Using modelling to extrapolate from TB trials – the STREAM experience

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Multi-drug resistant tuberculosis

- A public health crisis and a health security threat
- 558,000 cases with resistance to Rifampicine in 2017, of which 82% had MDR-TB
- TB incidence is currently falling at about 2% year, insufficient to reach the 2020 milestones of the End TB Strategy

STREAM I trial

- First phase-III RCT to test the efficacy, safety and economic impact of the 9-month Bangladeshi regimen

- Primary objectives:
  - Assess whether the proportion of participants with a favourable efficacy outcome on shorter regimen is non inferior to that on the WHO 20-24 months recommended regimen
  - Compare the proportion of participants who experience grade 3 or greater adverse events during treatment or follow-up

STREAM I Economic Evaluation

- Conducted in Ethiopia and South Africa only
- Collected 3 types of costs:
  - Patient direct costs (transport costs, food costs, OOPs to access healthcare services)
  - Patient indirect costs (work loss, reduced productivity from disease)
  - Health system costs (drug therapy, medical care, in-patient treatment, SAEs management, etc.)

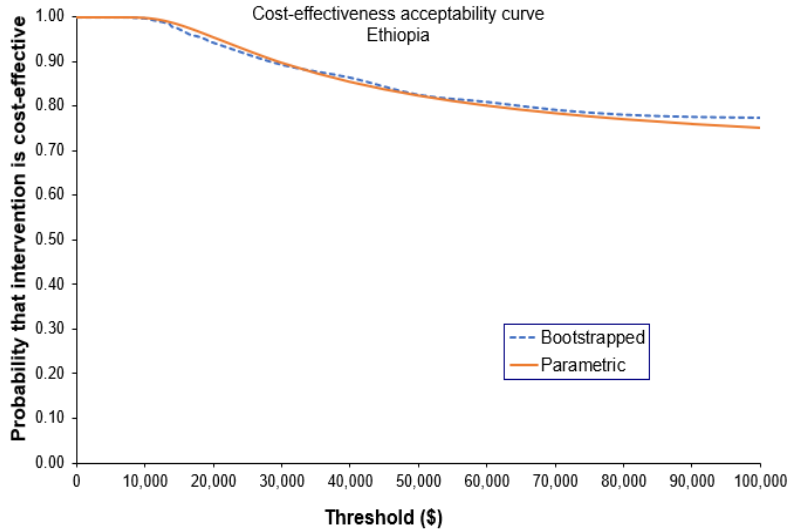
STREAM I Economic Evaluation- sources of cost data

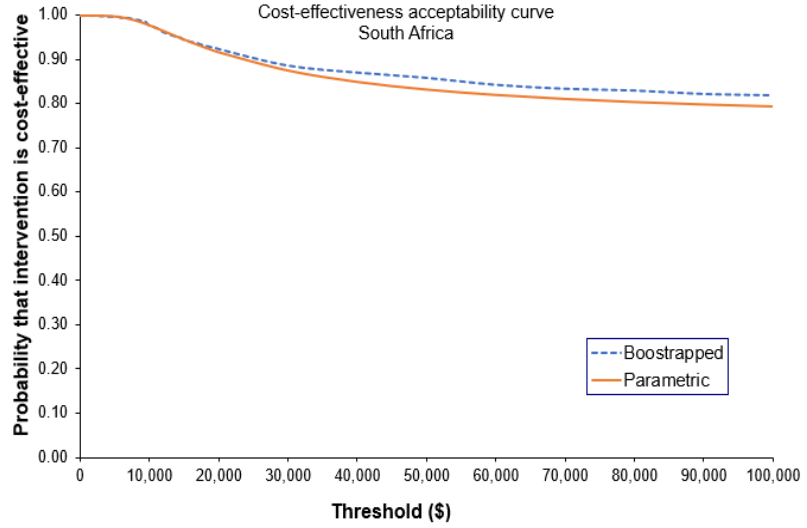
- Health system costs (routine)
  - Unit costs from local sources
  - Staff interviews (to establish clinical management, tests, examinations and durations where appropriate)
  - Patients clinical records
  - Serious Adverse Events costed using patients' records

- Patient costs and socioeconomic status
  - Captured using trial CRFs, every 12 weeks

Cost-effectiveness analysis of STREAM I

- No HRQoL data collected, so efficacy outcome results from the clinical trial have been used
- Conducted a probabilistic sensitivity analysis, by replicating costs and effects 1000 times
- Constructed CEAC curves

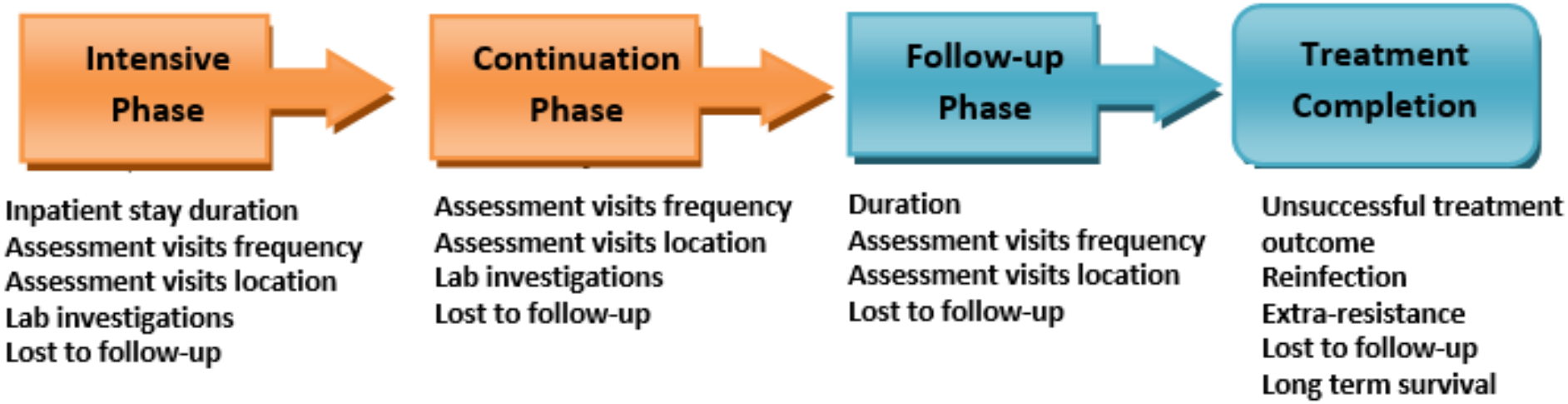




Within-trial economic evaluation issues

- Intermediate health outcomes rather than final outcomes (the follow-up period was of 132 weeks only)
- Neglects to account for relapses, acquired resistance, long term health
- Trial primary outcome was a composite outcome whose components vary in their likely consequences
- Care received in practice likely to vary between countries and can differ substantially from that received in STREAM

Care received in practice likely to vary



Using DAMs to extrapolate outcomes and costs

Predict the impact of the treatments received by:

- Evaluating the full absolute impacts of the two treatments on health outcomes and healthcare costs i.e. the impact on DALYs and healthcare costs primarily driven by unsuccessful treatment, reinfection, lost to follow-up and extra resistance
- Extrapolating beyond the composite outcome

Compare cost-effectiveness results based on trial data with corresponding analysis based on a model

Transition and model state-related effects and costs will be based on trial data and external resources

Value of Information

Uncertainty

Thank you!

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