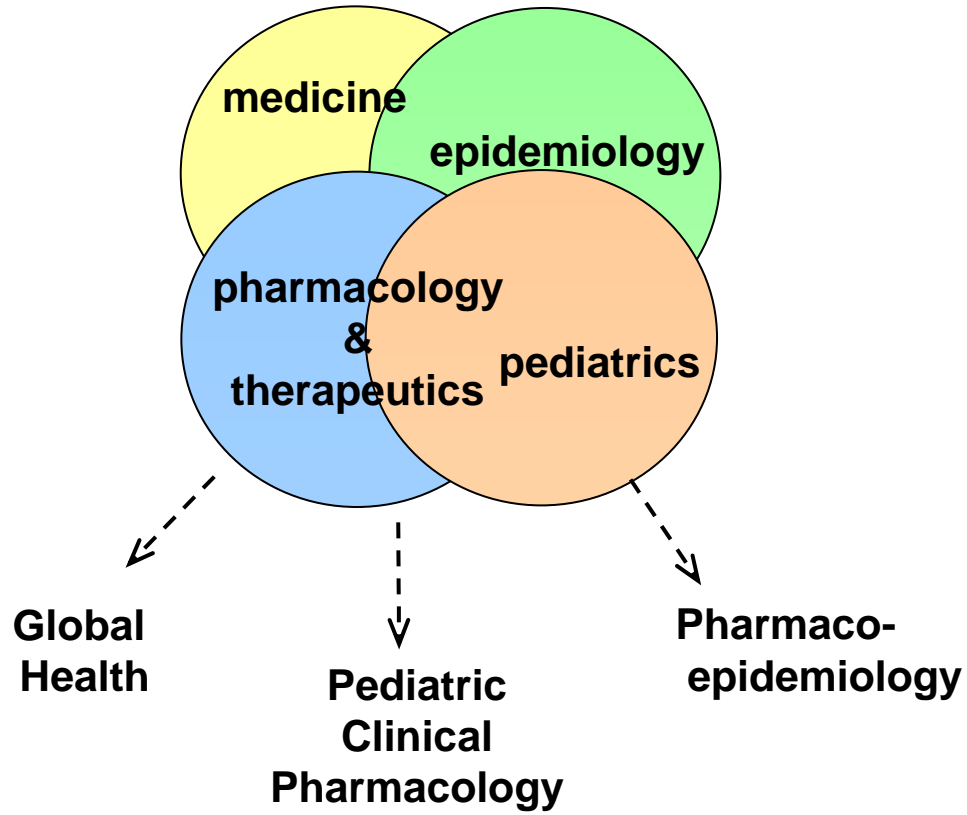
TAKE GOOD CARE OF  
HISTORICAL RELICS

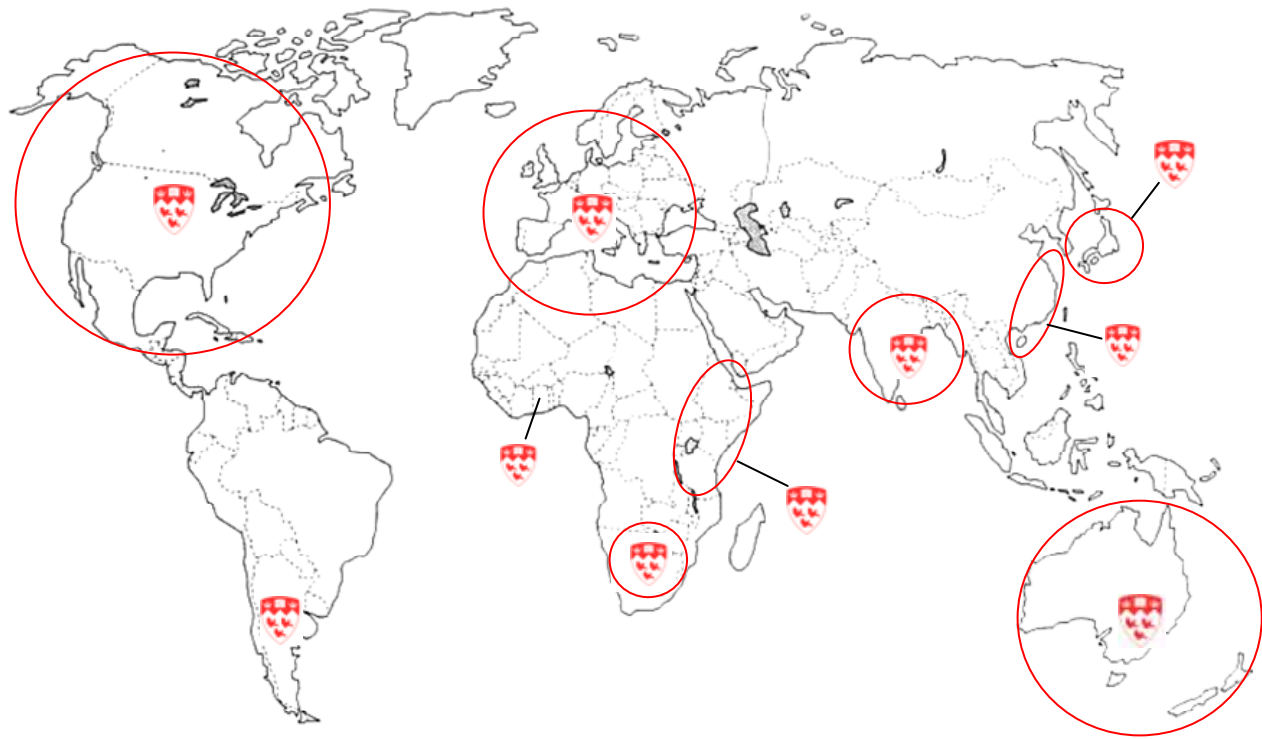


McGill

## McGill contributors in global child health

- Maurice McGregor
- Pat Cronin
- Alan Ross
- Doug Cameron
- Don and Liz Hillman
- Mary Ellen Avery
- Nick Steinmetz
- Yves Bergevin
- Charles Larson
- David Zakus
- Joyce Pickering
- countless trainees and indirect advocates





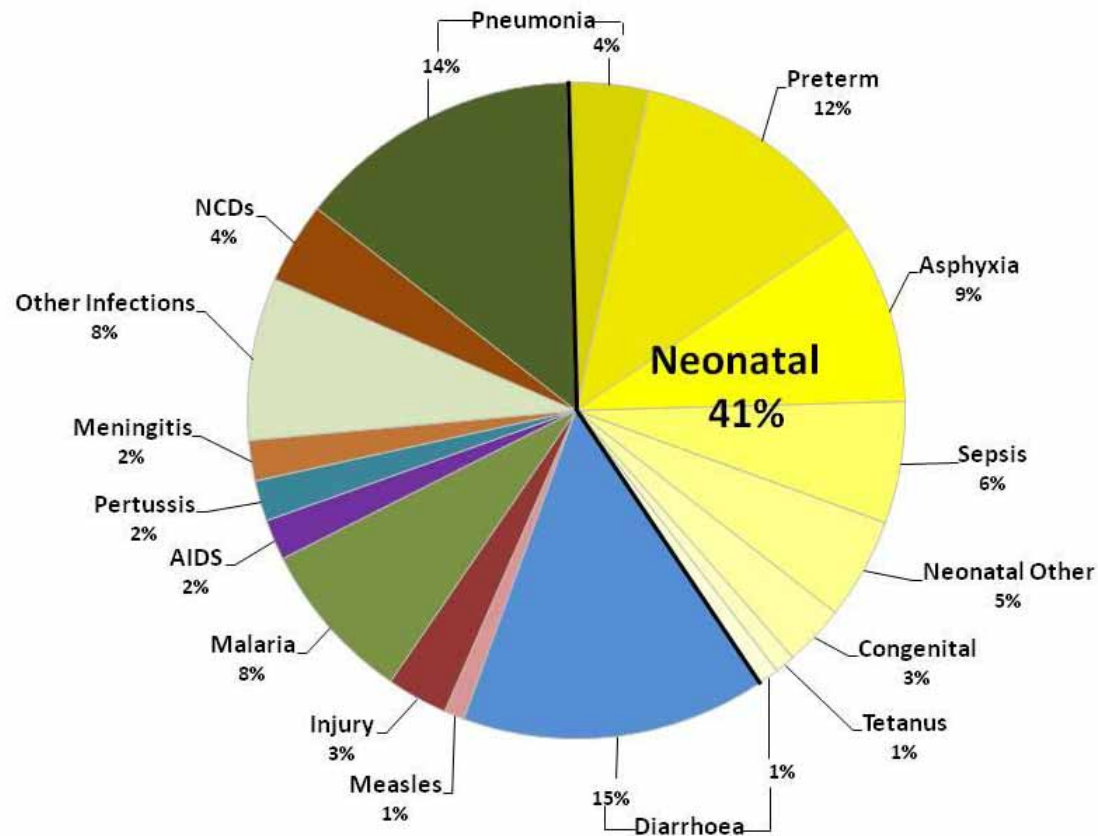
Department of Pediatrics – University of Nairobi



....a pace-setter for eastern, central and southern Africa



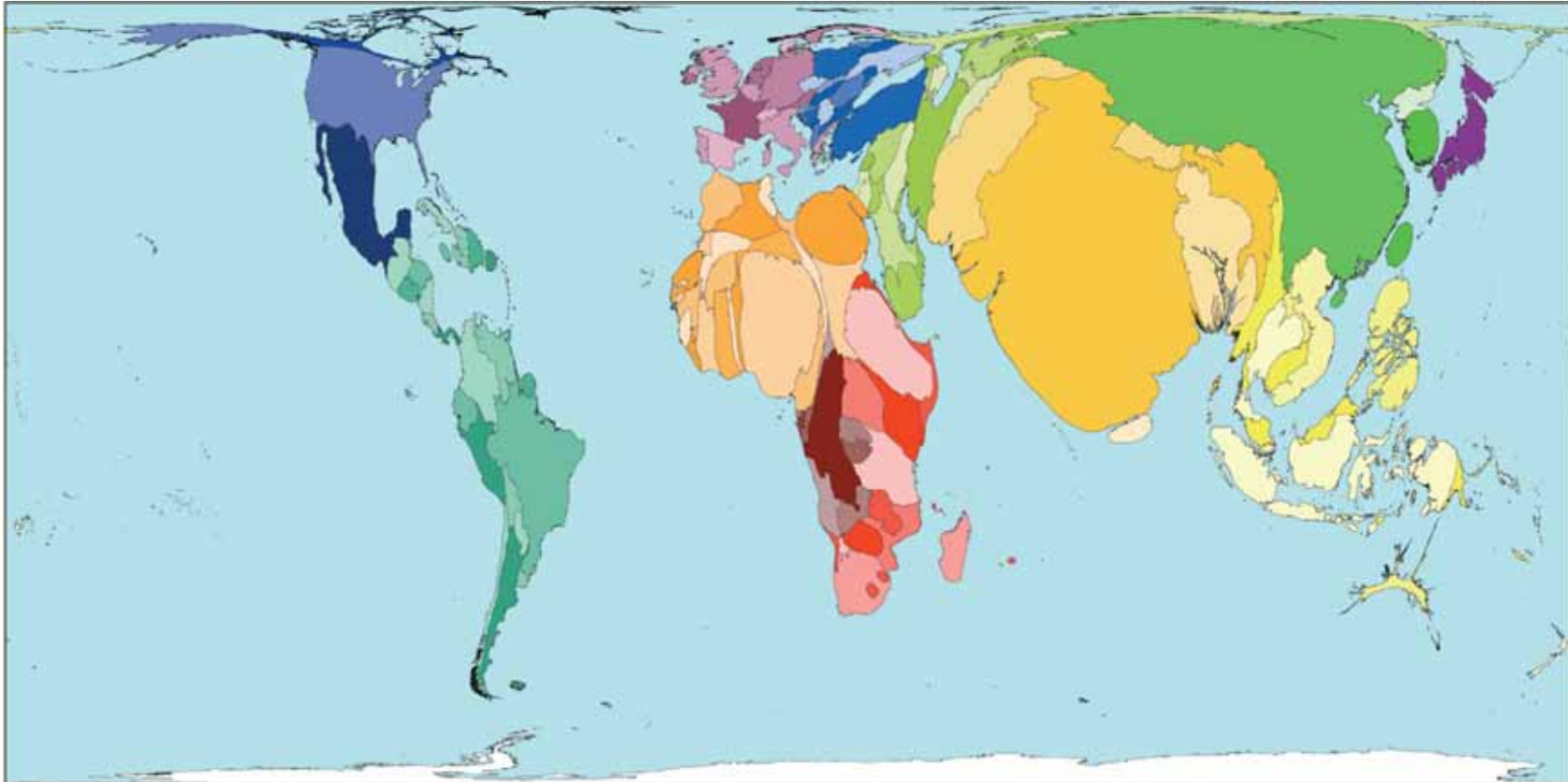
# Causes of under-five mortality



78% Pneumonia, diarrhea, malaria and neonatal illness  
 75 % in 18 countries, 50%: India, Nigeria, DRC, Pakistan,  
 China (5), 33% India & Nigeria (2); 19 out of the top 20 U5MR  
 countries, are in Africa (& Afghanistan)

Black et al. Lancet, 2010, WHO. The World Health Statistics 2010, Black et al. Lancet, 2008

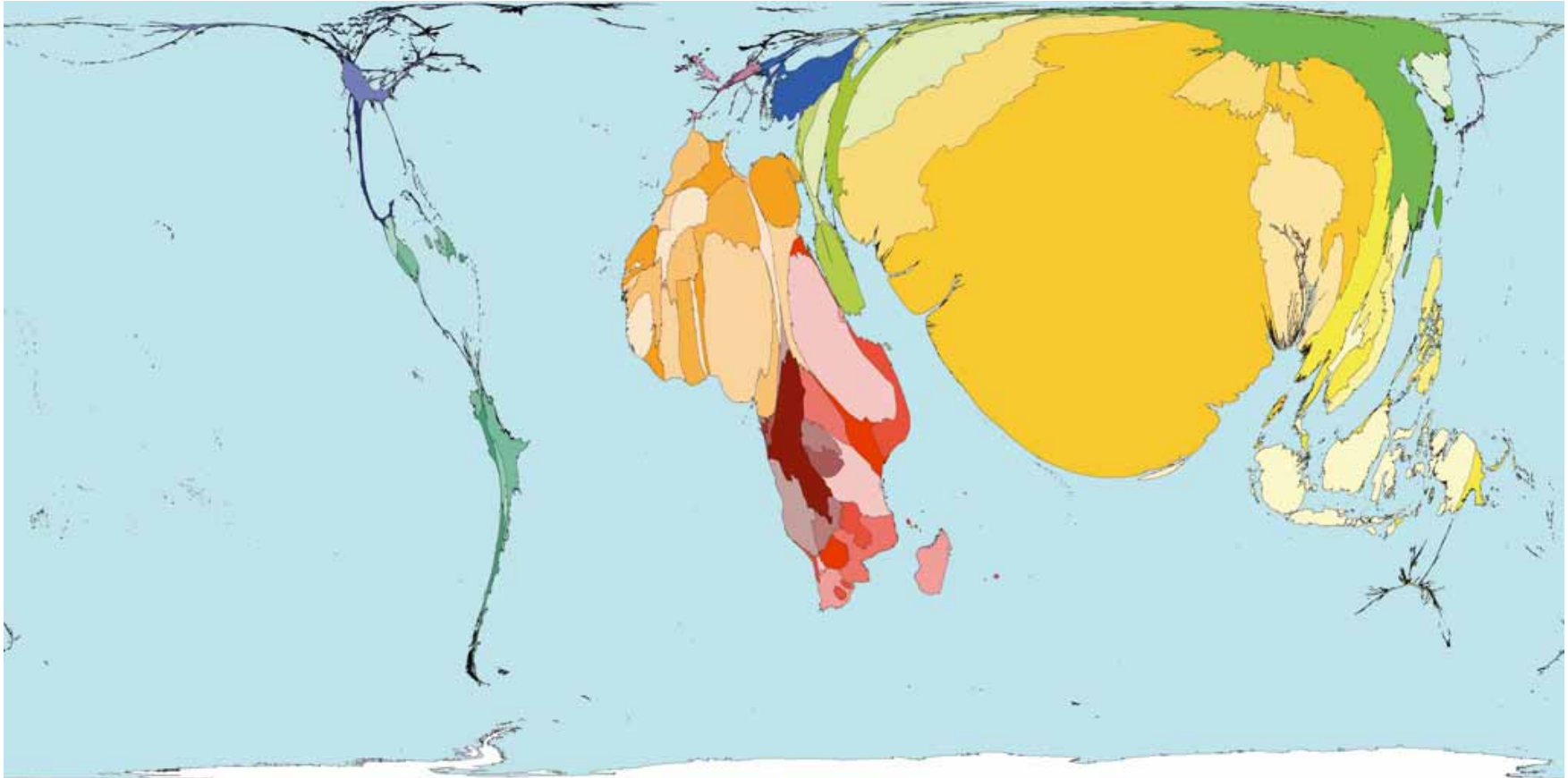
## Pediatric clinical pharmacology and child health: A global perspective



[www.worldmapper.org](http://www.worldmapper.org)

### Total Children

Children under 15 are shown. Africa has the highest percentage. In Uganda and Niger half the population is under 15. In Italy, Spain and Japan only 14% of the population are children aged under 15.



**Low Birth Weight Related Deaths**

# Better Medicines for 300 Million Children in China

## Report on Recent Progress

*Zhiping Li,<sup>1</sup> Li Wang,<sup>2</sup> Yi Wang,<sup>1</sup> Yonghao H. Gui,<sup>1</sup> Alexander A. Vinks<sup>3</sup> and Stuart MacLeod<sup>4</sup>*

1 Fudan Children's Hospital, Shanghai, China

2 Peking University First Hospital, Beijing, China

3 Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

4 Centre for International Child Health, University of British Columbia, Vancouver, British Columbia, Canada

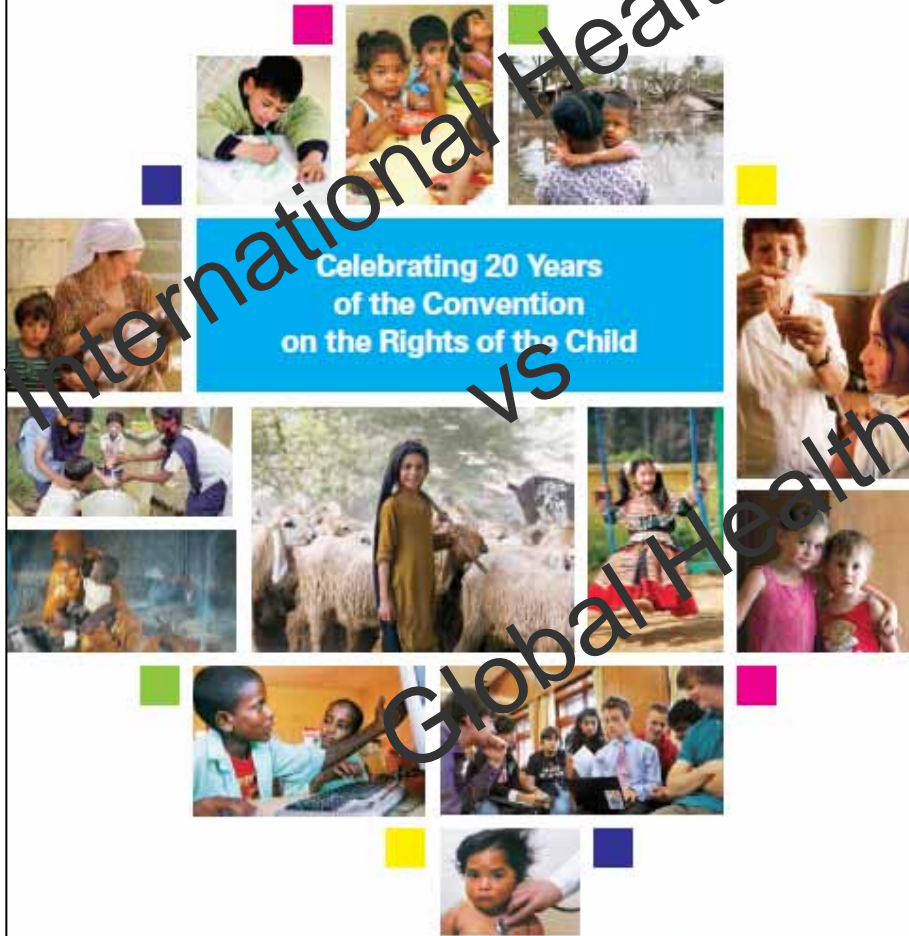
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China is home to nearly 300 million children and, as a consequence, poses a major challenge to those interested in pursuing better drug therapy for infants, children, and youth. While many of China's children are raised under developed country conditions there are still substantial numbers, partic-

represent some clinical trials, the apparent shortfall in Asian participation nonetheless presents a significant opportunity for Chinese clinical trialists.

In September 2010, a dual meeting was convened in Beijing. The first meeting was the inaugural regional meeting of the

**THE STATE OF THE WORLD'S CHILDREN**  
SPECIAL EDITION



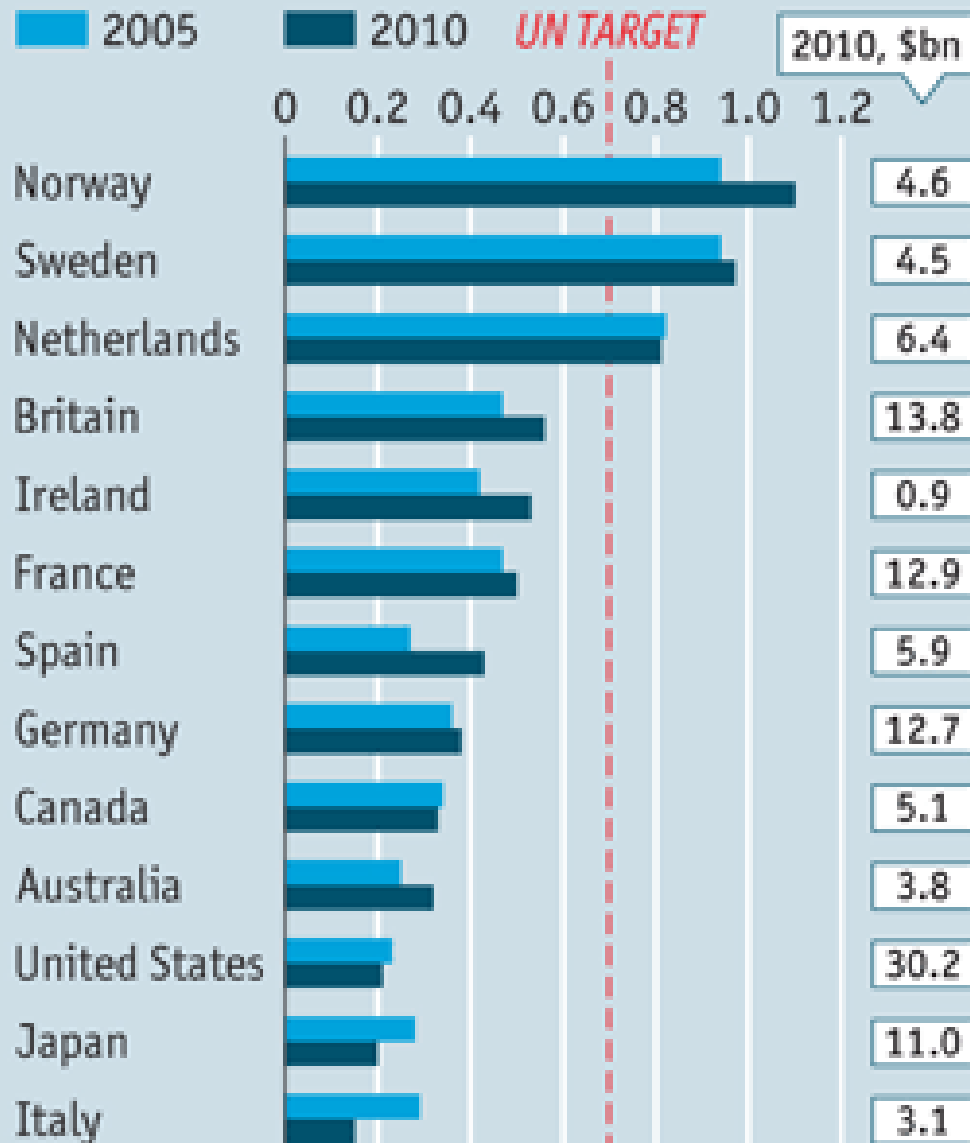
Celebrating 20 Years  
of the Convention  
on the Rights of the Child

unite for  
children

unicef 

## Aid

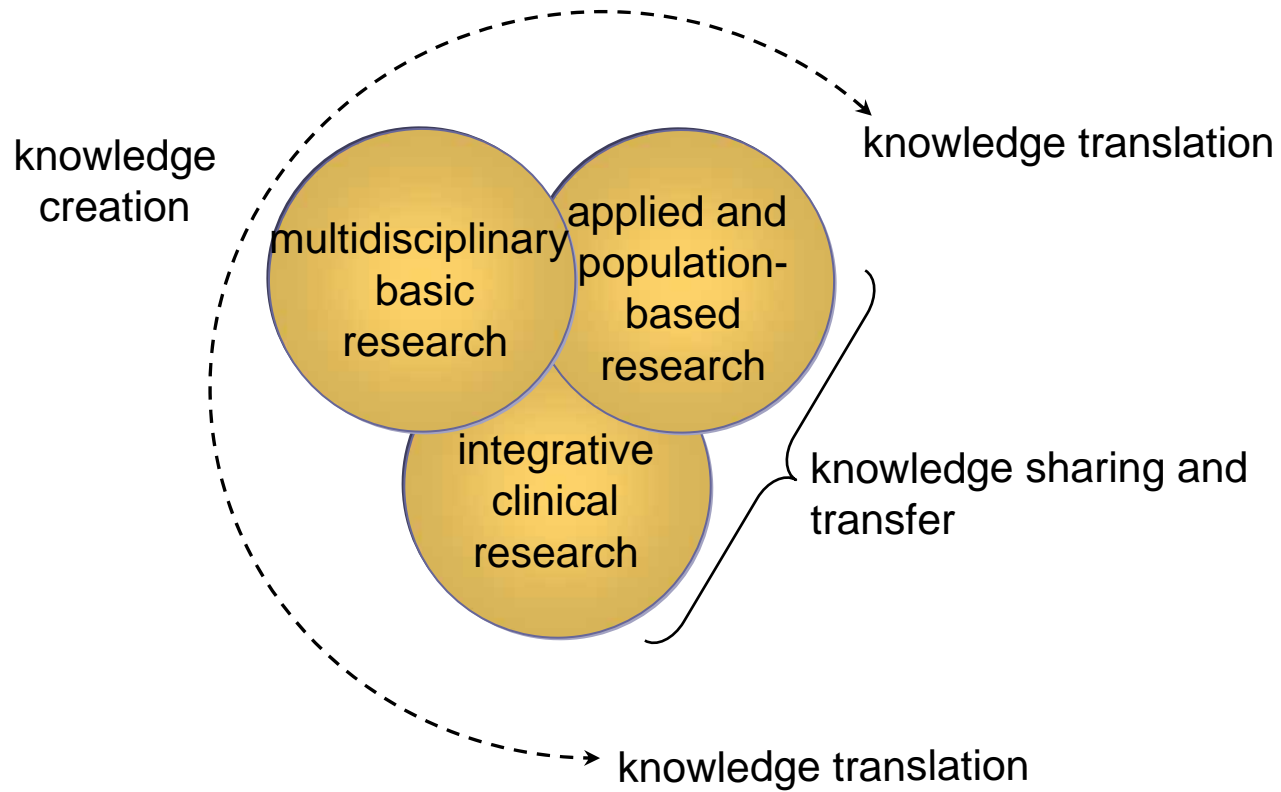
Net official development assistance as % of GDP



Source: OECD

# Better Medicines for Children

## A shifting paradigm



## Key trends in the evolution of pediatric clinical research

- ongoing adjustment of research balance
- ↑ importance of clinical and population health
- ↑ patient centred research and knowledge transfer
- ↑ pharmacogenomics, epigenetics, personalized therapeutics
- global research, ↑ child survival, reaching millennium development goals
- effective research networks
  - national – international – disease focused – discipline centred
- Changing environment for medical, educational and post-professional training

# THE SELECTION AND USE OF ESSENTIAL MEDICINES

Report of the WHO Expert Committee,  
October 2007  
(including the Model List of  
Essential Medicines for Children)

(including the Model List of  
Essential Medicines for Children)



World Health  
Organization

# Better medicines for children

## WHO priorities

- training / capacity building
- promoting multidisciplinary research
- closing the know-do gaps
- development of child friendly formulations and fixed dose combinations
- development of better pharmacotherapy for palliation and pain relief
- better management – supply chain management

Parallels between international and regional health Issues.

# Better Medicines for Children

## Key events

- |             |   |
|-------------|---|
| 2007        | World Health Assembly resolution<br>and Essential Medicines List for Children (EMLc)                              |
| 2006 - 2010 | meetings: Baltimore, Shanghai, Anaheim,<br>Quebec City, Athens, Orlando, Accra,<br>Copenhagen, Vancouver, Beijing |
| 2010        | WHO model formulary for children  |



## Better medicines for children

- ★ essential medicines lists
- ★ standard treatment guidelines
- ★ clinical trial methods
- ★ expanded use of WHO pre-qualification of medicines program
- ★ scaling up of established interventions for priority conditions
- ★ formulations

WHO / Bill and Melinda Gates Foundation 2008-2012



make medicines *child size*

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## Meeting Report

# WHO and StaR Child Health Use of Standards in Paediatric Clinical Trials in Developing Countries Meeting

Amsterdam, The Netherlands  
28 October 2009

This publication contains the Report of the WHO and StaR Child Health Paediatric Trials in Developing Countries Meeting and does not necessarily represent the decisions or policies of the World Health Organization

[http://www.who.int/childmedicines/progress/Amsterdam\\_Meeting.pdf](http://www.who.int/childmedicines/progress/Amsterdam_Meeting.pdf)

## Key recommendations

### Amsterdam 2009

- develop strategies to improve reporting
- develop standards for cluster randomized trials
- improve community participation in trial design
- develop KT strategies
- develop a code of conduct for research involving children in low/middle income countries

### The major challenge

- building human resource capacity for clinical and population health research

## Clinical trials in world by population of children: 2009

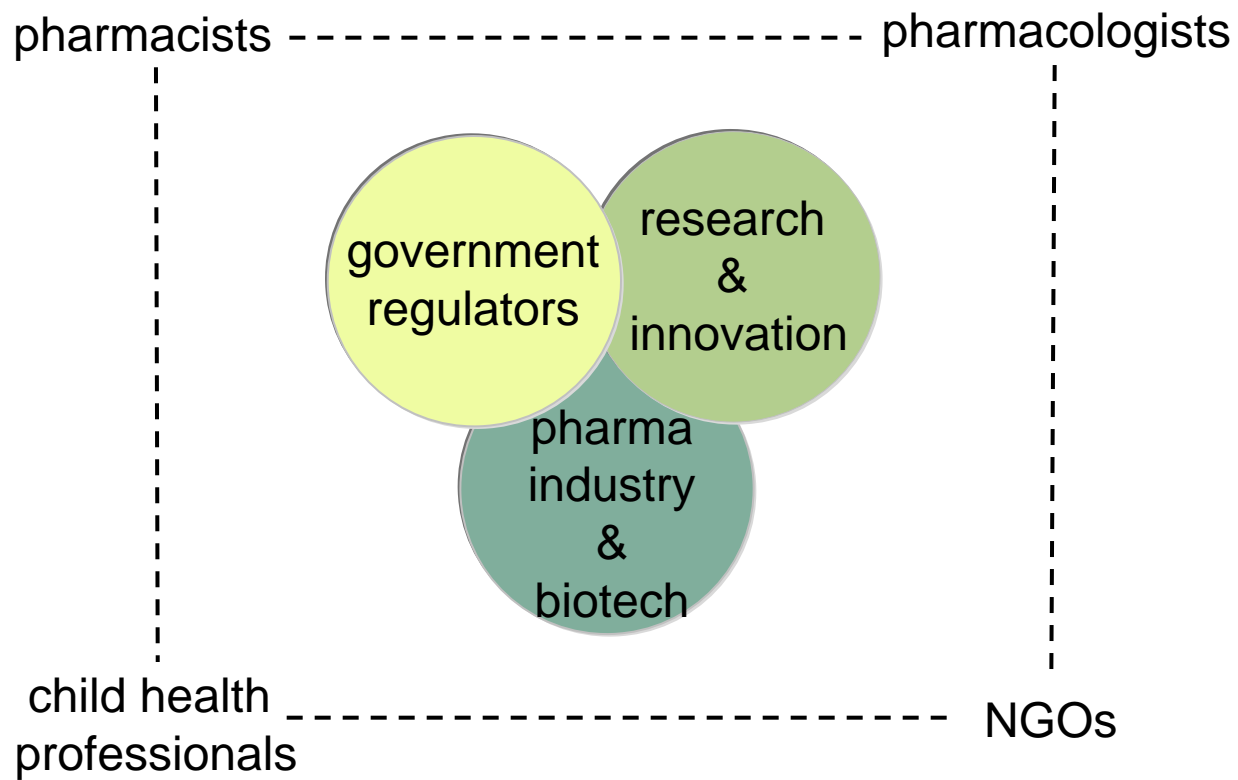
	# Clinical Trials*	% Total Trials	Trials per millions aged 0-14 years
Total Trials	5385		
USA	2788	52	46
Canada	459	9	86
Australia	394	7	99
UK	310	6	31
Netherlands	261	5	90
France	255	5	21
Germany	253	5	22
Japan	183	3	11
India	121	2	0.33
China	100	2	0.38

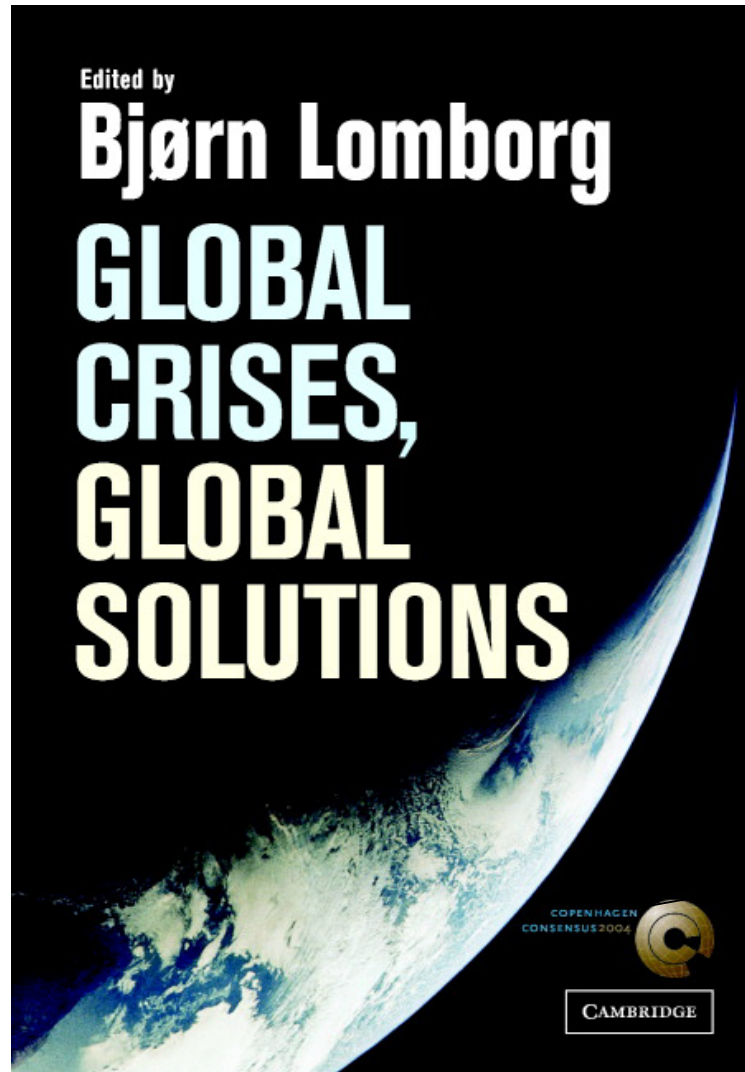
\* from: WHO <http://wwwl.who.int/ictrp/child/search/en/>

Population statistics from: <https://www.cia.gov/library/publications/the-world-factbook>



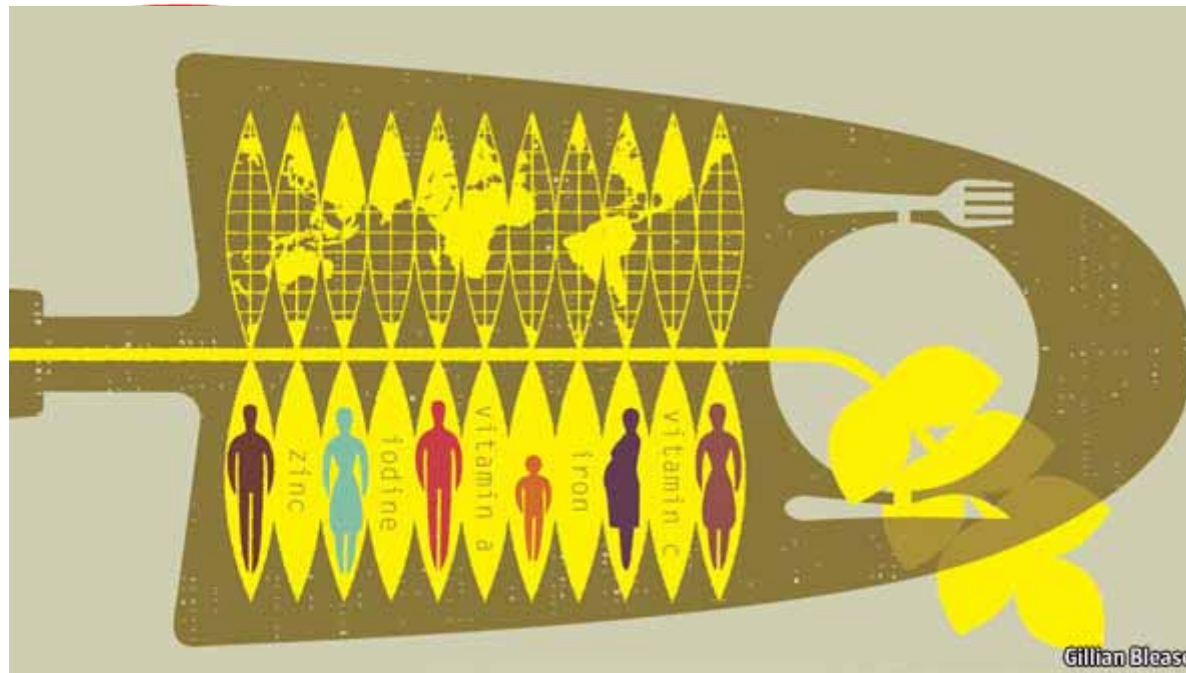
International Alliance for  
Better Medicines for Children





Copenhagen  
Consensus 2004

Why small doses of vitamins could make a huge difference to the world's health



Economist Mar 24th 2011

## Towards a better world: The Copenhagen Consensus 2008

1. micronutrient for children (vitamin A and zinc)
3. micronutrient fortification (iron and iodine)
4. expanded immunization coverage
6. anthelmintics
9. community nutrition
10. fertility management
12. malaria prevention
13. TB case finding and treatment
19. HIV prevention and treatment

## Role of networks in international pediatric clinical investigation

national: UK, Netherlands, USA, France, Germany

training / mentoring: GRIP, NICHD, INCLEN, INRUD, MSH

international organizations: IUPHAR, ESDP, ASCPT

pediatric trials: MICYRN, NICHD, EC FP7 / EMA,  
Infectious Disease Institute, Kampala

disease / condition specific: eg, neonatal, cystic fibrosis, thalassemia

# Pediatric clinical studies

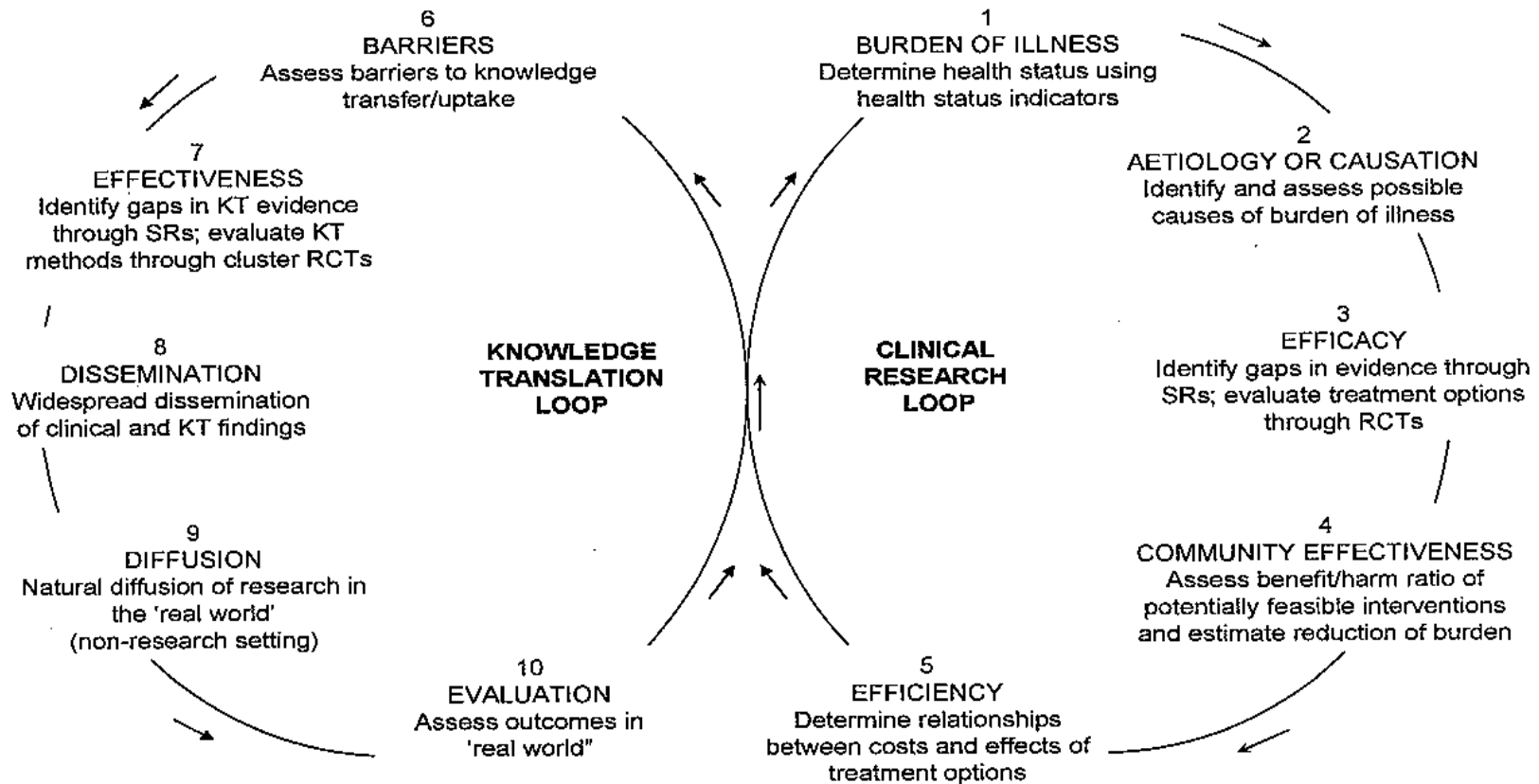
## Key components

- modeling / simulation capability
- clinical pharmacology design experts
- PK / PD
- analytic capacity
- dose response
- safety and efficacy
- data transfer
- data management
- data and safety monitoring (risk management)
- data sharing plan

## Pediatric Clinical Trials Environment

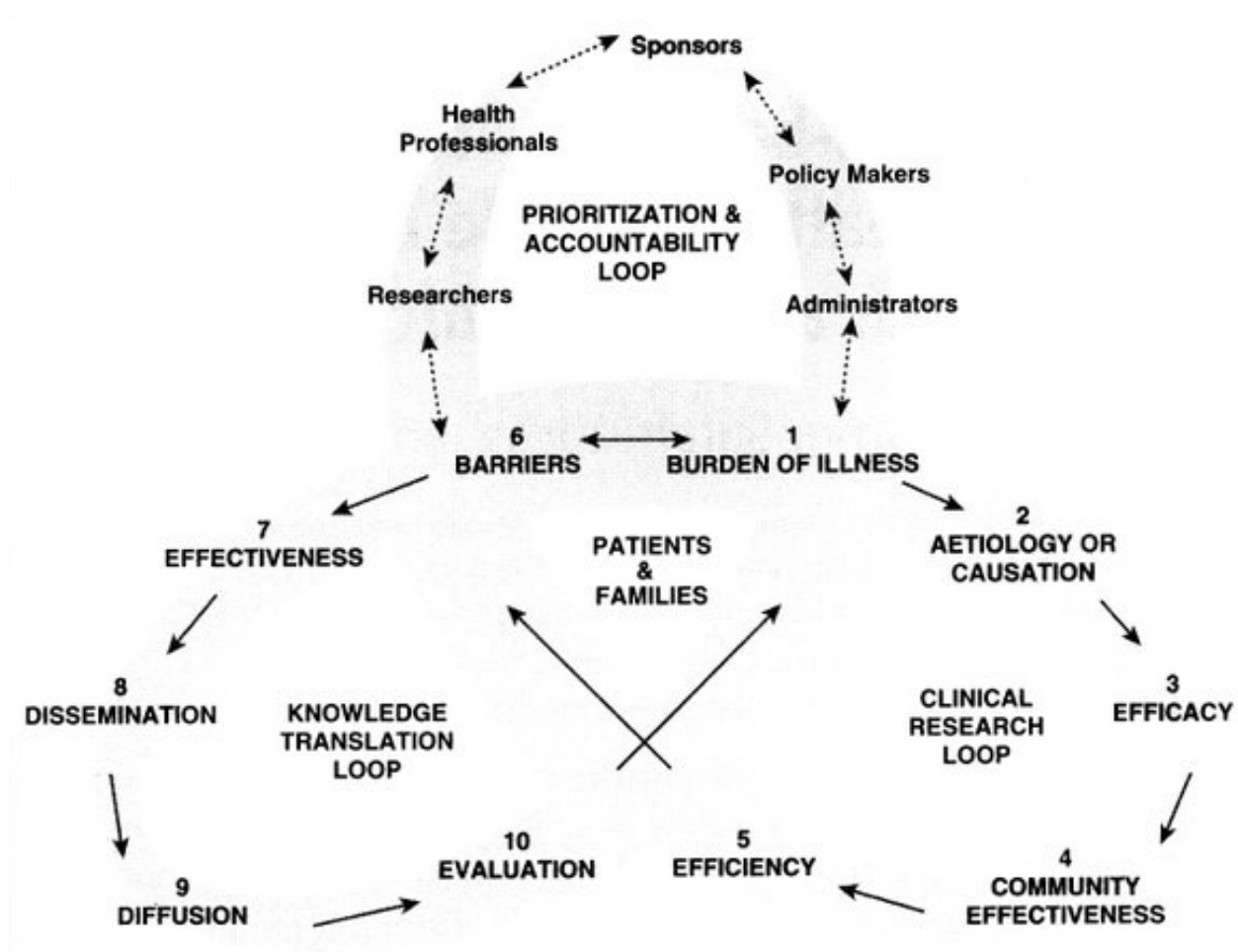
1997	FDAMA
1998	FDA Pediatric Rule
2000	ICH E11
2002	Best Pharmaceuticals for Children Act (BPCA)
2003 - 2008	Pediatric Research Equity Act (PREA)
2006	EMA agreement re pediatric drug testing
2007	FDA Amendments Act, including reauthorization of BPCA
2007	WHO Make Medicines Child Size
2009 – 2010	StaR Child Health meetings: Amsterdam, Vancouver
2010	European Community (FP7): Global research in pediatrics

# Child health research paradigm: The iterative figure-eight



L Hartling et al. Academic Emergency Medicine. 2007;14:968-77.

# Child health research paradigm: Conceptual framework



L Hartling. In: Economic Evaluation in Child Health  
Oxford University Press. 2010

The clinical-political gap in healthcare decision-making







*"My question is: Are we making an impact?"*



...when you're not the lead dog...



Gates-WHO project slides  
See Botswana