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

Department of Epidemiology & Public Health
Health Interventions Unit

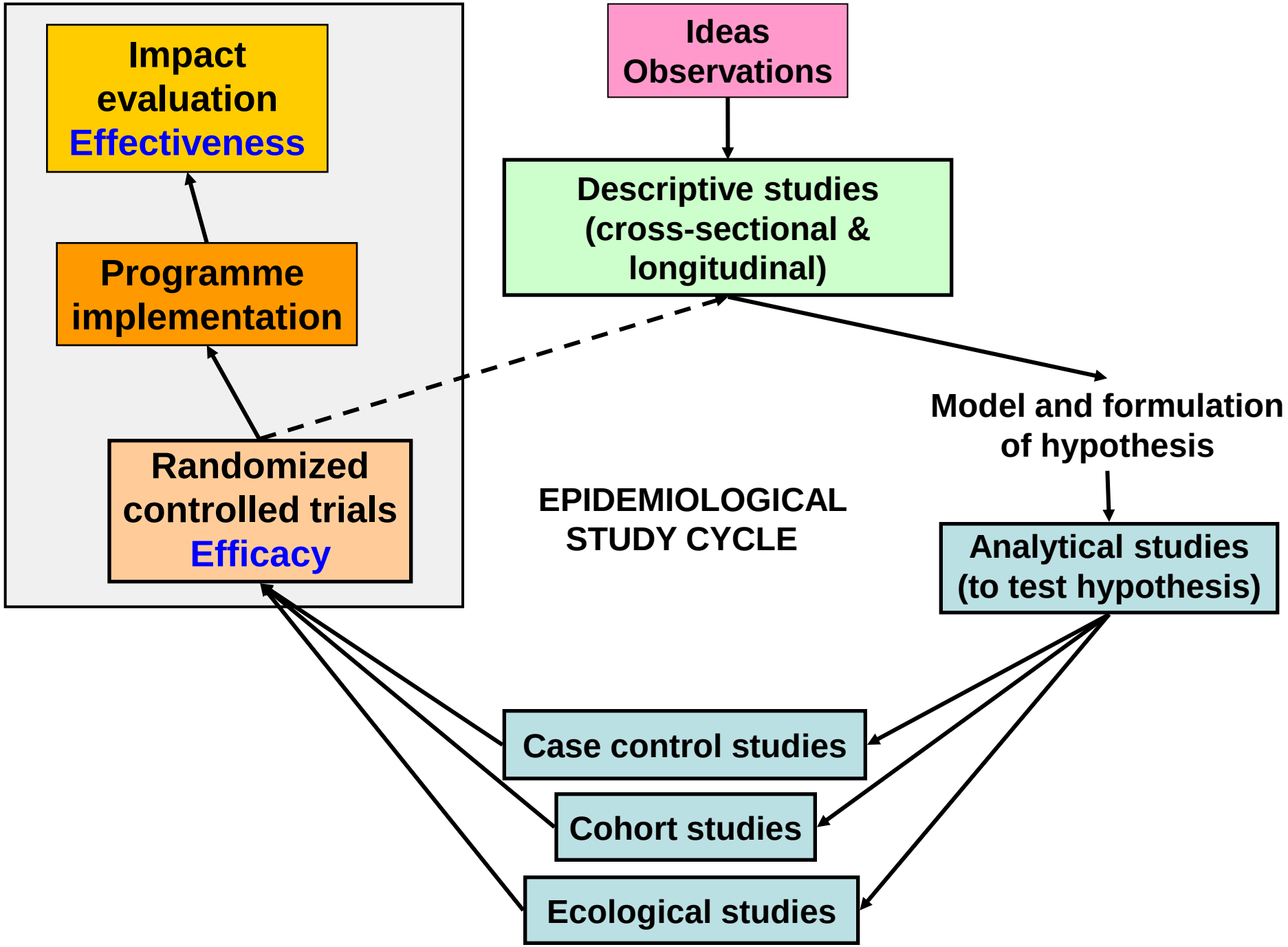
Implémenter et Evaluer des Programmes de Santé Publique:
de la Théorie à la Pratique

Christian Lengeler

Swiss Tropical and Public Health Institute
Basel, Switzerland

Content

1. Efficacy versus Effectiveness
2. Relative versus absolute risk
3. How to measure effectiveness?
   Evaluating public health programmes


Impact evaluation
Effectiveness
Programme implementation
Randomized controlled trials
Efficacy
Ideas
Observations
Descriptive studies (cross-sectional & longitudinal)
Model and formulation of hypothesis
EPIDEMIOLOGICAL STUDY CYCLE
Analytical studies (to test hypothesis)
Case control studies
Cohort studies
Ecological studies

1: Efficacy vs Effectiveness

Efficacy: measure of the impact of an intervention under ideal (maximal) conditions. Usually measured in Phase 3 RCTs and therefore likely to be bias-free. It gives the best possible measure of impact (the "goal" for programmes to reach).

"How well can it work ?"

Effectiveness: measure of the impact of an intervention under "real world" conditions. Usually measured in large-scale programmes.

"How well does it work in practice"

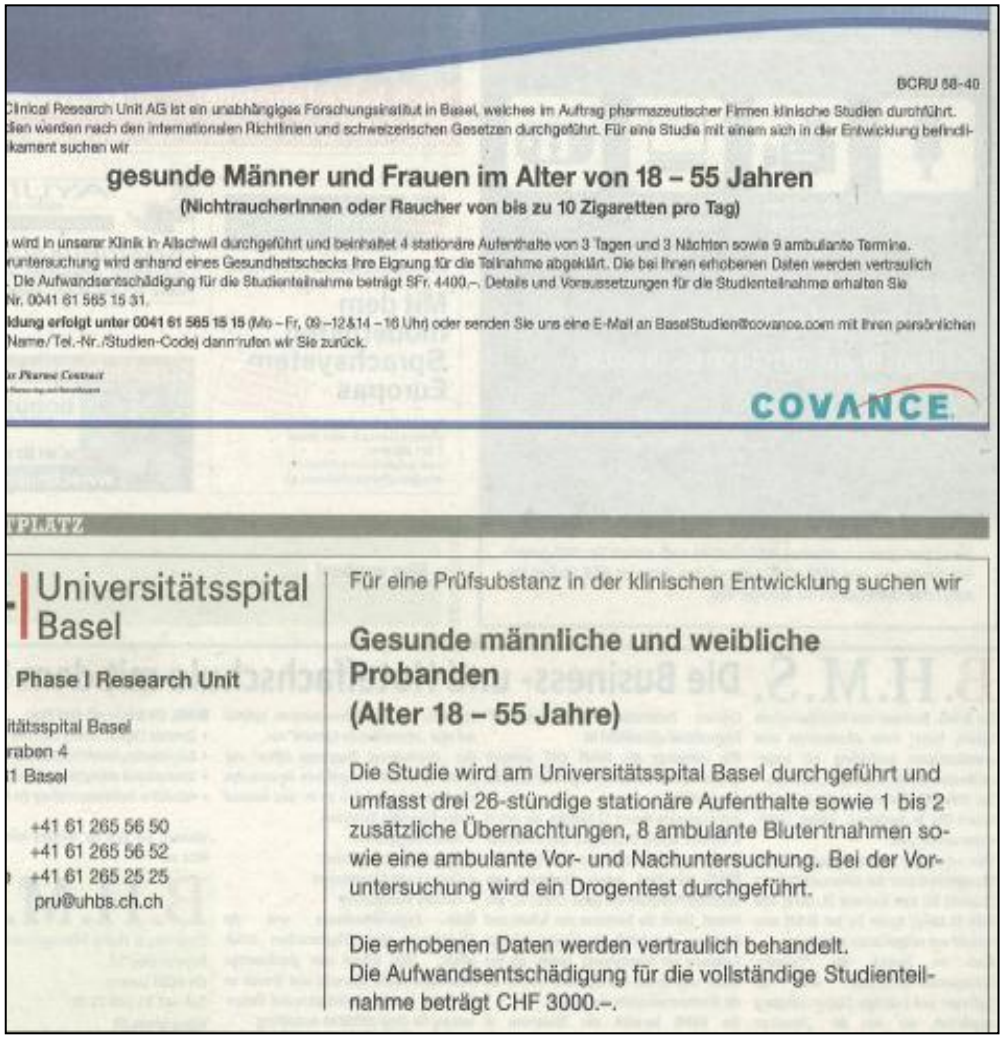
The two measures should ideally be very close.. but often this is not the case

For drugs: treatment compliance might be lower, the indications might be less rigorous, co-morbidity might affect treatment effect, ages might be different, etc.

For vaccines: There might be a problem with the cold chain that reduces the vaccine's performance. For multi-dose vaccines compliance might be low.

For public health programmes: coverage might be low, provider compliance and patient adherence might be sub-optimal (see below).

Usually, efficacy is higher than effectiveness… but not always (vaccines, vector control)



BCRU 58-40

Clinical Research Unit AG ist ein unabhängiges Forschungsinstitut in Basel, welches im Auftrag pharmazeutischer Firmen klinische Studien durchführt. Studien werden nach den internationalen Richtlinien und schweizerischen Gesetzen durchgeführt. Für eine Studie mit einem sich in der Entwicklung befindlichen Arzneimittel suchen wir

gesunde Männer und Frauen im Alter von 18 – 55 Jahren

(NichtraucherInnen oder Raucher von bis zu 10 Zigaretten pro Tag)

Die Studie wird in unserer Klinik in Allschwil durchgeführt und beinhaltet 4 stationäre Aufenthalte von 3 Tagen und 3 Nächten sowie 9 ambulante Termine. Bei der Voruntersuchung wird anhand eines Gesundheitschecks Ihre Eignung für die Teilnahme abgeklärt. Die bei Ihnen erhobenen Daten werden vertraulich behandelt. Die Aufwandsentschädigung für die Studienteilnahme beträgt SFr. 4400.–. Details und Voraussetzungen für die Studienteilnahme erhalten Sie unter Tel. Nr. 0041 61 565 15 31.

Anmeldung erfolgt unter 0041 61 565 15 15 (Mo – Fr, 09 –12&14 – 16 Uhr) oder senden Sie uns eine E-Mail an BaselStudien@covance.com mit Ihren persönlichen Angaben (Name/Tel.-Nr./Studien-Code) dann rufen wir Sie zurück.

COVANCE

PLATZ

Universitätsspital Basel

Phase I Research Unit

itätsspital Basel
raben 4
1 Basel

+41 61 265 56 50
+41 61 265 56 52
+41 61 265 25 25
pru@uhbs.ch.ch

Für eine Prüfsubstanz in der klinischen Entwicklung suchen wir

Gesunde männliche und weibliche Probanden (Alter 18 – 55 Jahre)

Die Studie wird am Universitätsspital Basel durchgeführt und umfasst drei 26-stündige stationäre Aufenthalte sowie 1 bis 2 zusätzliche Übernachtungen, 8 ambulante Blutentnahmen sowie eine ambulante Vor- und Nachuntersuchung. Bei der Voruntersuchung wird ein Drogentest durchgeführt.

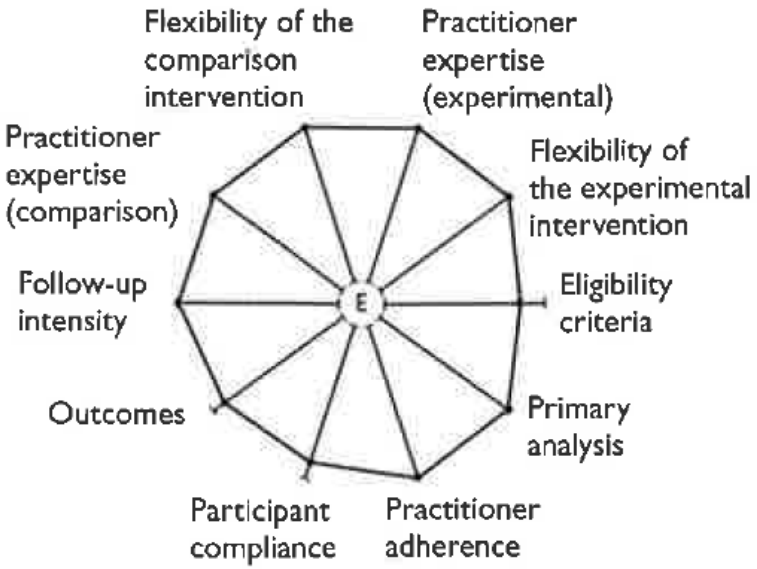
Die erhobenen Daten werden vertraulich behandelt.
Die Aufwandsentschädigung für die vollständige Studienteilnahme beträgt CHF 3000.–.

Healthy male and female volunteers (aged 18-55 years)

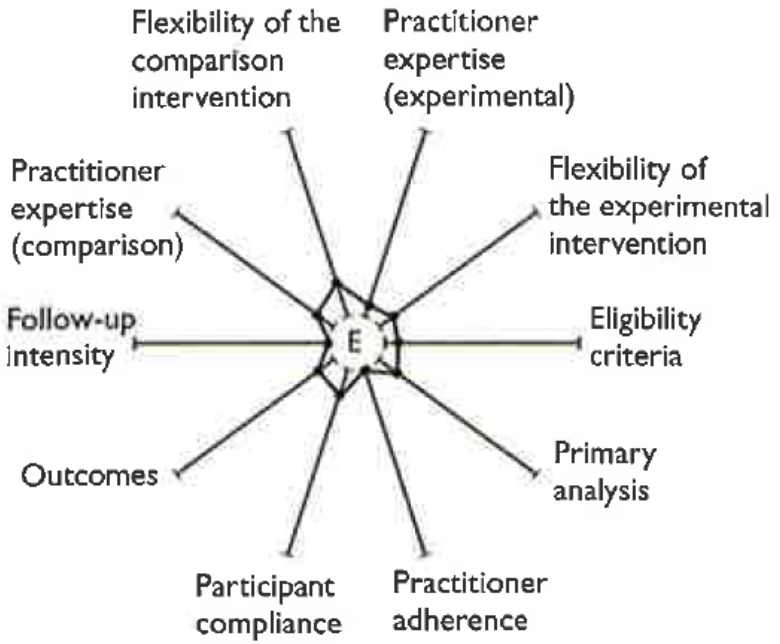
Eligibility in clinical trials (Phases 1-3)

Internal vs external validity

PRECIS: qualification of Randomized Controlled Trials: How close or how far away they are from «real life»



Close



Far away

Source: Senn *et al*., 2012. Adapted from Thorpe *et al*. 2009

Why Measure Effectiveness ?

For clinicians and public health managers it is important to know how much of the original efficacy can be retained under a "real world" programme situation.

- **Usually, the implementation of a new intervention under programme conditions is different from the implementation under a clinical trial situation.**

Ex: Vitamin A trials were done mostly in children aged 1-4 years.

In the real world, Vitamin A is given together with childhood vaccines around the age of one.

Can impact still be achieved? Are there unexpected side-effects ?

Ex: How safe is a new generation of pain killers when the target population is old and has multiple morbidity?

The effectiveness stair for health interventions

Modified from P. Tugwell, D. deSavigny, M. Tanner

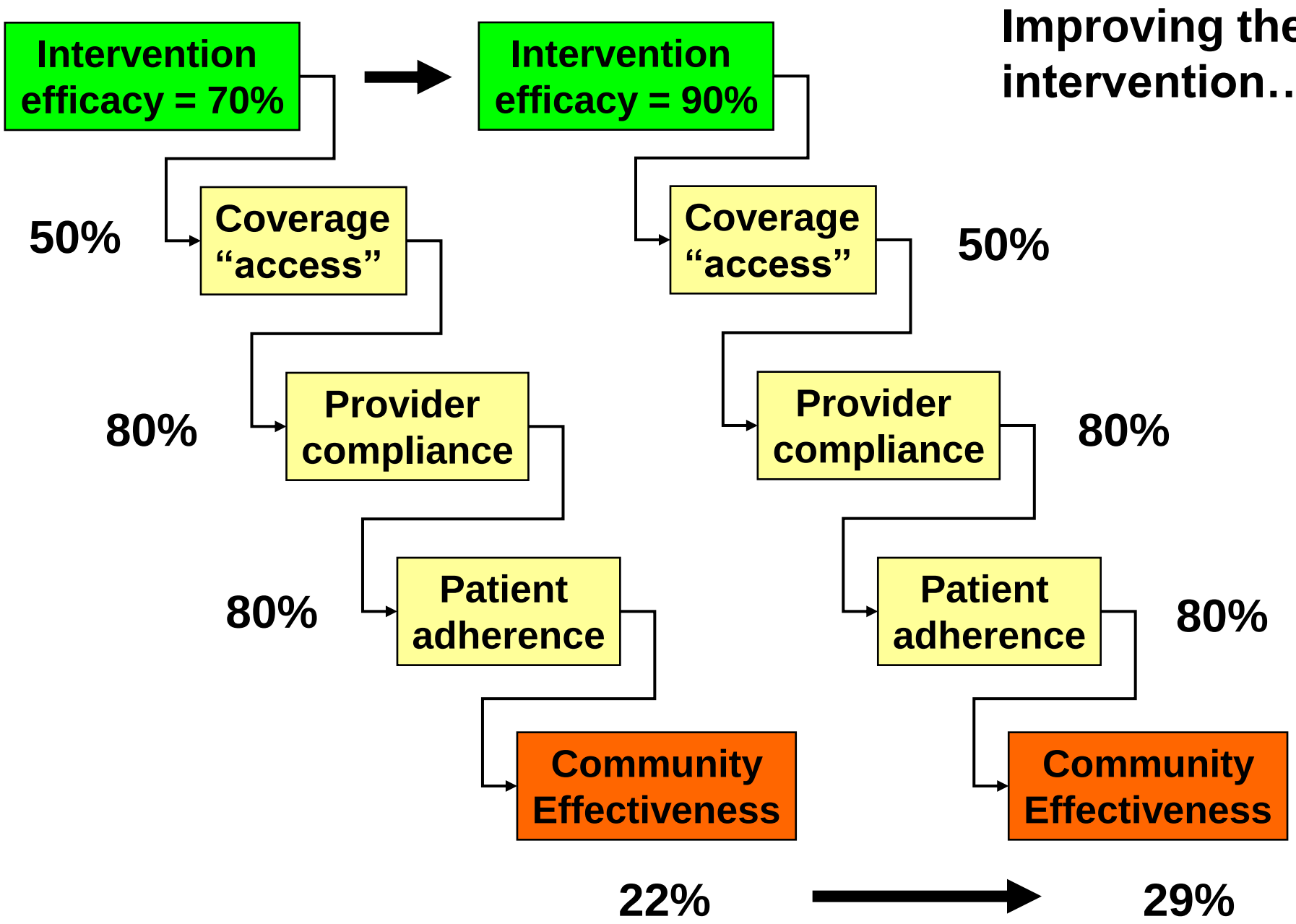
Intervention efficacy

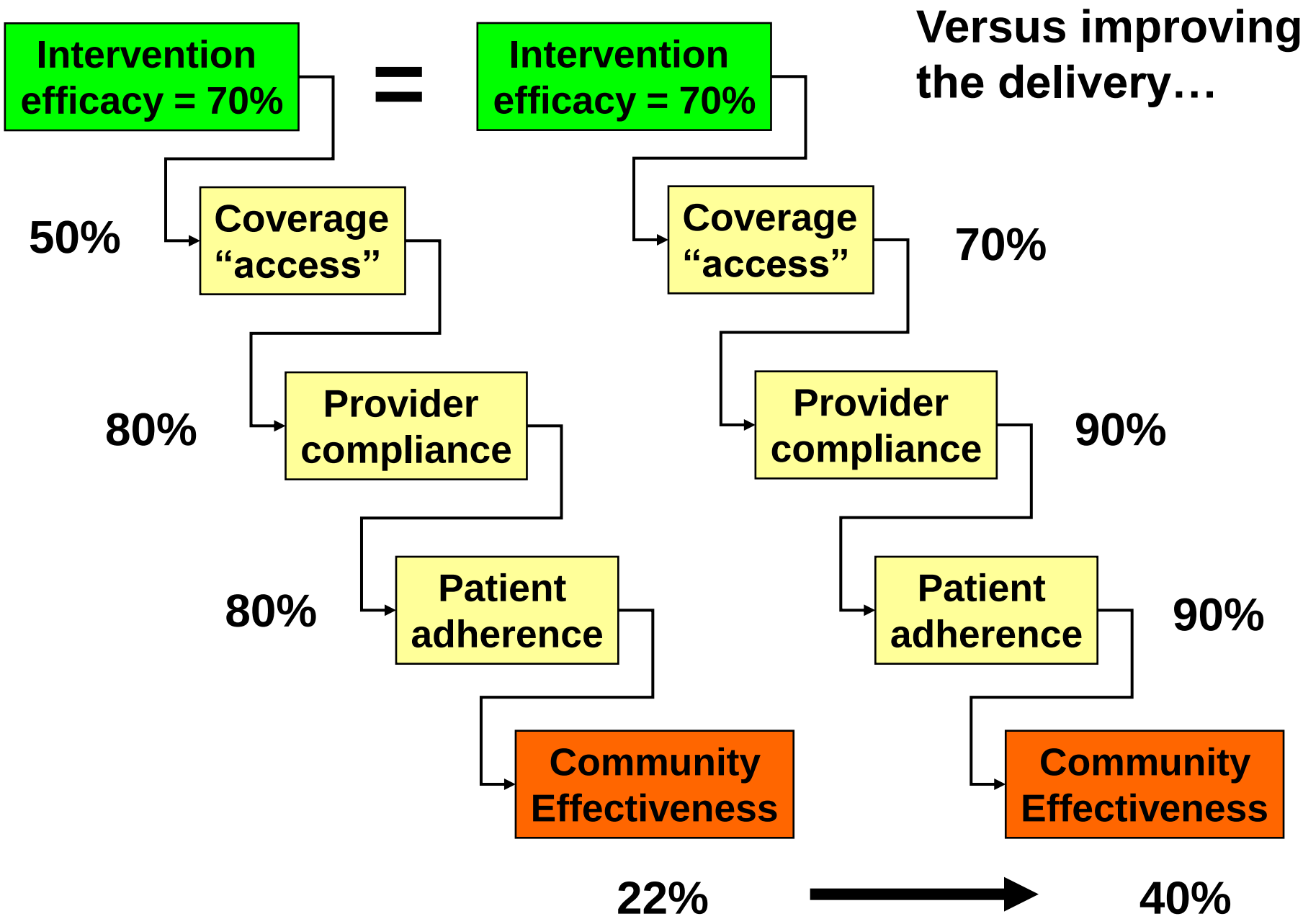
Coverage "access"

Provider compliance

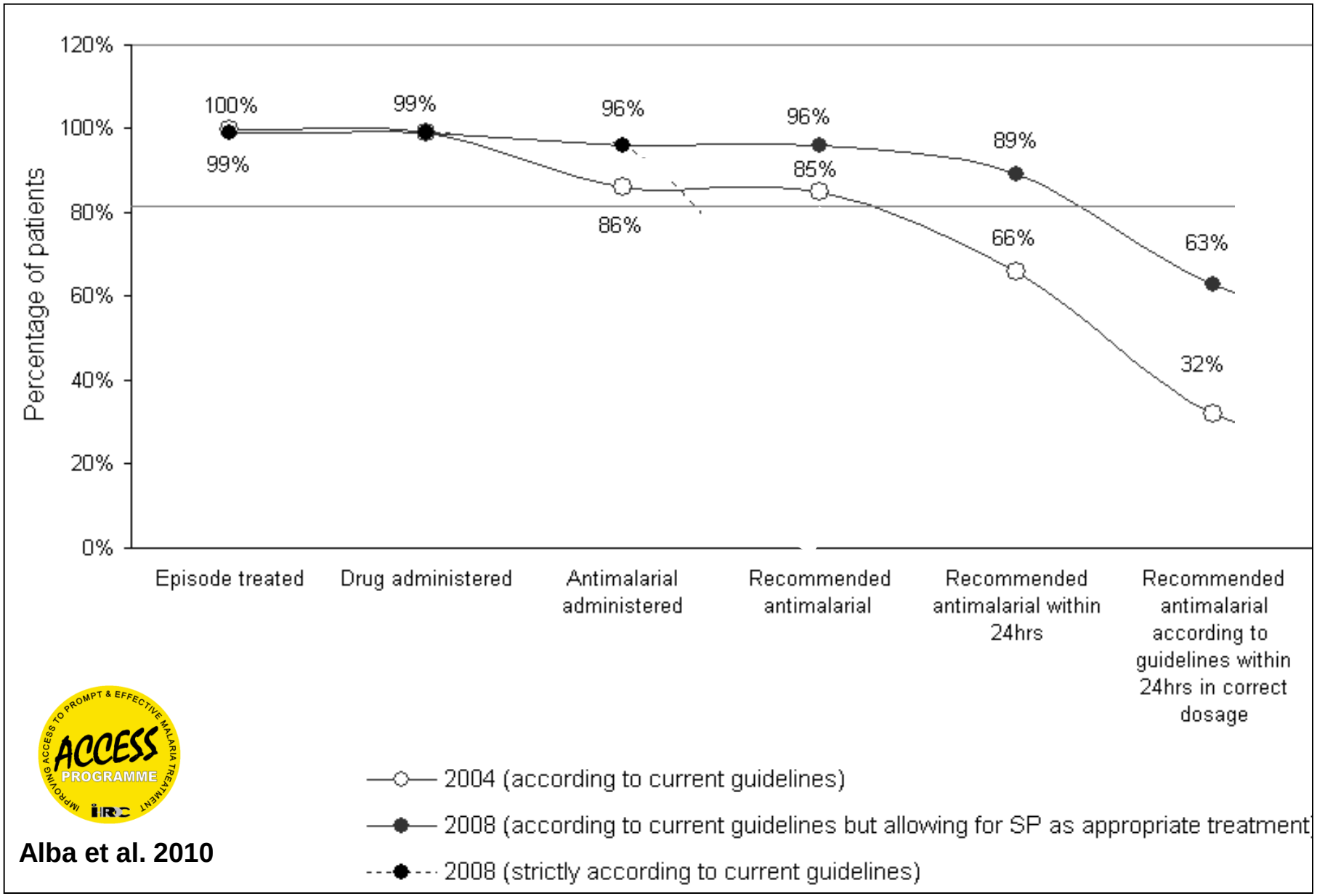
Patient adherence

Community Effectiveness


Improving the intervention…
Intervention efficacy = 70%
Intervention efficacy = 90%
50%
Coverage "access"
Coverage "access"
50%
80%
Provider compliance
Provider compliance
80%
80%
Patient adherence
Patient adherence
80%
Community Effectiveness
Community Effectiveness
22%
29%

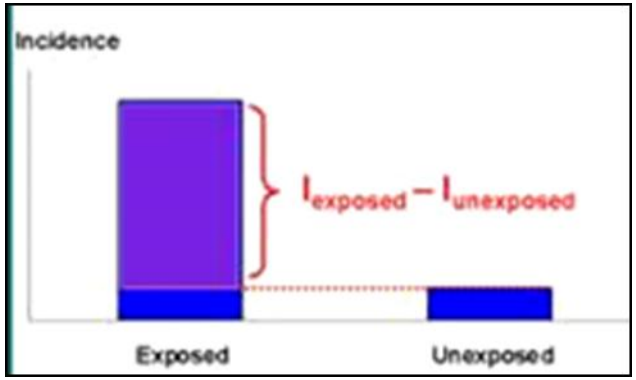

Intervention efficacy = 70%
=
Intervention efficacy = 70%
Versus improving the delivery…
50%
Coverage "access"
Coverage "access"
70%
80%
Provider compliance
Provider compliance
90%
80%
Patient adherence
Patient adherence
90%
Community Effectiveness
Community Effectiveness
22%
40%

Community effectiveness of malaria treatment



Alba et al. 2010

2. Relative versus Absolute Risk



The Relative risk (Ie / I0) is important for assessing exposure-outcome associations (and therefore causality). Very popular with academics.

But the Risk Difference (Ie – I0) converts protection/excess risk into "real" numbers, hence it expresses better the clinical and public health significance of a risk/protective factor.

Number Needed to Treat (NNT)

- **NNT expresses the number of patients that have to receive a preventive treatment in order to avoid one case of disease.**

- **NNT is the reciprocal of the risk difference: Ie – I0**

$$NNT = \frac{1}{RD}$$

Malaria vaccine RTS,S/AS01 :

From March 2009 - January 2011, almost 9000 children (age 5–17 months) and 6500 young infants (age 6–12 weeks) were enrolled at 11 centres in seven countries in SSA.

RTS,S Clinical trials partnership, Lancet April 24th, 2015.

Results for vaccine at month 0, 1, 2 and booster at 20 months for mild clinical malaria episodes:

- Incidence rate was 6616 episodes / 9958 PYR = **0.66** in *vaccine group*
- Incidence rate was 9585 episodes / 9995 PYR = **0.96** in *control group*

Hence crude RR is 0.69 and PE is therefore 31%.

But: Risk difference: Ie – I0: 0.66 – 0.96 = 0.30

For 1000 vaccinated children you prevent 300 malaria cases… Number needed to treat is 3.3

Criminality & violence in Switzerland
(Hebdo 28.03.2013)

- **March 2013: the Swiss media announced a 23% increase in violence with bodily harm compared to the previous year. This sounds very worrying.**
- **However, journalists did not explain that the baseline rate for this rate is extremely low (0.06 per 1000 in 2011).**
- **Hence, an increase from 0.060 to 0.074 per 1000 is indeed a 23% increase, but it only represent a difference of 0.014 per 1000, or 1 in 71,430 population.**

3. How to measure effectiveness?

Swiss TPH

How to measure effectiveness?: A good question in a clinical setting.

But in the case of public health, a necessary extension is:

How to measure public health programme impact?

The methodological problems for programme impact evaluation are usually substantial since it is rarely possible to have a control group (an intervention that has been found to be efficacious can not be withhold).

Hence great difficulty in proving causality.

Health impact assessment under programme conditions

Axis 1: Indicators

PROVISION ==> UTILIZATION ==> COVERAGE ==> IMPACT

Activities Outputs Outcomes

Axis 2: Type of inference

1. **Adequacy: Are key targets reached? Has predicted change occurred?**
2. **Plausibility: Can we exclude other explanations for the observed change? Is there a causal relationship?**
3. **Probability: formal testing of significance - implies the possibility to have an adequate control group**

Habicht *et al*. 1999; Victora *et al*. 2004

1. Before-after design (longitudinal study)

This is a simple and attractive design. But it can be seriously flawed because secular trends or year-to-year fluctuations can not be taken into account.

Ex: Stop AIDS in Switzerland: seemingly very successful… But hard to relate change in behaviour and drop in HIV incidence rates only to the campaign.

STOP AIDS

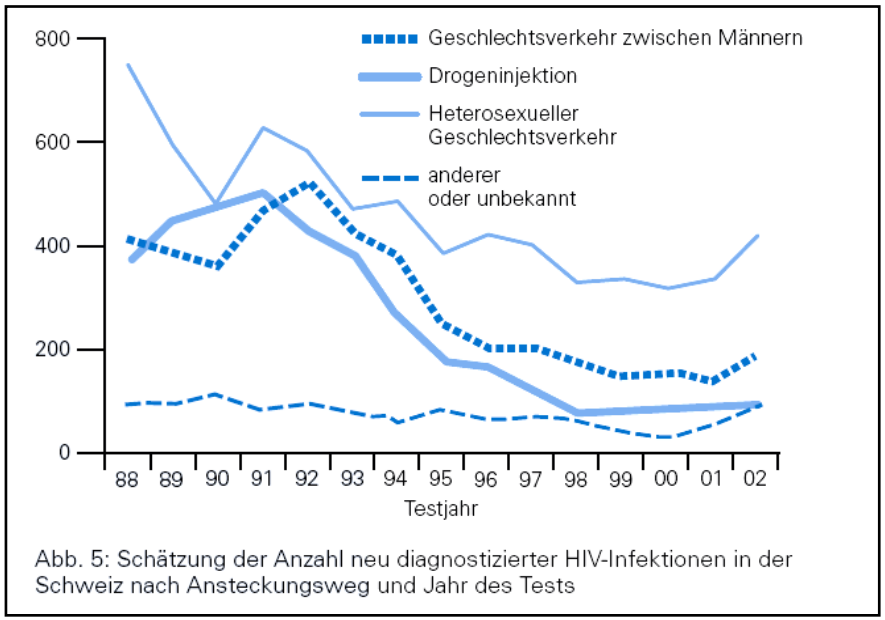


Abb. 5: Schätzung der Anzahl neu diagnostizierter HIV-Infektionen in der Schweiz nach Ansteckungsweg und Jahr des Tests

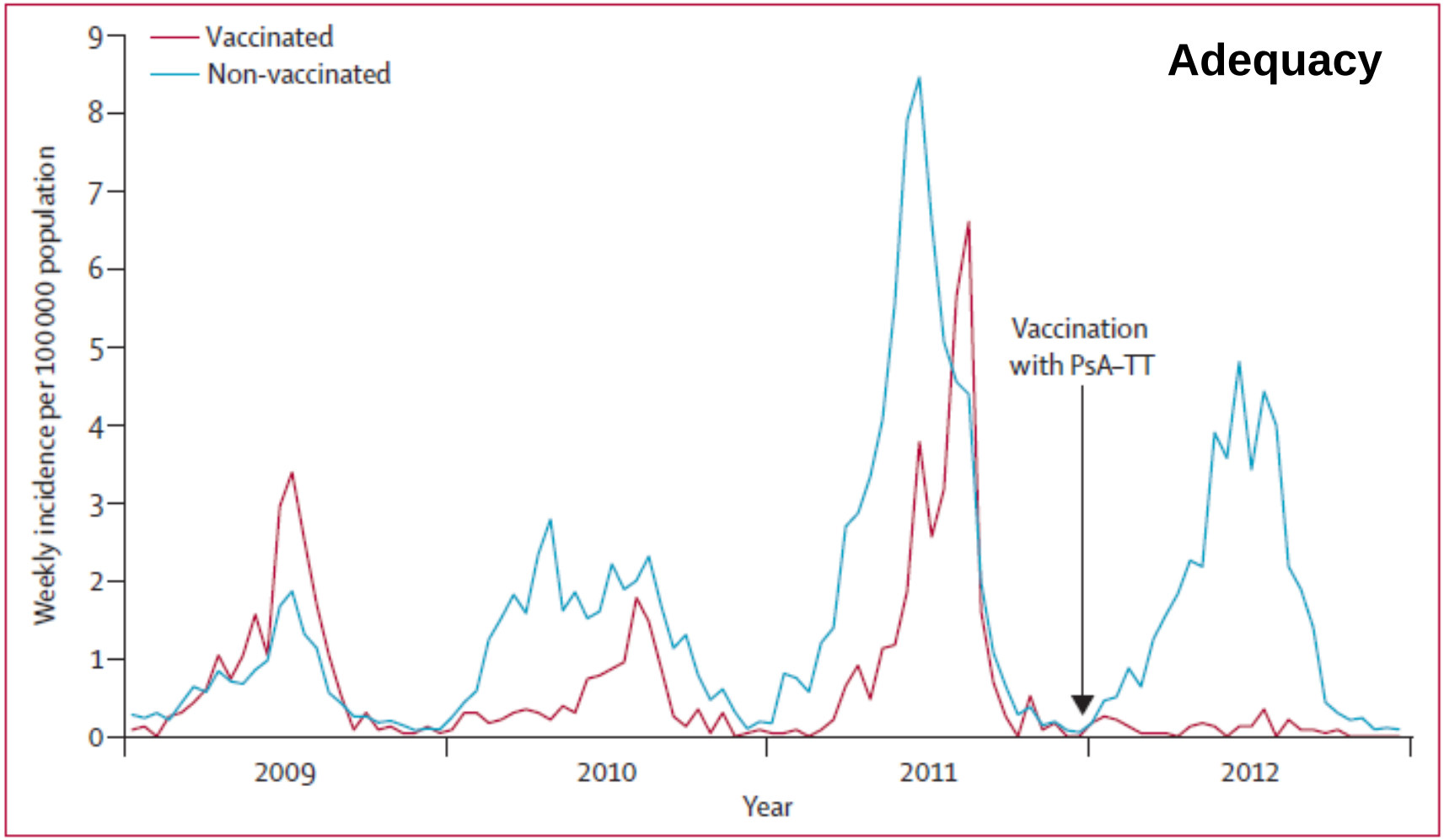
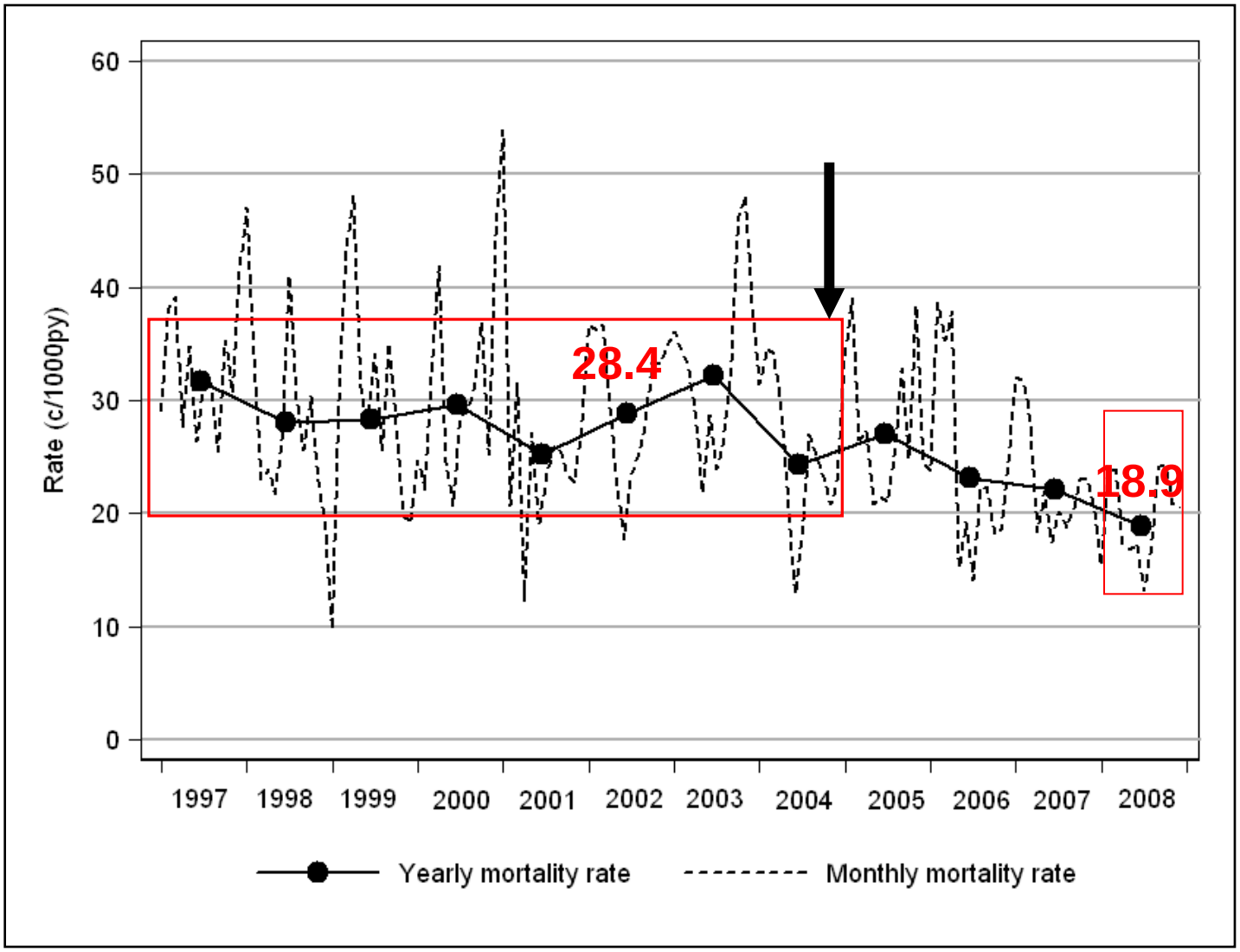


Figure 3: **Incidence of reported cases of meningitis in Chad, 2009–12**
Vaccination with PsA–TT was undertaken in patients aged 1–29 years at the end of 2011 (arrow).
PsA–TT=serogroup A meningococcal polysaccharide–tetanus toxoid conjugate vaccine.

D M Daugla et al. Lancet 2013

Mortality impact of malaria interventions

Under-five mortality rates (1997-2008)



Plausibility

33% overall decrease

17% decrease accounting for:

1) Change in mosquito net ownership
2) Changes of recommended drug for malaria

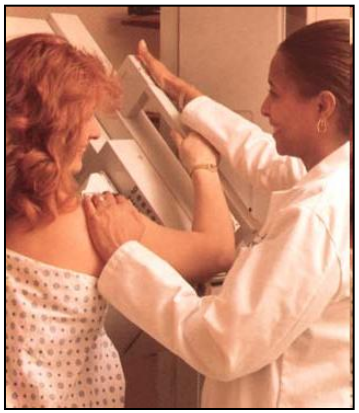
Contextual factors (rainfall and agricultural production) explain the rest

2. Users versus non-users

Often a useful approach, but users are likely to be different from non-users in many ways, and so it might be problematic to relate observed difference in health to the intervention under investigation.

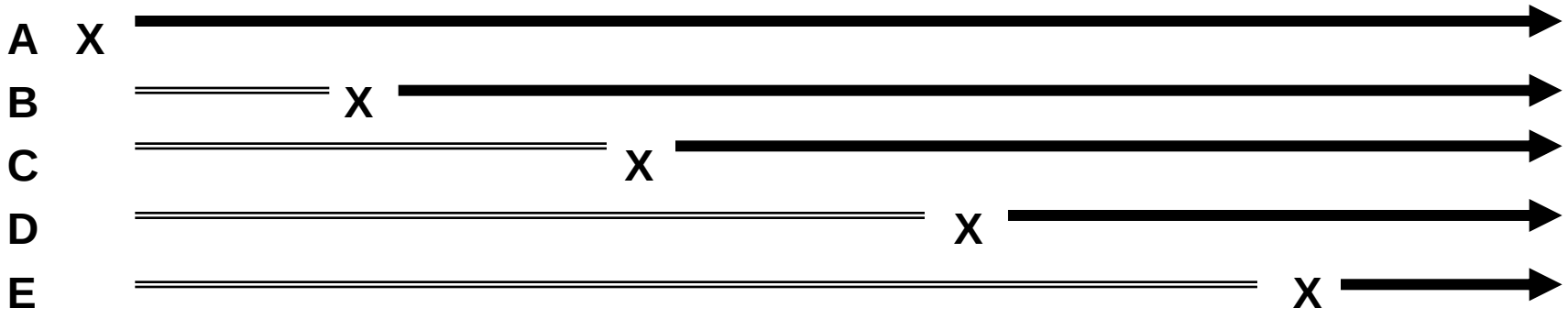
Ex: The effect of screening (mammography) on health outcome in women: women coming for screening are likely to be more health conscious and hence have a lower cancer risk.

Ex: Users versus non users of ITNs in Tanzania. Users had a 27% improved survival compared to non-users. But potential problem with selection bias (since users might be better off, etc.).



3. Stepped-wedge design (cohort)

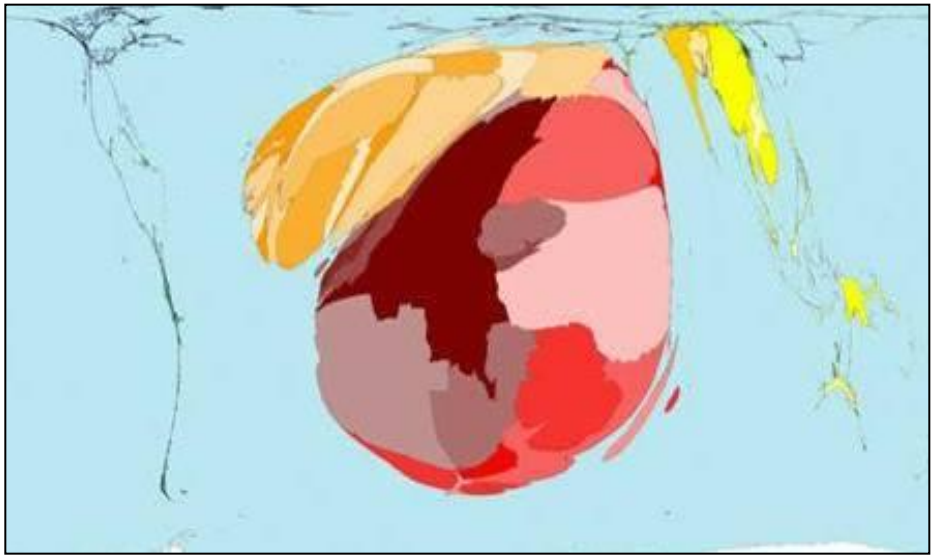
Many intervention can not be implemented instantly everywhere in a large area (for example a country). Through the phased introduction of an intervention there is a possibility to observe impact during a certain "time window" because areas without the intervention can serve as controls. The order of introduction can be randomized and then this is a very rigorous design.



Ex: THRio: a randomized phased implementation clinic-based study of a tuberculosis preventive therapy intervention in HIV+ subjects

Moulton LH, *et al*. 2007

www.worldmapper.org



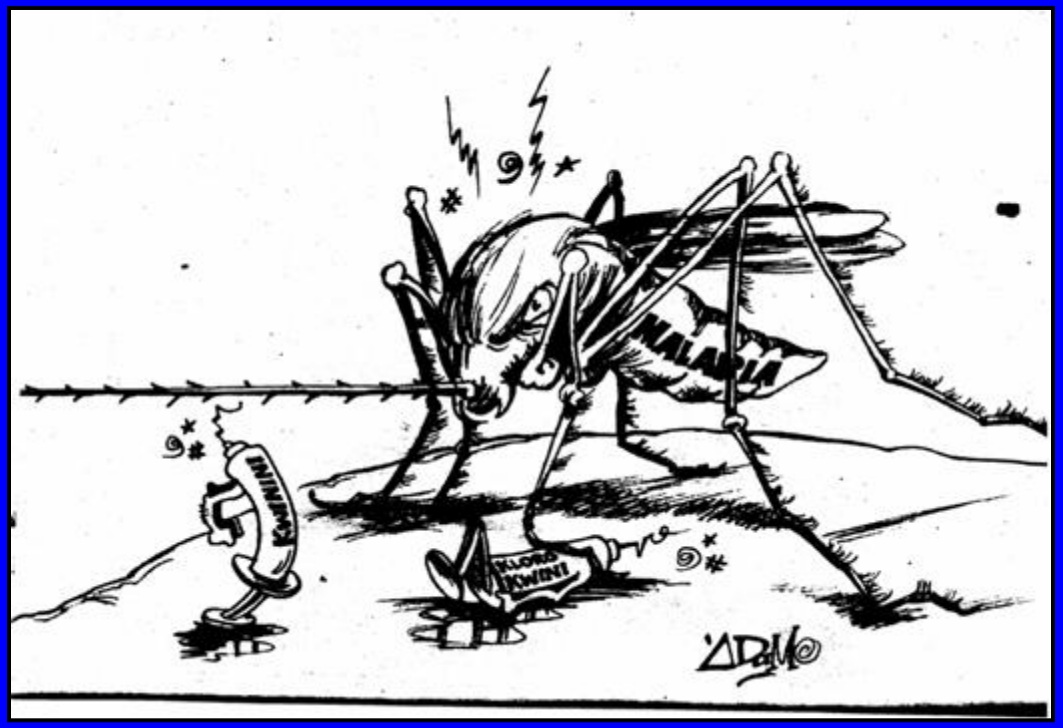
Malaria cases **Malaria deaths**

In 2015

- **214 million cases per year (vs 300 mio in 2000)**
- **438,000 deaths, mainly African children (vs 1 million in 2000 and 3 millions in 1980)**
- **2 billion people at risk of infection**

WHO - World Malaria Report 2015

The Challenge



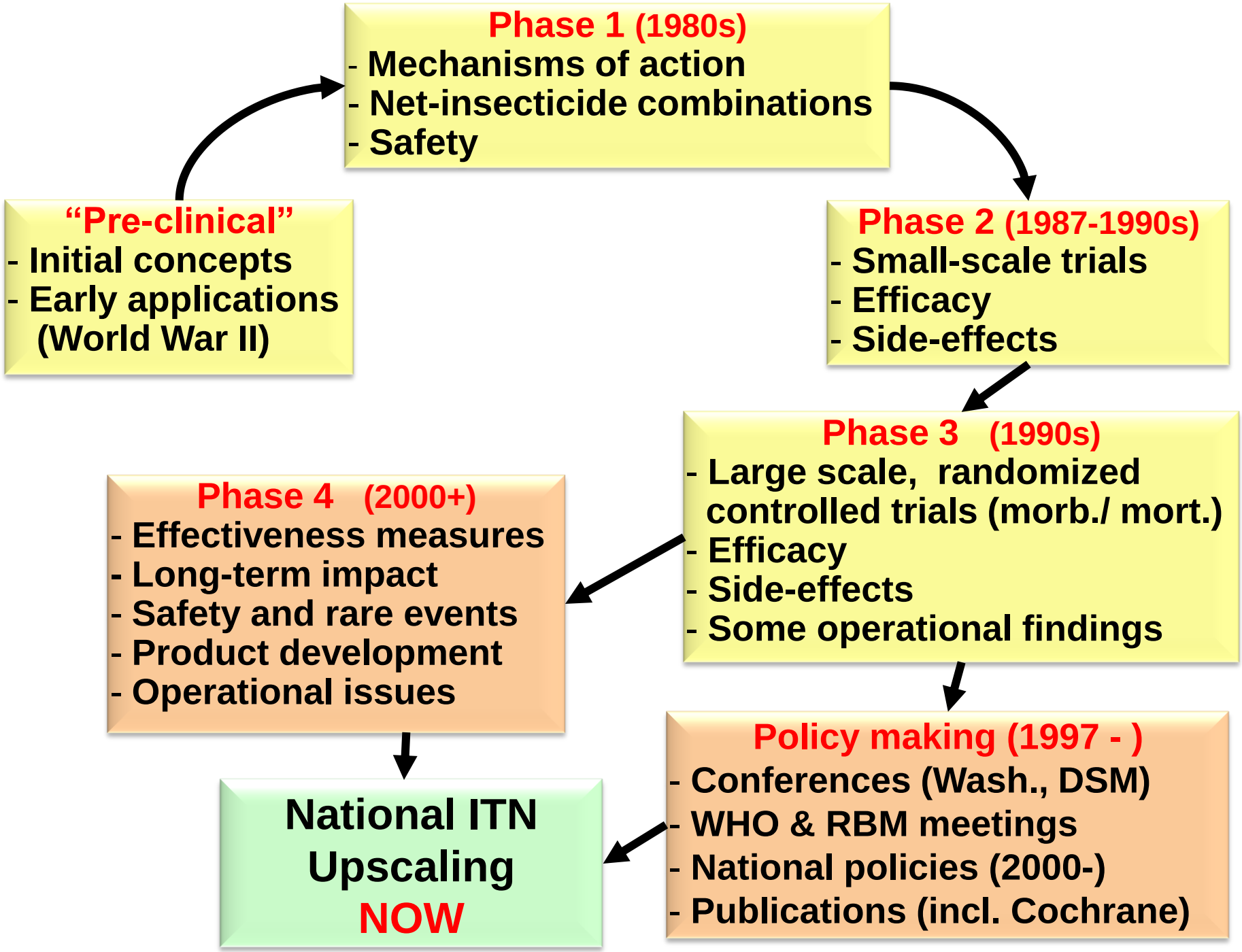
African Anophelines bite only late at night

+

A mosquito net...

treated with insecticide

= Insecticide-treated net (ITN)


Phase 1 (1980s)
- Mechanisms of action
- Net-insecticide combinations
- Safety
"Pre-clinical"
- Initial concepts
- Early applications
(World War II)
Phase 2 (1987-1990s)
- Small-scale trials
- Efficacy
- Side-effects
Phase 3 (1990s)
- Large scale, randomized controlled trials (morb./ mort.)
- Efficacy
- Side-effects
- Some operational findings
Phase 4 (2000+)
- Effectiveness measures
- Long-term impact
- Safety and rare events
- Product development
- Operational issues
Policy making (1997 -)
- Conferences (Wash., DSM)
- WHO & RBM meetings
- National policies (2000-)
- Publications (incl. Cochrane)
National ITN Upscaling NOW

Summary of impact of ITNs (Cochrane)

- **ITNs have a substantial impact on child mortality (1-59 months) in Africa: overall, there is a reduction of 18% in child mortality in 5 large-scale trials.**

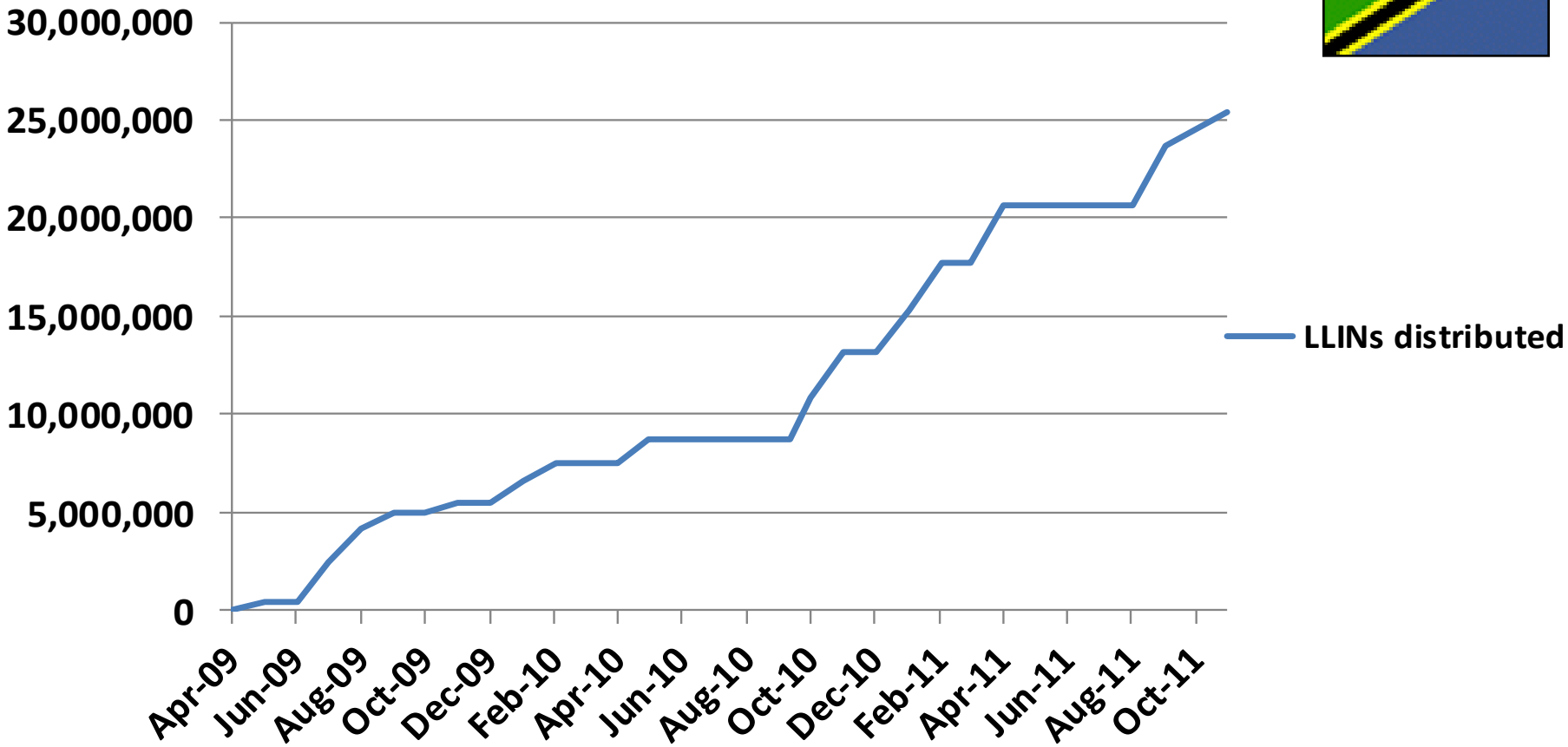
- **This is equivalent to 5.5 deaths averted per year and per 1000 protected children**

- **ITNs have a substantial impact on mild disease episodes:**

  - **In Africa: 50% reduction against *P. falciparum***
  - **In Asia and LA: 62% reduction against *P. falciparum***
  - **In Asia and LA: 52% reduction against *P. vivax***

Source: Lengeler 2004

Total LLINs distributed in 2009 - 2011

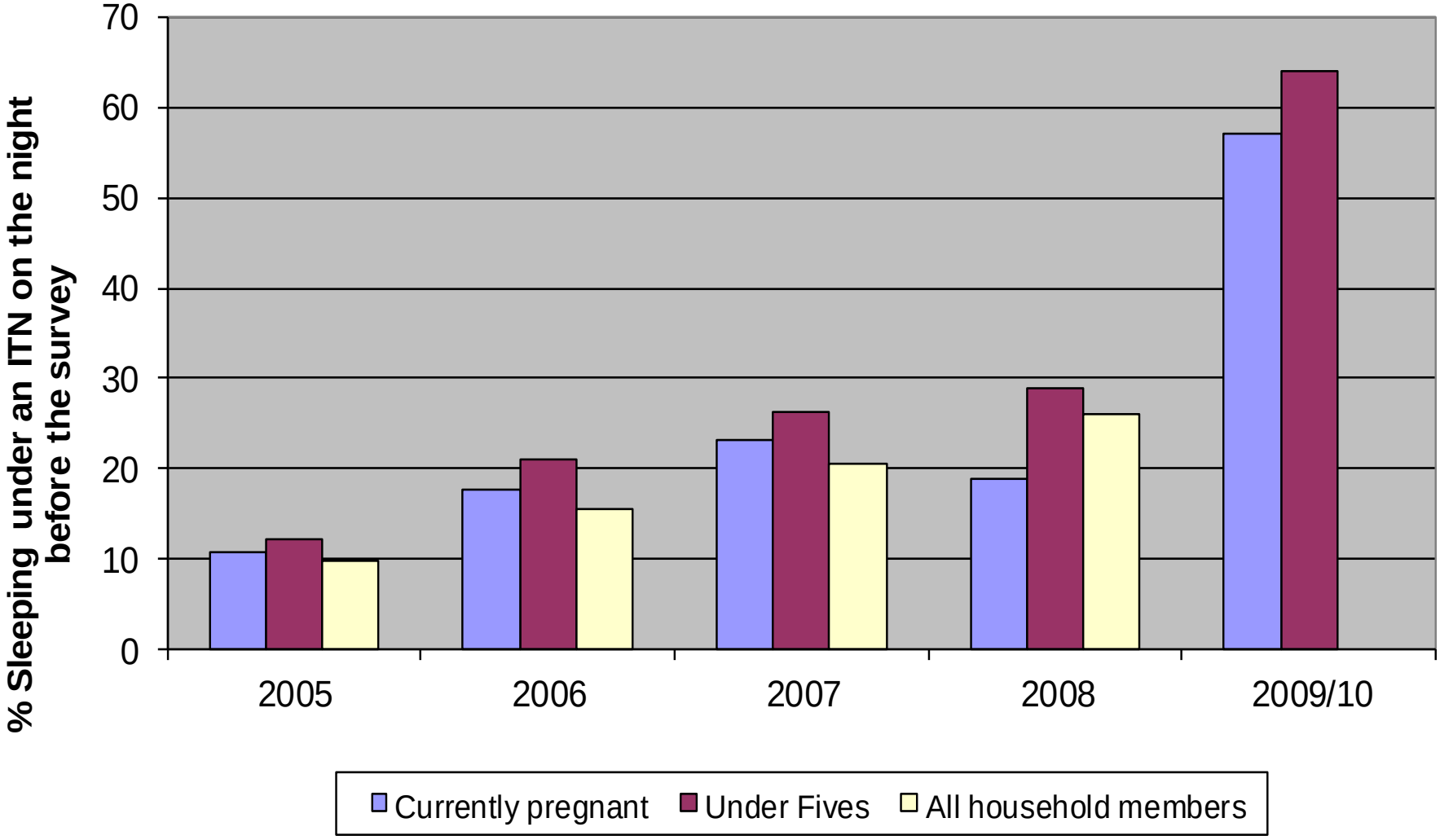


Source: ITN cell, NMCP


www.simbaoil.com

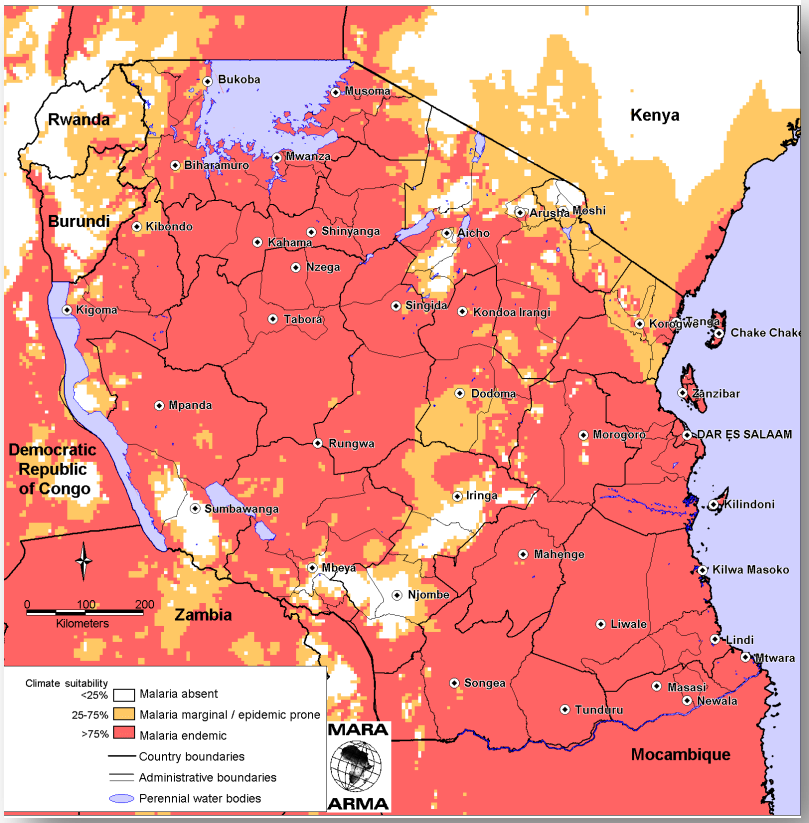
ITN Coverage for different risk groups

Source: TNVS household surveys (2005-2008) and DHS (2009-2010)
Ifakara Health Institute & London School of Hygiene Tropical Medicine



Malaria endemicity in Tanzania

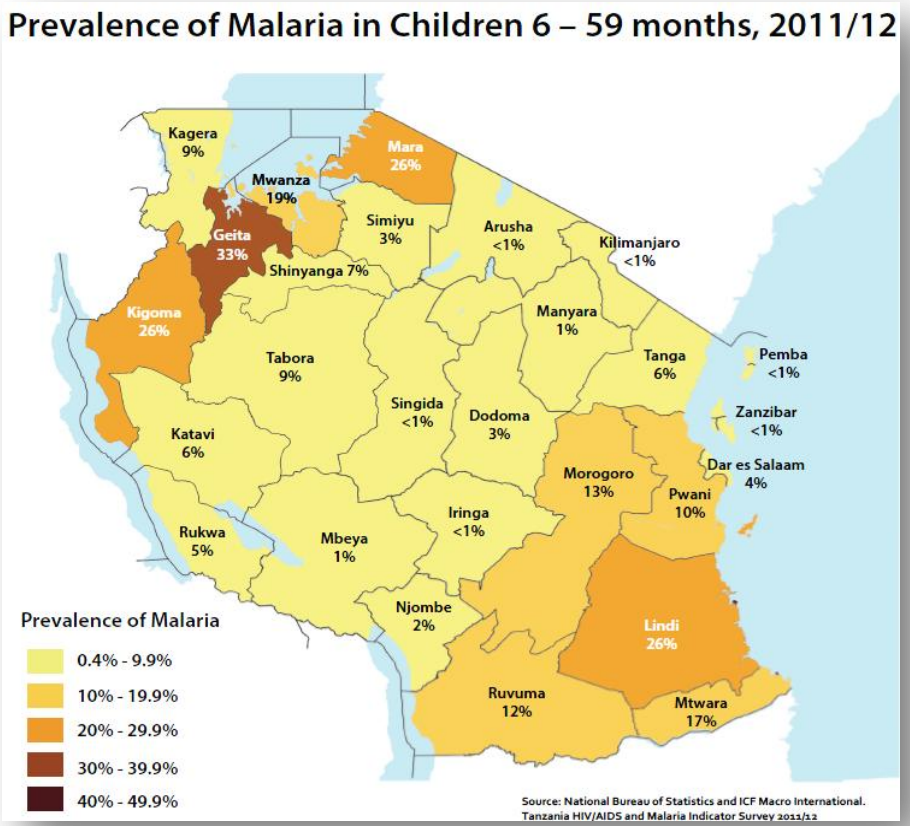
Historical situation (pre-1995)

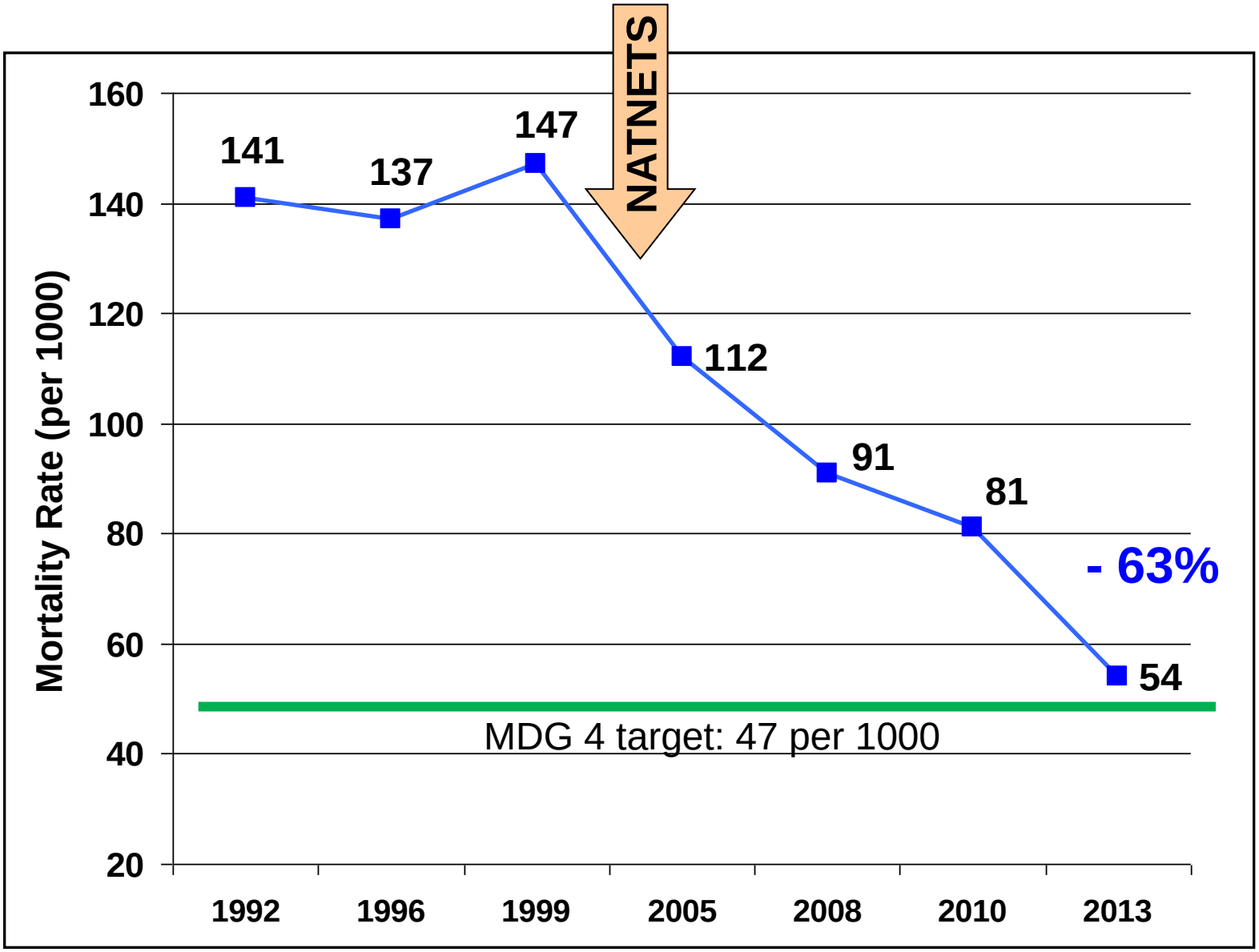


Ocre: 25-75%

Red: > 75%

Situation after first wave of control, 2012





An improvement of 63% in under 5 mortality represents
Over 130,000 deaths less each year

Tanzania DHS surveys Macro Int.

Conclusions

Swiss TPH

1. **Distinguishing between Efficacy and Effectiveness is very important in both clinical and public health settings.**

2. **The absolute impact is much more important in practice than the relative impact.**

3. **Measuring programme impact is often challenging … but it is important to understand truly how well an intervention works, and ultimately for securing long-term support.**