ROLE OF TREATMENT FOR LTBI IN THE CHANGING GLOBAL LANDSCAPE

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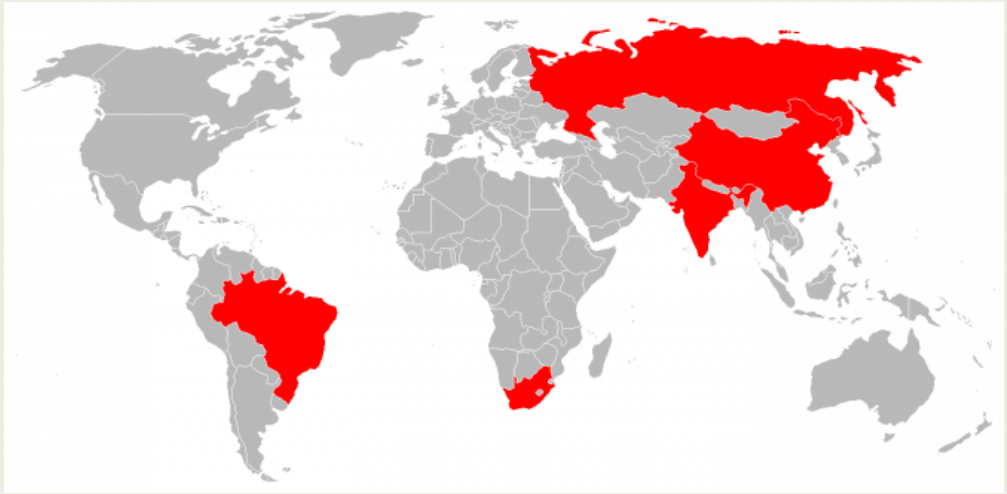
CHANGING LANDSCAPE: FOR BETTER OR FOR WORSE?

CoI disclosure

- Investigator in implementation/operational studies on treatment and diagnosis of LTBI and active TB
- Member of the Brazilian NTP advisory board
- No links to diagnostic or drug manufacturers/distributors

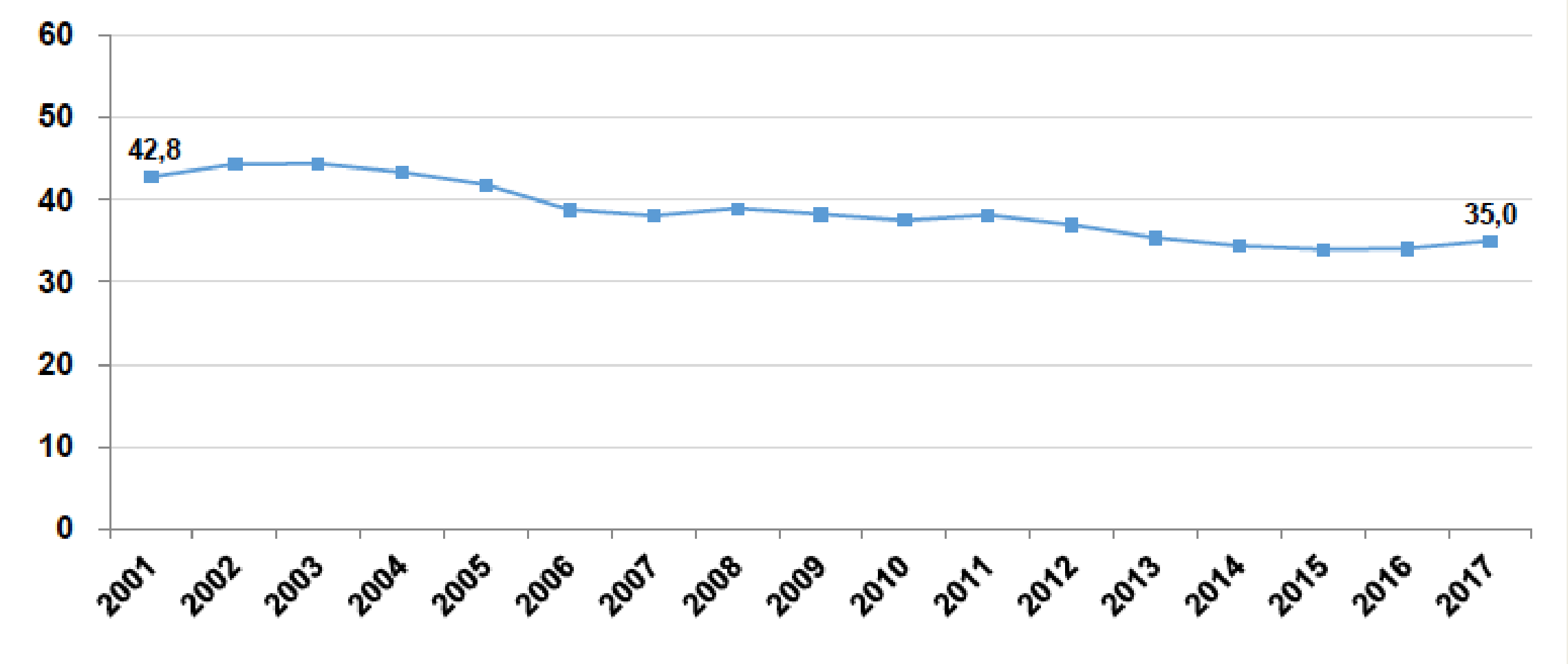
Brazilian context

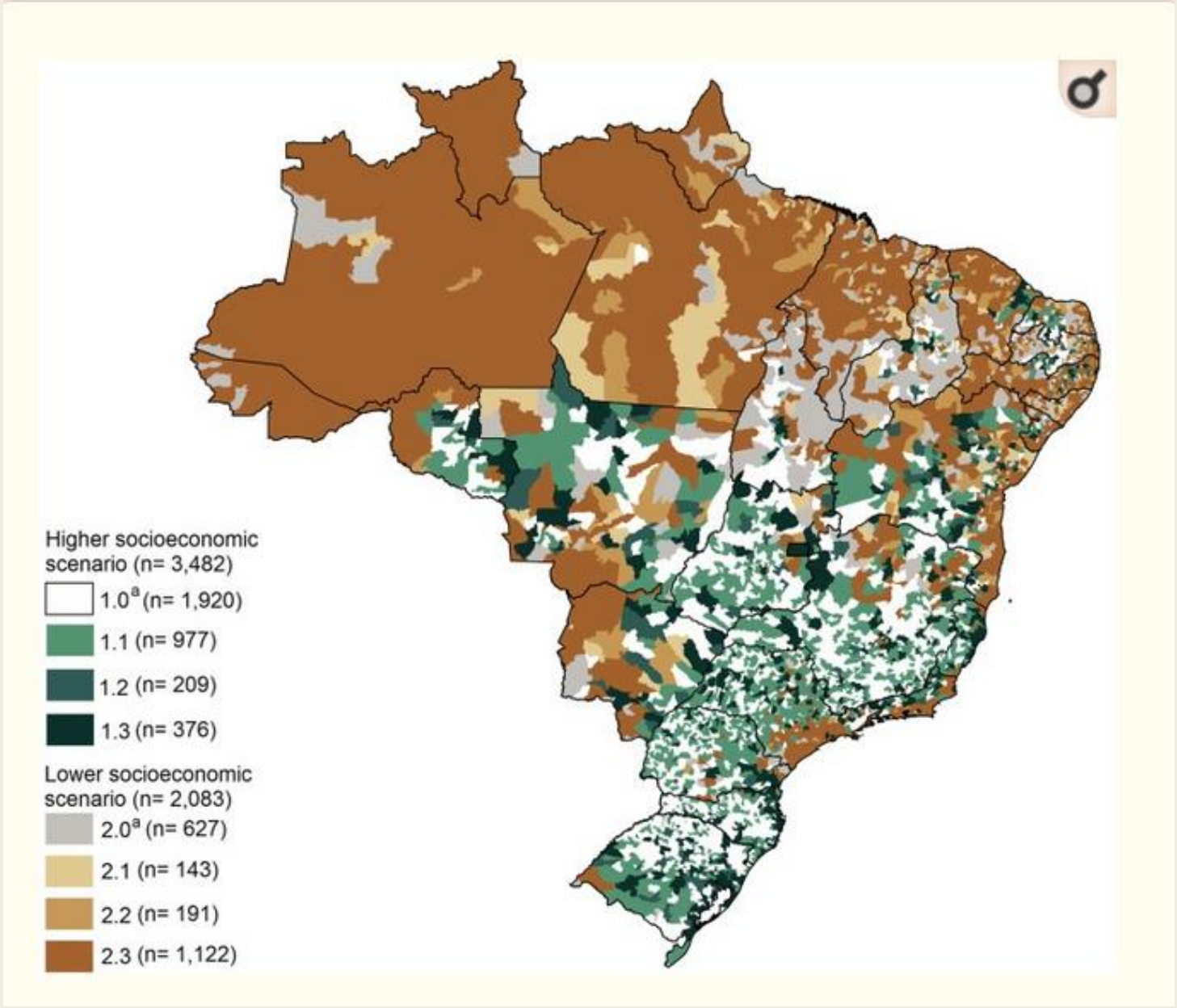


- Large country, upper-middle income, one of BRICS
- High inequity despite recent growth of class C
- Largest public health system; covers 140 million
- 72,000 new TB cases reported; 84,000 estimated; 20th in the world
- 42/100,000 estimated
- 9.5% HIV+, estimated 13%, 19th in the world

Q.1: REPORTED VS. ESTIMATED DATA

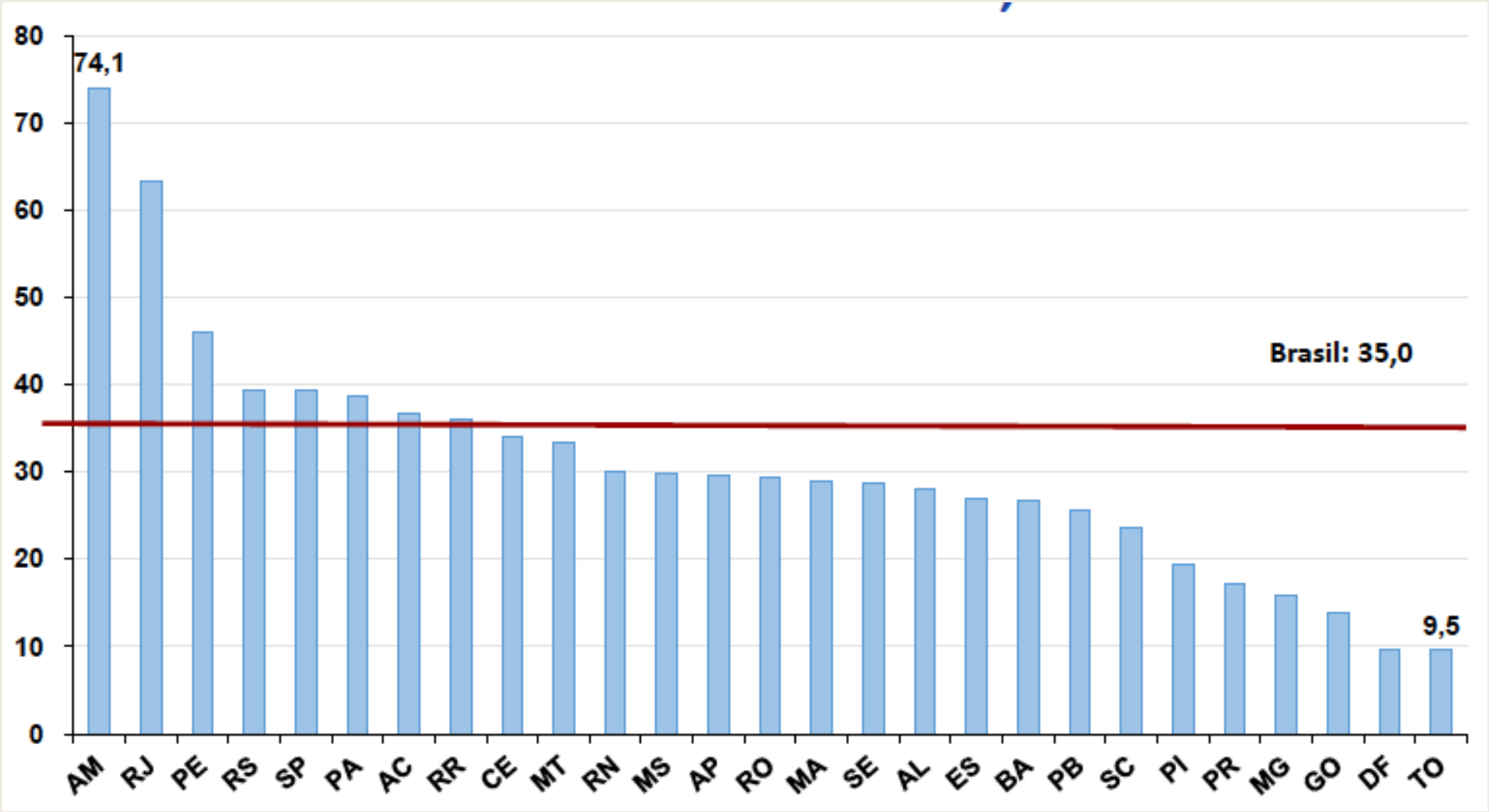
TB incidence per 100,000 pop., new cases





Pelissari, BMJ Open 2018, 8(6) :e018545

Incidence rates vary tremendously



Hotspots in *favelas* and prisons

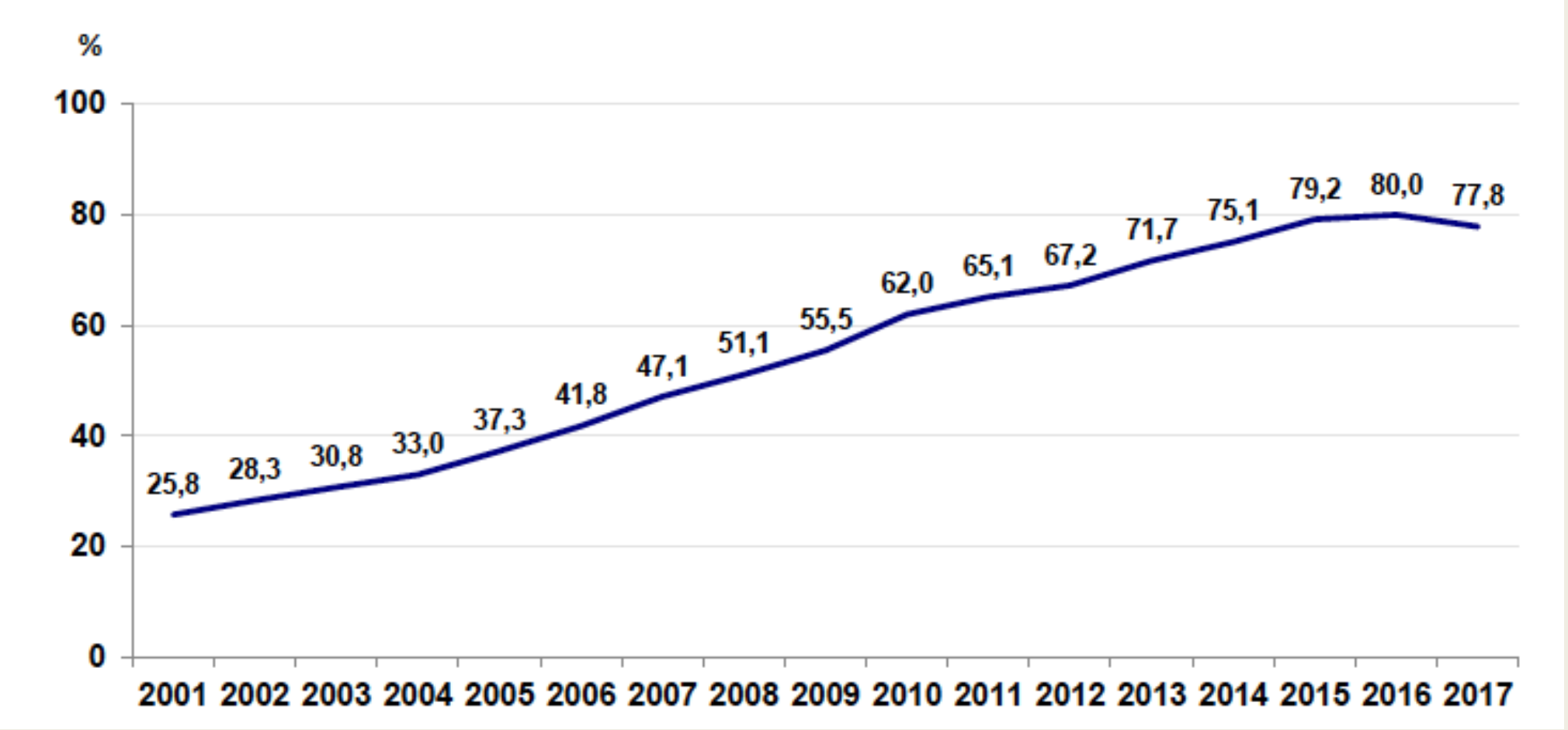
400/100,000

1,036/100,000

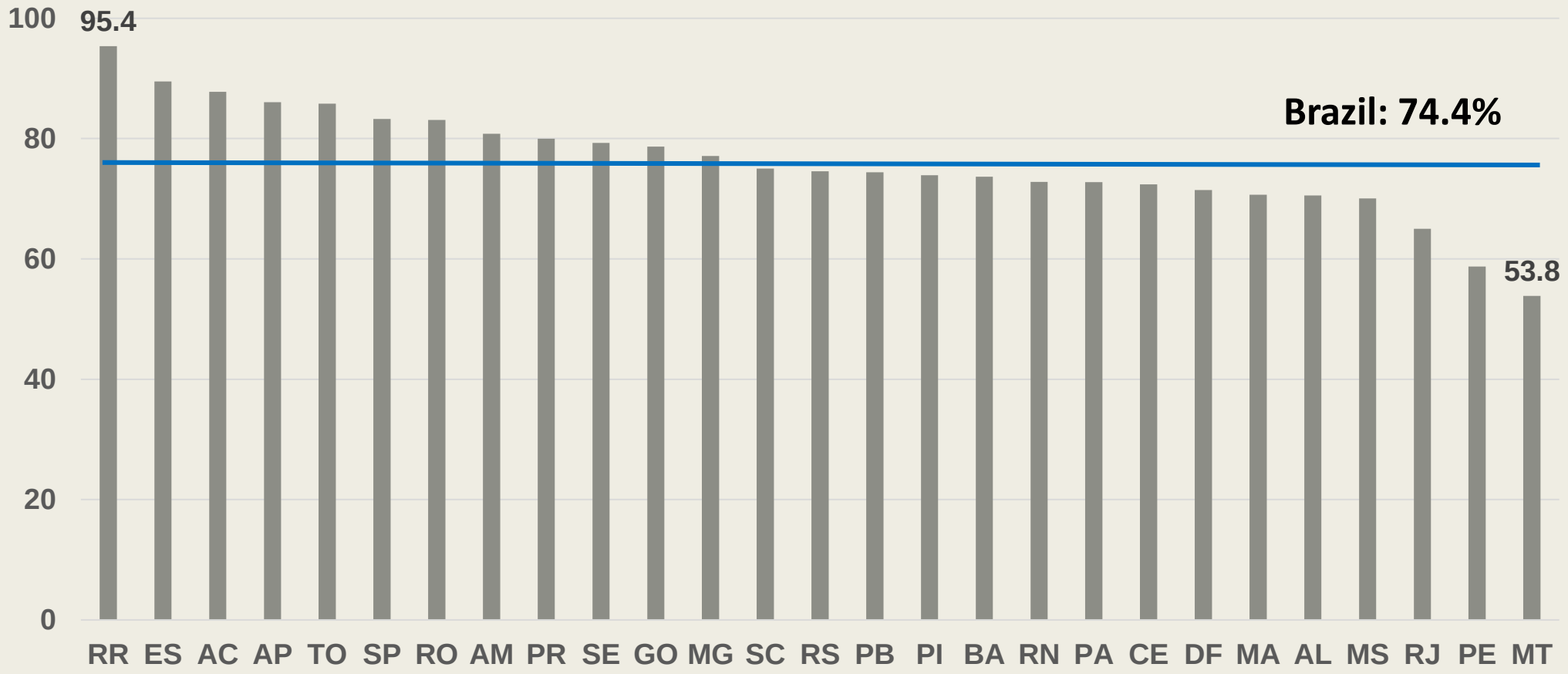
Q.2: VARIABILITY OF TRANSMISSION PROBABILITY

Q.3: UNCERTAINTY OF RISK OF PROGRESSION

HIV testing over years



Variable rates of confirmation of pulmonary TB (despite Xpert available for 70%)



Q.4: WHAT IS AN INDEX CASE?

Previous guidelines for LTBI treatment – contacts (2011)

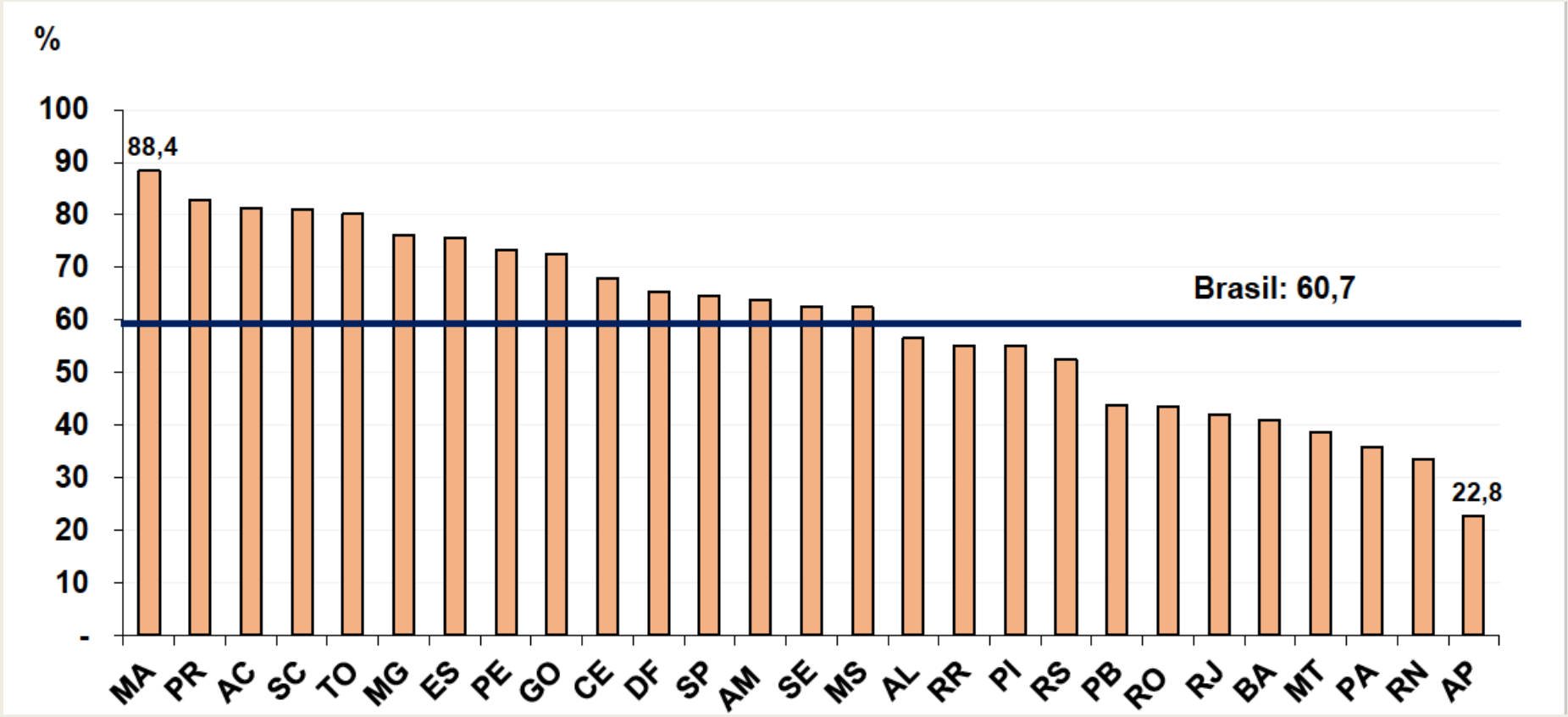
- Investigation of contacts recommended in cities where incidence rate < 50/100,000 and cure rates >80%
- TST is the current standard of care for diagnosis
- Treat all TST+ contacts, **regardless of age**, after ruling out active TB
- Treat all HIV contacts, regardless of TST
- 6 to 9 months of INH

Current guidelines (2018)

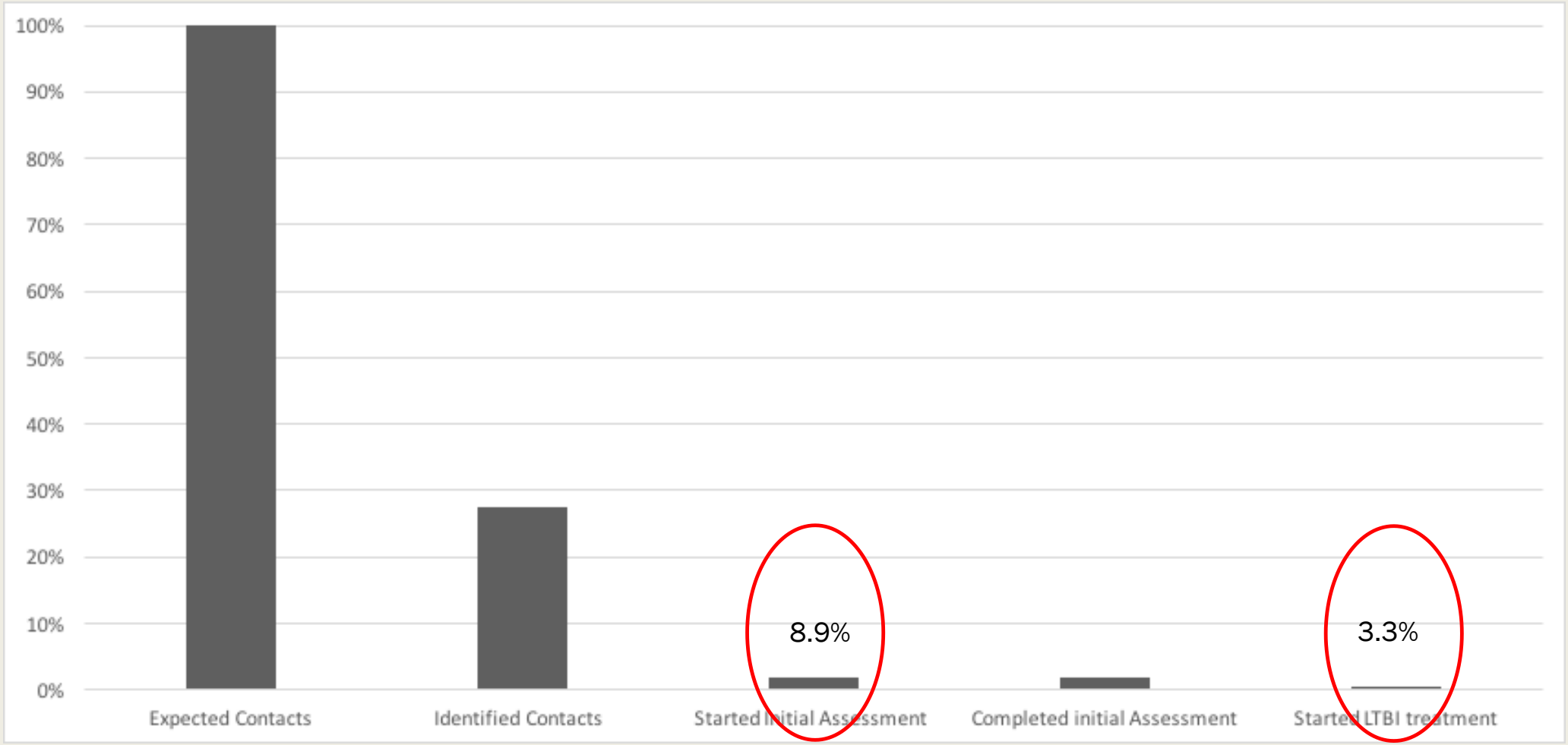
- LTBI treatment recommended for TST+ contacts **everywhere**
- 4RIF for <5y, >50y and liver disease
- RPT not available (not ”FDA”-approved)

- Incorporation of QFT (available in private sector) and RPT under discussion

Proportion of contacts “examined” – official data based on reporting system



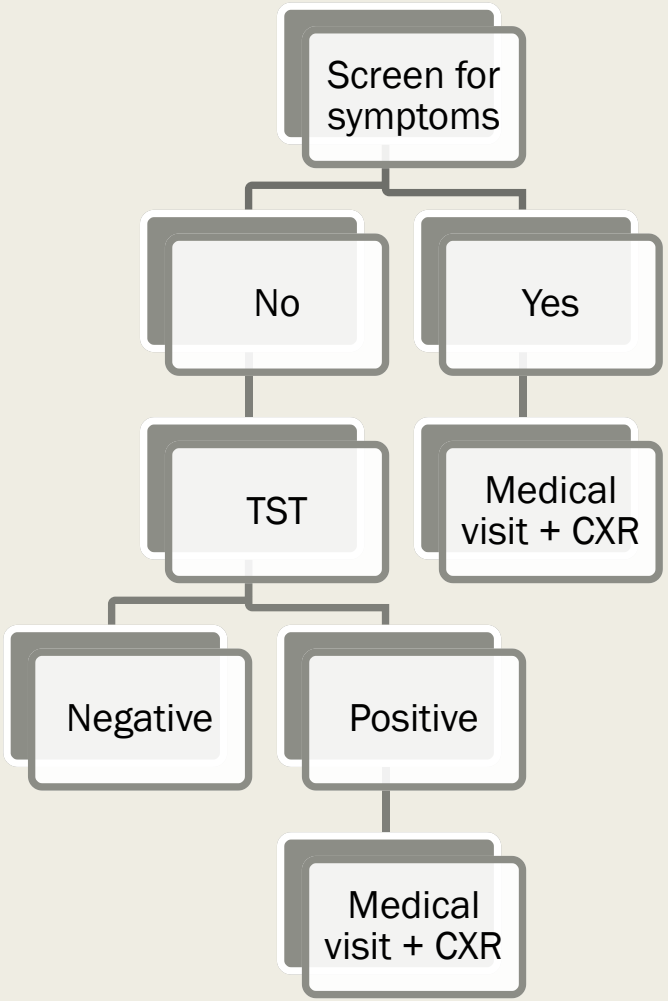
Proportion of contacts investigated – data based on ACT4 study: <9% underwent TST



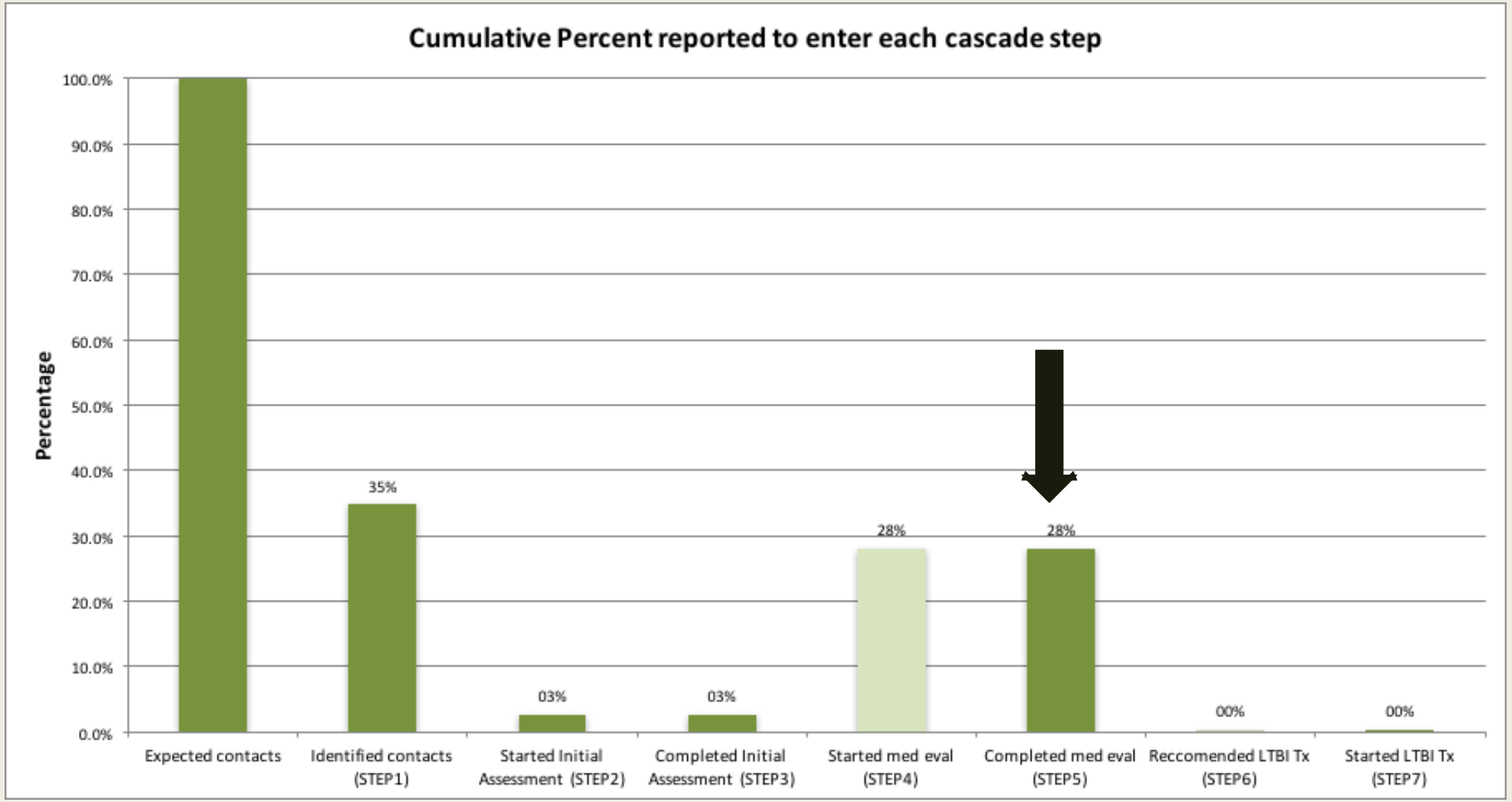
Q.5: WHEN IS A CONTACT CONSIDERED INVESTIGATED?

Q.6: ENTERING PARAMETERS IN MODELS - GUIDELINES VS. REAL LIFE DATA

Guidelines (HIV– adult contacts)



Real data from ACT4 study (one clinic in Rio)



DOT

- Recommended for all, but flexible
- 3 times weekly
- Officially: >80%…

- This means that 80% are covered by a clinic where DOT is available

ISSUES THAT NEED MODELING

Current guidelines for LTBI treatment – HIV

- Test yearly for CD4 and LTBI
- **For new cases, without previous treatment of TB/LTBI:**
  - ***If <350/mm^3, start LTBI treatment***
  - ***If ≥ 350/mm^3, treat if TST+***
- If (re)exposed: treat without testing at each exposure

- How much does it cost, how many will be in each group, how many treatments necessary, how much harm for "unnecessary" treatment?

Other current controversies in Brazil: do we need to test before treating?

- Benefit from IPT in PLWH even in TST- or unknown TST
- High QFT positivity of contacts in some settings (74% in a favela)
- CXR can delay LTBI treatment by 3-4 months. Can we rule out active TB based on symptoms in non-HIV?

- Does one model ”fit all”?

Indicator

- Should we have a programmatic “indicator”?
- How many contacts should be on LTBI treatment considering the number of index cases

Other universal issues also pertinent to Brazil should be taken into account

- Drug-resistance
- New regimens
- Population age (under 5s)
- Need for FU visits
- DOT, VOT, MOT (for effectiveness and AE monitoring)
- Complex training for TST
- Outcomes (TB case averted?)
- Shortage of consumables

Summary

- Variable transmission in different settings
- Underestimation of HIV and TB cases based on notification
- Real life vs. guidelines vs. notification data
- Low rates of bacteriological confirmation: who is an index case?

- Need for testing both for active and latent TB
  - *Will we overtreat if we don't test? Should we treat all?*
  - *"Unnecessary" treatments: costs and harm*
  - *Symptom vs image-based screening*
- We need an indicator

Thank you!