Outline

1. An example of a prospective, comparative, implementation research effort (Brazil)

2. Opportunities for operational research "bolted on" to implementation

3. A mapping tool of Xpert MTB/RIF operational research (TREAT-TB)

Policy Relevant Outcomes from Validating Evidence on ImpacT (PROVE-IT) of MTB/RIF and Line Probe Assay on Presumptive Diagnosis of DR-TB in Brazil

S Bertel Squire on behalf of REDE-TB Brazil and TREAT-TB/:

REDE-TB: Afranio Kritski, Claudia Vater, Fatima Scarparo, Gisele Huf, Jose Ueleres Braga
The Union: Anne Detjen
MRC UK: Patrick Phillips
LSTM: Gillian Mann, Ivor Langley, Kerry Millington

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PROVE-IT

an example of
"implementation research
– testing the whole system"

cardinal feature =

clinical and public health decisions about:
a) who is tested
b) what treatment is given
are made in routine practice on the basis
of the new technology

Background - Brazil

1. Xpert MTB/RIF, MTBDR Plus (LPA), and MGIT 960 – in private sector, but not incorporated into the public health system (MGIT partially incorporated)

2. 2008 - Commission on Technology Incorporation (CITEC) established.

3. CITEC reviews studies on new technologies to decide if they should be incorporated into the public health system

4. For approval, studies must:
   a) Be carried out under field conditions in different regions
   b) Have used the most appropriate design
   c) Have included an assessment of the impact on the health system
   d) Have provided knowledge to assist decisions on scale up

Objectives

To compare, amongst DR/MDR TB suspects, the following between MTB/RIF, LPA, and MGIT960:

Two primary outcome measures :

1. Effectiveness
   a) Time from sputum submission to starting appropriate regimen for DR-TB
   b) culture conversion at 6 months

Several secondary outcome measures:

2. Equity:
   a) Median costs incurred by patients in reaching DR-TB diagnosis
   b) Costs in relation to income (derived from asset measure)

Objectives (cont)

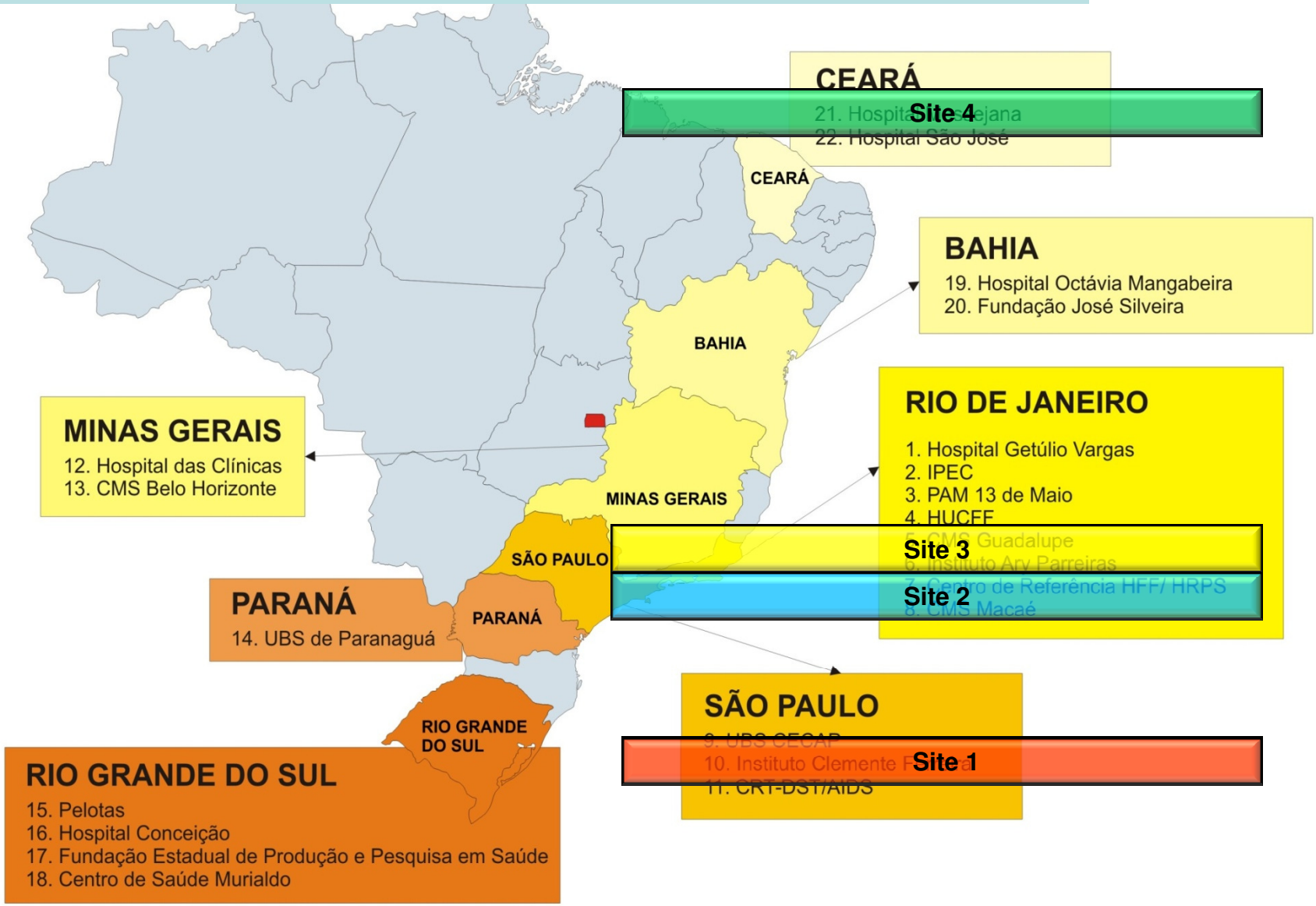
3. Health System impact :
   a) Health system costs (median cost per patient starting DR therapy)
   b) Health system requirements: disaggregated into component costs
      - Often discussed: e.g. laboratory human resources, training,
      - Less discussed: quality assurance, generators, disposal, human resources outside of laboratory – risk assessment, treatment decisions etc.

4. Scale up potential :
   a) Cost effectiveness in terms of: (e.g.) cost per case starting DR treatment, cost per case cured, cost per DR case averted
   b) Modelling of operational requirements (e.g. HR requirements across the whole algorithm, not just in the laboratory)

A Framework for Impact Assessment for New Diagnostics
[Mann, Squire et al, IJTLD 2010 ;14(12) :1518-1524]

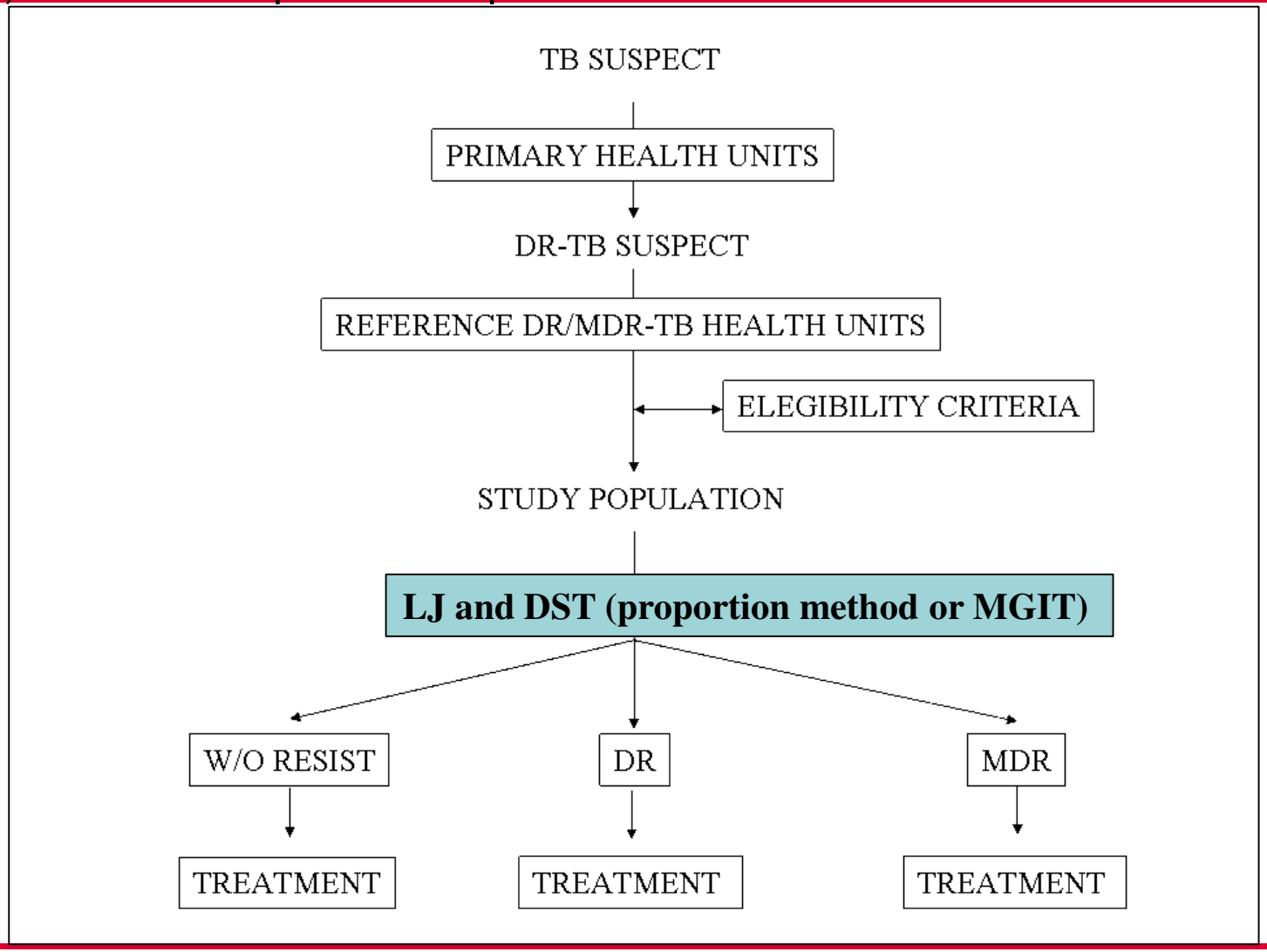
Layer of Assessment	*Kinds of question(s) being answered*
Layer 1: EFFECTIVENESS ANALYSIS	What is the programmatic impact on time to starting treatment? What is the effect on culture conversion at 6 months?
Layer 2: EQUITY ANALYSIS	Who benefits? (e.g. poor/less poor, adults/children) Why do these benefits accrue? (e.g. change in patient costs)
Layer 3: HEALTH SYSTEM ANALYSIS	What are the *total* human resource implications? What are the infrastructure implications? What are the procurement implications? What are the implications for quality assurance?
Layer 4: SCALE UP ANALYSIS	What are the projected impacts of going to scale? eg a) cost savings to patients in relation to income b) cost savings to the health system d) Effects on transmission
Layer 5: POLICY ANALYSIS	What other similar technologies are available or likely to become available? How do similar existing or emerging technologies compare?

Design:
pragmatic, cluster-randomised, implementation trial

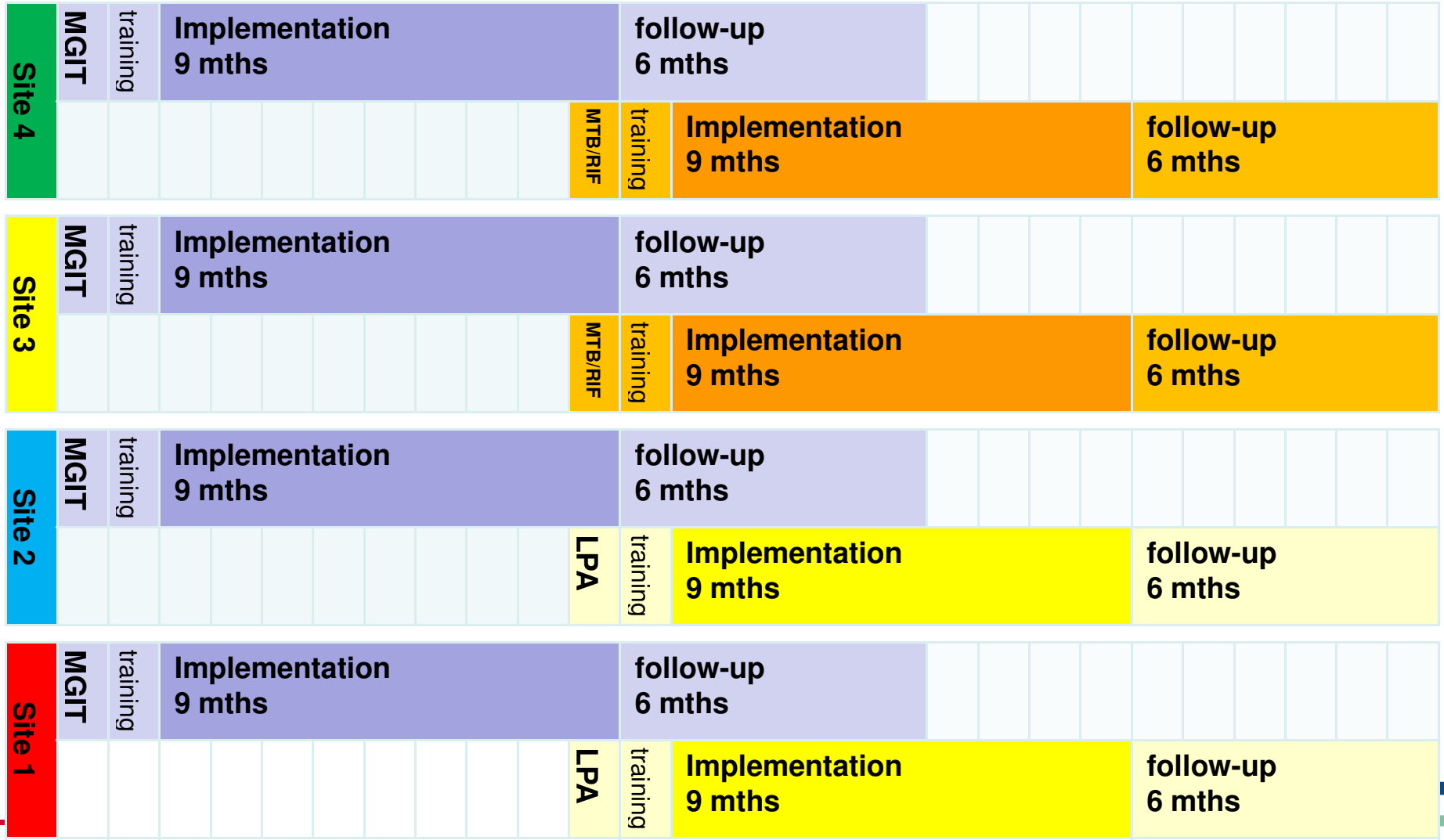


Baseline: All 4 sites – data collection 5 months

a) Site accounts – health system costs
b) Routine registers (clinical & lab)
c) Subset of patients – patients costs

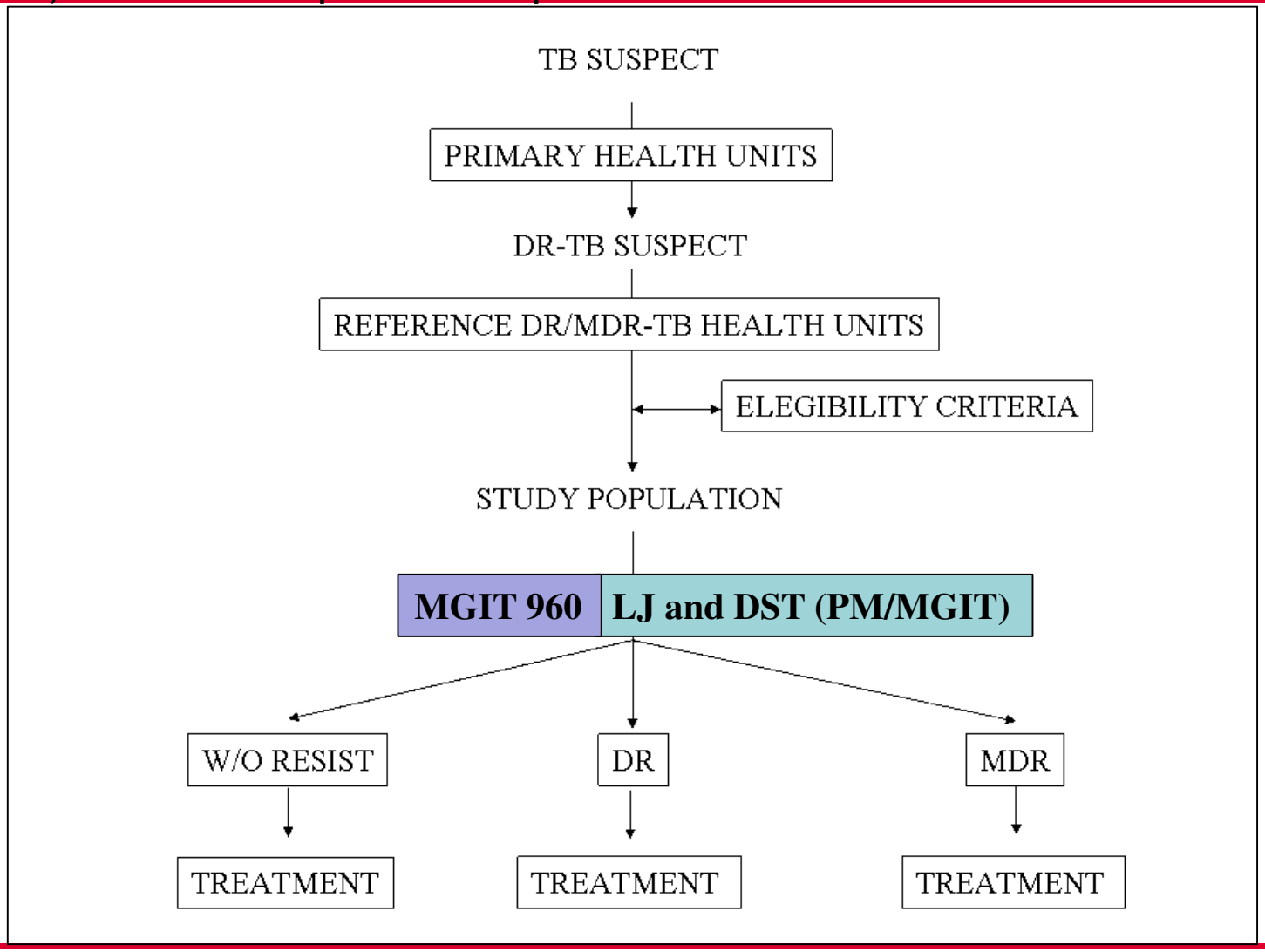


Implementation:
Pragmatic, cluster-randomised, cross-over



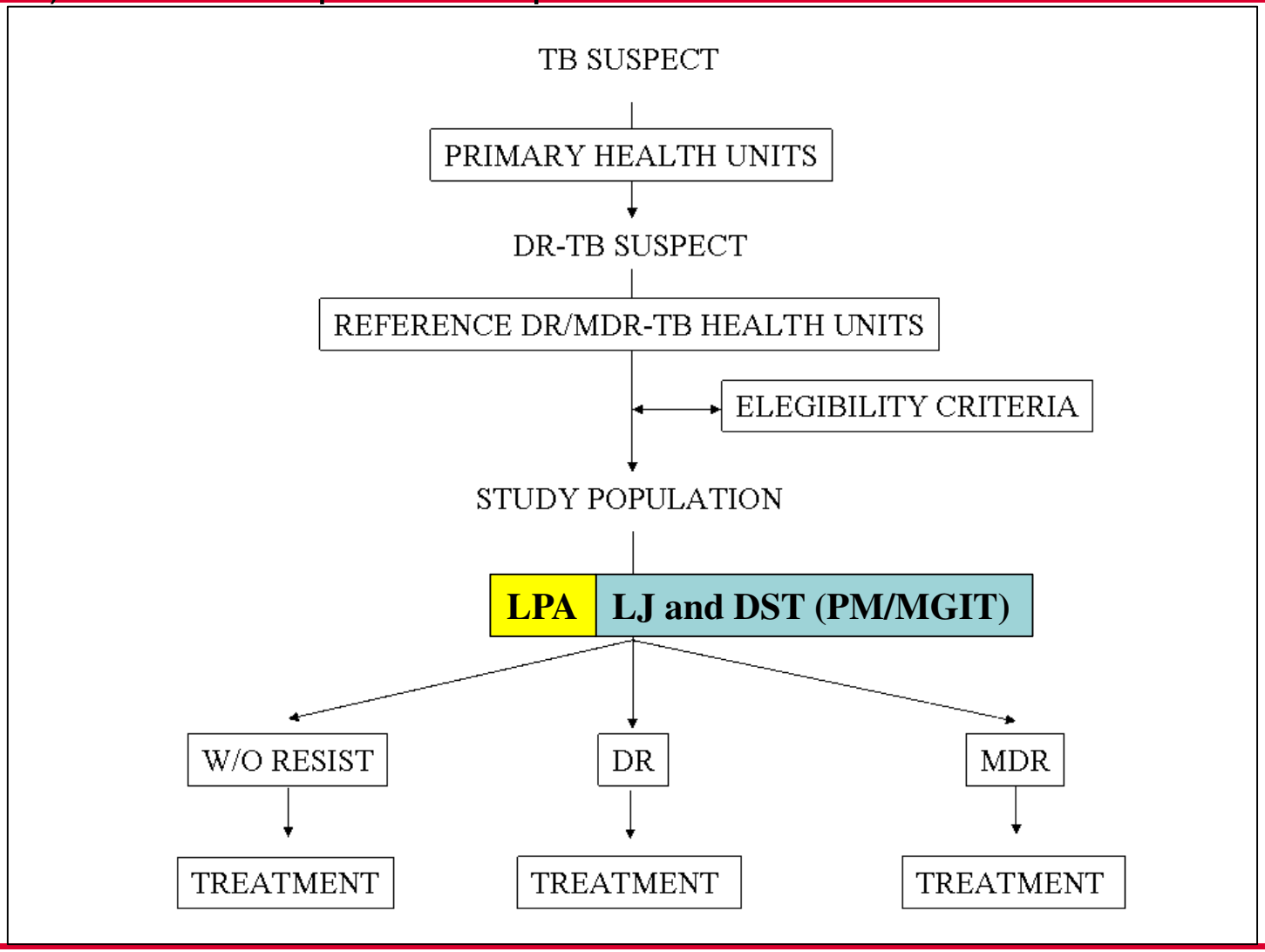
Implementation – e.g. Site 1, 1st 9 months

a) Site accounts – health system costs
b) Routine registers (clinical & lab)
c) Subset of patients – patients costs



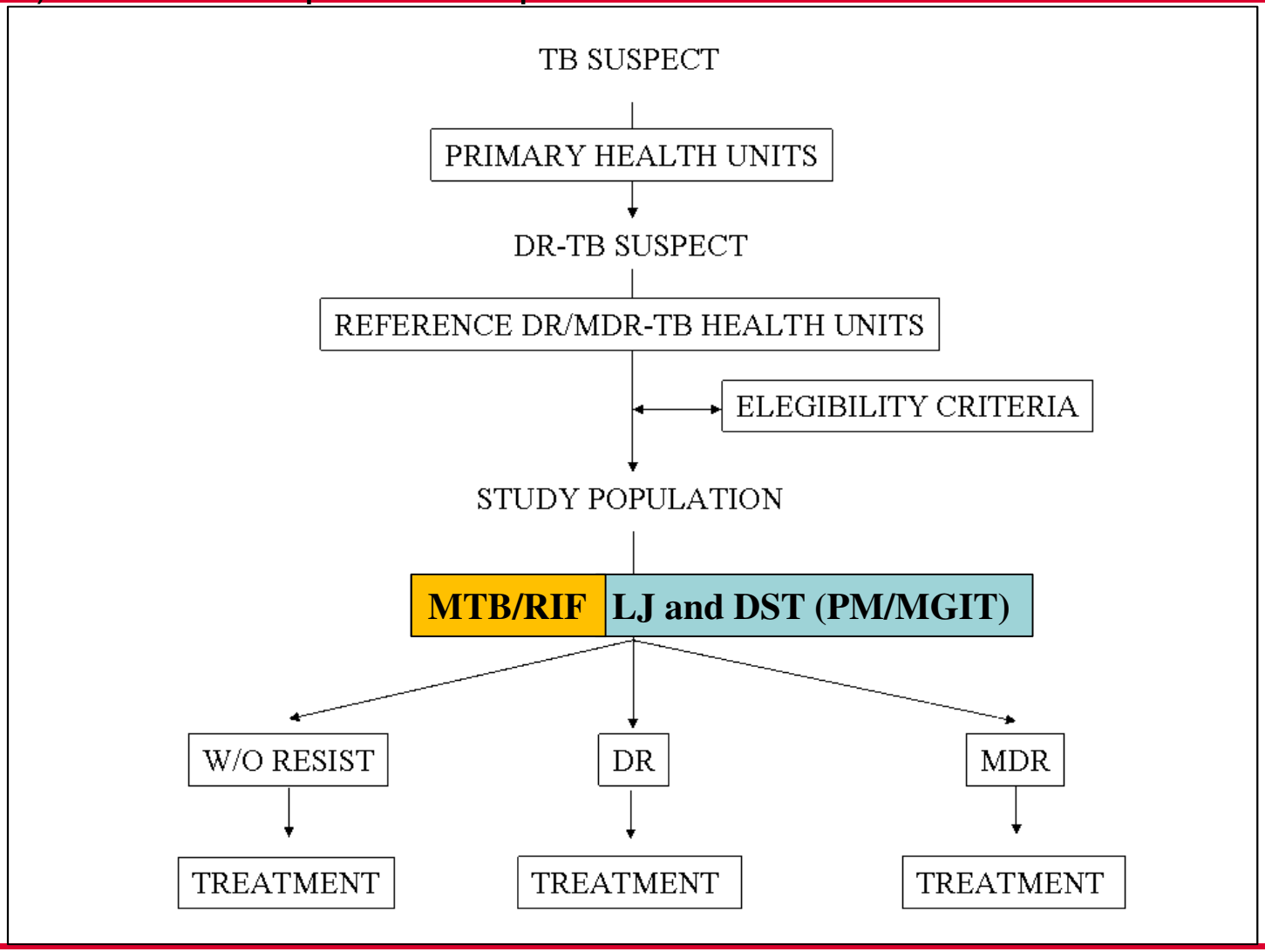
Implementation – e.g Site 1, 2nd 9 months

a) Site accounts – health system costs
b) Routine registers (clinical & lab)
c) Subset of patients – patients costs



Implementation – e.g. Site 3, 2nd 9 months

a) Site accounts – health system costs
b) Routine registers (clinical & lab)
c) Subset of patients – patients costs



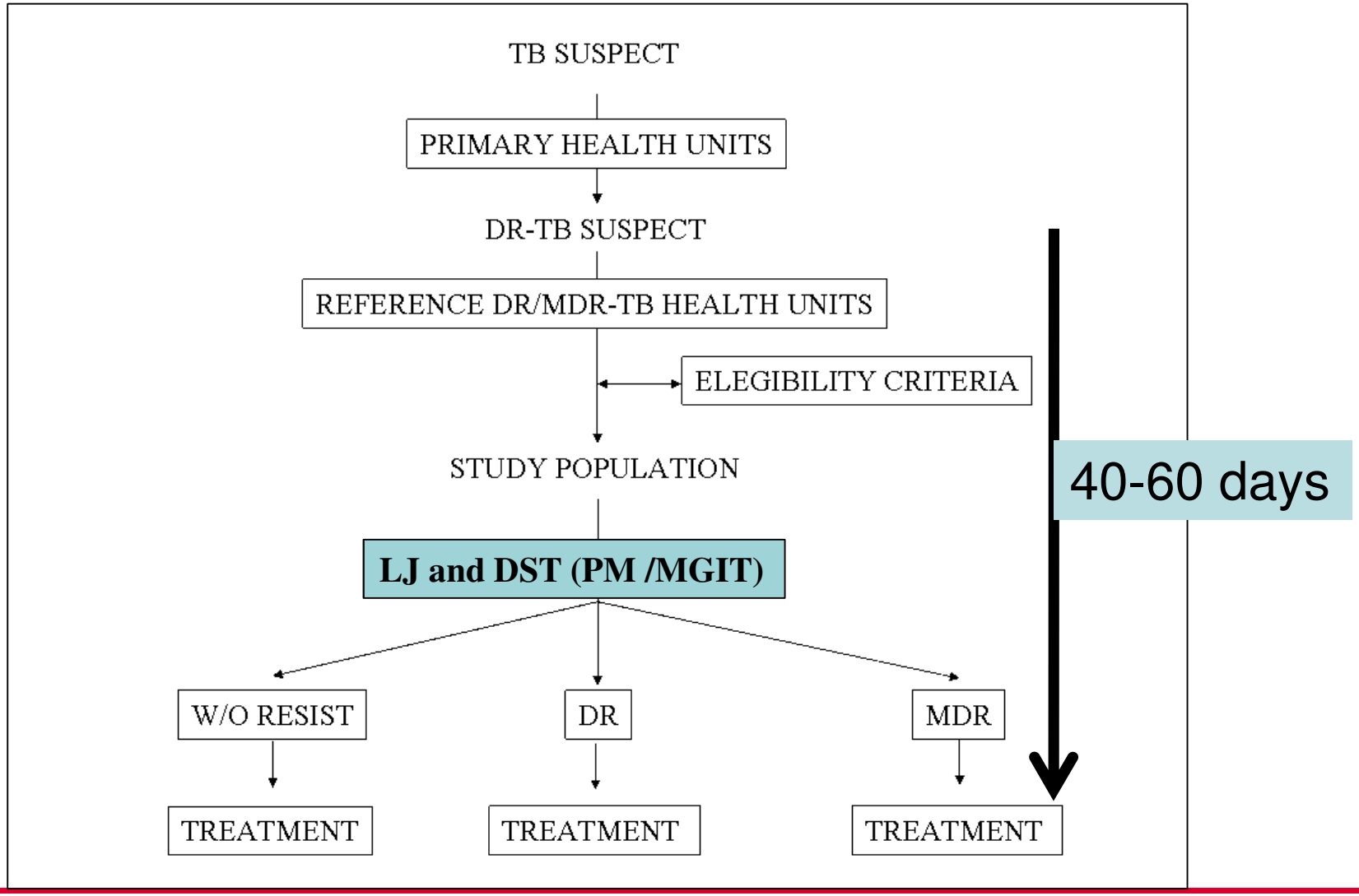
Participants – 3 types

1. Sites – health system costs

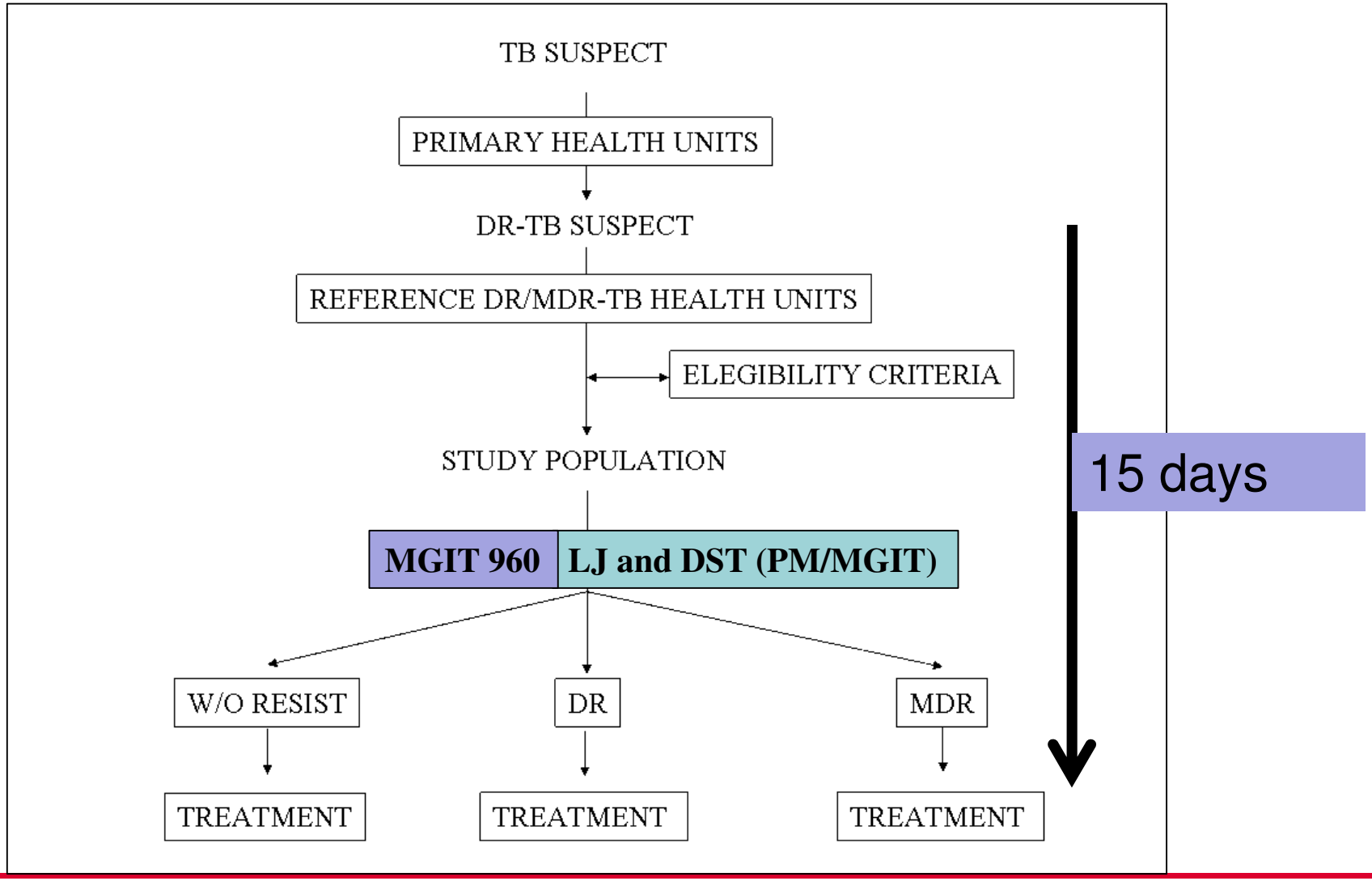
2. All MDR TB suspects
   a) TB in the past
   b) HIV positive
   c) Failure or smear positive at 2 months
   d) Special conditions: inmates, homeless

3. Subset of MDR TB suspects at each site and during each phase interviewed for socio-economic status and costs

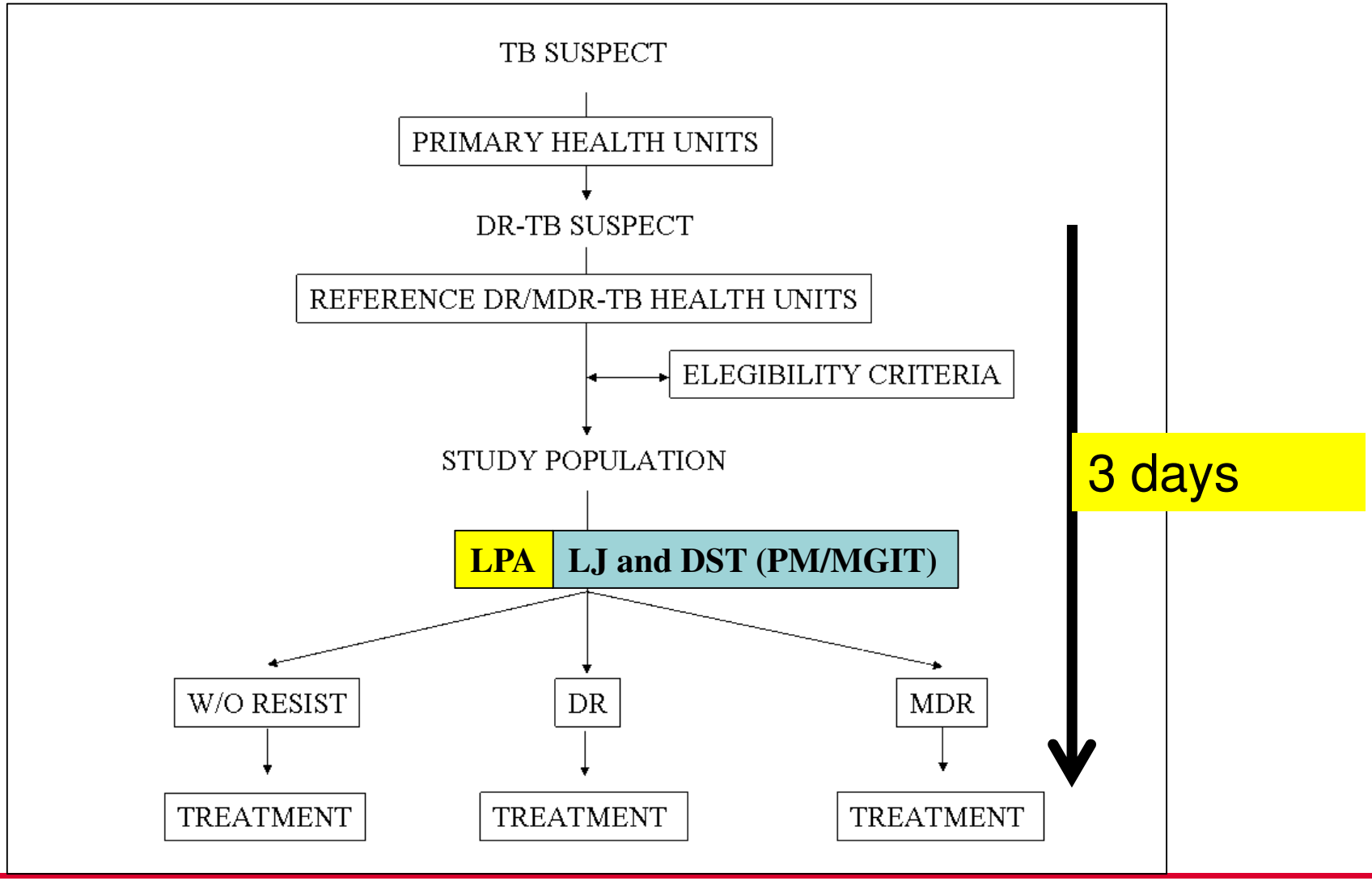
Sample size assumptions 1



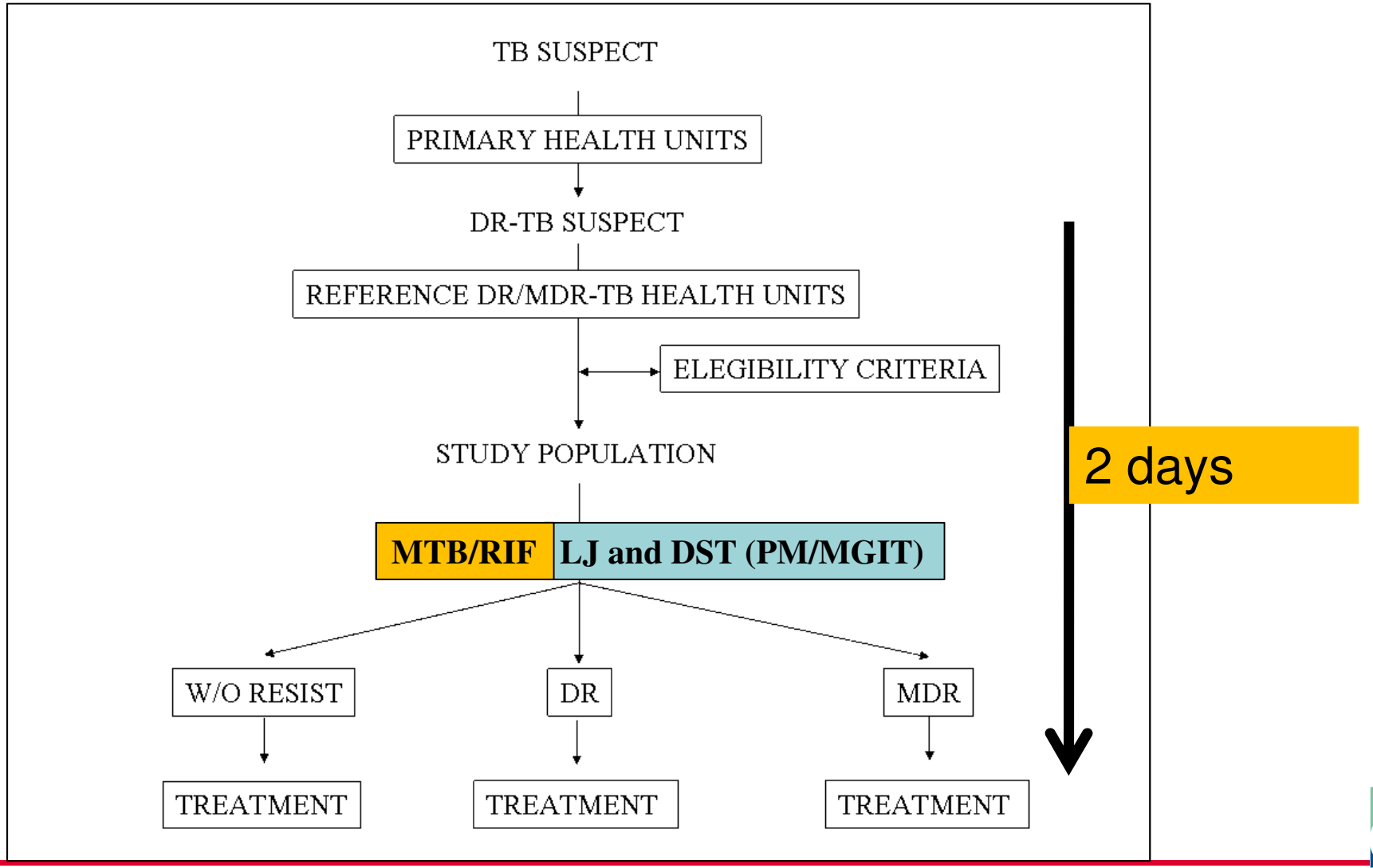
Sample size assumptions 2



Sample size assumptions 3



Sample size assumptions 4



Sample size projections

1. Two comparisons
   a) MTB/RIF vs MGIT in 2 arms
   b) LPA vs MGIT in 2 arms

2. Two main end-points
   a) Time to initiation of MDR therapy
   b) Outcome at 6 months in MDR patients

3. Power – main driver of the calculation was 6 month outcome:
   a) Assuming 40% culture negative at 6 months in MGIT arm, 242 patients per arm required to detect increase to 56%in culture negativity at 6 months, assuming 10% LTF, need 270 per comparison

Feasibility

1. From National data 2010, expect:
   a) >350 DR cases in 18 months for 2 arms comparing MGIT and MTB/RIF
   b) >550 DR cases in 18 months for 2 arms comparing MGIT and LPA

2. Thirty-two months total (including analysis and write-up) – results available October 2013

PROVE-IT Summary

Prospective, randomised implementation trial giving comparative results for DR patients on

1. **patient important outcomes**
   - **a) time to starting treatment**
   - **b) proportion culture negative at 6 months**

2. **health system costs (full economic)**

3. **patient costs**

Will facilitate rational decision by CITEC on how best to deploy MGIT, LPA, and MTB/RIF singly or in combination for national roll-out

USAID FROM THE AMERICAN PEOPLE

International Union Against Tuberculosis and Lung Disease
Health solutions for the poor

treat TB
Technology, Research, Education, and Technical Assistance for Tuberculosis

LSTM

What if a prospective, comparative study is not possible?

Layer of Assessment	*Kinds of question(s) being answered*
Layer 2: **EQUITY ANALYSIS**	**Who benefits from new tool? (e.g. poor/less poor, adults/children)** **Why do these benefits accrue? (e.g. change time to issue of results)**

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Layer of Assessment	*Kinds of question(s) being answered*
Layer 3: **HEALTH SYSTEM ANALYSIS**	**What are the human resource implications?** **What are the infrastructure implications?** **What are the procurement implications?** **What are the implications for quality assurance?**

A Framework for Impact Assessment for New Diagnostics

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Layer of Assessment	*Kinds of question(s) being answered*
Layer 4: **SCALE UP ANALYSIS**	**What are the projected impacts of going to scale with new tool? eg** **a) cost savings to patients in relation to income** **b) cost savings to health providers / the health system** **d) Effects on transmission**

Conclusions

1. More prospective, comparative implementation studies are needed to inform rational policy uptake in different settings.

2. Several cluster-randomised designs are possible – only one example has been shown here

3. If prospective, comparative studies are not possible, it is still important to conduct operational research in association with before-and-after implementation work

4. The Impact Assessment Framework provides a way of thinking about the kind of studies that could be "bolted on" to implementation