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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- Ted Cohen
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- Elana Robertson
- UNITAID
- USAID
- TB CARE

[Logos of various organizations]
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

- 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?

Quantify the level of TB burden

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

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1st set of WHO estimates (2011)

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Timeline:
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- Feb-15
- Dec-15
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
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- Publication of new estimation attempts

Events:
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- Dec-11
- Sep-12
- Jul-13
- May-14
- Feb-15
- Dec-15
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 JL Murray*, Katrina F Ortblad, Caterina Guinovart, Stephen S Lim, Timothy M Wolock, D Allen Roberts, Emily A Dansereau, Nicho
Heterogeneous findings, many data gaps
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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-reported
- Under-diagnosed

TB case notifications known to the NTP

Gap
## Summary of key decisions, timelines and requirements

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Incidence *data source* (2013)
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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STEP-TB end

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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