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

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Content

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2. Relative versus absolute risk
3. How to measure effectiveness? Evaluating public health programmes
Descriptive studies (cross-sectional & longitudinal)

Analytical studies (to test hypothesis)

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Cohort studies
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Programme implementation
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Impact evaluation
Effectiveness

Ideas
Observations

Model and formulation of hypothesis

Epidemiological study cycle
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)
Eligibility in clinical trials (Phases 1-3)

Internal vs external validity

Healthy male and female volunteers (aged 18-55 years)
**PRECIS**: qualification of Randomized Controlled Trials: How close or how far away they are from «real life»

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
Improving the intervention…

Intervention efficacy = 90%

Coverage “access”

Provider compliance

Patient adherence

Community Effectiveness 29%

Intervention efficacy = 70%

Coverage “access”

Provider compliance

Patient adherence

Community Effectiveness 22%
Intervention efficacy = 70% = Intervention efficacy = 70%

- Coverage “access”
  - Provider compliance
    - Patient adherence
      - Community Effectiveness

- Coverage “access”
  - Provider compliance
    - Patient adherence
      - Community Effectiveness

50% 70% 80% 90% 80% 90% 22% 40%

Versus improving the delivery...
Community effectiveness of malaria treatment

Alba et al. 2010

ACCESS Programme

2004 (according to current guidelines)
2008 (according to current guidelines but allowing for SP as appropriate treatment)
2008 (strictly according to current guidelines)
2. Relative versus Absolute Risk

The **Relative risk** \((I_e / I_0)\) is important for assessing exposure-outcome associations (and therefore causality). Very popular with academics.

But the **Risk Difference** \((I_e - I_0)\) 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: $\text{le} - \text{l0}$

  $$\text{NNT} = \frac{1}{\text{RD}}$$
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: \( I_e - I_0: 0.66 - 0.96 = 0.30 \)

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?

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 cannot 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.
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.
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 cannot 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
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... 

+ 

= Insecticide-treated net (ITN)

= 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 Up-scaling NOW

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
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

% Sleeping under an ITN on the night before the survey

Currently pregnant
Under Fives
All household members

% Sleeping under an ITN on the night before the survey

Ifakara Health Institute & London School of Hygiene Tropical Medicine
Malaria endemicity in Tanzania

Historical situation (pre-1995)

Situation after first wave of control, 2012

Ocre: 25-75%
Red: > 75%
An improvement of 63% in under 5 mortality represents Over 130,000 deaths less each year
Conclusions

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.