Operations Research Mini Course

University of Washington Center for AIDS Research

Scientific Program on
Health Services and Strategies Research

July 29, 2011

CFAR
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University of Washington

Agenda for the day

Time	Session	Presenter
9:00 – 9:30	Welcome, Overview, and Data Validation	Steve Gloyd, MD, MPH
9:30 – 10:45	Introduction to OR and OR Methodology	Mark Micek, MD, MPH
10:45 – 11:00	Break	
11:00 – 12:00	OR Study Methodologies: Stepped Wedge	James Hughes, PhD
12:00 – 1:00	Lunch	
1:00 – 2:00	OR Study Methodologies: Qualitative	James Pfeiffer, PhD, MPH
2:00 – 3:00	Introduction to Optimization Models	Archis Ghate, PhD
3:00 – 3:15	Break	
3:15 – 4:00	Quality Improvement	Sarah Gimbel, RN, MPH
4:00 – 4:45	OR and Policy Change	Kenneth Sherr, PhD, MPH
4:45 – 5:00	Wrap-up and Course Evaluations	Mark Micek, MD, MPH

An Introduction to Operations Research

------- or -------

How can I make my health program better?

Mark Micek, MD, MPH

Quiz: which ones are OR/IS?

1. Does male circumcision reduce risk of HIV transmission/ acquisition?
2. What is the rate of HIV resistance in the population that comes to my ART clinic?
3. Is a 3-months of INH + Rifapentine better than 9 months of INH for treatment of LTBI in Africa?
4. Can rapid CD4 tests improve the proportion of patients starting ART?
5. How can I reduce the time required to respond to disease outbreaks?
6. Can plumpy-nut reduce mortality among malnourished children in my health program?

Defining features of OR

- Focus of research
  - Health program (not epi or clinical causality)
- Goal of research
  - Help health program (not contribute to generalizable knowledge)
- Study outcomes
  - Improve process, outputs, outcomes (less impacts)
- Study designs
  - Integrated into health program (not large separate study)

Why is operations research necessary?

- What we know ≠ what we do

Quality indicator	Median (World)	Median (Low income)
Antenatal care coverage (>1 visit)	94%	71%
Births by skilled health personnel	96%	40%
Measles vaccination	92%	78%
ARVs for advanced HIV infection	30%	34%

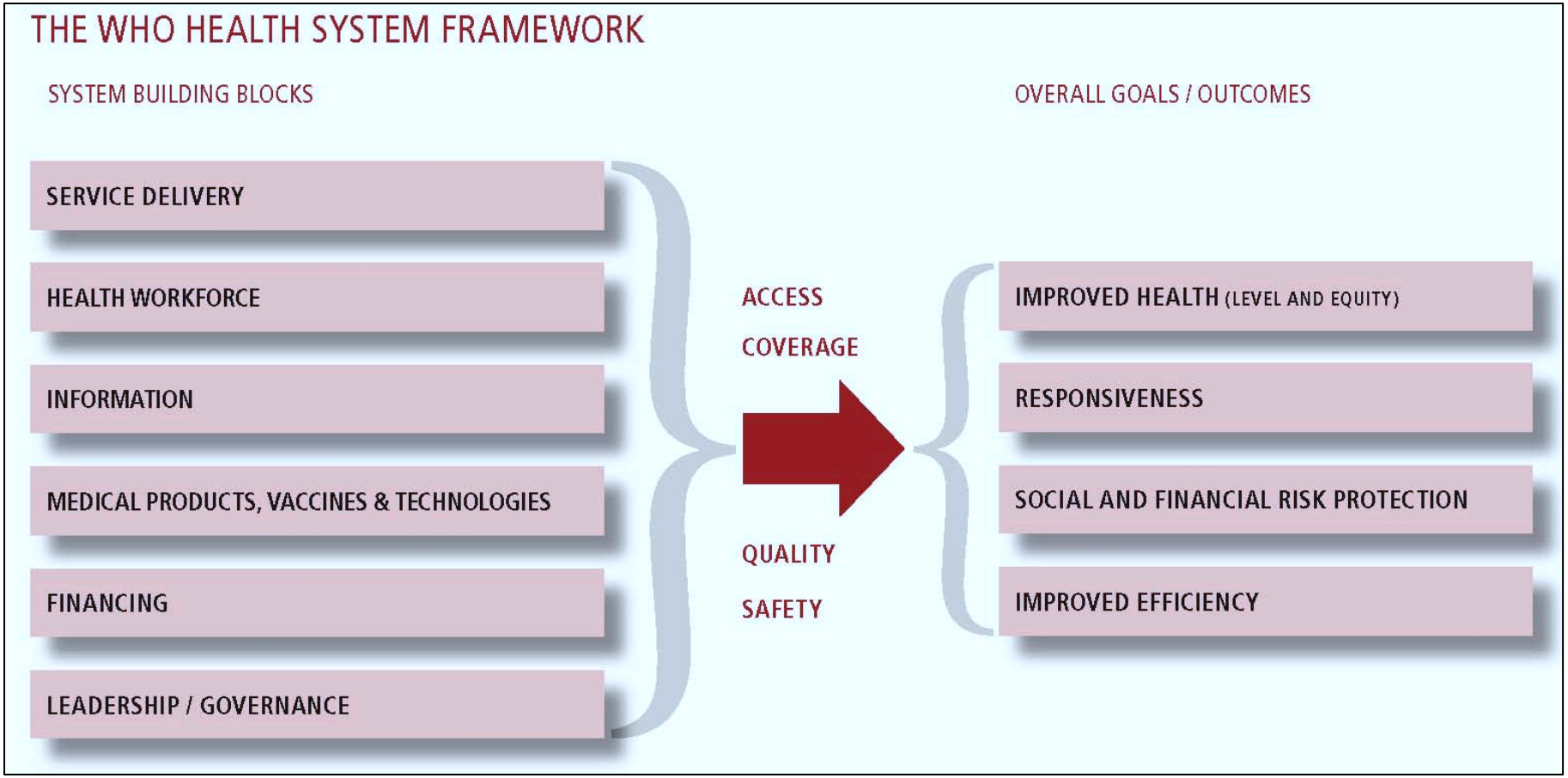
Source: WHO. World Health Statistics 2011.

Quality indicator (US)	Median 2000-2001
B-blockers <24hrs in MI	69%
Antibiotics <8hrs for pneumonia	87%
Mammogram q2yrs	60%
Lipid panel q2yrs in diabetics	60%

Source: Jenks SF et al, Change in the quality of care delivered to Medicare beneficiaries, 1998-1999 to 2000-2001. JAMA. 2003;289:305-312.

Why is it difficult to achieve targets of health care delivery?

Components of health system affect the know-do gap



Source: Measuring health systems strengthening and trends: A toolkit for countries. WHO, 2008.

Why is it difficult to achieve targets of health care delivery?

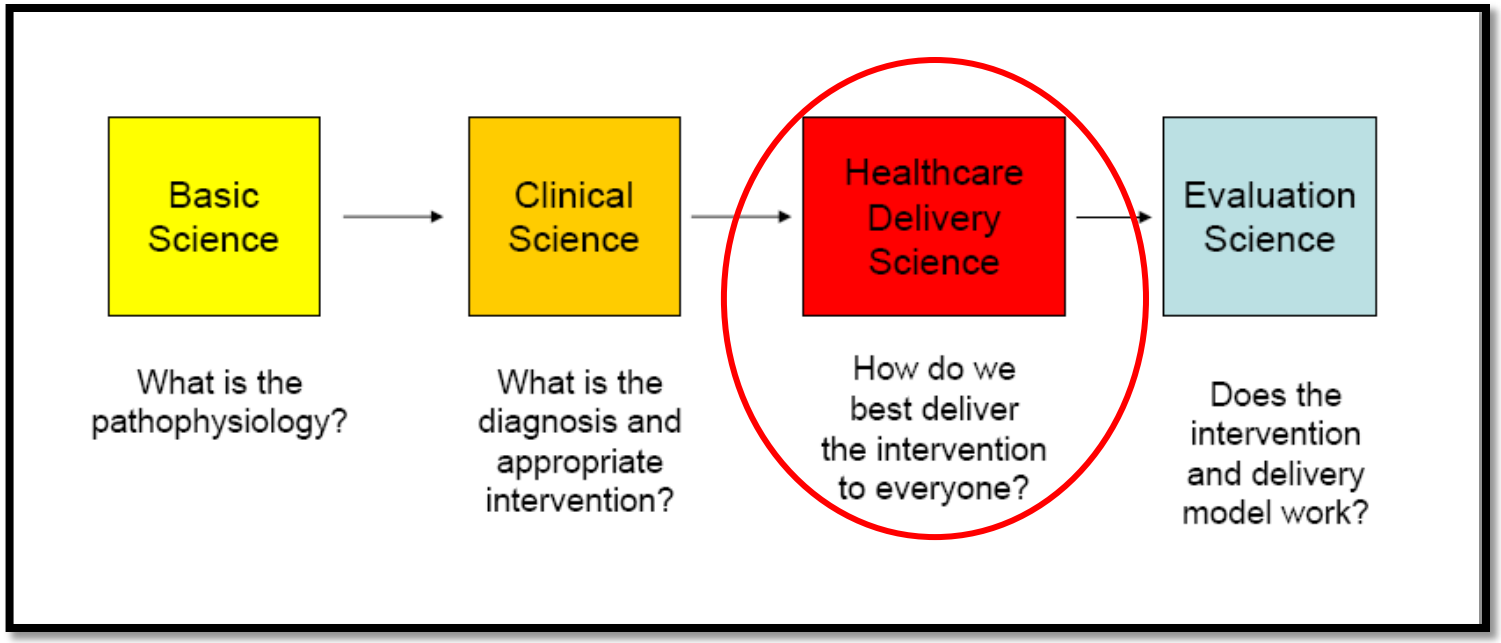
- Major constraint = weak health systems
  - Cannot provide adequate services given realities of target population
    - Human and capital resource limitations
    - Management and supervision
    - Poor process design
      - "Every process is perfectly designed to give you exactly the outcome you get." *– Don Berwick, IHI*

The question for OR/IS

- Is it possible to improve the efficiency of health programs? Even within significant resource constraints?
- If so, can research methodology help to do this?

Application of research to improve health care delivery

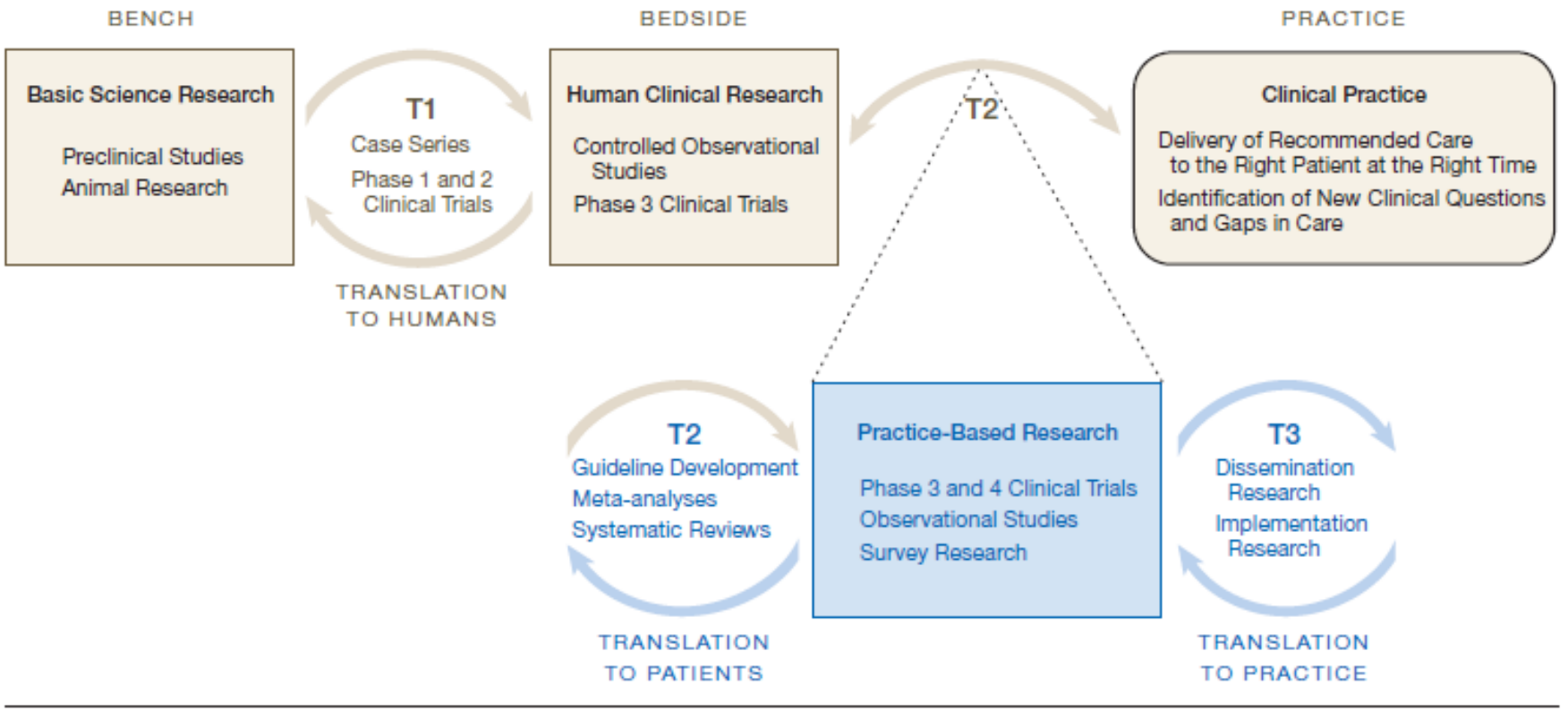
- i.e. Operations research, implementation science, translational science, health systems research, quality improvement



Source: Kim JK, Bridging the implementation gap in global health. 2nd Annual Conference on the Science of Dissemination and Implementation. Bethesda, MD; Jan 2009.

Translational research: The "T's"

Figure. "Blue Highways" on the NIH Roadmap



Source: Westfall JM et al, Practice-based research– "Blue Highways" on the NIH Roadmap. JAMA. 2007;297(4):403-406.

Is there a meaningful difference in terms?

Table 1. Defining research to improve health systems.

Research Domain	Primary Characteristic		
	Focus of the Research	**Users of the Research Outputs**	**Utility of the Research Outputs***
Operational	Operational issues of specific health programmes	Health care providers programme managers	Local
Implementation	Implementation strategies for specific products or services	Programme managers, R&D managers	Local/broad
Health System	Issues affecting some or all of the building blocks of a health system	Health system managers, policy makers	Broad

*How amenable the research outputs are to adaptation, scaling up or use or in other contexts or locations.
doi:10.1371/journal.pmed.1001000.t001

- Which is which?
  - What supervision strategy can increase rates of syphilis screening in ANC?
  - Does fragmented donor funding streams affect integration of health programs?
  - Can CD4 testing in ANC improve rates of ART among HIV+ pregnant women?

Source: Remme JHF et al, Defining research to improve health systems. PLoS Medicine. Nov 2010;7(11).

Defining features of OR

- Focus of research
  - Health systems (not epi or clinical causality)
- Goal of research
  - Help health program (not contribute to generalizable knowledge)
- Study outcomes
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- Study designs
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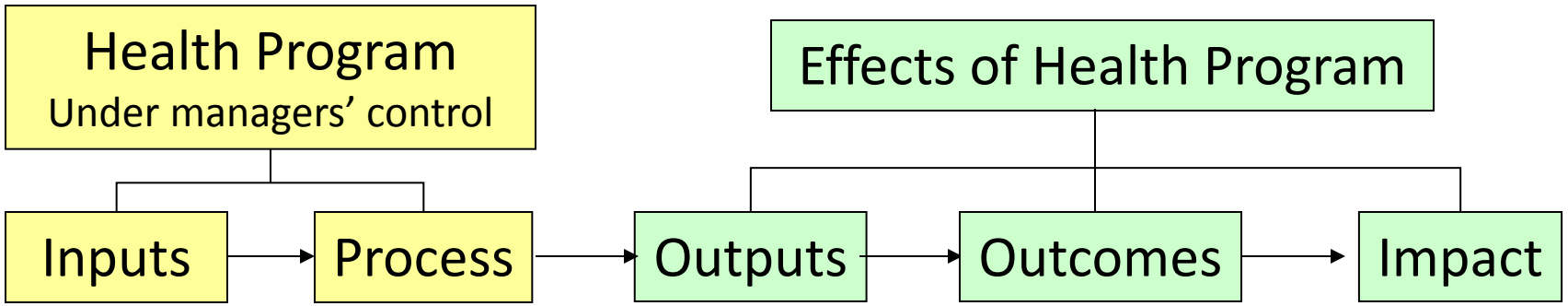
Focus of OR: Study health programs

- The health program is the focus of OR
- Start with a program problem, not a generic theoretical problem
  - Research methodology responds to the program problem
- Need to understand the workings of the health system
  - "Literature review" = understanding the program, not the disease
  - Why things are done the way they are, how they can be different
  - Flow mapping

➢ Without involvement of a health program, it's not OR

Schematic of a health system



Raw Materials:

- Finances
- Costs
- Staff
- Facilities

Activities:

- Trainings
- Supervision
- Logistics
- Reporting
- Record keeping
- Patient flow strategies

Products of program activities:

- # condoms distributed
- # people tested for HIV
- # enrolling for HIV care

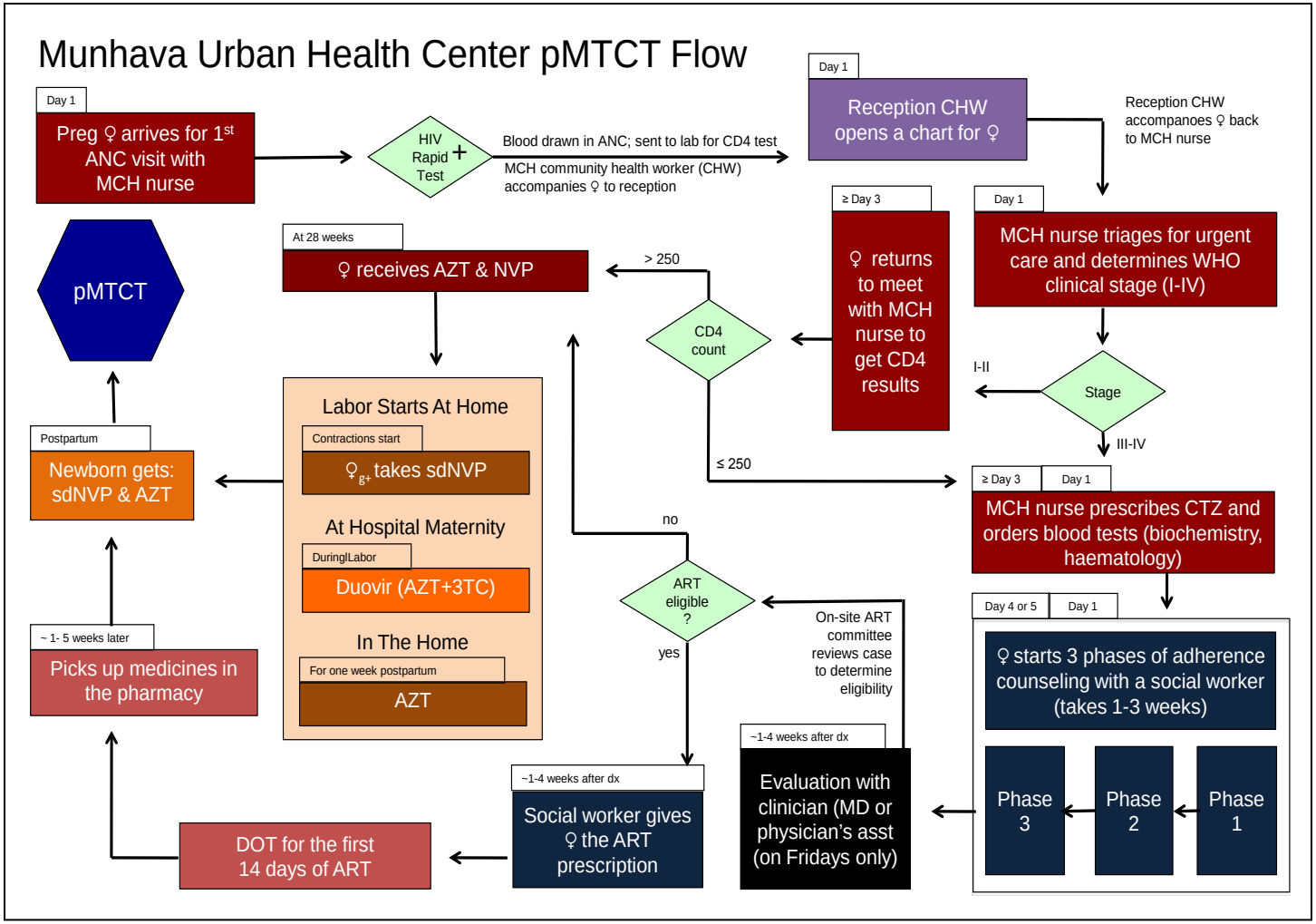
Effect on knowledge or behavior:

- # youth using condoms
- # women using pMTCT services
- # starting ART
- % adhering to ART

Change in health/well-being

- HIV/STD incidence
- # deaths

Mapping pMTCT flow in Mozambique



Goal of OR:
Make the health program better

- Better "understanding" of situation is not enough
- Better can mean…
  - Improve access to services
  - Improve quality
  - Limit costs (improve cost-effectiveness)
  - Improve health
- Use results
  - Implement new strategy on a local / national scale
  - Influence national / international policy
  - Dissemination of results, develop "best practices"

➢ OR successful only if results used to improve the program
  - Published papers are NOT a valid indicator of OR success

OR requires collaboration between managers and researchers

- Program managers & policy-makers
  - Should be involved in ALL aspects of research process
    - Understand that health care system
    - Help ensure problem is important, solutions are feasible
    - Help ensure results will be implemented
- Researchers
  - Understand research methodology
  - Responsible for recommending and implementing appropriate research techniques
- Can be the same person

Broad methodologies of OR

- Modeling (classic)
  - Develop mathematical model to mimic health care system
  - Manipulate to find the best possible “solution”
    - Optimize efficiency
    - Maximize Y given constraints X
- Intervention-based (Population Council)
  - Identify bottlenecks in service delivery
  - Design/test better ways to deliver services

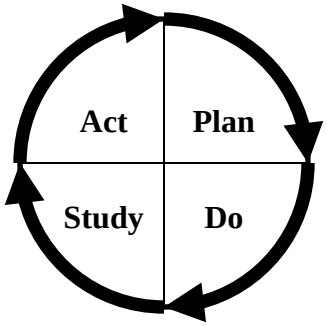
How to do OR:
Find a problem, try to fix it

Population Council
Linear

1. Identify program problem
2. Generate program solution
3. Test program solution
4. Use/disseminate results

IHI Collaborative
Cyclical

1. Plan
2. Do
3. Study
4. Act



How to do OR: HAI/UW

- Problem identification
  1. Validate data
  2. Identify variability in performance: Disaggregate
  3. Map steps/identify bottlenecks in the system: compare high and low performers, other studies as necessary (quantitative, qualitative)
- Intervention study
  4. Make changes to address bottlenecks
  5. Measure impact of changes
  6. If it works, expand changes and inform policymakers

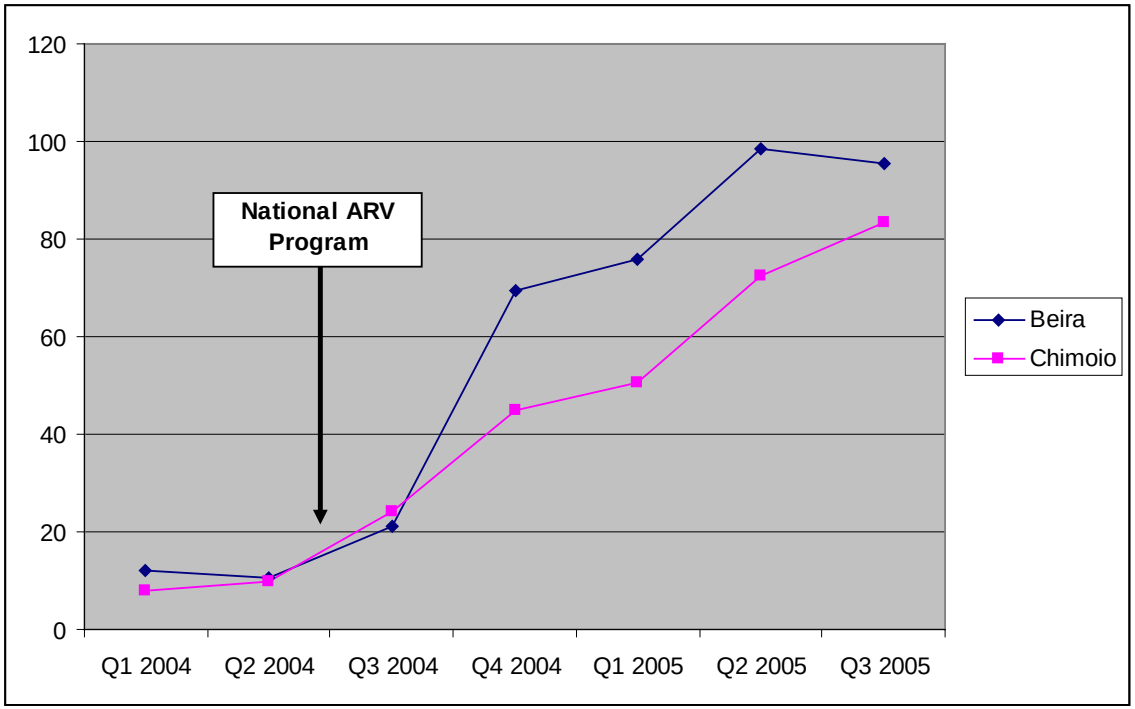
Problem identification

- Usually determined in ongoing program
- Defined by a specific indicator which is not as hoped
- Discovered by routine (M&E, surveillance) vs. non-routine (program evaluation, research study) data
- Check validity of data

- Examples:
  - Only 20% of HIV+ pregnant women start ART
  - Only 40% of women are screened for syphilis in ANC
  - NOT:
    - We need to increase TB medication adherence
    - We need a better drug to prevent pMTCT

Example of a program problem

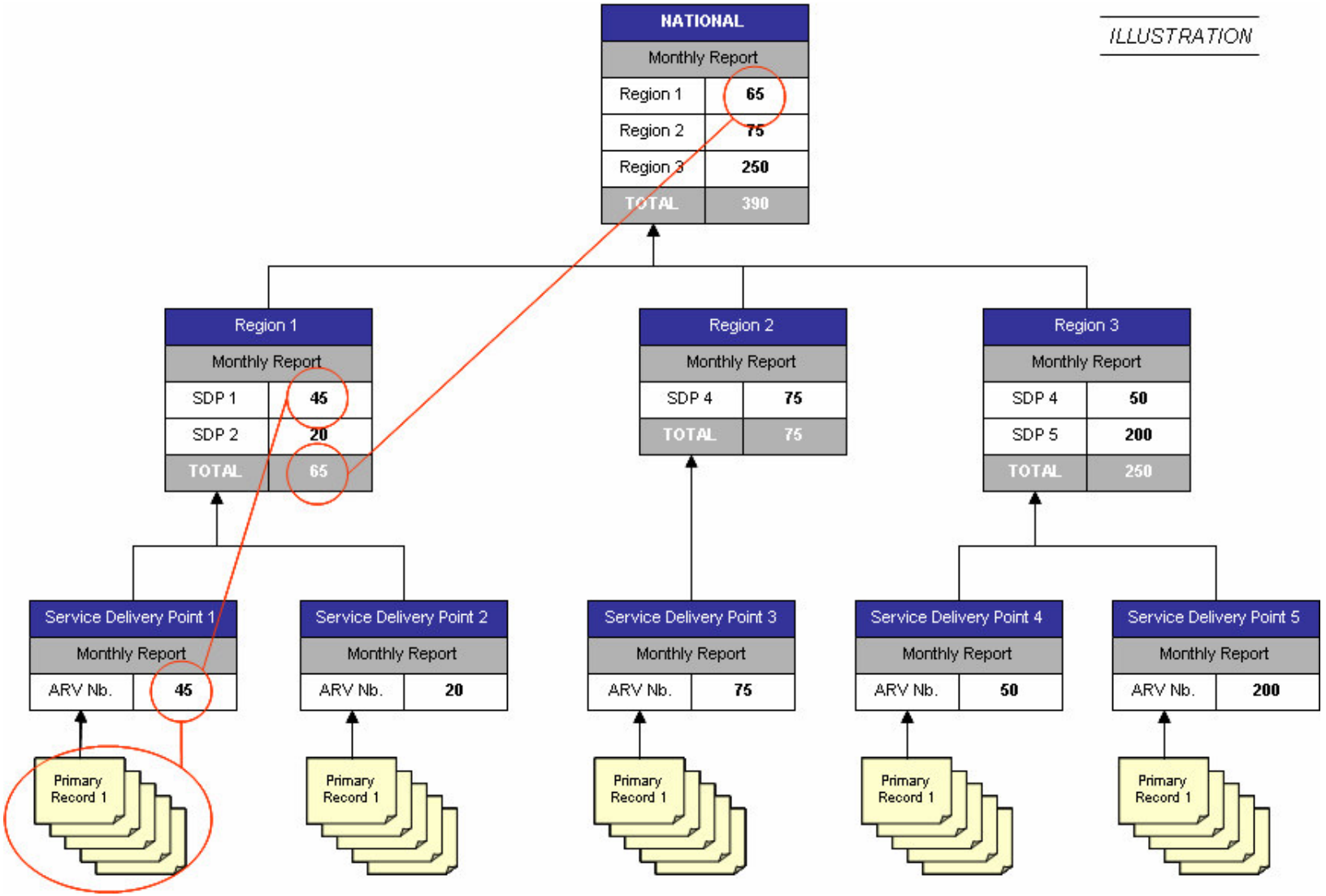
- ART medications are available to start 150 people on ART in Beira and Chimoio, but we are far short of this



OR Step #1: Validate data: Is it true?

- Ways to check health system data
  - Look for consistency over time
    - Outliers? Missing data?
    - Consistency from one level of reporting to another? (Bottom-up audit)
  - Compare data to other data sources
    - Surveys: often "gold standard" but have limitations too
    - Compare facility reports to other health systems data (patient charts, prenatal records, pharmacy records)
    - Directly observe clinical services → compare with point-of care registries

Bottom-up audit trail



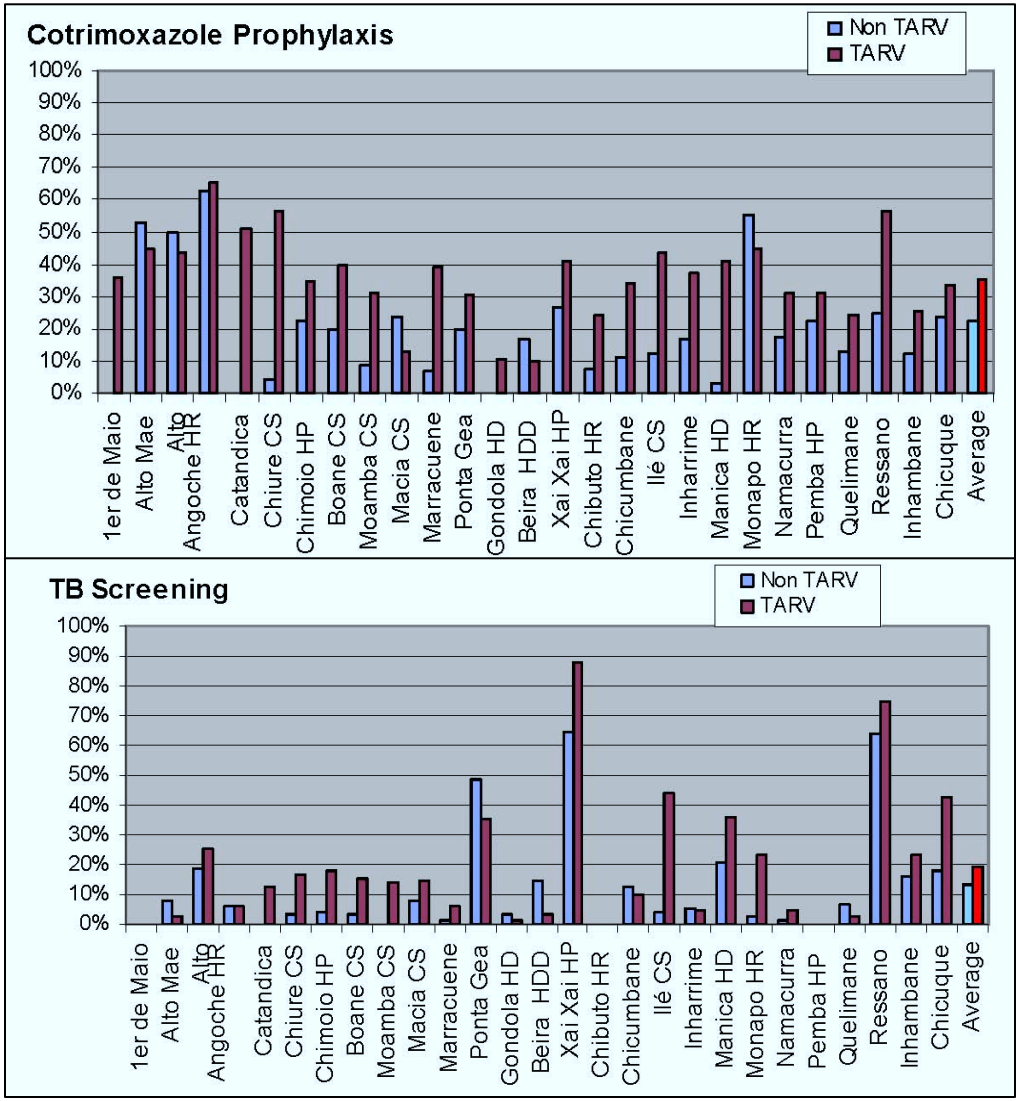
OR Step #2:
Identify variability

- Disaggregate to find out WHERE the problem is
  - Is it a problem at all sites, or only a few?

- Why do we do this?
- What does it mean?

Look and you will find

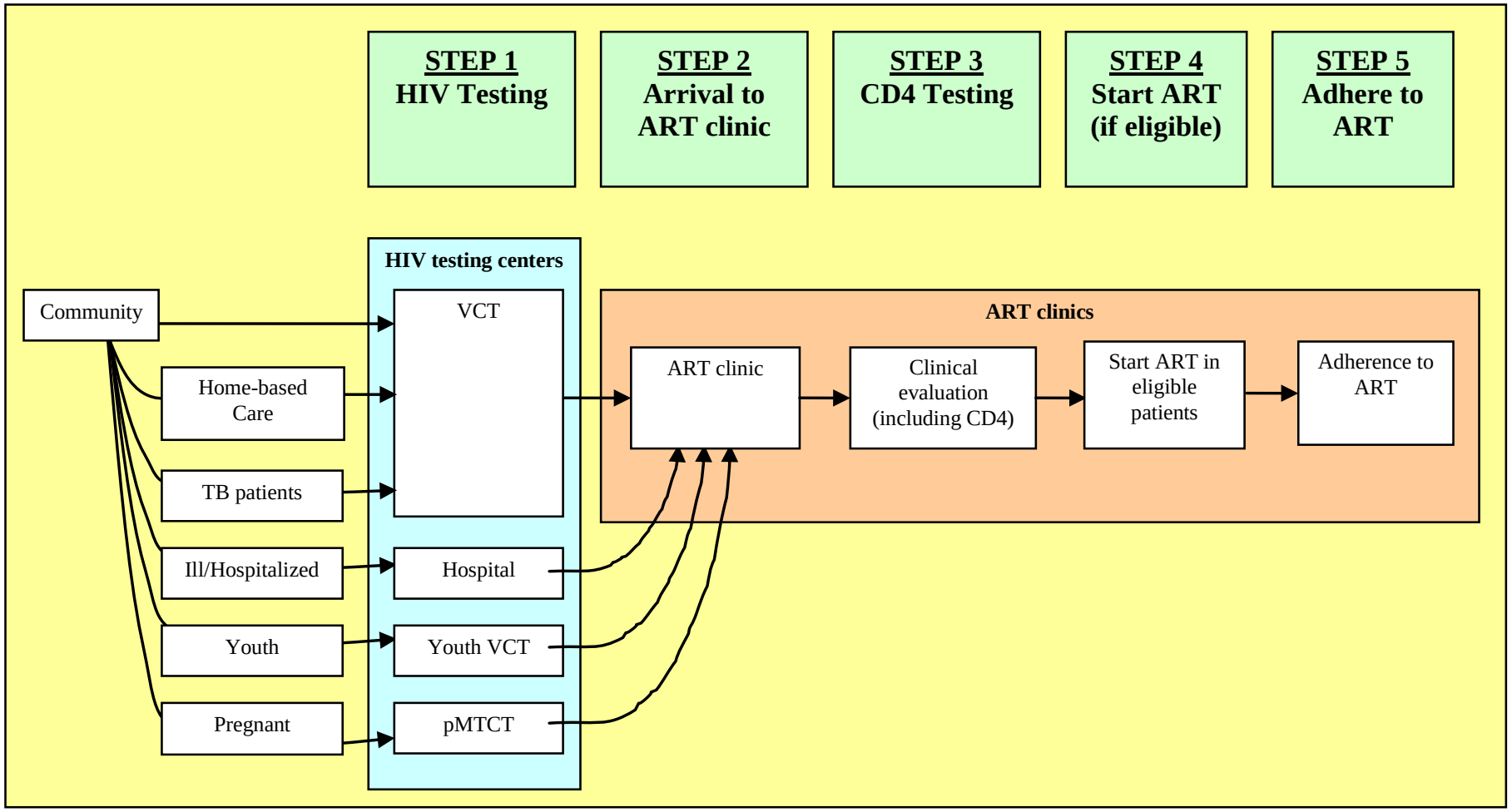
- Performance indicators in ART sites in Mozambique



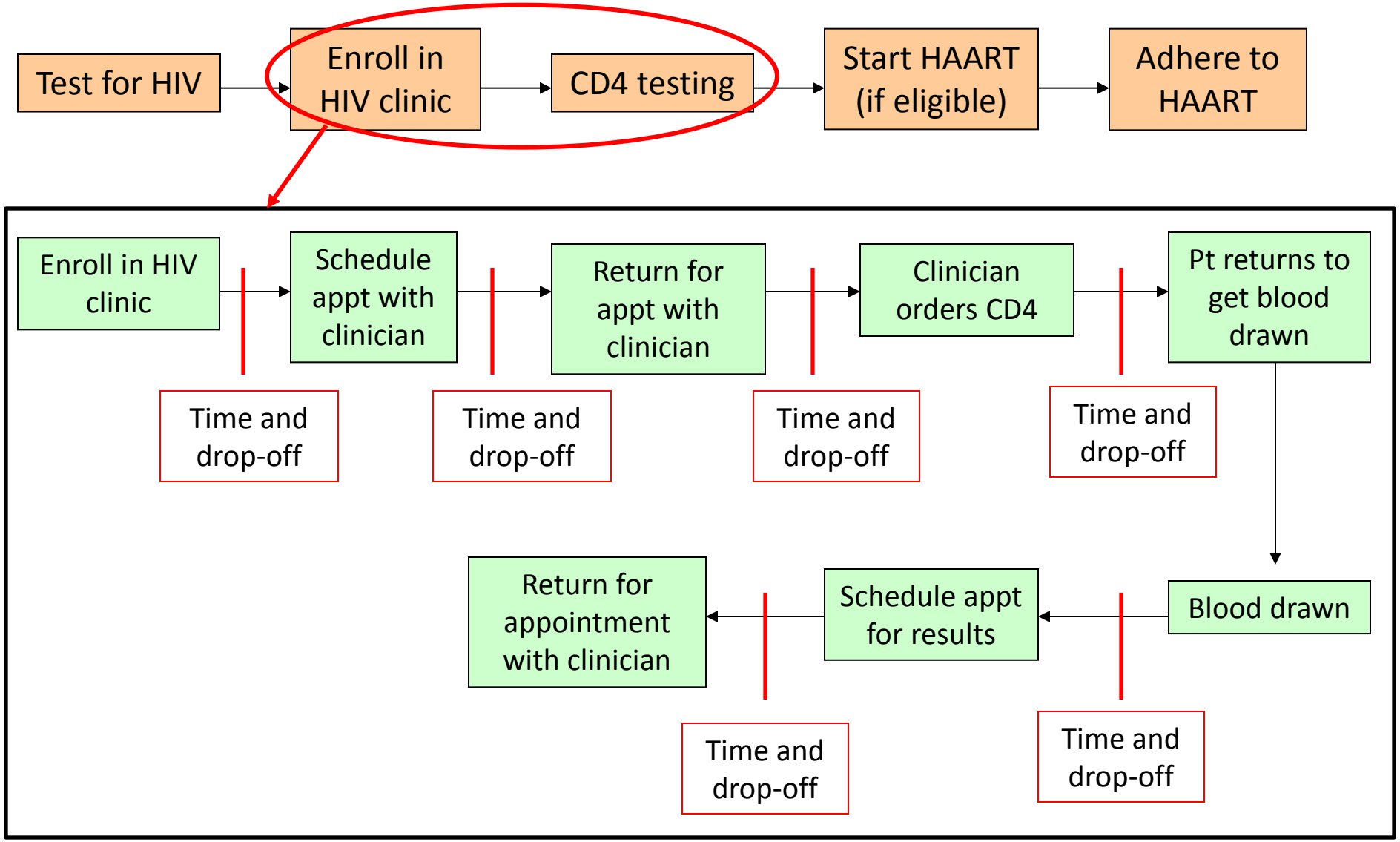
OR Step #3: Map flow & find the bottlenecks

- Mapping gives detail about what is really happening on the ground
  - Cannot do it without *observing*
- Find the bottlenecks:
  - Is the flow inefficient?
  - Compare good and bad sites- why are they different?
  - Other “exploratory” quantitative and qualitative studies

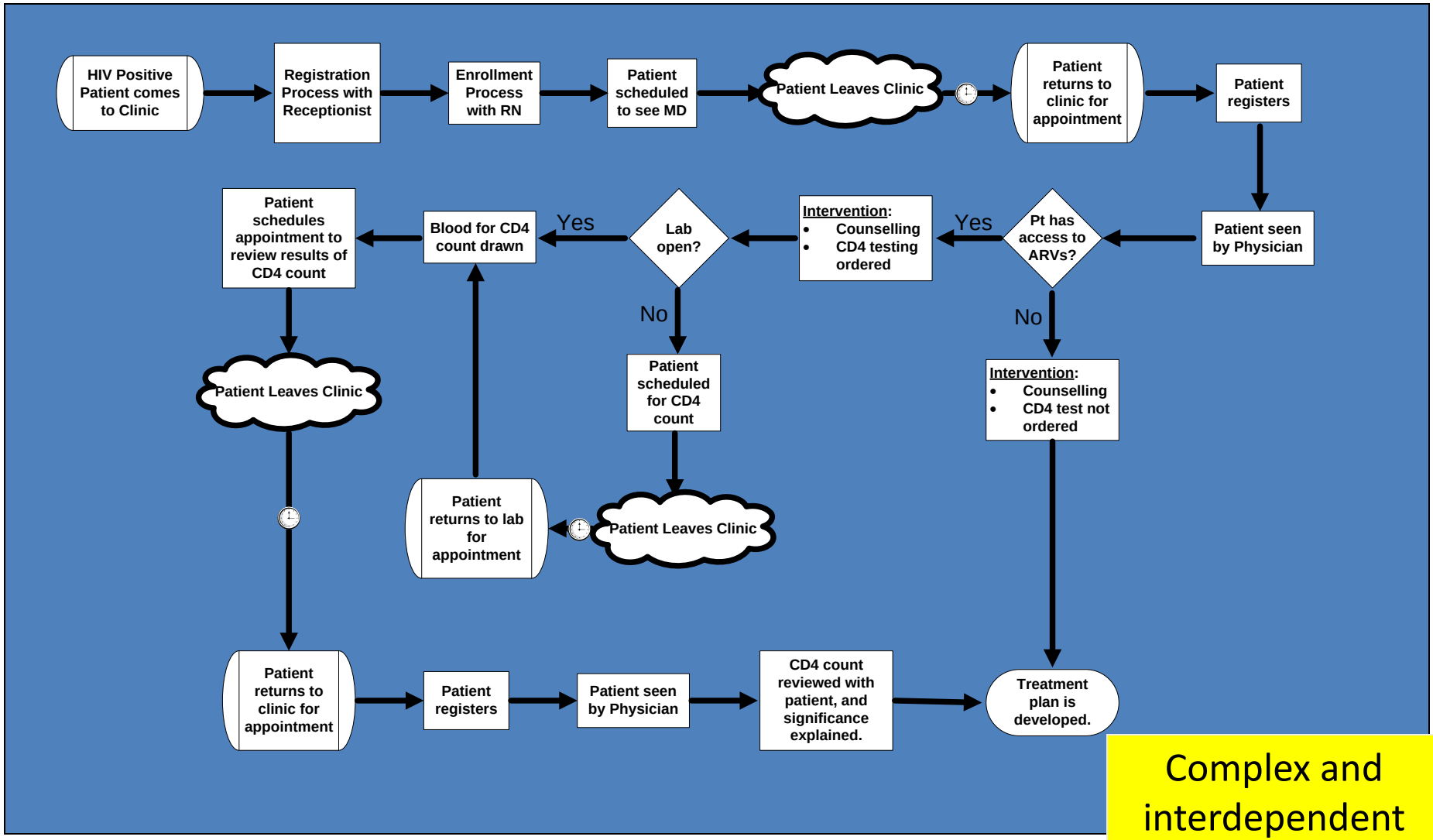
Steps towards starting ART



Health programs are complex systems

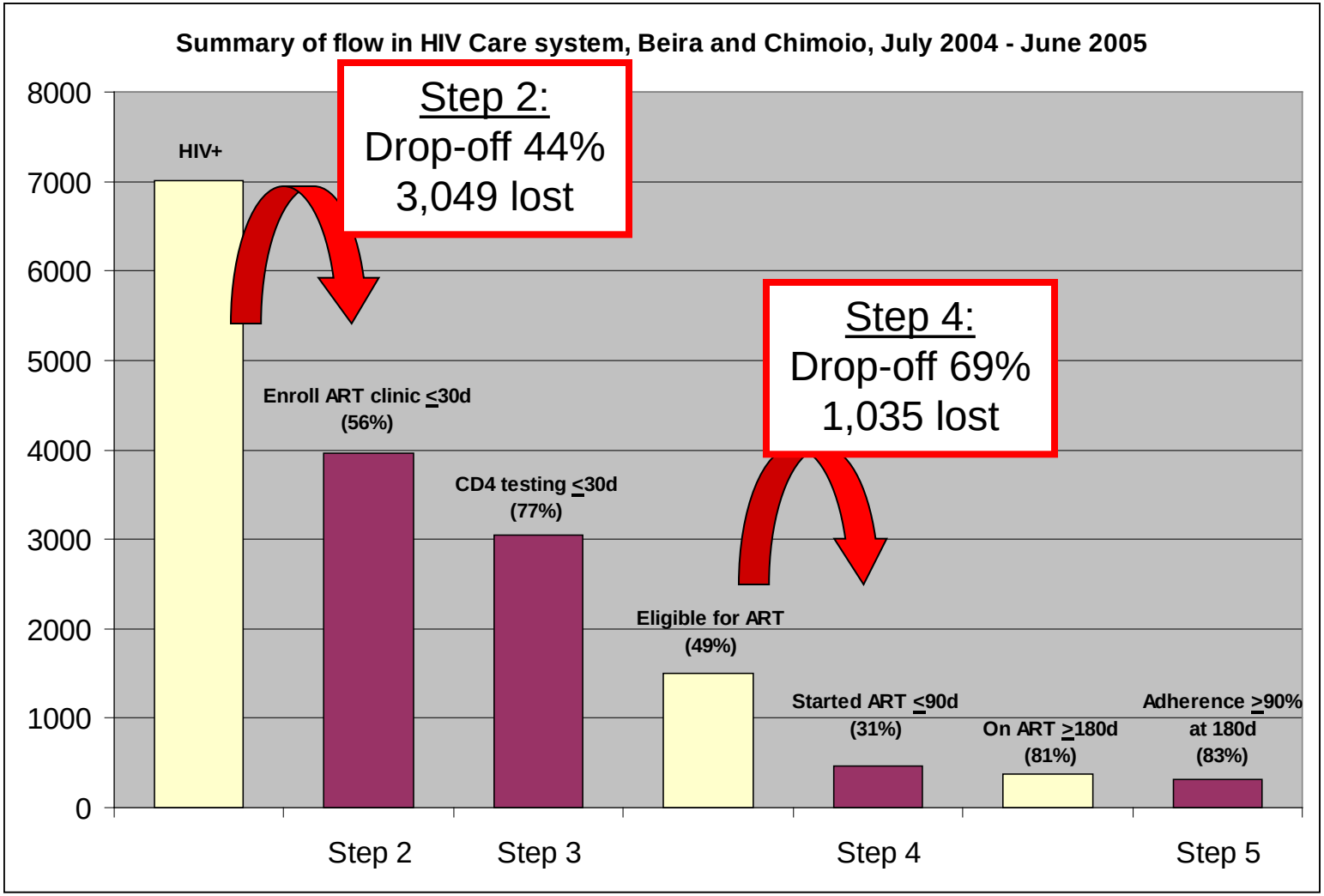


Workflow model: Obtaining a CD4



Complex and interdependent

Mapping and measuring flow



Source: Micek MA, et al, Evaluating the flow of adults in HIV care systems in Mozambique: Identifying obstacles to care. 17th International AIDS Conference, Mexico City, Mexico; August, 2008.

Flow disaggregated by HIV testing site

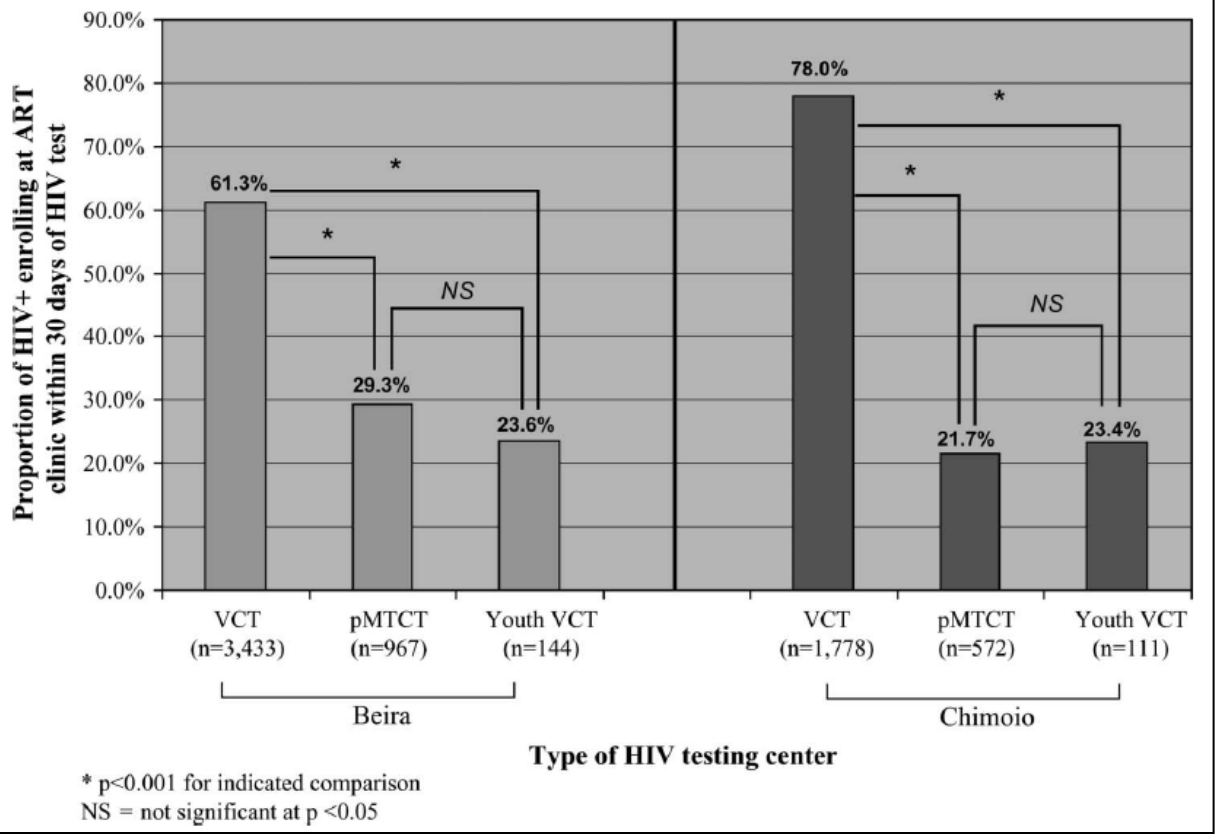


FIGURE 2. Step 2: Successful referral rates from VCT, pMTCT, and youth VCT centers in Beira and Chimoio, Mozambique. The proportion of HIV-positive people who enrolled at an ART clinic within 30 days of HIV testing differed among those tested at the various types of HIV testing centers in Beira (left section of figure) and Chimoio (right section of figure).

Source: Micek MA, et al, Loss to follow-up of adults in public HIV care systems in central Mozambique: Identifying obstacles to treatment. JAIDS. 2006;52:397-405.

Comparison of good vs. bad sites: Treatment of malnourished children*

- 11 hospitals in South Africa received training and support from university (UWC) and department of health to improve care of malnourished children (WHO 2000 guidelines)
  - Evaluation included retrospective assessments of case-fatality rates pre vs. post intervention
  - Some reduced mortality by >50%, others did not
  - ➢ WHY?

* *Puoane T et al, Why do some hospitals achieve better care of severely malnourished children than others? Health Policy and Planning, 2008. 23:428-437.*

Qualitative study

- 4 hospitals chosen: 2 “good”, 2 “bad”
  - Similarly remote, serve similar populations, staffing mix

Table 1 Case-fatality rates in 1999 (before training) and in 2002–04 (after training)[a]

Hospital	1999	2002	2003	2004
A	30%	13%	8%	6%
B	45%	14%	8%	6%[b]
C	34%	22%	32%	30%
D	36%	26%	36%	33%

[a]Three hospitals received training in November 1999 and the fourth in March 2000.
[b]Figure excludes period in unsanitary temporary accommodation (January–March).

- Methods:
  - 3-day structured observations (care, communication)
  - Quantitative data (staff, staff/pt ratios)
  - In-depth interviews & focus groups (staff, managers)

Results (1)

- Staffing and staff/pt ratios similar
- Drugs/supplies similar
- Quality indicators very different

Table 2 Indicators of quality of care from observations and record reviews in the four hospitals (June–July 2004)

Practice	Hospital A	Hospital B	Hospital C	Hospital D
Environment				
Clean	Yes	Yes	Cockroaches	Cockroaches
Warm ward	Yes	Yes	Intermittent	Intermittent
Rehydration				
Nurses responsible for dispensing oral fluid	Yes	Yes	No (mothers help themselves)	No (mothers help themselves)
Amount recorded	Yes	Yes	No	No
Diuretics avoided	Yes	Yes	Yes	No
Feeds				
Washed hands	Yes	No	No	No
Correct content	Yes	Yes	Yes	No (wrong recipe + overdiluted)
Well mixed	Yes	Yes	Yes	No (oil separates out)
Nurses use feed chart and dispense	Yes	Yes	No (mothers help themselves)	No (mothers tell nurse the volume)
Nurses supervise mothers while feeding	Yes	Yes	No	No
Fed on time	Yes	Yes	Yes	Sometimes
Intake recorded	Yes	Yes	No (or fabricated)	No (or fabricated)
Antibiotics				
Prescribed from day 1	Yes	Yes	Yes	Mostly
Correctly prescribed	Yes	Yes	Yes	No
Given on time	Yes	Yes	No	Yes
Electrolytes/minerals				
Vitamin A high dose	Yes	Yes	Yes	Mostly (but dose often incorrect)
Multivitamins	Mostly	Mostly	Yes	No
K	Yes	Yes	Some doses missed	Yes
Mg, Zn, Cu	None for 4m	Yes	Yes	Yes
Vital signs	Yes	Pulse/respirations fabricated	Pulse/respirations fabricated	Omitted except by student nurses
Toys/play	Yes	Yes	No	No
Friendly to mothers	Yes	Yes	Yes	Mostly
Shift handover				
Thorough	Yes	Yes	Yes	No (some critically ill children omitted)
All nurses attend	Most	Half	One-third	One-third

Results (2)

- Institutional culture very different
  - Attention to rehydration procedures, recording vital signs
  - Emphasis on in-service training, induction of new staff, supervision
  - Nurses' attitudes towards malnourished children
- Reflected differences in leadership, teamwork, managerial supervision & support

OR Step #4: Make changes to address bottlenecks

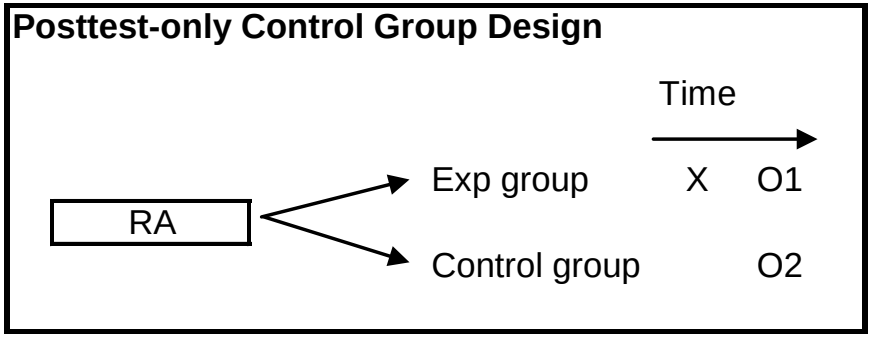
- Intervention should grow from Steps #1-3
- Inexpensive = feasible and sustainable
  - Most feasible solutions costs nothing
  - Workflow reorganization more feasible than large community-based interventions
- Must be acceptable to health workers, managers, and policy-makers
  - Higher chance of uptake after the intervention

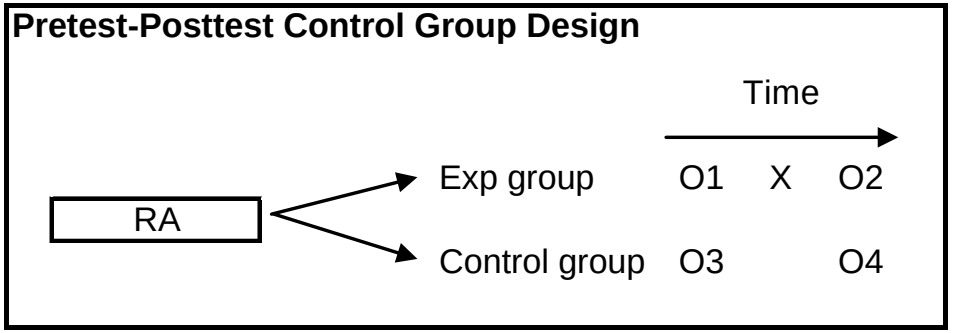
OR Step #5: Measure impact of changes

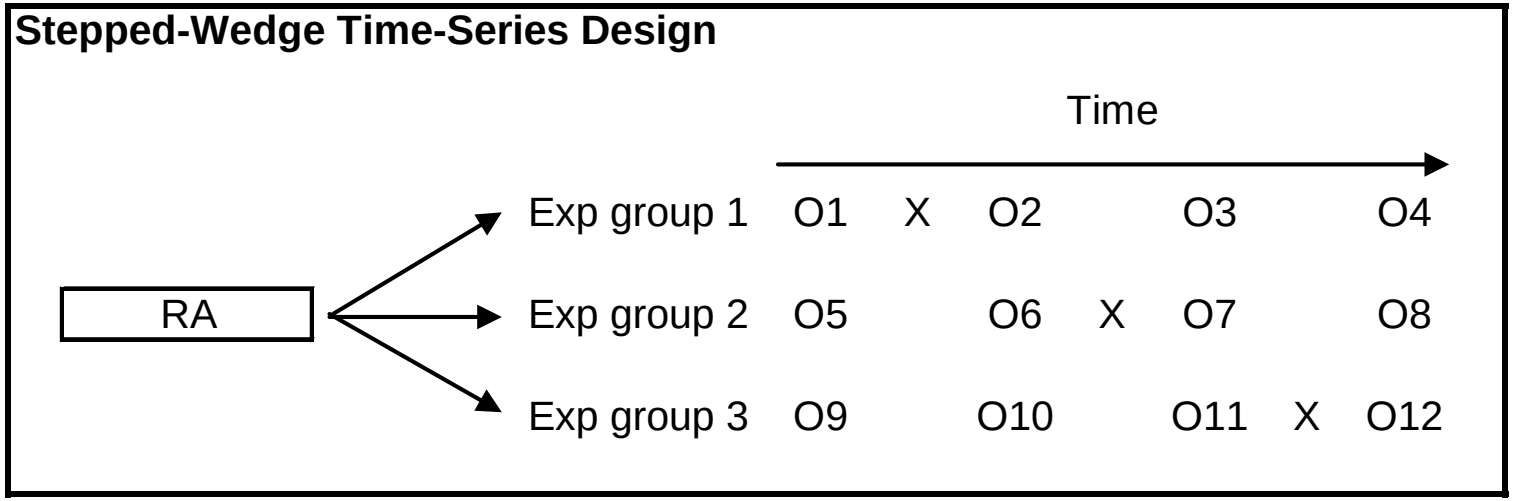
- Common attributes of OR intervention studies
  - Level of intervention: facility > intervention
  - Indicator types: outputs/outcomes > impact
  - Data measurement: routine > added procedures
  - Allocation: non-randomized > randomized

Type of study	Randomized	Good control group	Comments
Experimental	+	+	Best design; most expensive; longest duration
Quasi-experimental	-	+	Less expensive; main threat = selection bias
Non-experimental	-	-	Least valid, least expensive, often retrospective

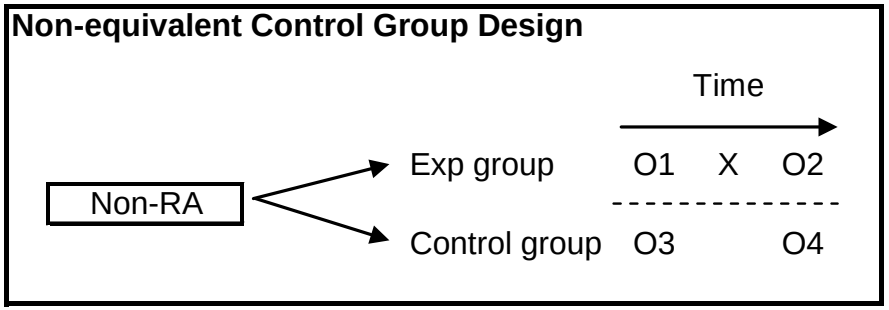
Experimental designs:
Random assignment & control group

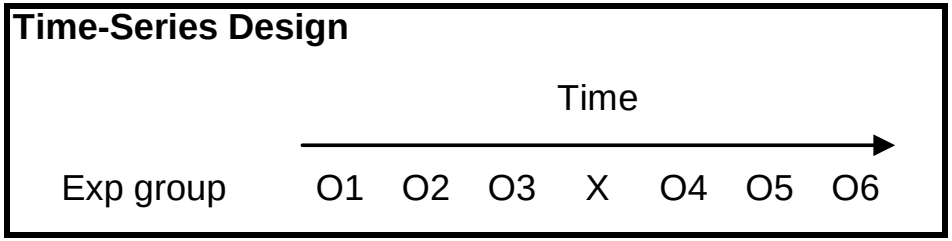


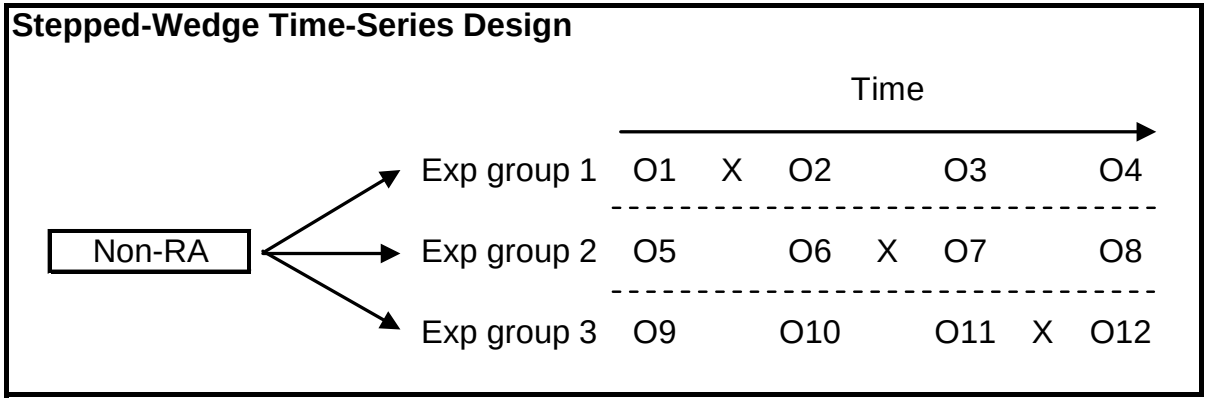




Quasi-experimental designs:
Non-random assignment & control group



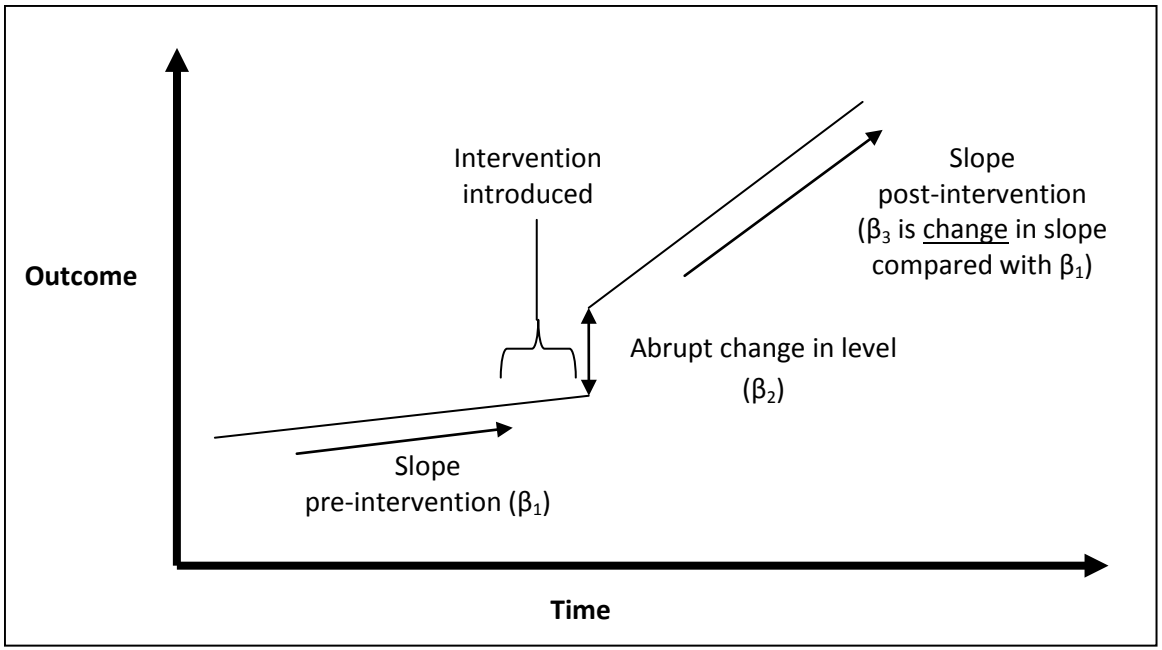




Time series design

- Helpful to analyze data with “natural” repeated measures
- One of few designs that allows following trends over time
  - Geared towards programs rather than research only
- Most valid design if only 1 site, but can also be adopted for multiple sites
- Basic concept:
  - Compare the mean of values prior to the intervention to the mean after the intervention: *just like a t-test*
  - Adjust for trends over time: *add linear regression*
  - Adjust for autocorrelation (measurements closer in time are more similar than those farther apart): *need a special function but available in Stata or SPSS*

$$Y_t = \beta_0 + \beta_1 \text{time}_t + \beta_2 \text{int}_t + \beta_3 \text{time after int}_t + e_t$$

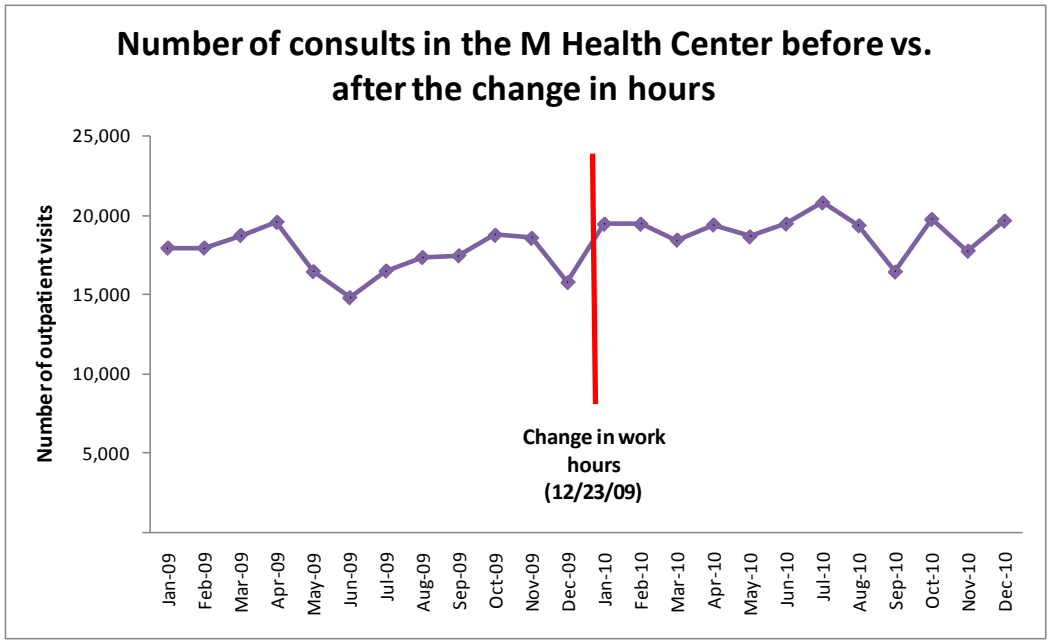


- Basically linear regression
- Data must be set up with one data-point per time period per panel (site)
- Outcome value must be numbers, means, or proportions
  - Each time-point treated as "1" observation (solves "over-power" issue of individual-level data)
  - Cannot use with individual-level data with time-series functions
- Can enter other covariates (usually vary by time period)
- Use time-series / panel-data operators to estimate e_t

Example of time-series design: Work hours extension in Mozambique

- Problem: Patients with chronic diseases not receiving enough attention in Mozambique health care system
- Intervention: MOH pilots extension of work hours in one health facility (Munhava) from 3:30pm to 7:30pm
- Research objective:
  - To determine if outpatient visits increased after the work hour extension
  - Analysis compared number of monthly visits 12 months before vs. after intervention

Results: Work hour change

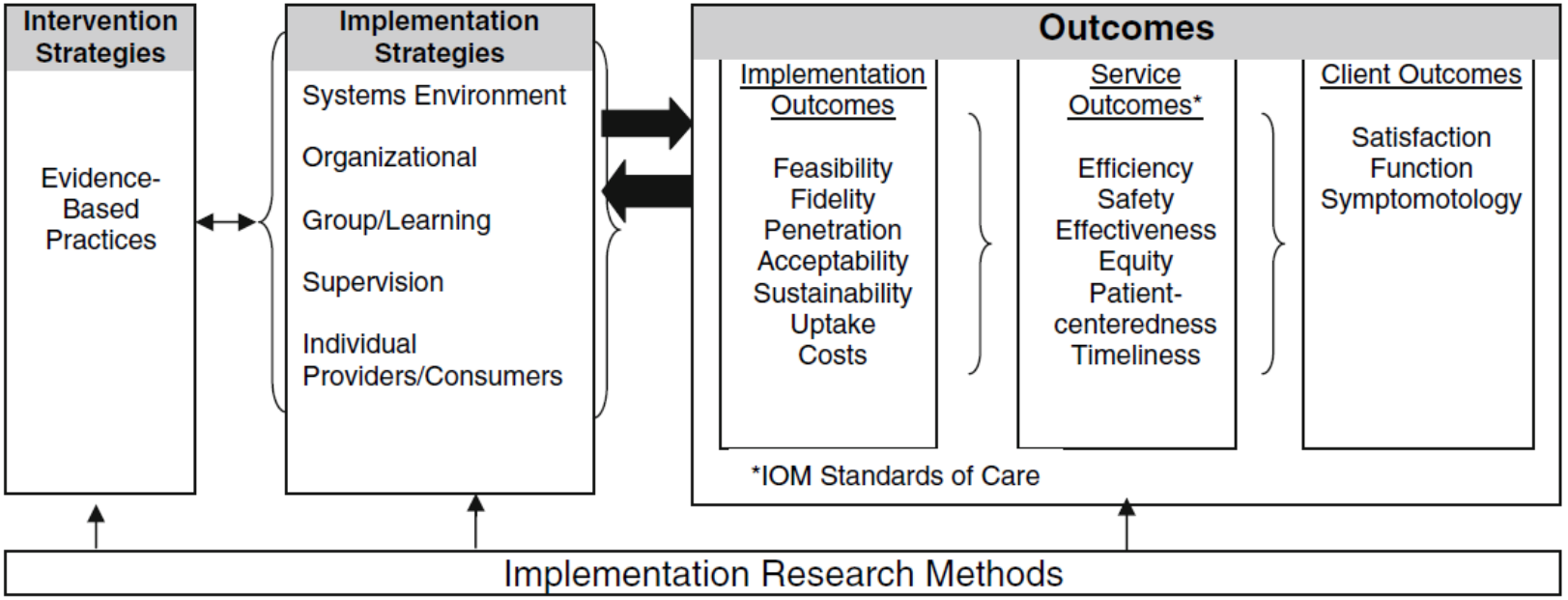


- Simple t-test: mean prior 17,490 vs. after 19,049; change = +1,559, p=0.006
- Controlled for time (regression): change = +2,395, p=0.03
- Controlled for time & autocorrelation (prais): change = +2,439, p=0.03

Another difference between OR and clinical studies

- Clinical studies: primary goal = understand causality
  - Studies are rigid, controlled, lots of study resources going into adhering to strict study protocol
- OR: primary goal = improve system
  - Rigid studies are less relevant in real world
  - Implementation of an intervention is subject to multiple influences that are difficult to control
    - These influences can become an OUTCOME of OR/IS: “What influences the implementation of my intervention?”

What influences implementation of an intervention?



Source: Proctor EK et al, Implementation research in Mental Health Services: an emerging science with conceptual, methodological, and training challenges. Adm Policy Ment Health. 2009;36:24-34.

Variation in implementation

- Often responsible for differences in outcomes
- Should have plan to measure:
  - Fidelity: whether primary components of intervention were implemented
  - Sustainability: whether intervention continues over time
  - Causes of variations (sometimes difficult to measure)
    - Staff turn-over
    - Local champion
    - Degree of supervision
    - Presence of external funding
    - ➢ Often times the most enlightening part of the study

Example of variation in implementation

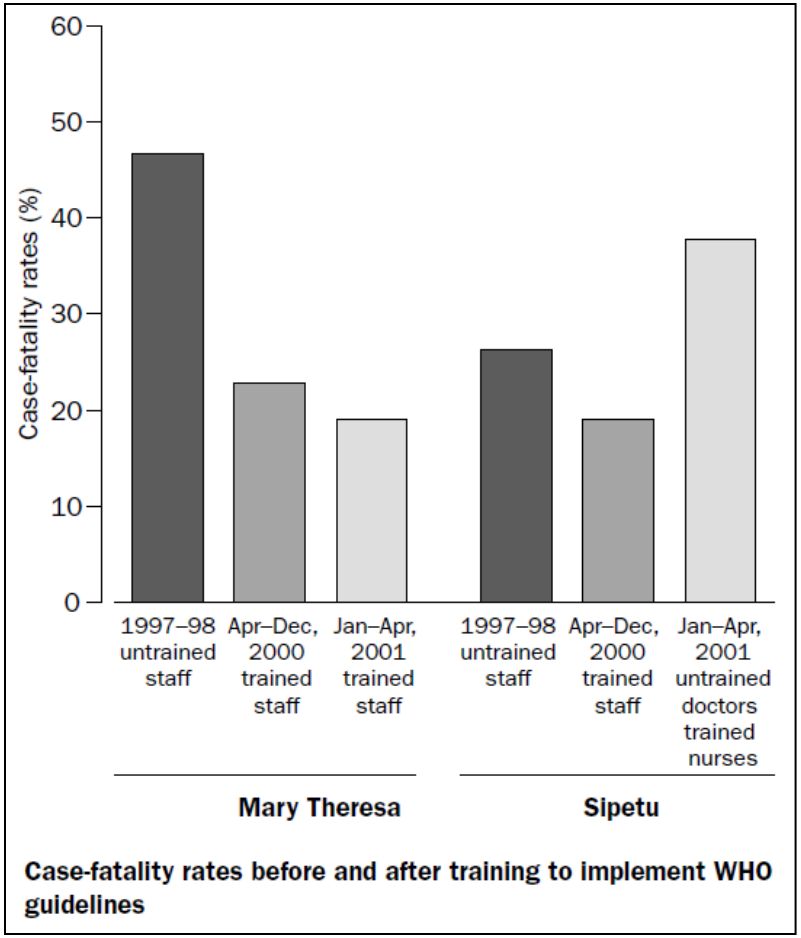
- Introduction of new WHO guidelines to manage inpatient severe malnutrition in rural South Africa*
- Intervention:
  - 2-day workshops to (1) assess local case-fatality rates, review treatment practices; and (2) explain malnutrition & guidelines, overcome barriers to adoption
  - 5 monthly 1-day visit by trainer: support, ad-hoc training, assistance in getting supplies

** Ashworth A et al, WHO guidelines for management of severe malnutrition in rural South African hospitals: effect on case fatality and the influence of operational factors. Lancet 2004;363:1110-1115.*

WHO malnutrition: Study design

- Pre-post study without control (non-experimental) in 2 rural health facilities
- Outcomes:
  - Case-fatality rates 12 months pre vs. 12 months post
  - Assessment of quality of care, adherence to guidelines (qualitative, direct observation, chart review); post-intervention phase only

Main outcomes



Case-fatality rates before and after training to implement WHO guidelines

- Case fatality decreased in MT ($p<0.02$), and initially decreased in S ($p=0.28$) but then rose ($p=0.01$)
- Many barriers to implementation identified in both sites
- Most deaths due to MD error (esp S in last period), coincided with changeover of 2 MDs who were not trained → less appropriate antibiotic coverage

OR Step #6:
Expand changes & inform policymakers

- Continue / expand successful interventions
- Influence national / international policy
- OR not typically generalizable, but can be relevant for similar programs (“best practices”)
- A measure of OR success = adoption, change
  - What makes OR more usable?

OR Example: Increasing ART in HIV+ pregnant women*

- Program problem: small proportion of HIV+ pregnant women start ART during pregnancy (<3%)
  - ART clinic physically separate from ANC care (although within same facility)
  - ART team = health officer, counselor, peer educator
  - CD4 done in ANC, then referred to ART clinic

- Potential solution: ART integrated in ANC clinics
  - ART team visits ANC clinic 1-2 days per week

** Killam WP et al, Antiretroviral therapy in antenatal care to increase treatment initiation in HIV infected pregnant women: a stepped-wedge evaluation. AIDS. 2010;24(1):85-91.*

Study design: Stepped-wedge

- Stepped implementation into 8 clinics in Lusaka
- CD4 done in ANC
- Study followed ART-eligible women with CD4<250
  - Deals with policy change to <350 during implementation
- Study outcomes
  - ART clinic enrollment <60 days after CD4 count
    - Deals with contamination during implementation of new strategy
  - ART initiated prior to delivery
- Routine data (retrospective)

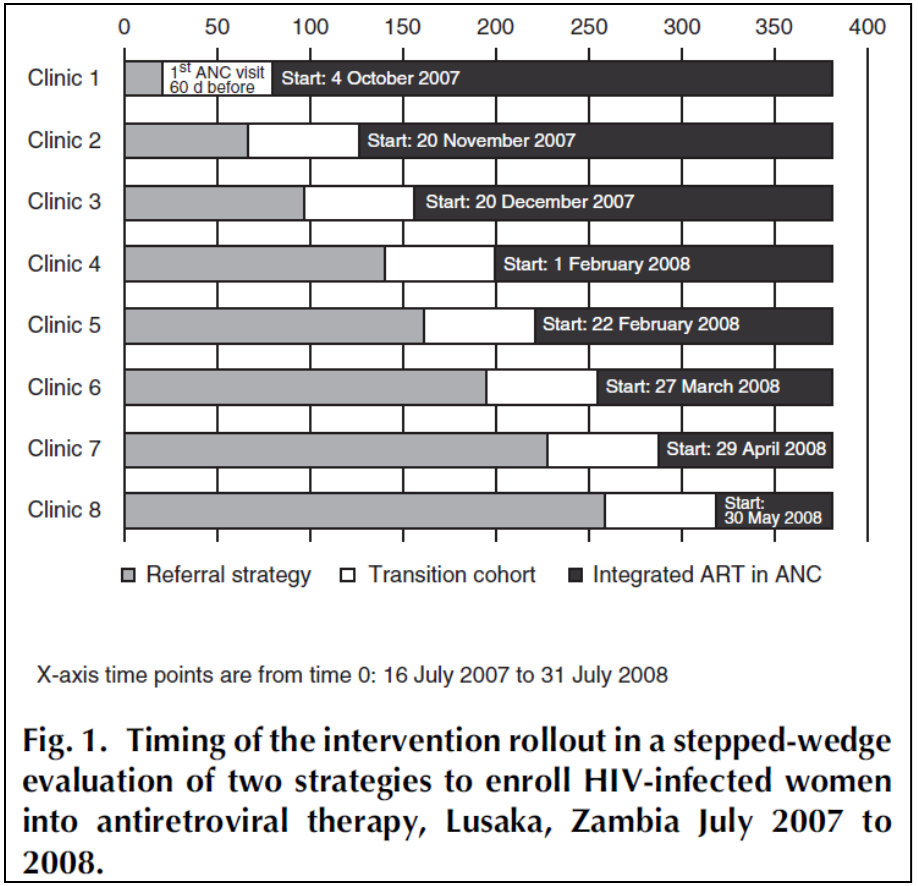


Fig. 1. Timing of the intervention rollout in a stepped-wedge evaluation of two strategies to enroll HIV-infected women into antiretroviral therapy, Lusaka, Zambia July 2007 to 2008.

Results

- Increased proportion of ART-eligible women starting ART prior to delivery

Table 3. Enrollment and ART initiation outcome of ART eligible patients by strategy cohort.

Outcomes	Referral to ART (control), $n = 716$	ART in ANC (intervention), $n = 846$	Crude OR (95% CI)	Adjusted OR[a] (95% CI)
Enrolled on ART (within 60 days and before delivery or EDD) [n (%)]	181 (25.3)	376 (44.4)	2.36 (1.90–2.94)	2.06 (1.27–3.34)
Initiated on ART (within 60 days and before delivery or EDD) [n (%)]	103 (14.4)	278 (32.9)	2.91 (2.26–3.75)	2.01 (1.37–2.95)

ANC, antenatal care; ART, antiretroviral therapy; CI, confidence interval; EDD, estimated date of delivery.
[a]Odds ratio (OR) adjusted for clinic site cluster and time effects.

- 90-day ART retention rates similar in pre/post cohorts (91.3% vs. 87.8%, p=0.3)

OR Example: Strategy to increase MCH service utilization in Senegal*

- Program problem: Low utilization of available MCH services in health units
  - Pre/post natal visits
  - Child vaccinations
  - STD testing & treatment
  - Child growth monitoring
  - Family planning

** Sanogo D, et al, Using Systematic Screening to Increase Integration of Reproductive Health Services Delivery in Senegal, Frontiers in Reproductive Health Program, 2005.*

Interventional study

- Potential solution: Integration of services via "check-list"
  - Used during outpatient visits
  - Serves as clinical reminder
  - Improve documentation of services provided

Figure 1.
Short screening checklist used in Senegal

To be filled in by screener **Client's age** _____		**Principal reason for visit** _____ _____		
Before the consultation, always ask the client if, in addition to the principal reason for her visit, she would like to receive one of the following services (circle number)		*After the consultation, always note the result of the visit (write the number of the corresponding code)*		
		1 Offered	2 Appointment	3 Referral
1	Prenatal consultation			
2	Vaccination for tetanus			
3	Postnatal consultation			
4	Family planning			
5	Screening or treatment for RTI/STI			
6	Vaccination of child			
7	Growth monitoring of child			

Source: Sanogo et al. 2005.

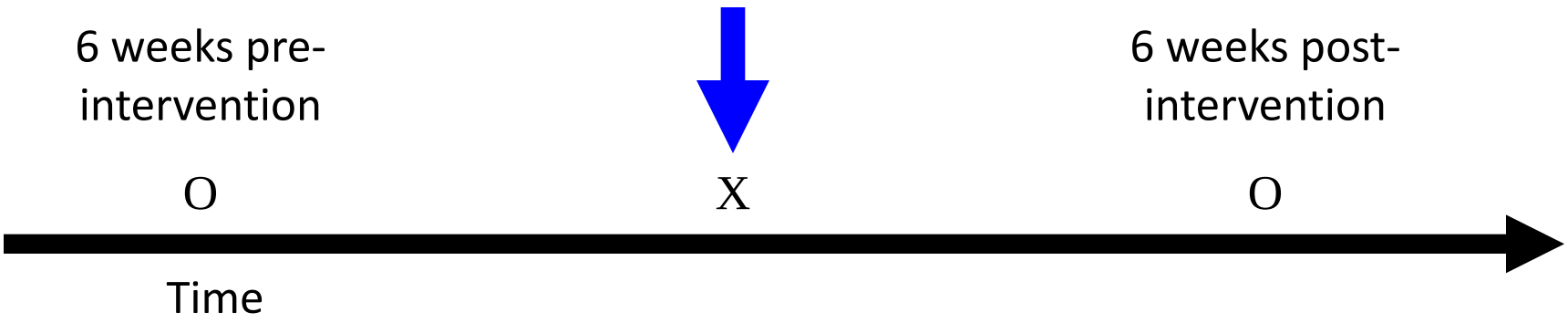
How could we study if this intervention worked?

Study design: Pre/post non-experimental

Pre-intervention measurement (7 sites)
- Interview women after clinic visit
- Ask about number of services received

Implementation of intervention
- Clinical training (1/2 day)
- Supervision of use of checklist (2 days)

Post-intervention measurement (7 sites)
- Interview women after clinic visit
- Ask about number of services received



Results

Table 2. Mean Services and Appointments per Visit by Health Post and Area

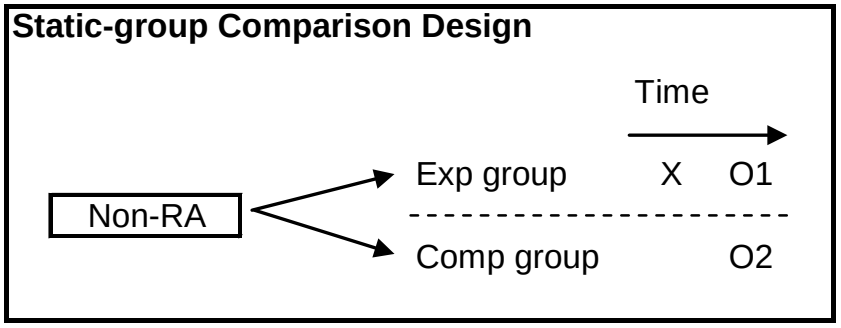
Health Posts	Mean Services per Visit		% Change	Mean Appointments per Visit	
	Pre	Post		Pre	Post
Total Dakar	1.17	1.40*	20	0.15	0.20*
HLM1	1.20	1.51*	25	0.20	0.21
Georges Lahoud	1.16	1.46*	26	0.11	0.09
Derklé	1.12	1.28*	16	0.11	0.40*
Liberté IV	1.21	1.30*	7	0.10	0.01*
Total Kebemer	1.44	1.79*	35	0.18	0.20
Diokoul	1.38	1.95*	41	0.05	0.07
Gueoul	1.61	1.81*	12	0.56	0.37
Sagatta	1.27	1.59*	25	0.40	0.56*

*p<.001

- Overall mean services 1.23 (pre) → 1.51 (post), 23% difference, p<.001

OR Example: Strategy to increase HIV care utilization in TB patients in Malawi*

- Comparison of TB programs in 2 districts (2001)
  - Intervention district with on-site VCT (Thyolo, n=1,103)
  - Control district without on-site VCT (Mulanje, n=1,239)
- Non-experimental design = static group comparison



- Outcome = TB treatment outcome (cure, treatment success, death, other)

** Chimzizi R et al, Voluntary counseling, HIV testing and adjunctive cotrimoxazole are associated with improved TB treatment outcomes under routine conditions in Thyolo District, Malawi. Int J Tuberc Lung Dis, 2004. 8(5):579-585.*

Results (1)

- High proportion of TB patients tested for HIV in Thyolo district, and started CTX
  - Not determined for Mulanje district

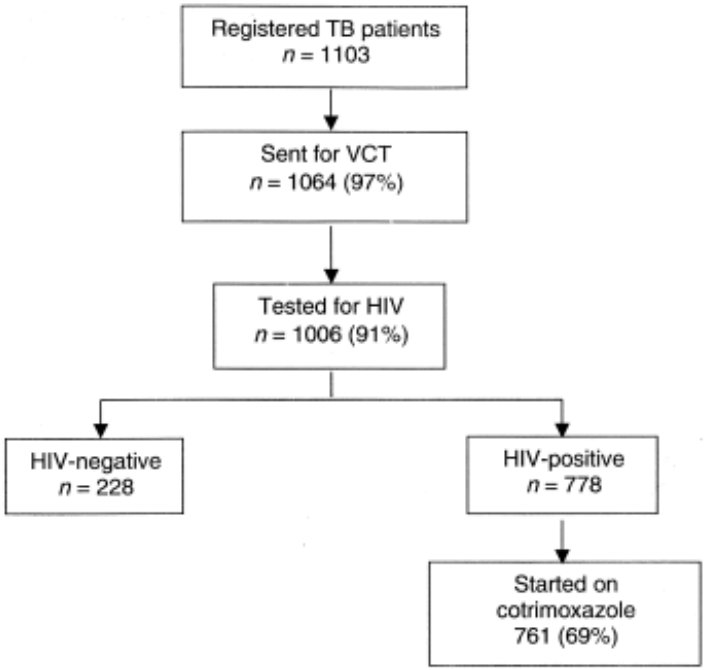


Figure Uptake of VCT and cotrimoxazole in TB patients registered in Thyolo District. TB = tuberculosis; VCT = voluntary counselling and HIV testing; HIV = human immunodeficiency virus.

Results (2)

- Thyolo district had higher treatment success & lower death, but lower "other outcomes" too (defaults, transfers out, or unknown)
- Adjusted ORs:
  - Treatment success RR 1.23 (95%CI 1.19-1.29, p<.001)
  - Death RR 0.84 (95%CI 0.78-0.91, p<.001)
  - Other outcomes RR 0.27 (95%CI 0.23-0.32, p<.001)

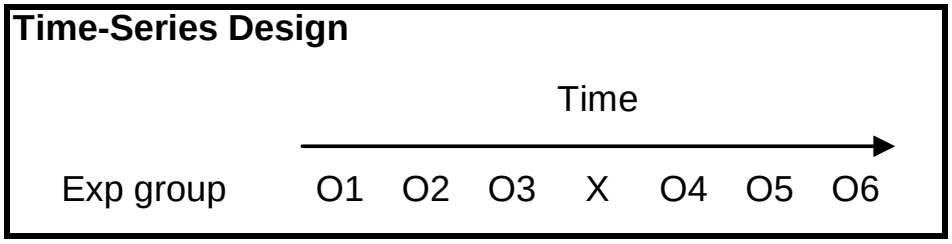
Potential biases

- Could something *else* be different about Thyolo district?
  - Intervention district had high proportion of “other outcomes” → may account for some of the differences in treatment success/cure
  - Only intervention district had support of NGO (MSF)
    - Infrastructure support
    - Health center management support
    - Home-based care
    - Community mobilization
    - Referral networks
    - VCT

- How could a different design help sort this out?
- Do we really need a another study?

OR Example: Time-series design*

- Strategies to improve perioperative antibiotic prophylaxis administration after C-section in Bogota, Colombia
  - 2 sequential interventions in one hospital:
    - Introduction of protocol to administer antibiotics
    - Identification of anesthesiologist as responsible person
  - Outcomes: antibiotic administration (utilization), antibiotic administration within 1 hour of delivery (timing), infection rate
  - Linear regression to examine immediate and gradual change over time using time-series analysis



** Weinbert et al, Reducing infections among women undergoing cesarean section in Colombia by means of continuous quality improvement methods. Arch Intern Med. 2001;161:2357-2365.*

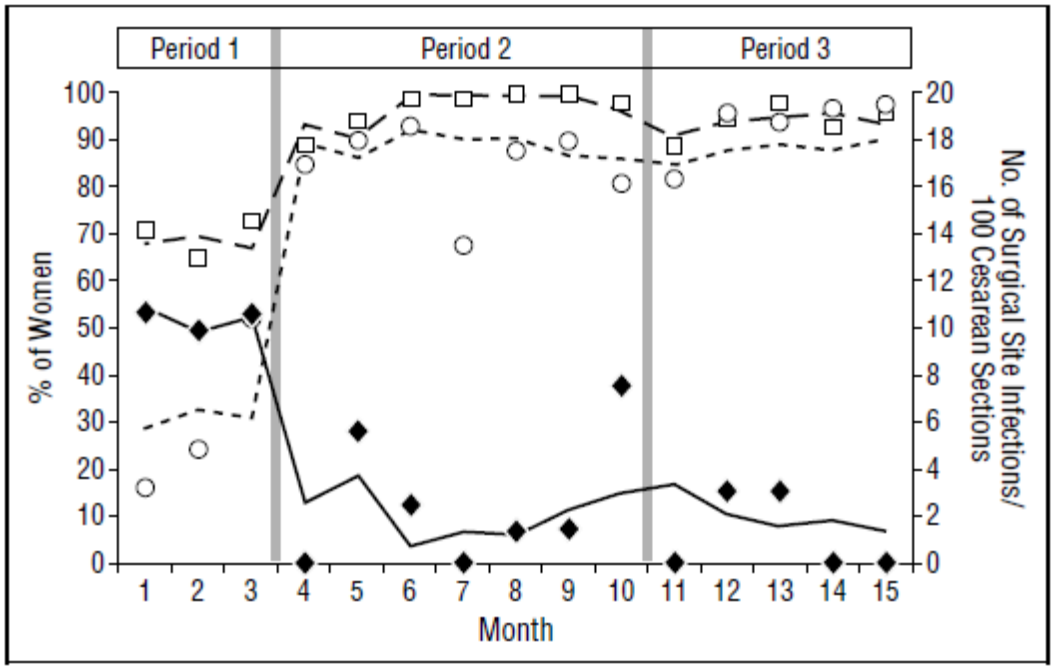
Time-series study: Results

- Period 2 vs. Period 1: Immediate increase in utilization (+31.6; p<0.001) and timing (+62.2, p<0.001); reduction in infection (-9.8/100 C-sections, p<0.001)
- Period 3 vs. Period 2: Utilization degraded (-4.9, p<0.001), others unchanged

Utilization (squares)

Infection (diamonds)

Timing (circles)



The End