TB disease burden estimation in children: an overview of progress

Childhood TB subgroup: annual meeting
Barcelona, 27 October 2014

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GLOBAL TB
PROGRAMME

World Health Organization

Acknowledgements

- National TB Control Programmes
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WHO Global Task Force on TB Impact Measurement

www.who.int/tb/advisory_bodies/impact_measurement_taskforce

National TB Programmes of many countries
& key technical and funding agencies

Task Force mandate (2006–2015)

- Produce robust, rigorous, widely-endorsed assessment of whether 2015 international TB targets are achieved
  - Promoting direct measurement of TB disease burden

- Regularly report on progress towards impact targets in years leading up to 2015

- Strengthen national capacity in monitoring and evaluation of TB control

What do we offer countries?

GLOBAL TUBERCULOSIS REPORT 2014

World Health Organization

INDONESIA

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden[a] 2011

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	65 (29–120)	27 (12–48)
Prevalence (includes HIV+TB)	680 (310–1 200)	281 (130–489)
Incidence (includes HIV+TB)	450 (370–540)	187 (155–222)
Incidence (HIV+TB)	15 (11–20)	6.2 (4.4–8.3)
Case detection, all forms (%)	70 (59–85)	

Quantify the level of TB burden

TB mortality, HIV-negative
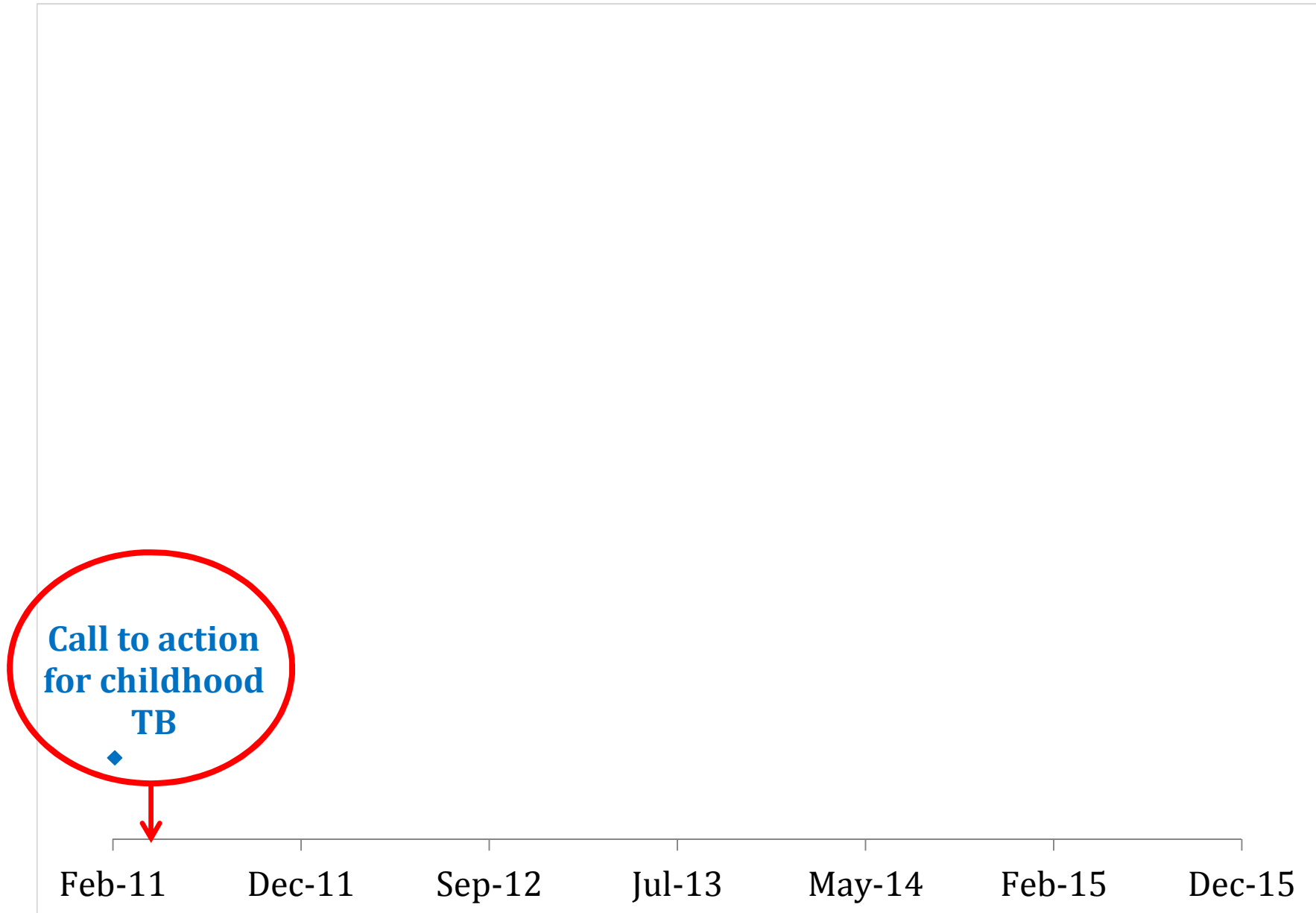
TB mortality, HIV-positive
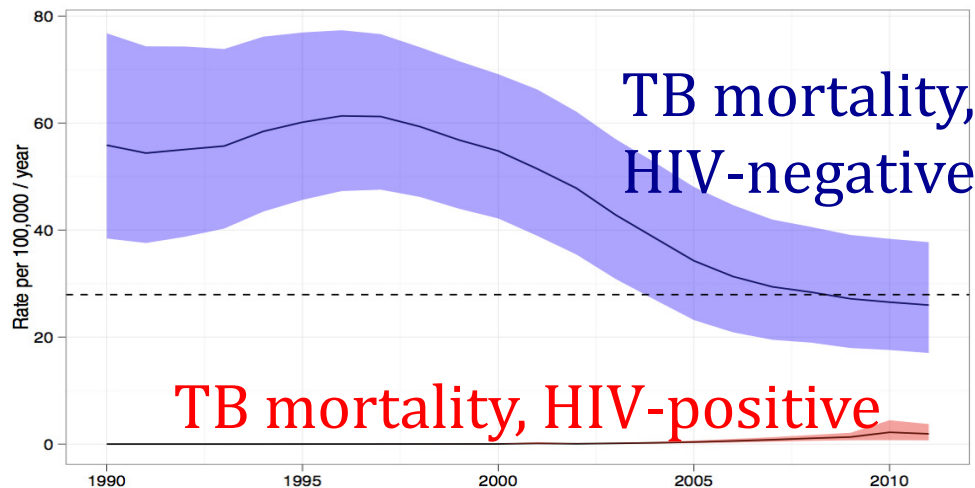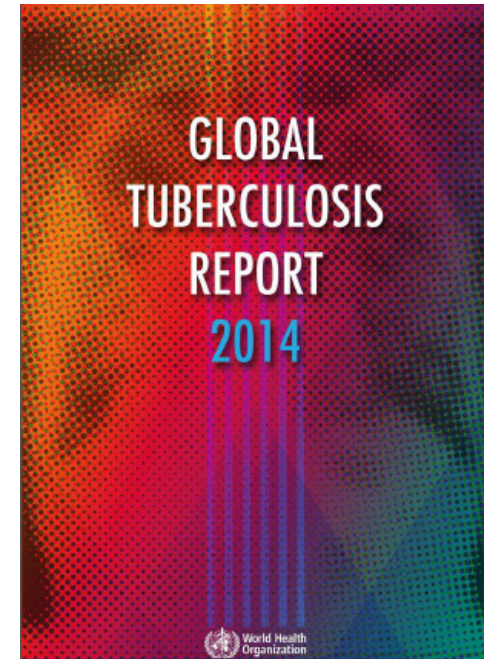
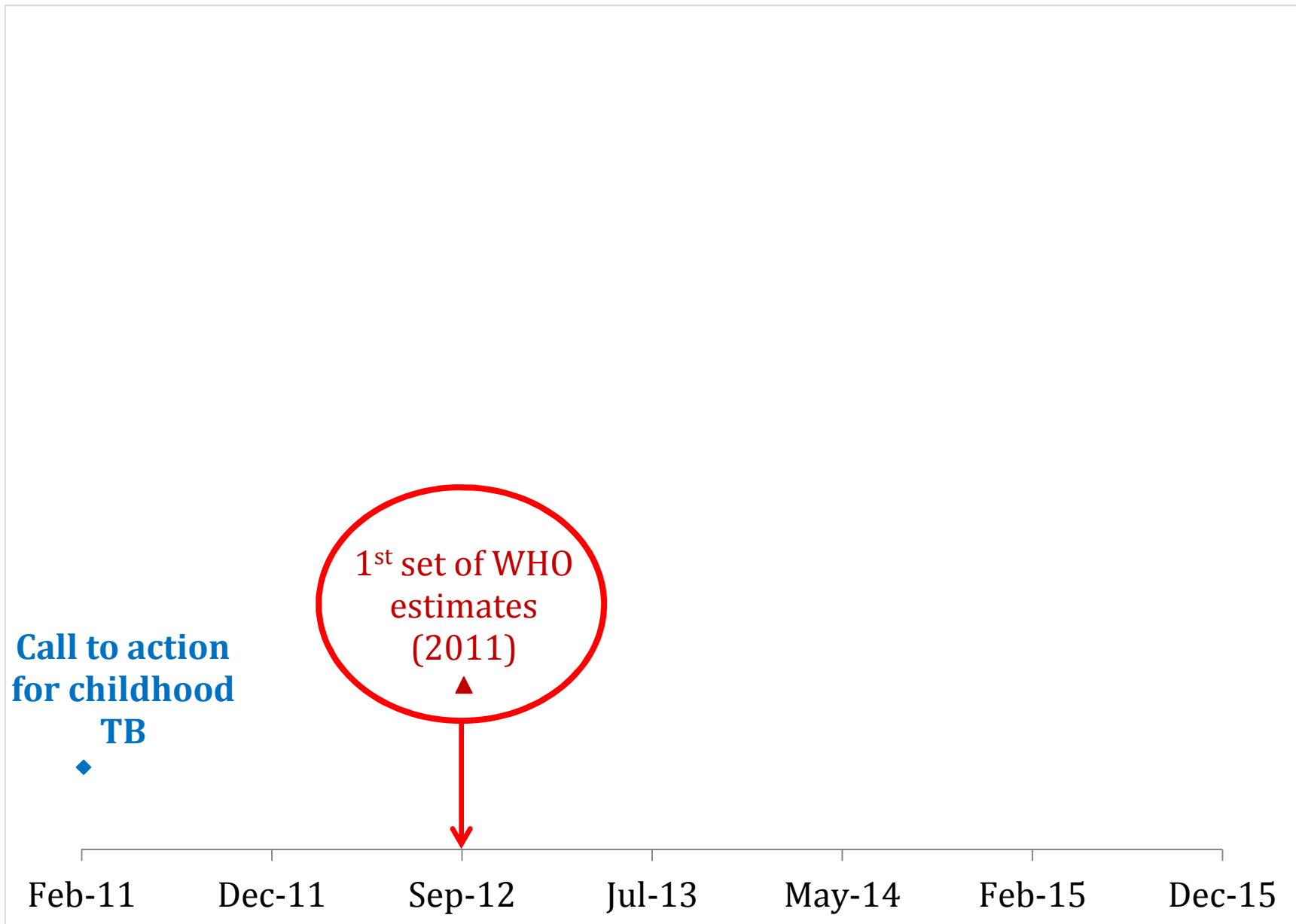**Monitor effectiveness of control programs by quantifying trends**

What makes paediatric TB disease burden estimates problematic?

- Lack of gold-standard, point-of-care, diagnostic tool (difficulties with case definitions)

- Neglect of recording and reporting of the "non-infectious" childhood TB cases

- Scarcity of robust, nationwide data on children

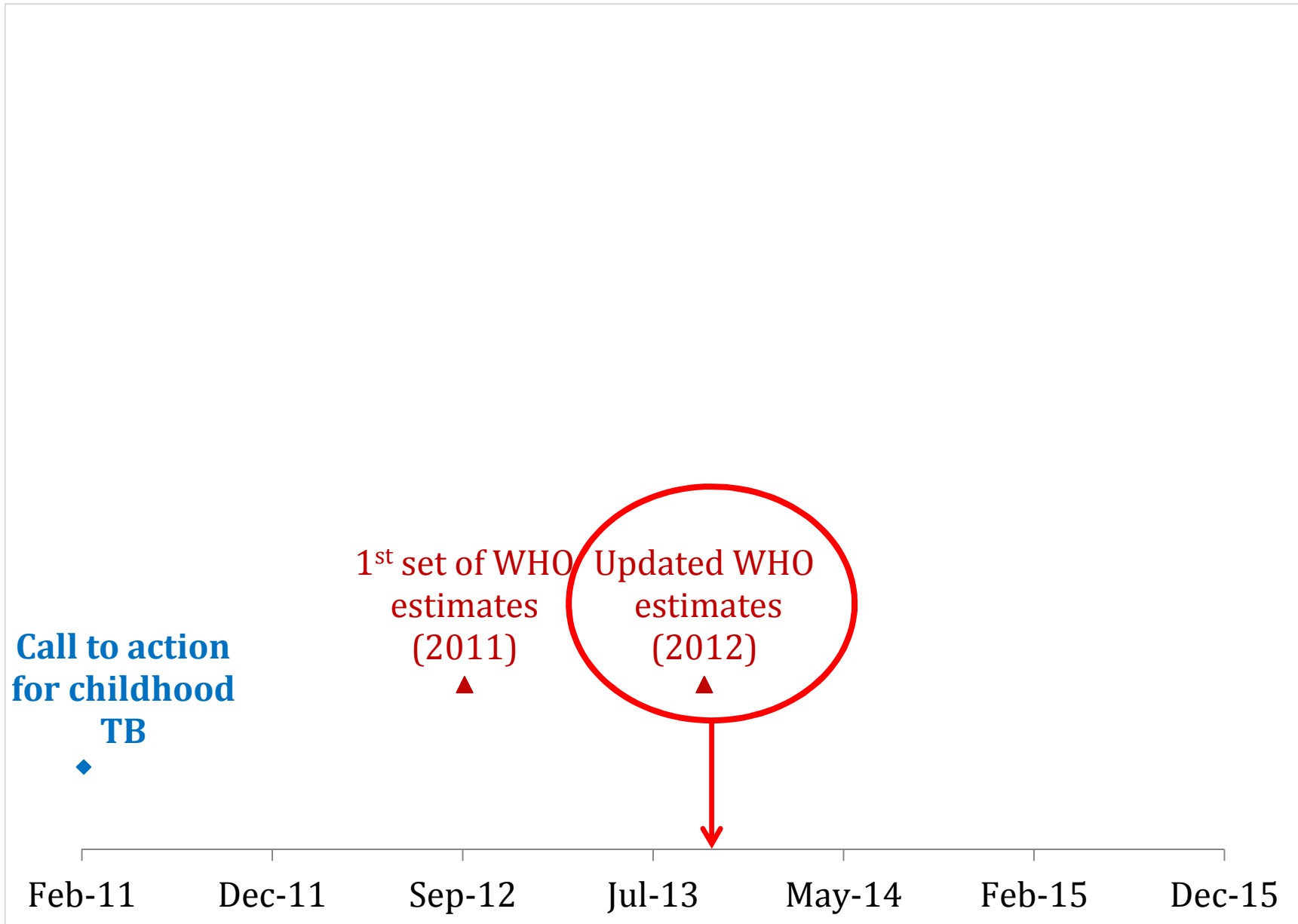# Paediatric TB disease burden: past, present, future

Call to action for childhood TB

Feb-11   Dec-11   Sep-12   Jul-13   May-14   Feb-15   Dec-15

Paediatric TB disease burden: past, present, future

Call to action for childhood TB

1ˢᵗ set of WHO estimates (2011)

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Paediatric TB disease burden: past, present, future

1st set of WHO estimates (2011)

Updated WHO estimates (2012)

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Paediatric TB disease burden: past, present, future

Start of STEP-TB

1st set of WHO estimates (2011)

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Global Consultation on Paediatric Tuberculosis: Disease Burden Estimation and Quantification of Its Drug Market

25-26 September, 2013

Hosted by the Speeding Treatments to End Paediatric Tuberculosis (STEP-TB) Project
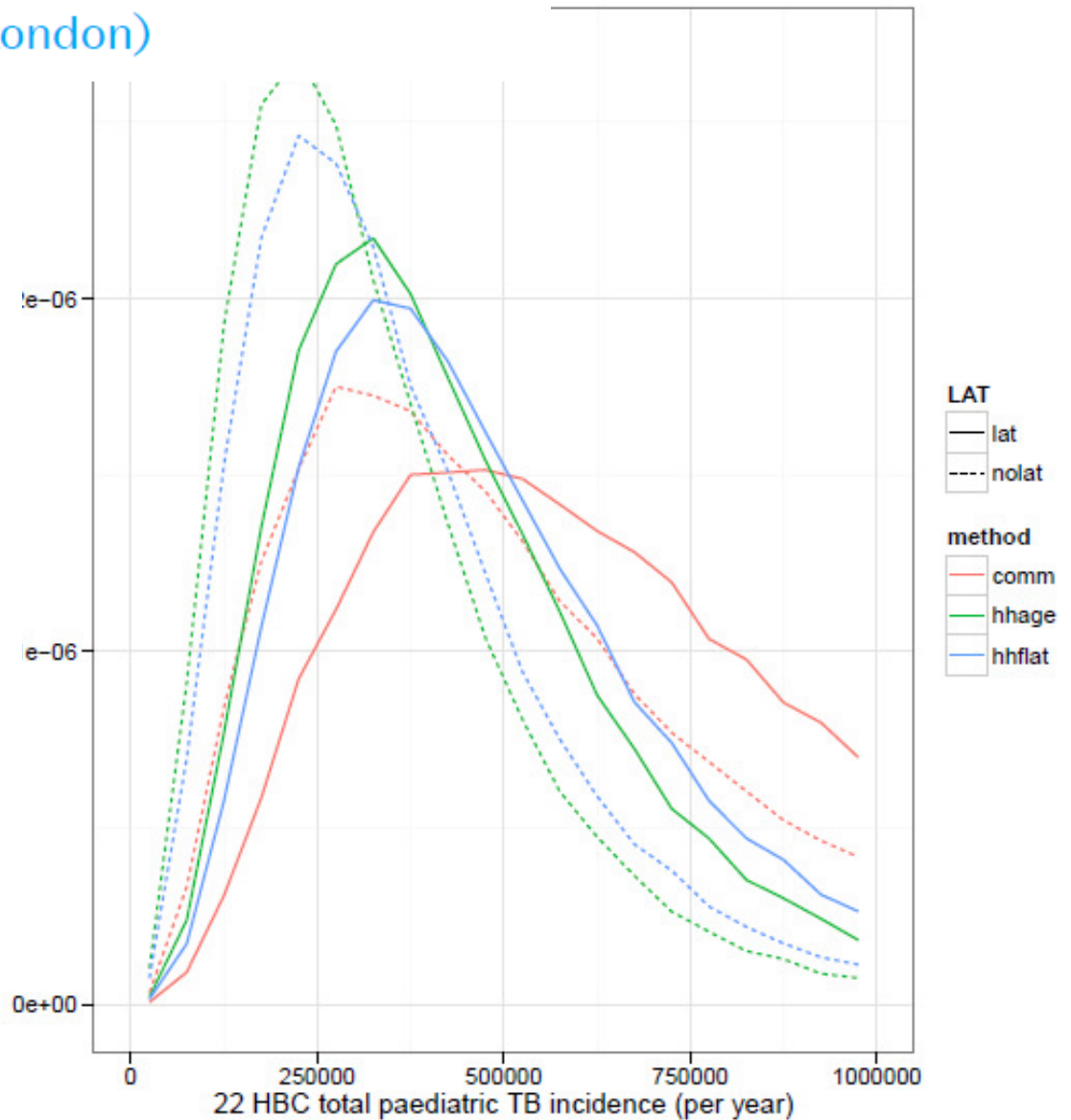*Sponsored by USAID and UNITAID*

Objectives

1. To review available data and **highlight gaps**

2. To **review analytical methods** and epidemiological indicators

3. To **define and prioritise specific actions** that can be taken by TB Alliance, WHO, and other participating organizations

4. To **catalyse efforts to strengthen routine surveillance** and promote consensus in disease burden estimation
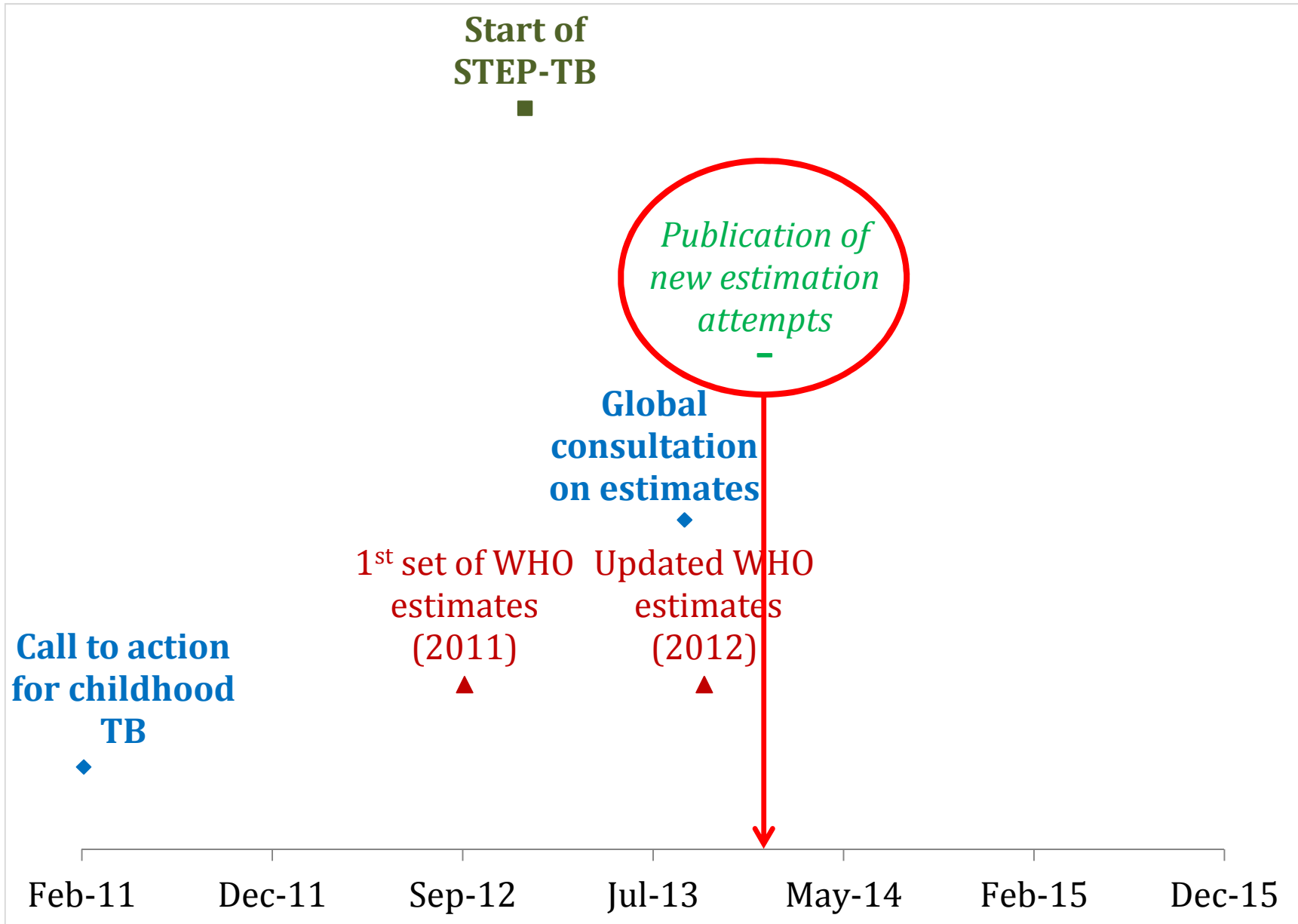
A modelling approach to estimating the burden of paediatric TB

Pete Dodd (University of Sheffield)
& James Seddon (Imperial College London)

- Ongoing **complementary analytical work** to increase our understanding and **build a richer, more consistent picture**

- Not based on TB case notifications

- Deterministic model: pool of children at risk, adult disease, child infection, child disease

- Largely consistent results

Paediatric TB disease burden: past, present, future

Start of STEP-TB
■

Publication of new estimation attempts
–

Global consultation on estimates
◆

1st set of WHO estimates (2011)
▲

Updated WHO estimates (2012)
▲

Call to action for childhood TB
◆

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Independent attempts to estimate TB incidence

Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates

Helen E Jenkins, Arielle W Tolman, Courtney M Yuen, Jonathan B Parr, Salmaan Keshavjee, Carlos M Pérez-Vélez, Marcello Pagano, Mercedes C Becerra,* Ted Cohen*
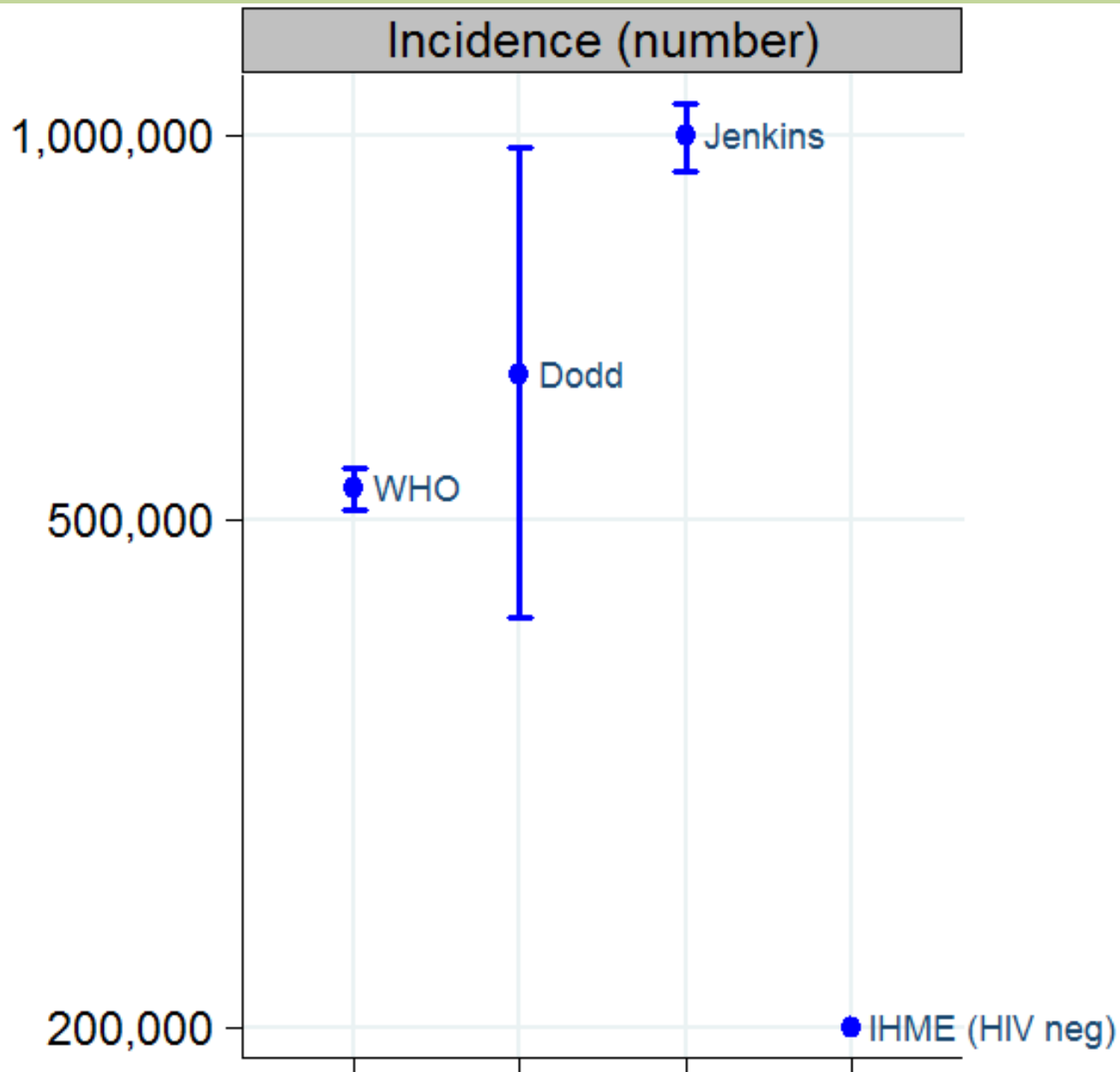
Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study

Peter J Dodd, Elizabeth Gardiner, Renia Coghlan, James A Seddon

Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013
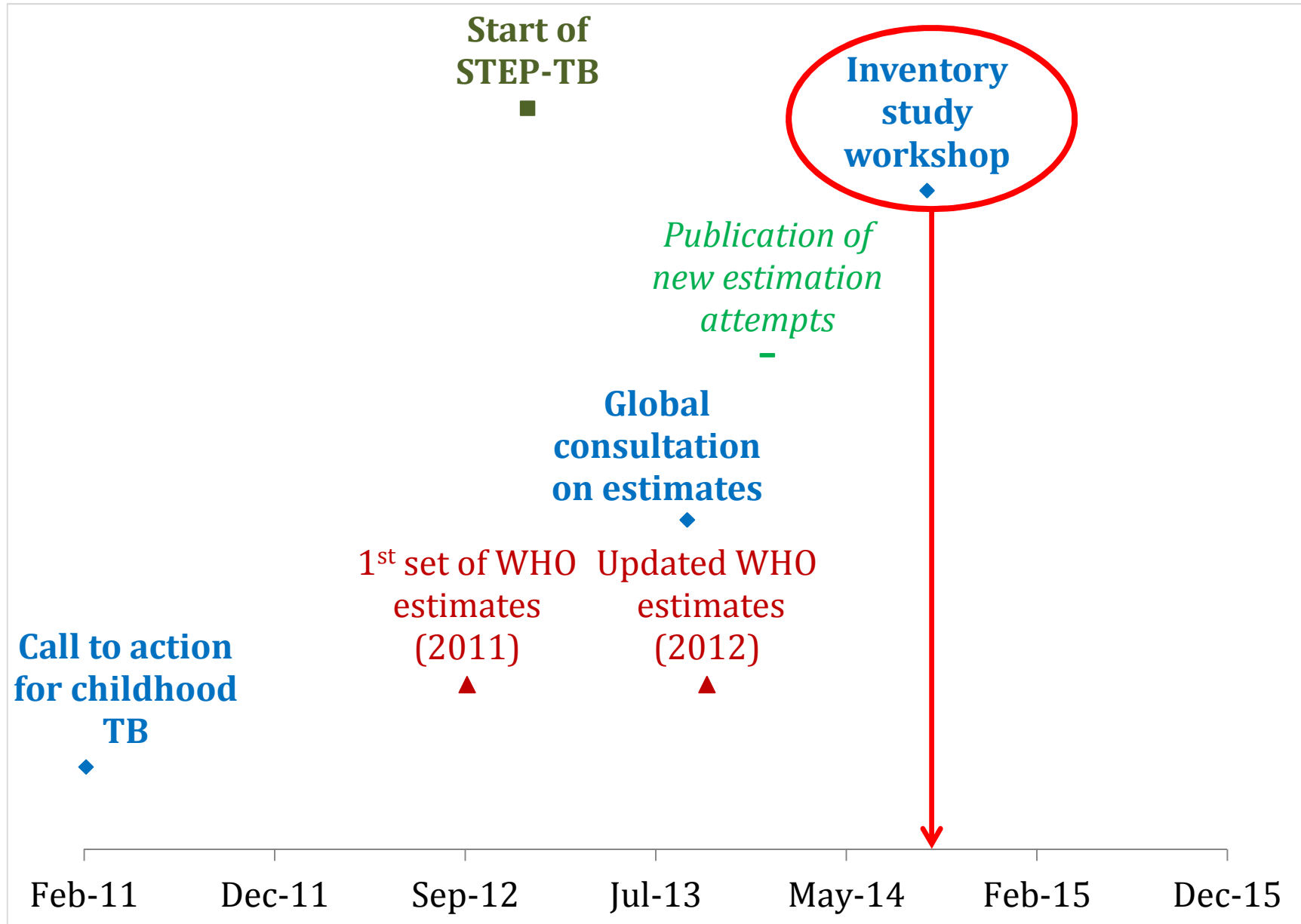
Christopher J L Murray*, Katrina F Ortblad, Caterina Guinovart, Stephen S Lim, Timothy M Wolock, D Allen Roberts, Emily A Dansereau, Nicho

Heterogeneous findings, many data gaps

Paediatric TB disease burden: past, present, future

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Inventory study workshop

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Design and protocol development workshop: TB inventory studies to measure under-reporting of TB cases

24-26 September, 2014

Objectives

1. To explain and promote the role and value of inventory studies to TB care and control

2. To explain (i) major alternative study design & (ii) key issues concerning the implementation and analysis of inventory studies

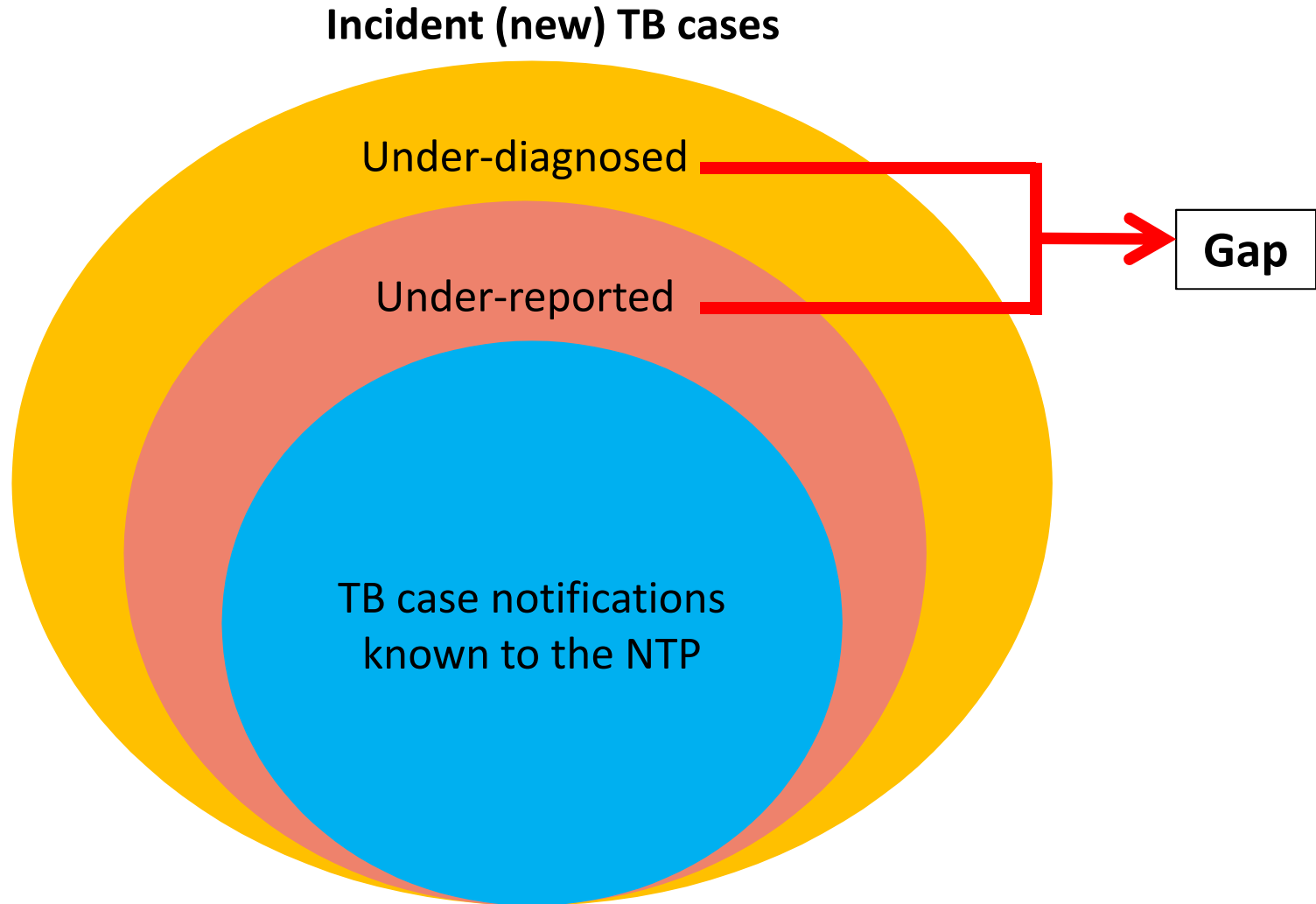3. To facilitate the development of a draft protocol outline for a TB inventory study

Getting to TB incidence

Incident (new) TB cases

Under-diagnosed

Under-reported

TB case notifications
known to the NTP

Gap

Summary of key decisions, timelines and requirements

	China	Indonesia	Pakistan	Philippines	Thailand	Viet Nam
Objectives	Under-reporting (retrospective)	Under-reporting (prospective)	Under-reporting (prospective)	Data quality assessment (NTP and non-NTP)	Under-reporting (retrospective & continuous)	Under-reporting & incidence (prospective)
Case definitions	Bact-conf (all ages)	• All-form TB • Bact-conf • Children	Children	• All-form TB • Bact-conf • Children	• All-form TB • Bact-conf • Children	• All-form TB • Bact-conf • Children
Timelines • *Protocol* • *Study end*	• Q1 2015 • Q4 2015	• Q4 2014 • Q4 2015	• Q4 2014 • Q4 2015	• Q2 2015 • Q4 2016	• Q4 2014 • Q4 2015	• Q4 2014 • Q4 2015
Support required	• TA	• TA • Funding	• TA • Funding	• TA • Funding	• TA • Funding	• TA • Funding

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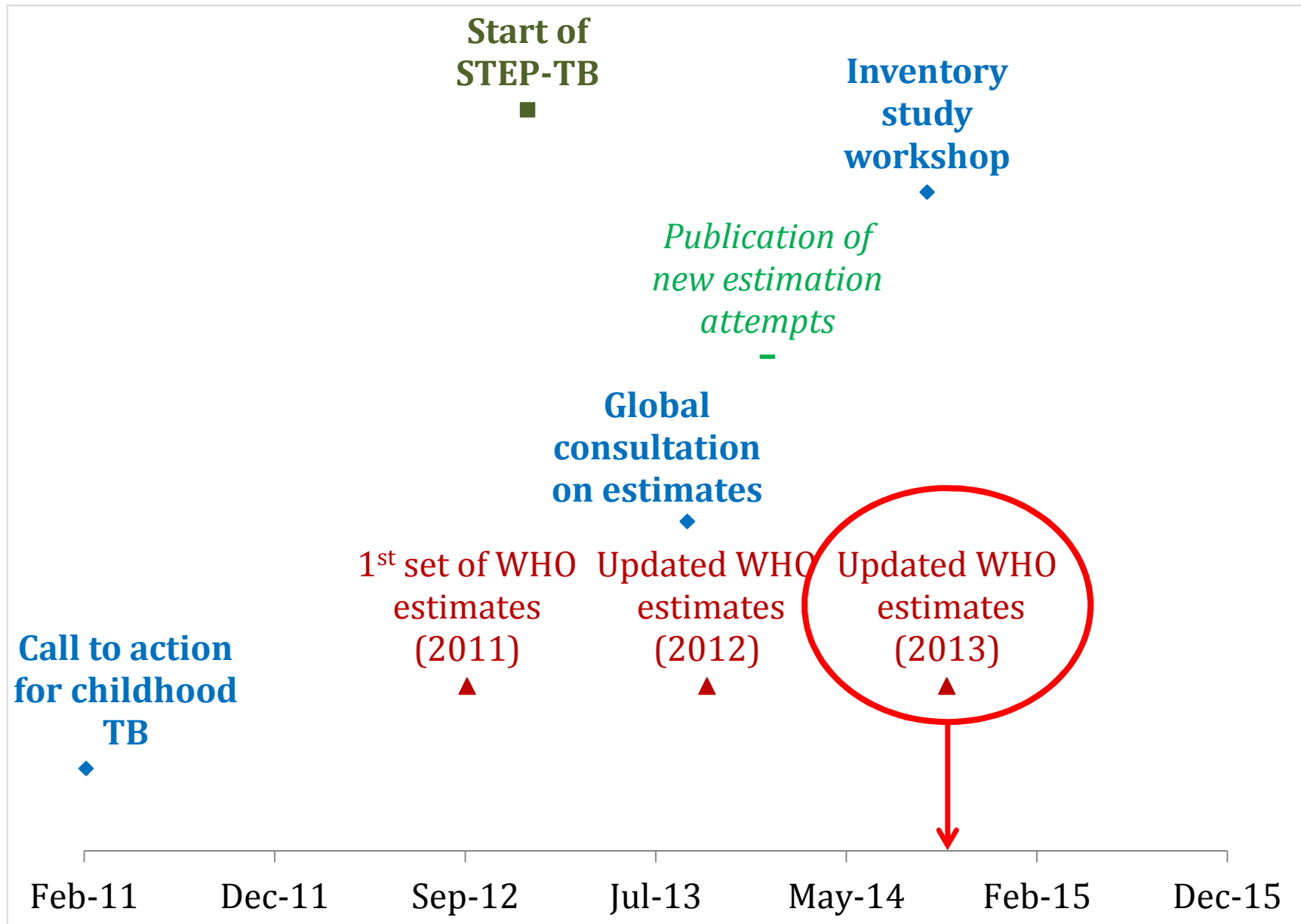
Incidence *data source* (2013)

Reporting of new and relapse TB case notifications disaggregated by age, 2013

Legend:
- Age disaggregation
- No age disaggregation
- No data reported
- Not applicable
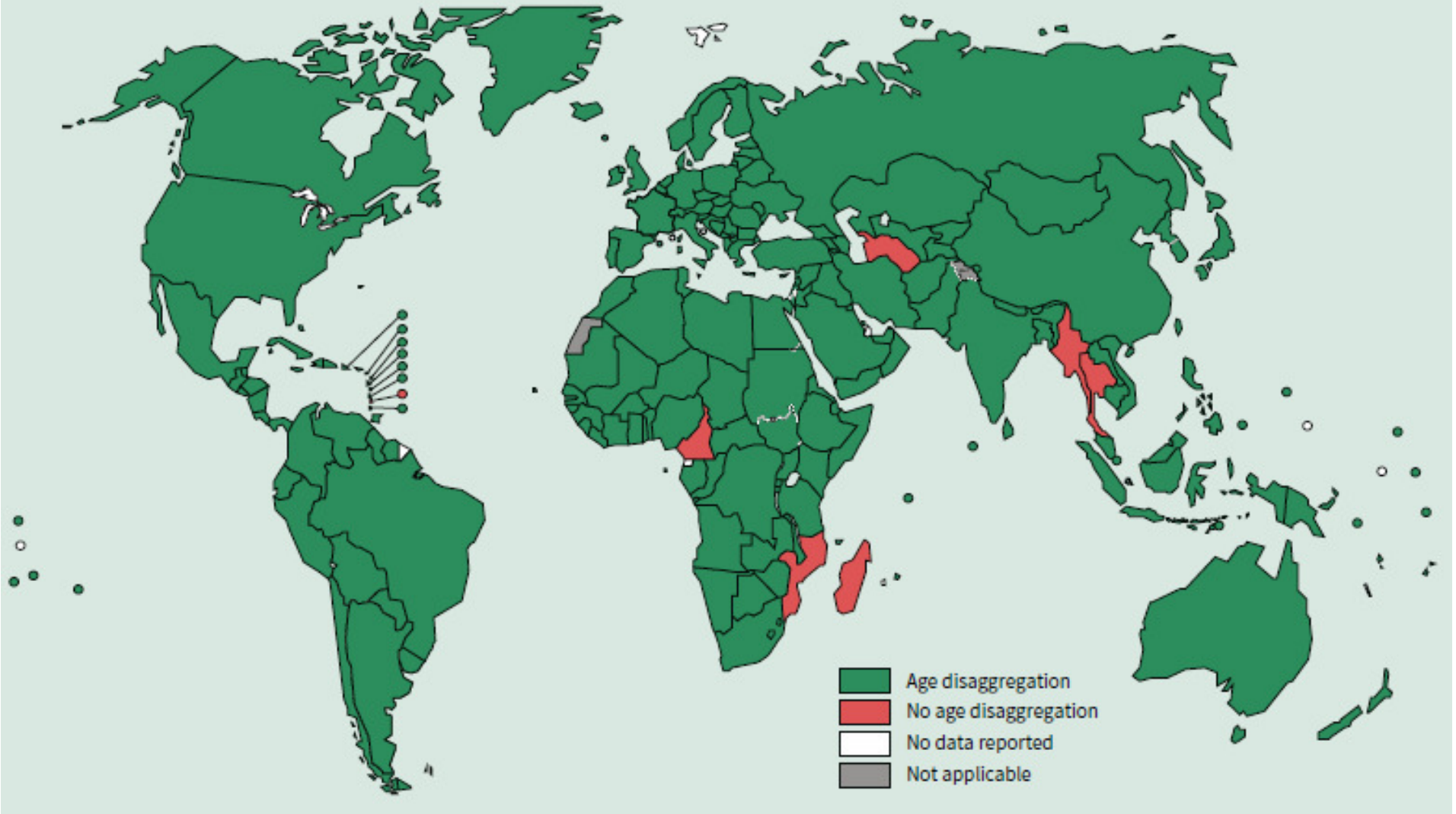
Incidence *estimation* (2013)

- *Method I*:
  - Age-disaggregation is now only requested for totals of all-form (bacteriologically-confirmed and clinically diagnosed), new and relapse case notifications (estimated total: 300 000)
  - Ratio of child to adult case notification is used to age disaggregate total TB incidence (all ages)

- *Method II*: results from Dodd et al

- Ensemble approach is used to combine the two independent methods

Estimated total incidence:

550 000 (95% CI 470 000 – 640 000)

6% of total 9 million incident cases are children

Incidence
next steps

Short-term

- Further complementary mathematical modelling work
  - disaggregation of incidence by HIV status

- Generation of new, nationwide data (particularly on informing the gap between notifications and real incidence)

Longer-term

- Promote the use of case-based electronic recording & reporting (*getting to the under-reported*)

- Strengthening links outside the NTP network e.g. paediatricians (*getting to the under-reported*)

- TB integration in MCH programmes (*getting to the under-diagnosed*)

Mortality *data source* (2013)

Countries (in orange) for which TB mortality is estimated using measurements from vital registration systems (n=124) and/or mortality surveys (n=2, India and Viet Nam)
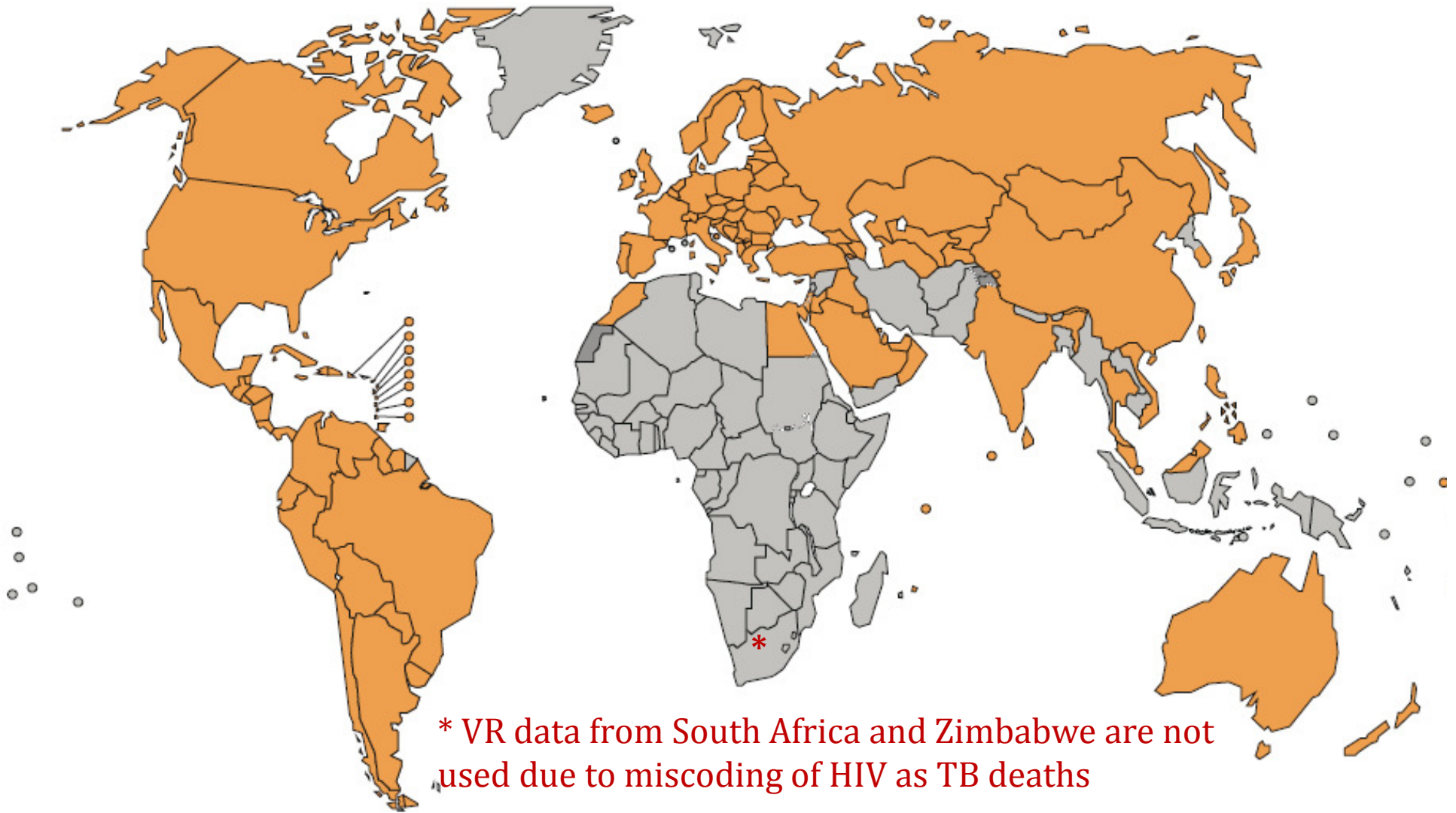
* VR data from South Africa and Zimbabwe are not used due to miscoding of HIV as TB deaths

Mortality *estimation* (2013)

- Underlying cause of death is TB (excludes TB deaths among PLHIV)
  - ICD-10: codes A15-A19
  - ICD-9: codes 010-018

- Adjust reported d deaths from VR: $d_a = \frac{d}{c(1-g)}$

  where c denotes system coverage and g proportion of ill-defined causes

- *For countries with VR data*: use adjusted reported paediatric TB deaths d_a

- *For countries without VR data*: use statistical modelling (including multiple imputation) to predict the ratio of paediatric to adult adjusted TB deaths and disaggregate totals (all ages)

80 000 (64 000 – 97 000) TB deaths (HIV-negative)

### 7% of total 1 100 000 TB deaths (HIV-negative)

Mortality
next steps

- Additional analytical work
  - Mathematical modelling (e.g. TB deaths in HIV co-infected children)

- Collaboration with CHERG*: investigate options to quantify the miscoding of TB deaths in VR systems (e.g. due to pneumonia, malnutrition, HIV/AIDS)

- Investigate options for "correcting" VR data from South Africa and Zimbabwe

- Advocate for the development of and investment in VR systems
  - Allows for a direct measurement of mortality: level of & time trends
  - Serving many health programmes, not only TB
  - Interest from funding agencies: Global Fund investment in VR, part of HIS strengthening grants (e.g. Indonesia)

* UNICEF & WHO's Child Health Epidemiology Reference Group

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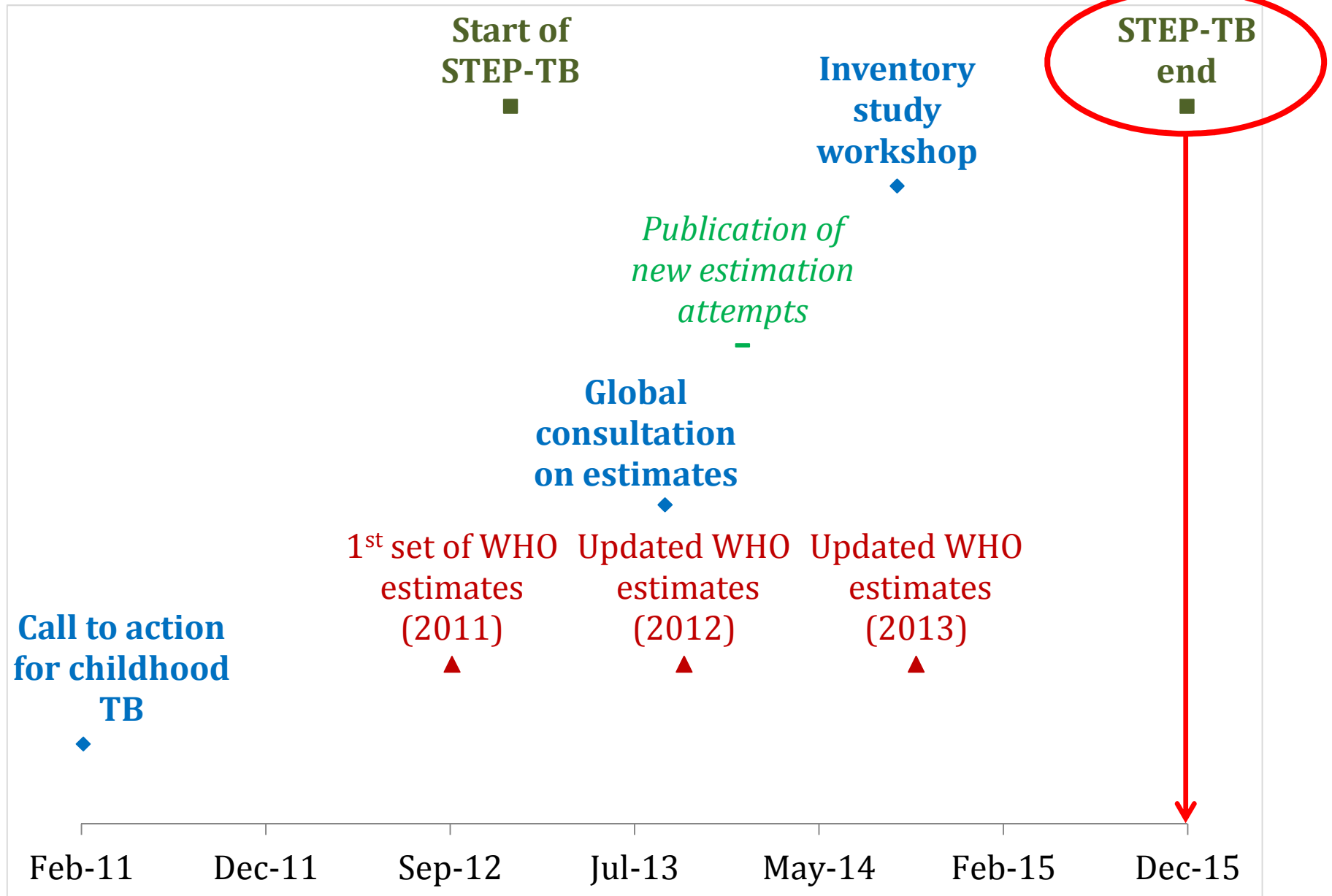
Ongoing analytical work

- **TB incidence**
  - Global and regional estimates
  - Disaggregated by HIV-status
  - Disaggregated by MDR-TB status

- **TB mortality**
  - Global and regional estimates
  - Disaggregated by HIV-status

- **Data gaps**
  - Set priorities in empirical studies that could most improve precision of model-based estimates

Over to Kathryn

TB IN ADOLESCENTS