Economic considerations for novel regimens of TB prevention

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Key considerations for modelling of TB prevention
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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

TB Modelling and Analysis Consortium

Overview

Novel regimens for TB prevention: economic considerations

Focus: economic evaluation (costs too, but not only!)

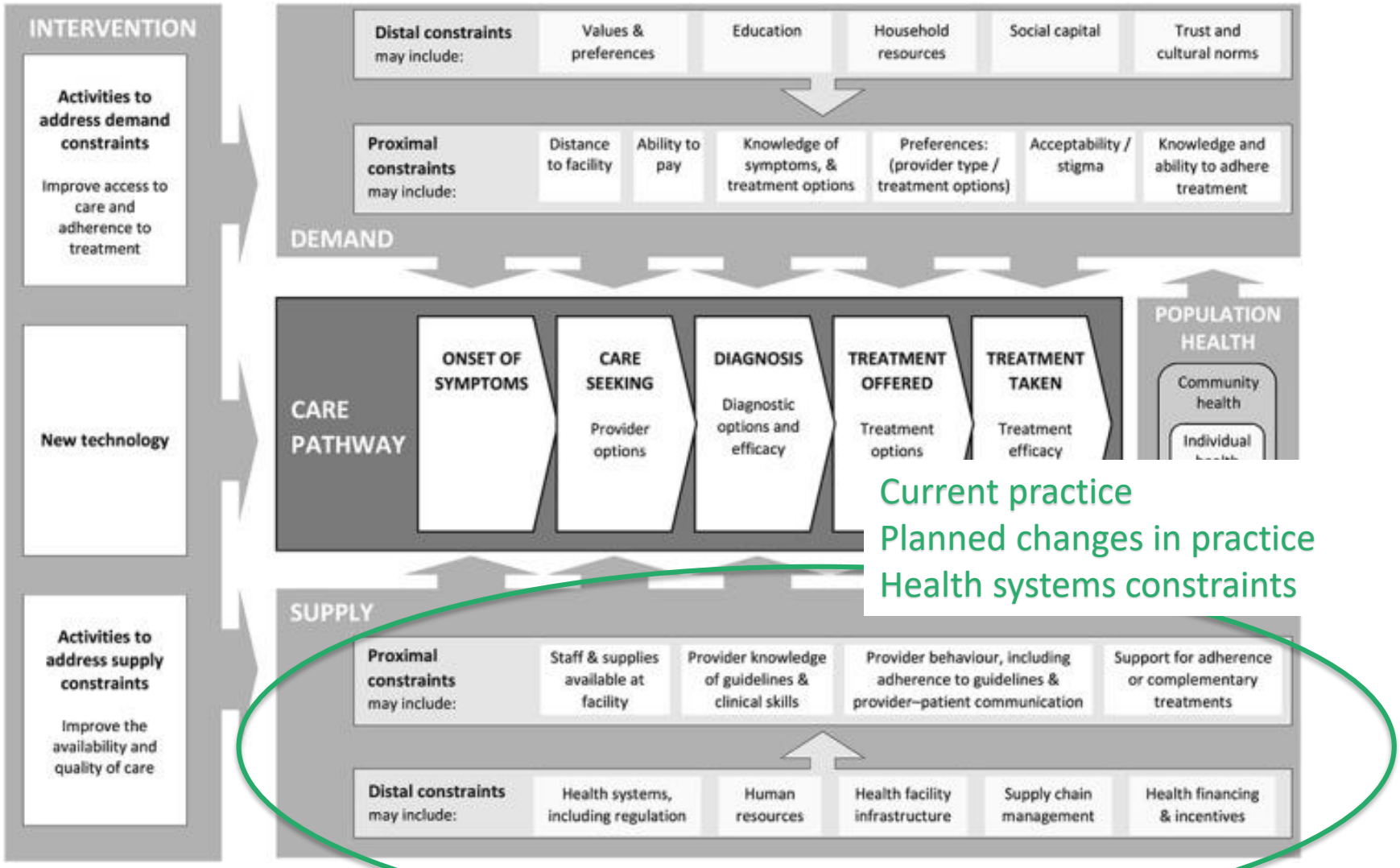
And within economic evaluation…

- Communicating uncertainty around comparator assumptions

Sources of uncertainty depend on the purpose of the analysis:

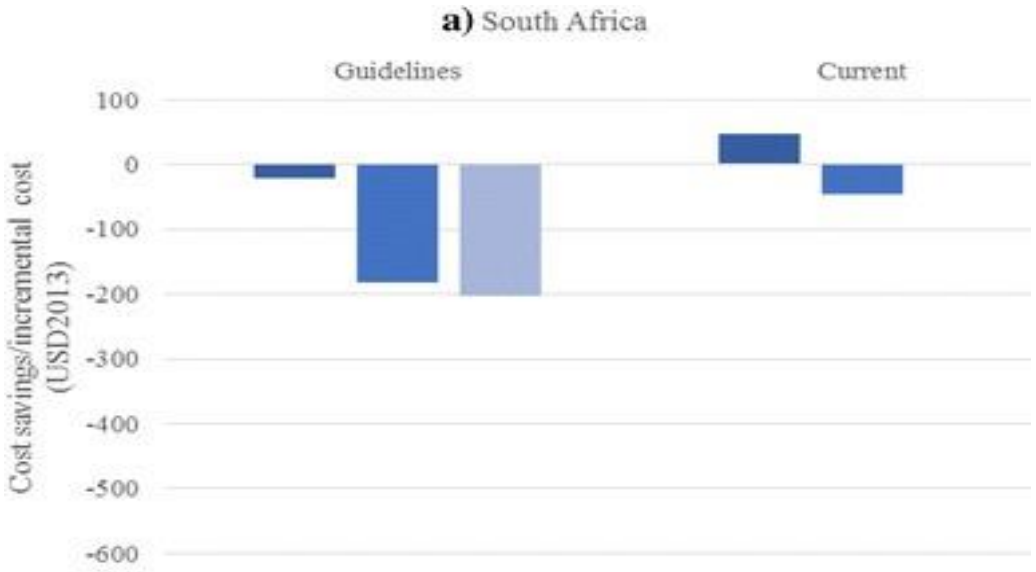
- Economic evaluation for short term scale up of new but existing prevention regimen – planning for next NSP? Local HTA?
- Economic evaluation for long term product development – informing country of potential impact and CE of a potential future regimen?

Introduction of new preventions regimens: how does current practice look like?



Incorporating Demand and Supply Constraints into Economic Evaluations in Low-Income and Middle-Income Countries. Vassall A, Mangham-Jefferies L, Gomez GB, Pitt C, Foster N. Health Econ. 2016 Feb;25 Suppl 1:95-115.

Current practice and possible cost savings from treatment shortening



Cost and cost-effectiveness of tuberculosis treatment shortening: a model-based analysis. Gomez GB, Dowdy DW, Bastos ML, Zwerling A, Sweeney S, Foster N, Trajman A, Islam MA, Kapiga S, Sinanovic E, Knight GM, White RG, Wells WA, Cobelens FG, Vassall A. BMC Infect Dis. 2016 Dec 1;16(1):726.

GeneXpert introduction and empirical treatment

- Local practice influence in the estimation of both health gains and costs

	Xpert scenario *vs* smear scenario	Percent difference* compared with original analysis[1]
Incremental costs over 10 years	US$216 000 000 (112 000 000–371 000 000)	49% lower
DALYs averted over 10 years	139 000 (50 000–280 000)	68% lower
Incremental cost-effectiveness ratio over 10 years	$1554 (858–4202)	62% higher
Incremental costs over 20 years	$572 000 000 (279 000 000–1134 000 000)	49% lower
DALYs averted over 20 years	473 000 (142 000–973 000)	67% lower
Incremental cost-effectiveness ratio over 20 years	$1208 (621–3995)	55% higher

An annual discount rate of 3% applied to incremental costs and DALYs averted. Parentheses indicate equal-tailed 95% posterior intervals. DALYs= disability-adjusted life years. *Values calculated as a percentage of result obtained in original analysis.[1]

Table 2: **Revised analysis of incremental outcomes and cost-effectiveness of Xpert scenario versus smear scenario**

Lancet Infect Dis. 2015 Jan;15(1):16-7. Effect of empirical treatment on outcomes of clinical trials of diagnostic assays for tuberculosis. Menzies NA, Cohen T, Murray M, Salomon JA.

Planned changes in practice: local national strategic plans

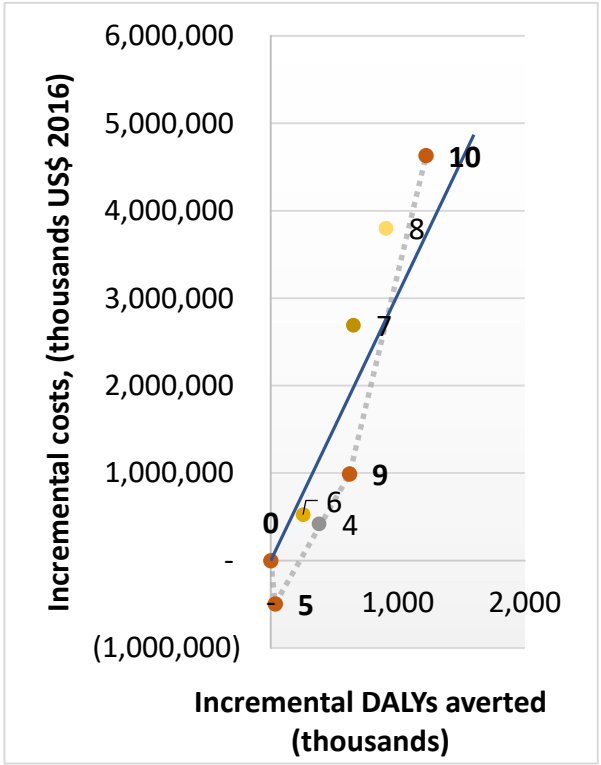
	National strategic plan
India	country-wide private sector engagement Improved diagnosis accuracy and treatment uptake: Xpert scale up (TB/RIF) Improved treatment outcomes: patient financial/m health support Improved MDR costs: MDR Tx decentralized
South Africa	Improved prevention: IPT for HIV+ n ART Improved diagnosis accuracy and treatment uptake: Xpert scale up (TB/RIF) Improved MDR costs: MDR Tx decentralized

Health systems constraints to scale up

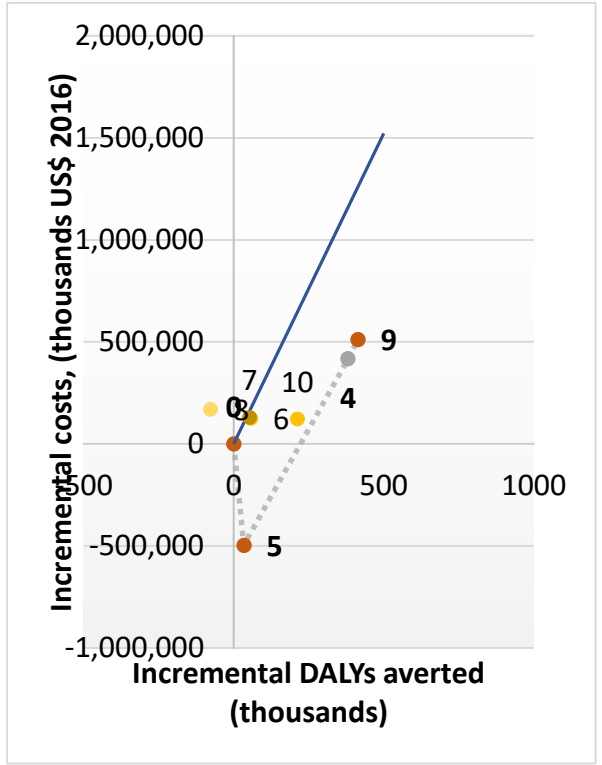
Work from South Africa's TB think tank

Different screening strategies for intensified case finding in South Africa

- Unconstrained scenario
- Coverage constrained by human resources availability



Unconstrained

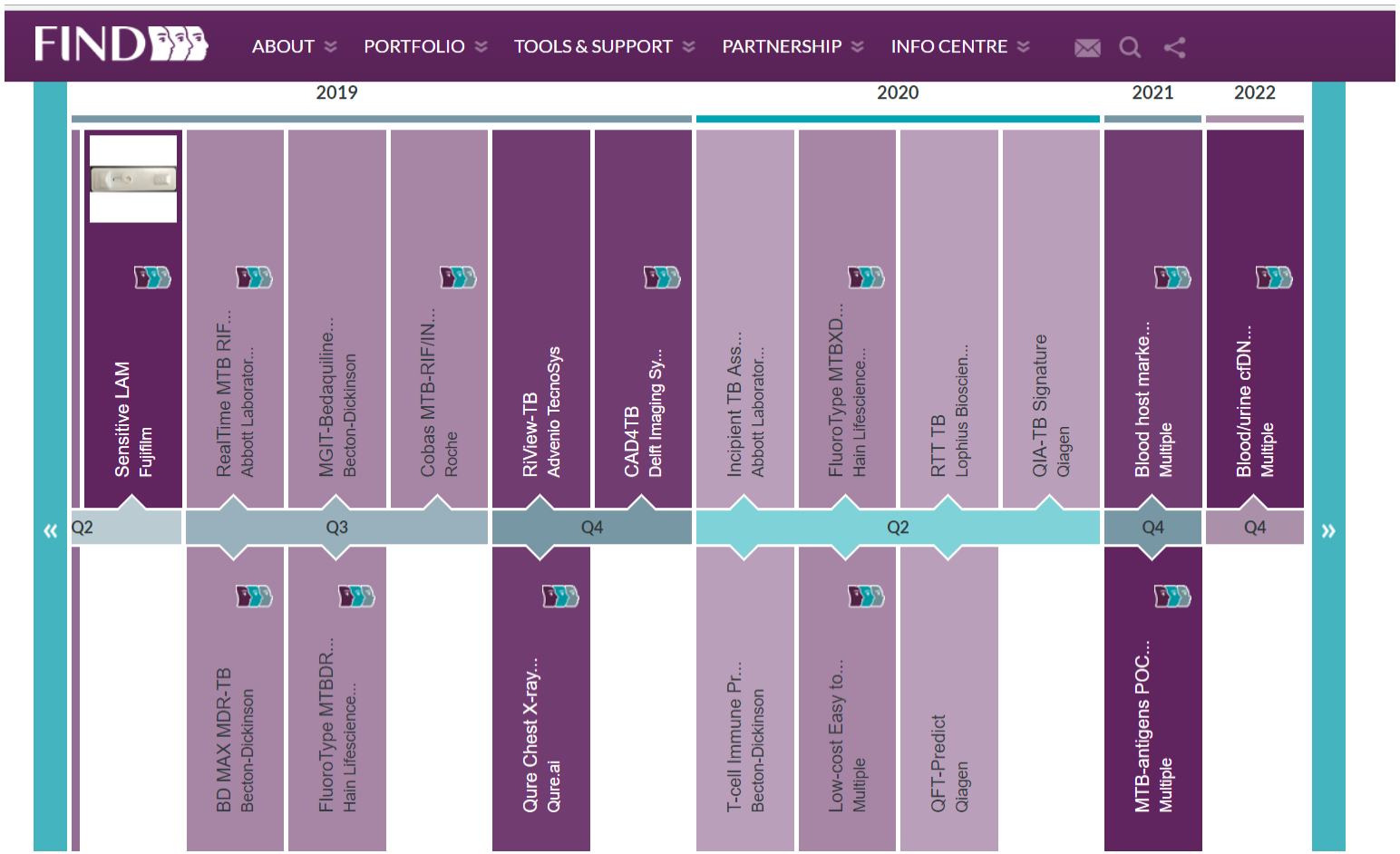


Medium HR constraint

Introduction of future prevention regimens: what will future comparator look like?

- Development pipeline for other technologies
  - New products
  - New strategies
- Local vision and medium/long term planning

Diagnostic pipeline



Treatment pipeline

2018 Global TB Drug and Regimen Clinical Research [1]

Ongoing Clinical Development Research: Strategy/Optimization/Regimen Development

Phase 2

Bedaquiline-Delamanid (ACTG 5343)

Bedaquiline - Pretomanid - Pyrazinamide (BPaZ) (NC-005)

Bedaquiline - Pretomanid – Moxifloxacin - Pyrazinamide (BPaMZ) (NC-005)

Levofloxacin with OBR for MDR-TB (OPTI-Q)

Linezolid Dose-Ranging

Nitazoxanide

Beta-Lactams

High Dose Rifampicin (PANACEA)

TB PRACTECAL - regimens with Bedaquiline-Pretomanid-Linezolid

Phase 3 Regimens

Bedaquiline-STREAM MDR-TB Trial Stage 2 with oral OBR (9 mo) or OBR with injectables (6 mo)

Bedaquiline-Pretomanid-Linezolid (NiX-TB)

Delamanid with OBR for MDR-TB

High Dose Rifampicin for DS-TB (RIFASHORT)

Rifapentine - Moxifloxacin for DS-TB (CDC TBTC 31)

Pretomanid-Moxifloxacin-Pyrazinamide (STAND)

Optimization/Post Market

Bedaquiline-Linezolid with OBR for MDR-TB (NExT Trial)

endTB 5-Regimen Trial for MDR TB

PredictTB – PET/CT, biomarkers DS-TB, 4 mo

Clofazimine - formulation development

Known chemical classes are color coded: fluoroquinolone, rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone , imidazopyridine amide.

[1] Strategy trials, regimen development, open label, repurposed drug studies. Details for projects listed can be found at http://www.newtbdrugs.org/pipeline/clinical

[2] OBR = Optimized Background Regimen

WORKING GROUP ON NEW TB DRUGS

www.newtbdrugs.org

Updated: March 2018

Vaccine pipeline

Discovery	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III
Approximately ***20 novel TB vaccine strategies*** in development, several R&D partners, TBVI	***Combination vaccines prime-boost*** GSK, TBVI	***MVA85A (ID, Aerosol)*** University of Oxford, TBVI	***RUTI*** Archivel Pharma	***VPM1002*** VPM, SII, MPIIB, TBVI	***M.Vaccae*** AnHui Longcom
	H64 + CAF01 SSI, TBVI	***MTBVAC*** Biofabri, University of Zaragoza, TBVI	***H1/H56 : IC31®*** SSI, Valneva, Aeras	***M72 + AS01E*** GSK, Aeras	
	rBCGΔais1/zmp1 University of Zurich, Aeras, TBVI	***ChAdOx1.85A MVA85A*** University of Oxford,	***H4 : IC31 ®*** SSI, Sanofi Pasteur, Aeras	***DAR-901*** Dartmouth University, Aeras	
	ChAdOxPPE15 University of Oxford, TBVI	***Ad5 Ag85A*** McMaster University, Can Sino	***ID93 + GLA-SE*** IDRI, Aeras		
	Therapeutic vaccine –MVA platform Transgene SA, TBVI	***TB/FLU-04L*** Research Institute for Biological Safety Problems, Kazakhstan			
	CysVac2/Advax University Sydney, TBVI				

Vaccine candidates currently receiving technical and / or financial or other support from TBVI

Vaccine candidates formerly receiving technical and / or financial support from TBVI

Other candidates in the global pipeline

Source: Phase I-III: TAG pipeline report
Update: May 2017

Local vision

Small improvement in technologies

Large improvement in technologies

	A (NSP)	B (5y, NSP + medium term tech)	C (15y, NSP + medium and long term tech)
India	country-wide private sector engagement Improved diagnosis accuracy and treatment uptake: Xpert scale up (TB/RIF) Improved treatment outcomes: patient financial/m health support Improved MDR costs: MDR Tx decentralized	A + Improved diagnosis accuracy and treatment uptake: Xpert scale up (expanded DST) Improved treatment outcomes: DS Tx: 4m, less costs Improved treatment outcomes: MDR Tx: 9m, less costs	B + Improved prevention: vaccine
South Africa	Improved prevention: IPT for HIV+ n ART Improved diagnosis accuracy and treatment uptake: Xpert scale up (TB/RIF) Improved MDR costs: MDR Tx decentralized	A + Improved diagnosis accuracy and treatment uptake: Xpert scale up (expanded DST) Improved treatment outcomes: DS Tx: 4m, less costs Improved treatment outcomes: MDR Tx: 9m, less costs	B + Improved prevention: vaccine

Reflections

Conclusions and recommendations will vary depending on your comparator assumptions – important to be transparent about this source of uncertainty

Large number of moving parts – how to explore different possible futures with policy makers in the same way we explore different introduction scenarios for new technologies

Discussion on what uncertainty to reflect and how to communicate it will depend on the purpose of the analysis

- Introduction of an existing technology in the short term: current practice, local NSP and health systems constraints
- Introduction of future technologies in medium to long term: pipelines of other technologies and long term country plans

Thank you

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