A review of methods to incorporate health systems in infectious disease models

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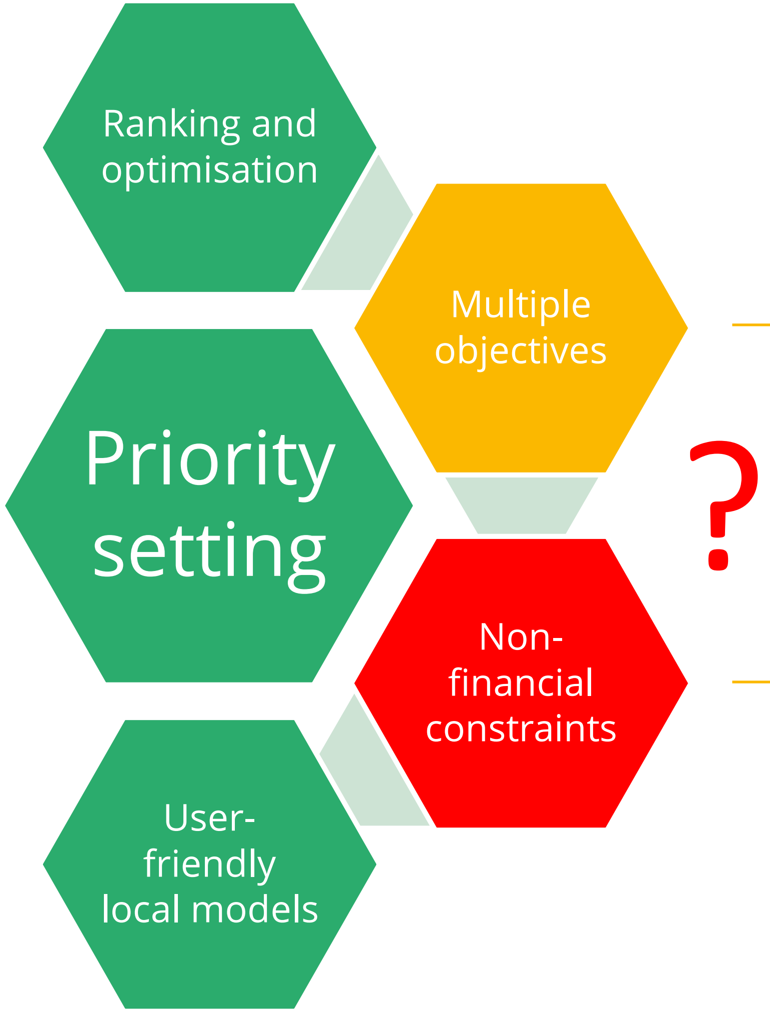
Feasibility – what it is and why it matters



Local norms determine policy priorities as well as structure of health systems and institutions

Feasibility/ acceptability or "ease of implementation" is an objective?

Local demand- and supply-side constraints around the **feasibility of implementation** must be considered

- Limit pace of scale-up
- May incur costs for relaxing (if possible)

Systematic literature review methods

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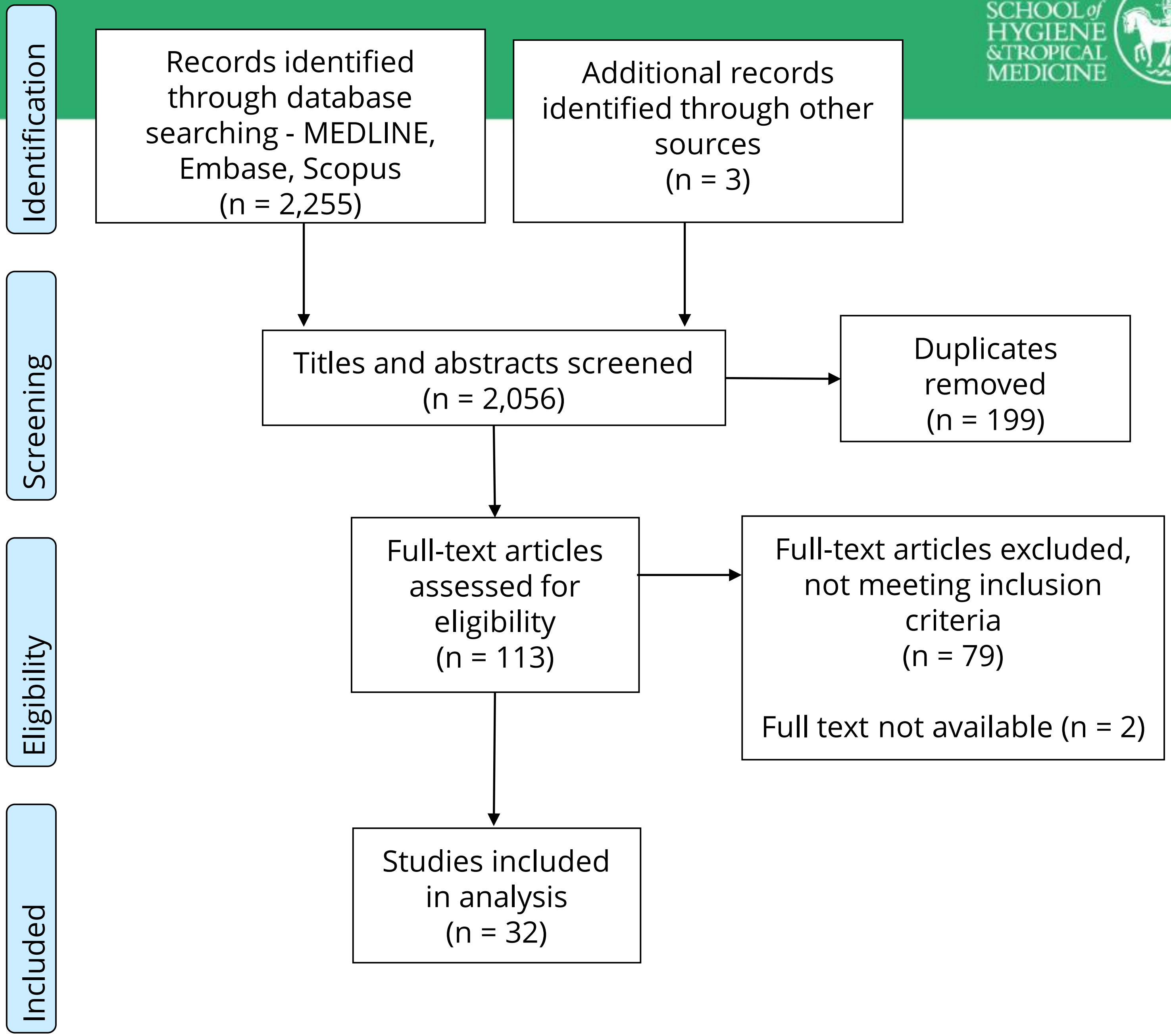
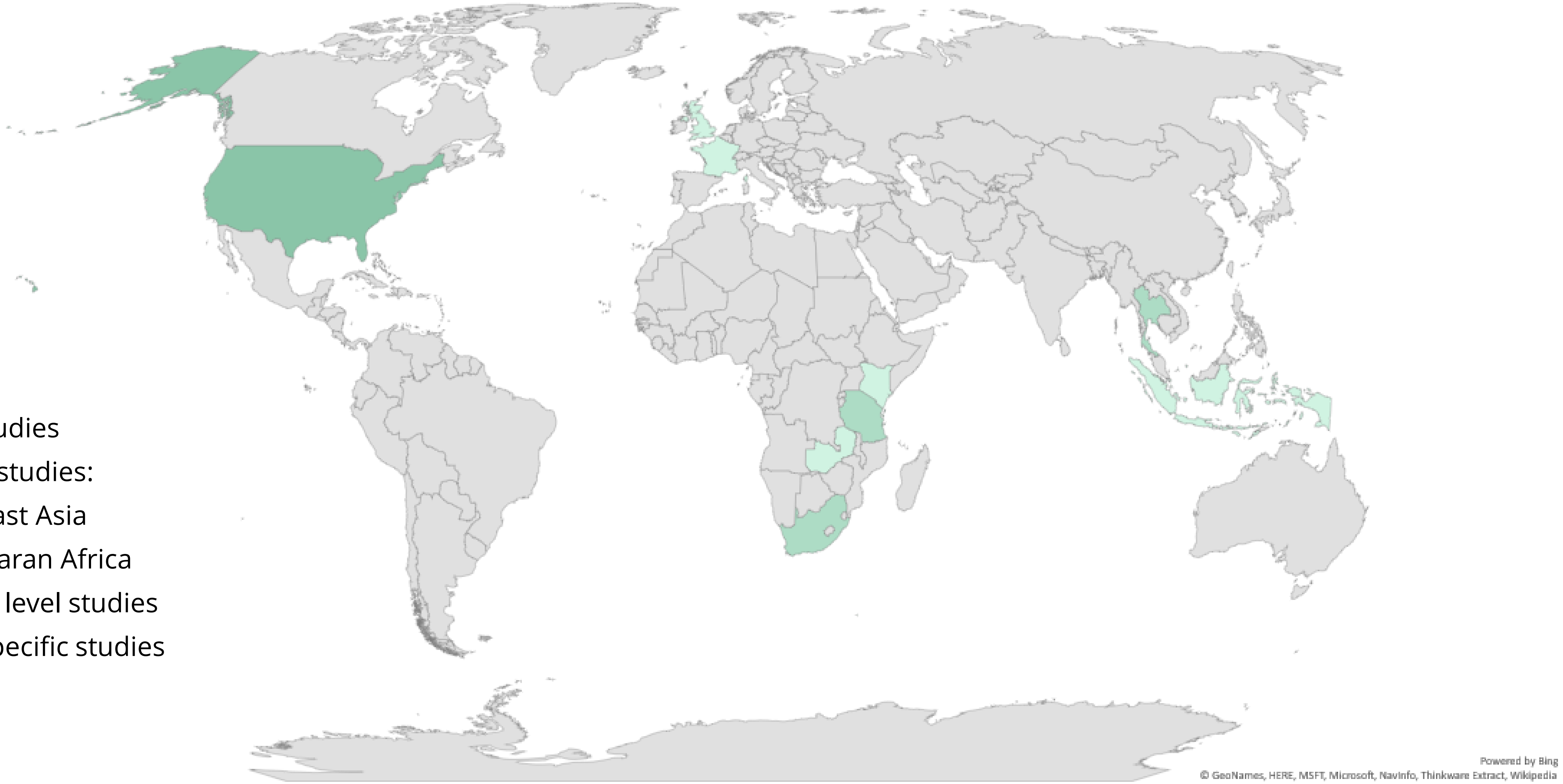
- Research question: how have health system elements (non-financial constraints, policy objectives) been incorporated in mathematical model-based analyses of infectious disease control interventions?
- Databases searched on 9th May 2019: Medline, Embase, Scopus
- Inclusion criteria:
  - English language
  - Topic related to human health
  - Reference to a **formal method of applying non-financial constraints in priority setting using an infectious disease control model**
  - Eligible article type:
    - Infectious diseases modelling study
    - Systematic review

Search results



Study settings



8 Global studies

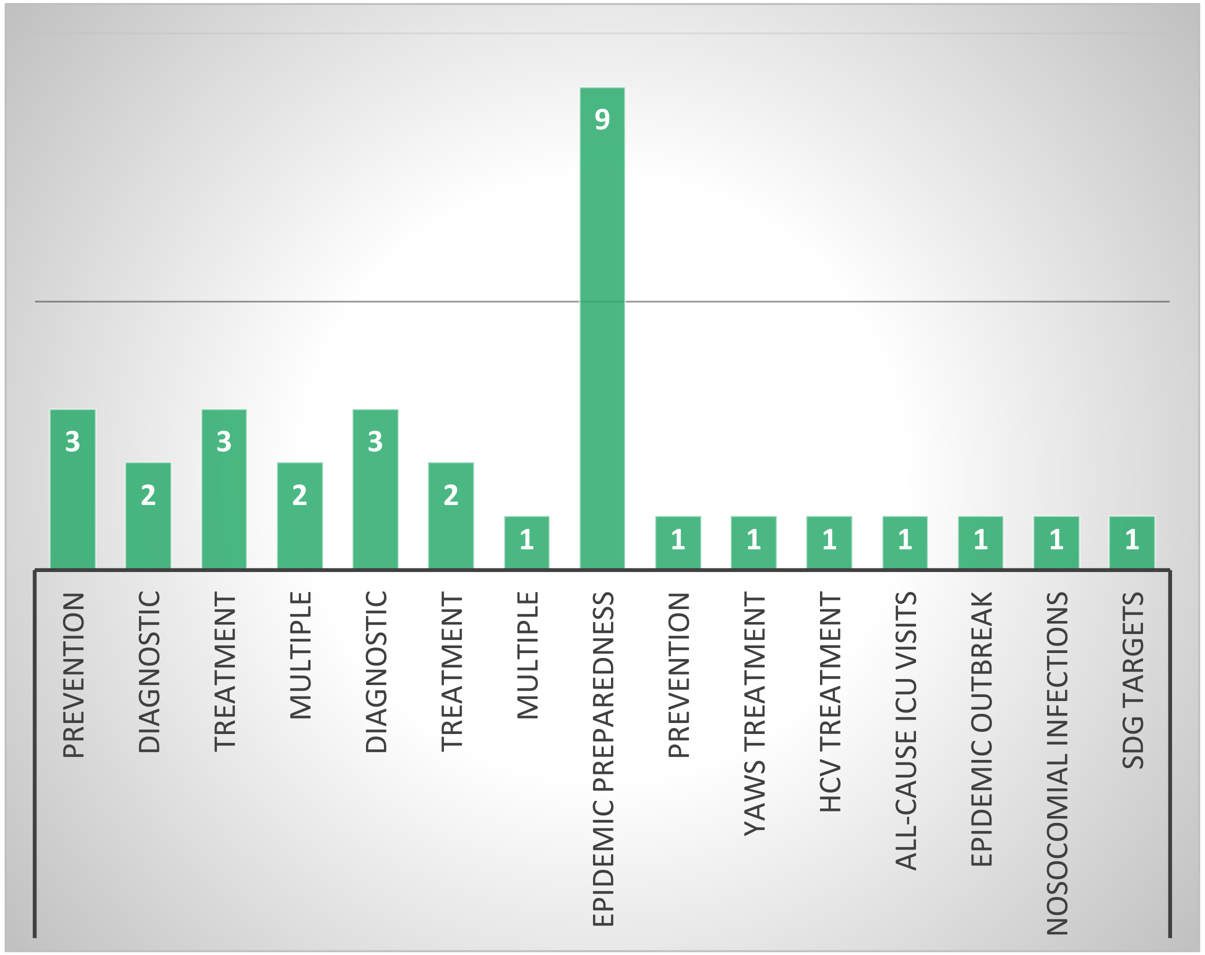
2 Regional studies:

- South East Asia
- sub-Saharan Africa

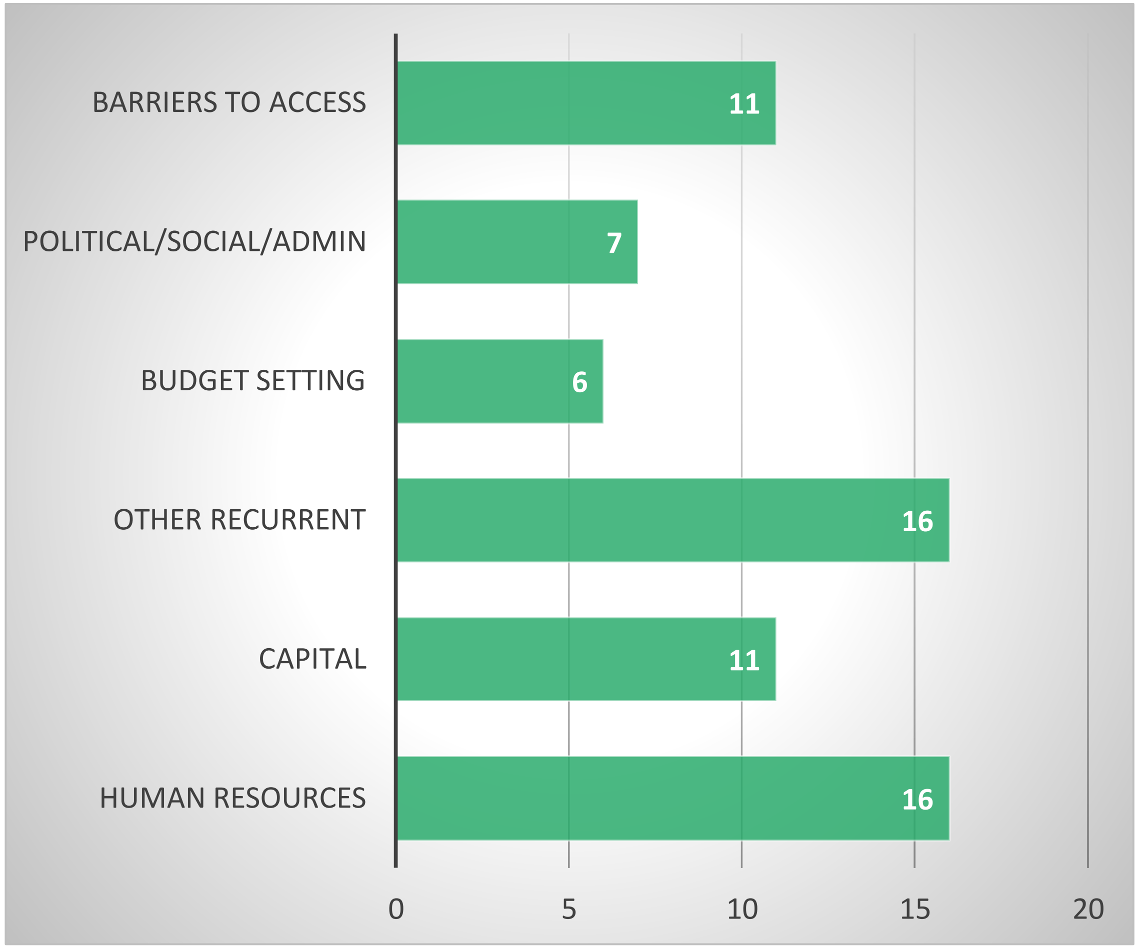
13 Country level studies

8 facility specific studies

Study characteristics



Disease area and intervention types

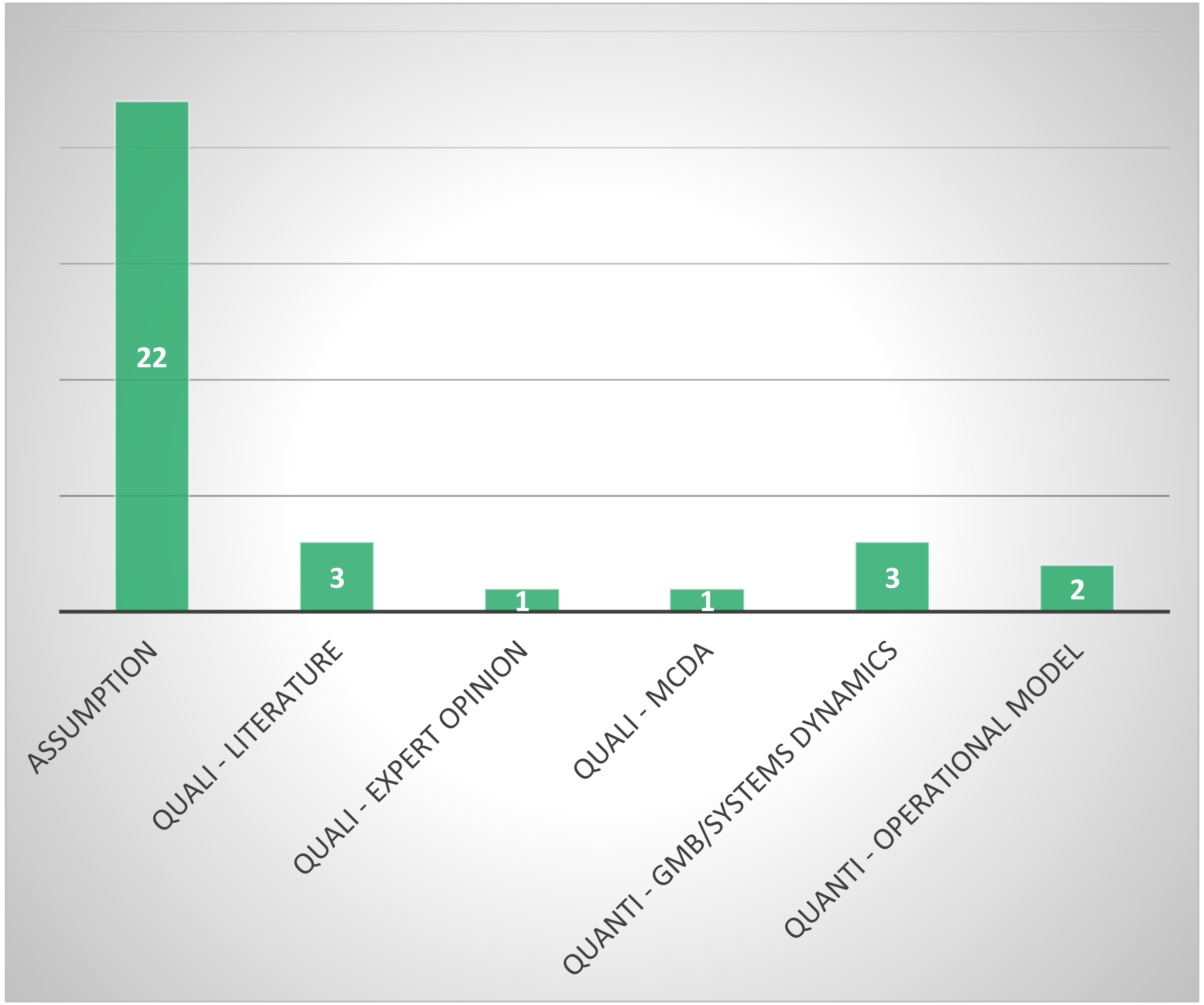


Types of constraints

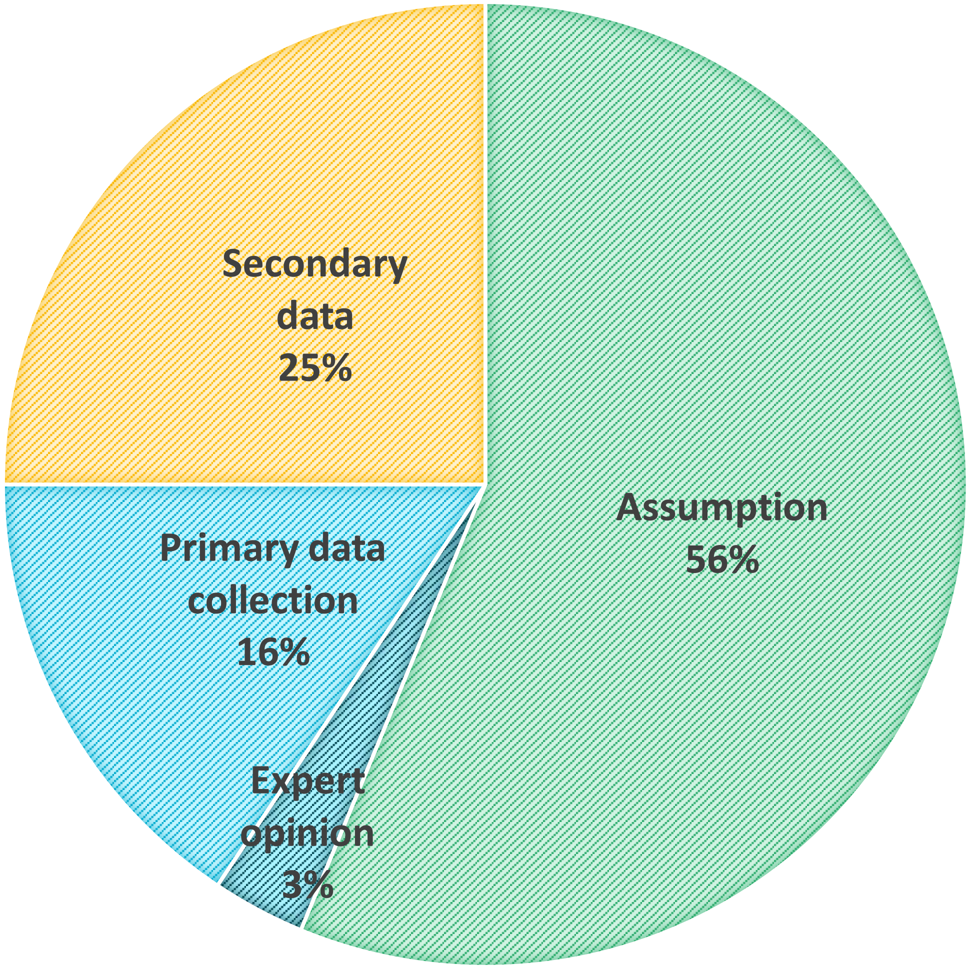
Model characteristics and methods

- Vast majority (n=25, 78%) are deterministic compartmental models
- Four analyses use agent-based simulations
- One influenza study compares a compartmental model to an agent-based simulation
- One study on yaws uses a stochastic compartmental model (transmission rates not determined by ordinary differential equations)
- Three models are 'static' (force of infection does not change over time)
- 13 studies included some kind of economic analysis:
  - 5 cost-effectiveness analyses (2 on HIV and 3 on TB)
  - 8 cost analyses
- 5 studies set priorities by optimising under a budget constraint

Constraints identification and quantification



Method for identifying constraints



Method for quantifying extent and impact of constraints

How do studies consider constraints?

Constrained estimation	Unconstrained estimation	Combination
• Limit effects of the specific intervention • Limit effects along the diseases cascade • Limit effects system-wide	• Include costs of relaxing the constraints • Include estimate of non-financial resource requirements	• Constrained estimation + costs • Constrained estimation + resources • All of the above

Example 1 – Constrained model limiting intervention effects

Shim (2011)

- Objective: compare age-specific H1N1 vaccination allocation between a Nash (own interest) and a utilitarian (optimal for the population) strategy
- Method: model compartments further subdivided based on whether or not individuals decide to vaccinate. Model calculates probability of infection based on the decision. Expected costs of infection and vaccination are then calculated for vaccinated and refusers based on probabilities

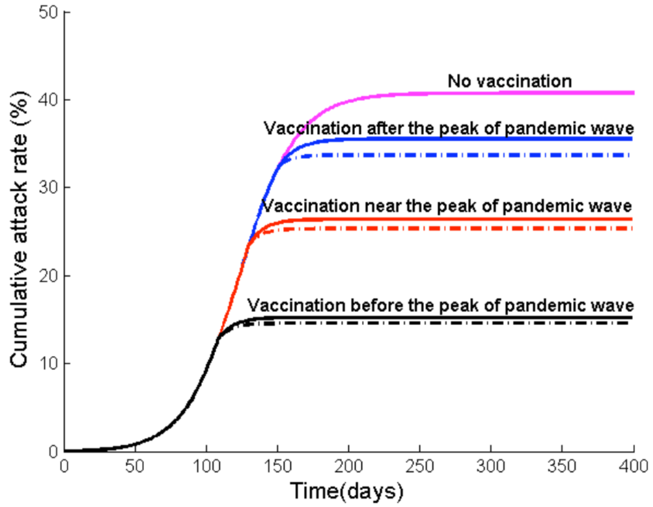


Figure 5 Cumulative incidence of influenza A/H1N1 when vaccination is guided by the Nash or utilitarian strategies. Vaccination is implemented at free of charge the three weeks before, exactly at, or three weeks after the peak of a pandemic influenza. Solid lines show the cumulative attack rate when vaccination is in alignment with utilitarian strategies when vaccination and is offered free of charge, whereas dotted lines show the cumulative attack rate assuming the vaccination is in alignment with the Nash strategies. For comparison, cumulative incidence without vaccination is also shown.

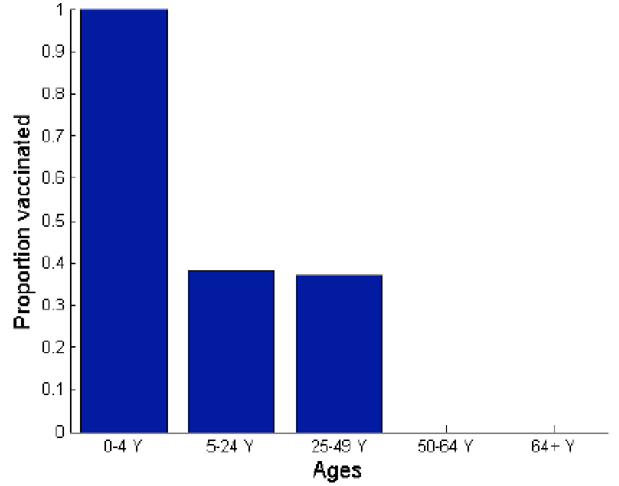


Figure 9 Nash strategy when vaccine is available at the beginning of an influenza pandemic and when vaccination is offered free of charge.

Example 2 – Unconstrained estimates including costs of ‘relaxing’

Stebnerg (2017)

- Objective: estimate impact of scaling up interventions to reach health-related SDGs as well as resource gaps under different health system constraints scenarios
- Methods: projections generated using Spectrum models for the respective disease areas. Gap estimated between current provision and universal coverage and country-specific programme costs multiplied by this gap. Costs estimated from OHT (WHO-CHOICE) and from the literature for disease/programme areas not covered. Progress towards 2030 targets adjusted by level of 'strength' of the health system

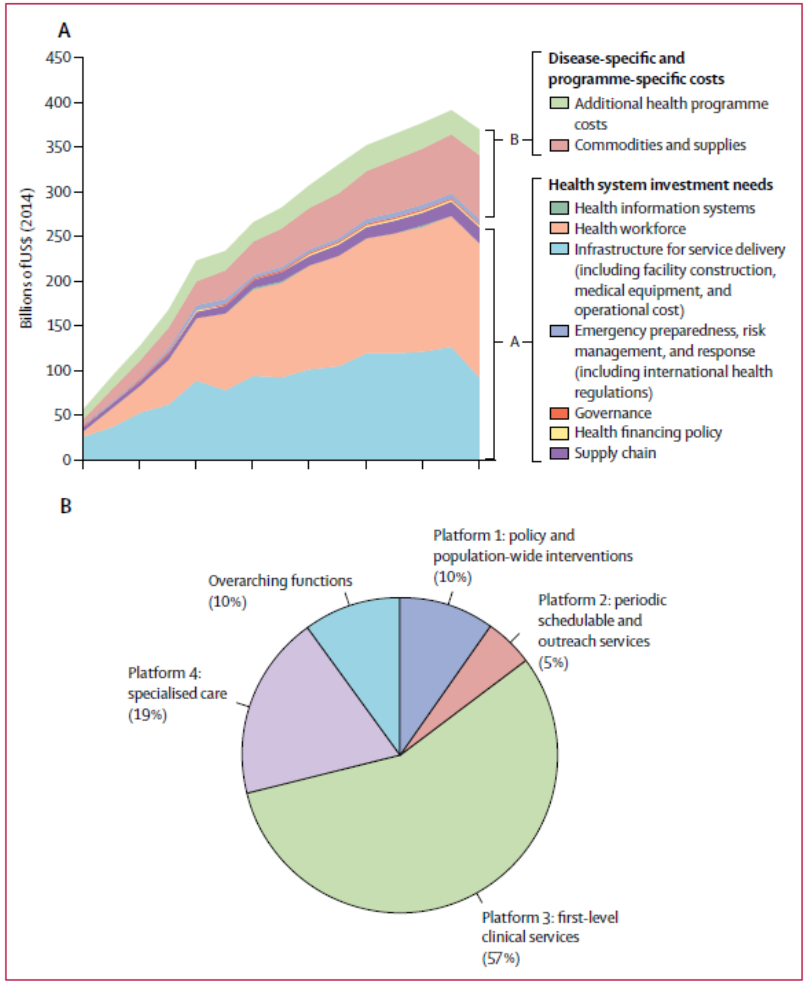


***Figure 2:* Additional investments required in 67 low-income and middle-income countries to meet Sustainable Development Goal 3 (US$ 2014 billion) (A) and additional resource needs by service delivery platform (B) in the ambitious scenario**
Additional health programme costs include those that are programme specific but do not refer to specific drugs, supplies, or laboratory tests. Examples include costs for programme-specific administration staff, supervision, and monitoring relative to the services for which the programme provides leadership and oversight (eg, the national malaria programme provides implementation guidance, and monitors and supervises service delivery for malaria). Other examples include mass media campaigns and demand generation. These data are presented as a table in the appendix.

Example 3 – Unconstrained estimates including non-financial resource requirements

Krumkamp (2011); Rudge (2012); Adisasmito (2015)

AsiaFluCap simulator

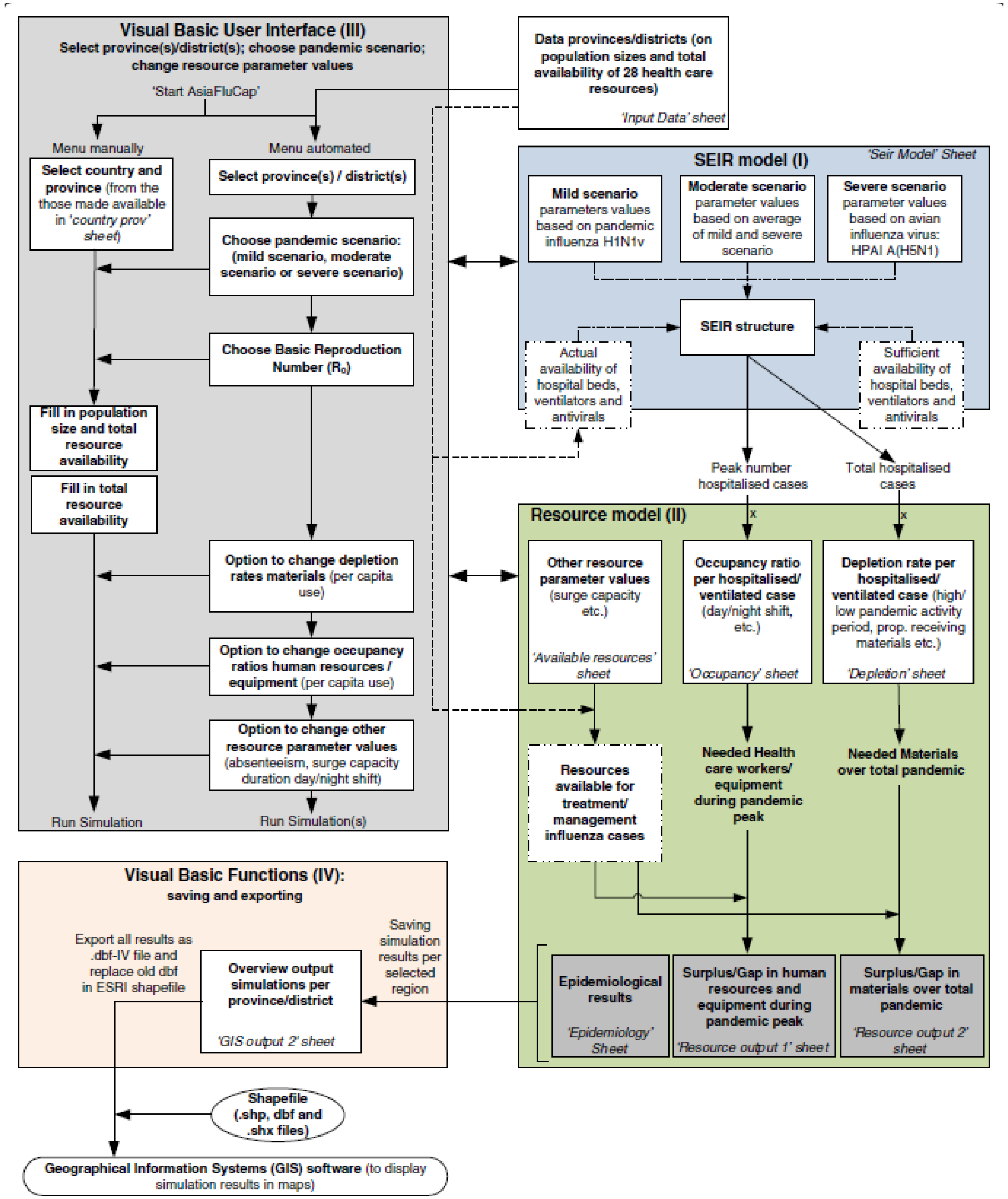
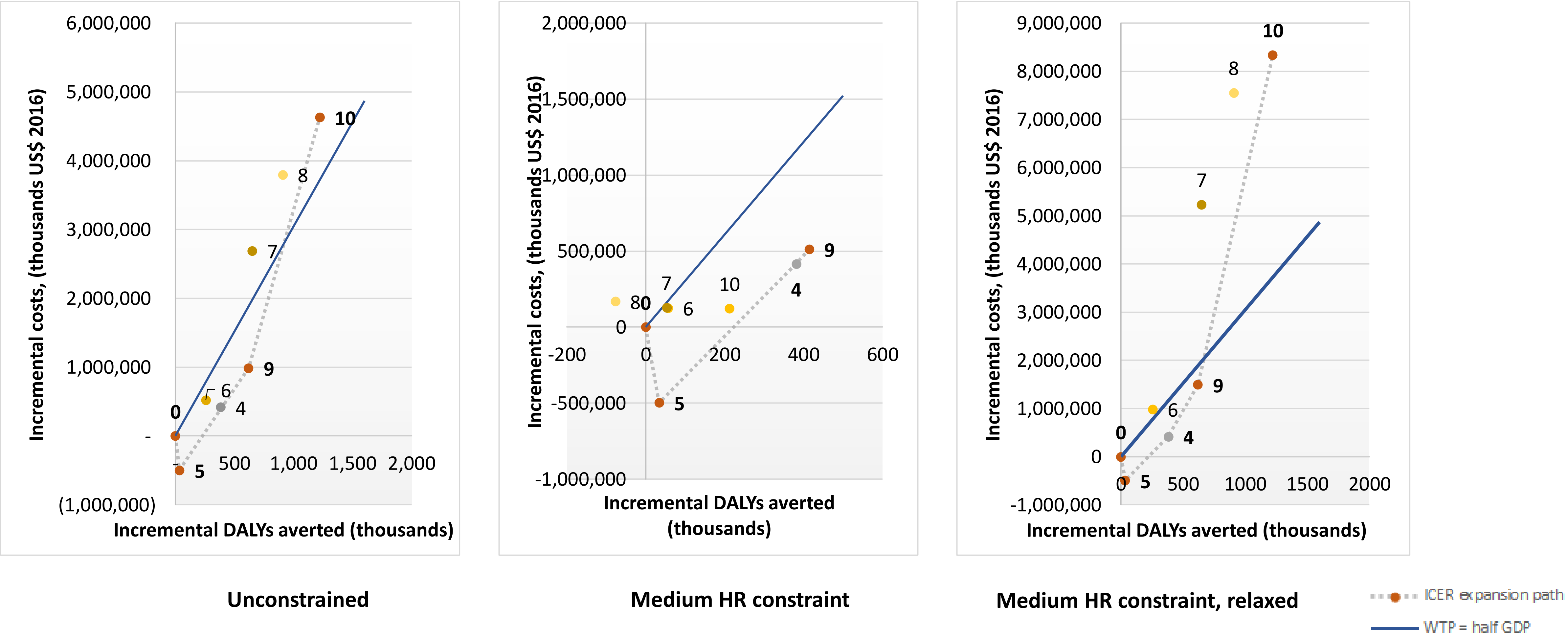


Figure 1 Schematic overview of the AsiaFluCap Simulator structure and processes.

Source: Stein M.L., et *al*. (2012). Development of a resource modelling tool to support decision makers in pandemic influenza preparedness: The AsiaFluCap Simulator. BMC Public Health, 12.

Example 4 – Combination (effects + costs) Bozzani (2018)

4. Xpert utilisation + Xpert negative algorithm
5. Cough triage in 100% of known HIV+ clinic attendees
6. Cough triage in 90% of PHC attendees
7. Symptom screen in 100% of known HIV+ clinic attendees
8. Symptom screen in 90% of PHC attendees
9. 4 + 6
10. 4 + 8



Approaches for implementing constraints in models

1. Transmission model-based estimation
2. Linking models: transmission + operational
3. Linking models: transmission + system dynamics
4. Constrained optimisation (other than budget)

Attaching unit costs/resources to model outputs

Bozzani (2018)

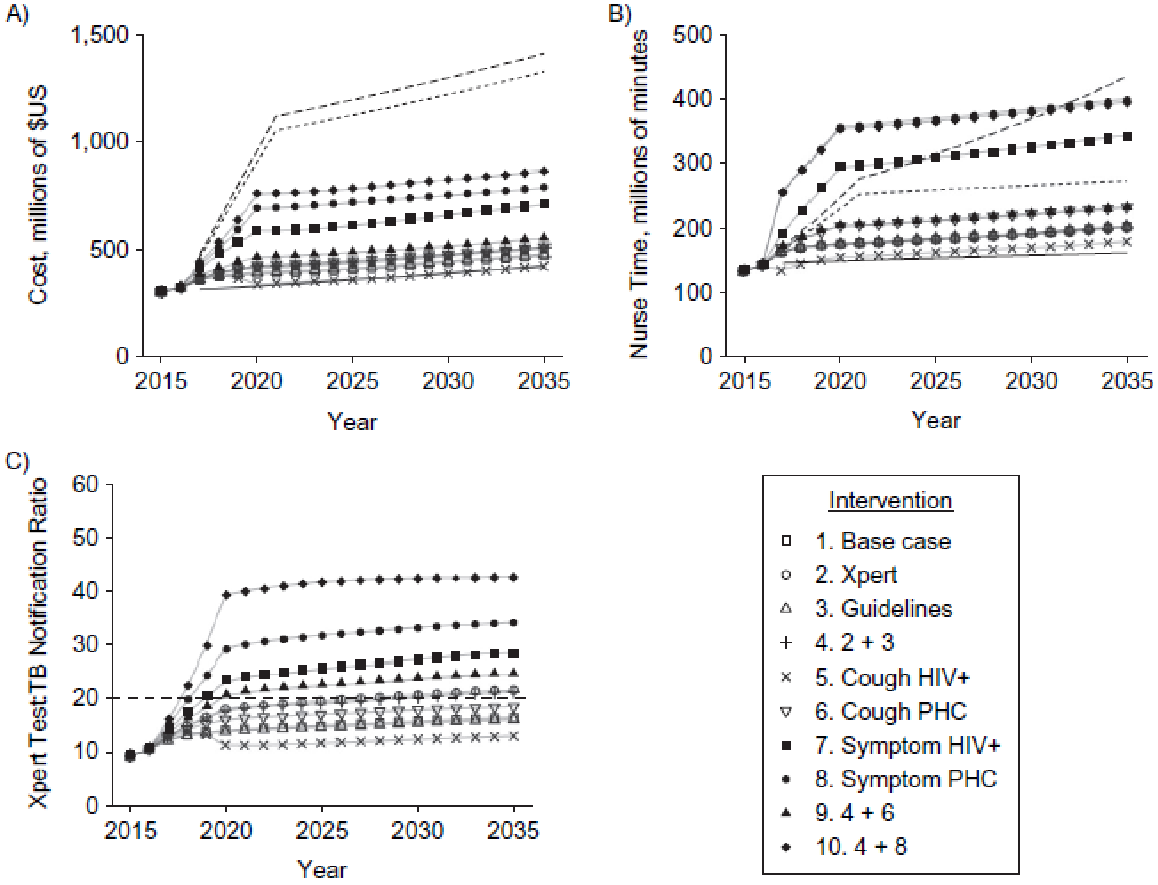


Figure 2. Model projection of future costs, human resource requirements, and Xpert test:tuberculosis (TB) notification ratio (ratio of number of Xpert tests (Xpert MTB/RIF assay; Cepheid Inc., Sunnyvale, California) to number of TB notifications) of the TB control program in South Africa, 2016–2035. Symbols show the median model prediction for each intervention from 2016 to 2035. A) Total costs of TB control activities, in millions of US dollars; B) nurse time spent on TB activities, in millions of minutes; C) Xpert:notification ratio. In panels A and B, solid lines show results for the low (most restrictive) constraints, dotted lines show results for the medium constraints, and dashed lines show results for the high (least restrictive) constraints. In panel C, results are shown (dashed line) for only a single constraint (a ratio of 20:1). HIV+, positive for human immunodeficiency virus; MTB, *Mycobacterium tuberculosis*; PHC, public health clinic; RIF, rifampin.

Source: Sumner T., et *al*. (2019). Estimating the impact of tuberculosis case detection in constrained health systems: An example of case-finding in South Africa. Am J Epidemiol, 188(6):1155-1164

Table 2 List of inputs into and outputs from the operational and transmission models. The linkage between the two models results from using model outputs from one model as inputs for the other

Operational model	
Input	**Output**
Average number of tuberculosis suspects coming for diagnosis per diagnostic centre per day	Average time to receive diagnosis
Proportion of smear-positive tests	Loss to follow-up (diagnostic default)
Treatment times	Number of visits to diagnostic centre
Number of microscopy staff at diagnostic centre	Diagnosis outcomes
Laboratory time per sample	Treatment outcomes
Staff shift patterns	Time to complete treatment
Physician availability	Default in treatment
Probability of default during diagnostic and treatment pathways	Number of samples processed
Transport availability for samples	Health system costs
Unit costs	Patient costs

Transmission model	
Output	**Input**
Tuberculosis incidence	Transmission rate
Tuberculosis prevalence	Primary progression rate
	Reactivation rate
	Natural cure rate
	Tuberculosis-specific mortality
	Diagnostic test performance—sensitivity
	Loss to follow-up (diagnostic default)
	Duration parameters (e.g., from symptom onset to health centre visit, from seeking diagnosis to receiving diagnosis)
	Tuberculosis treatment parameters (e.g., fraction of initial defaulters, treatment success rate, treatment failure and death rate)

Linking transmission and operational models

Lin (2011) and Langley (2014)

- Objective: use operational modelling to assess impact of new TB diagnostics on health system costs, infrastructure, patient access and outcomes
- Methods: operational model used to parametrise a transmission model, limiting intervention effects based on HR availability, diagnostic pathway bottleneck and affordability

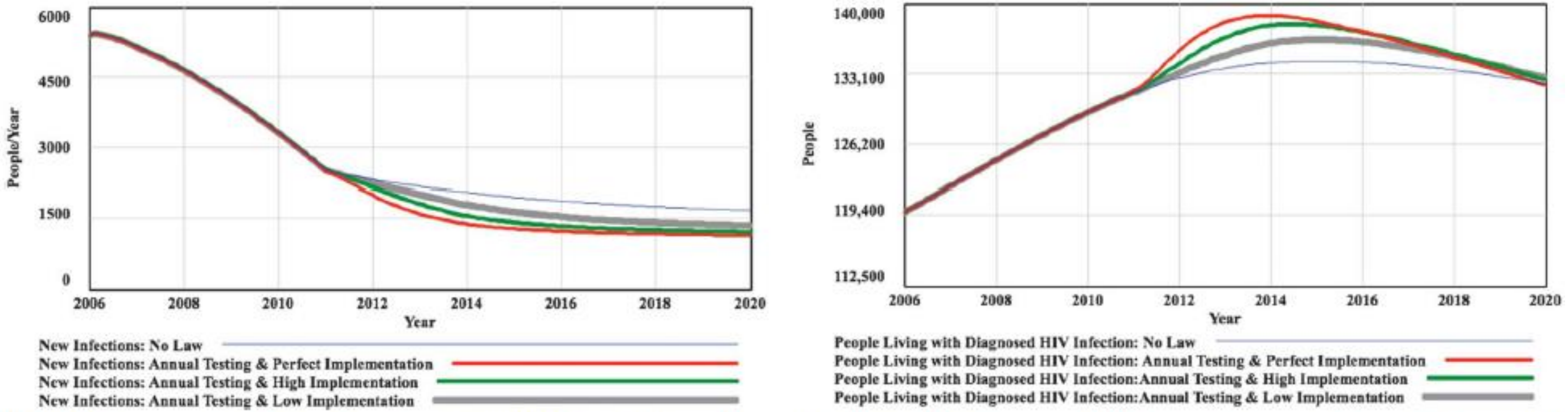


FIGURE 2. Projected differences in new infections (left) and people living with diagnosed HIV infection (right), for scenarios with annual testing offers in routine medical care and 3 levels of implementation.

Linking transmission and system dynamics models

Martin (2015a and 2015b)

- Objective: assess how changes in HIV testing and care law impact epidemic outcomes and resource needs at different levels (low, high and perfect) and timings of implementation
- Methods: system dynamics model integrating stock and flow diagrams of HIV testing and care and of the HIV testing law structure. Transmission rates determined based on ‘HIV stage’ stock, which determines CD4 count

Source: Martin 2015b

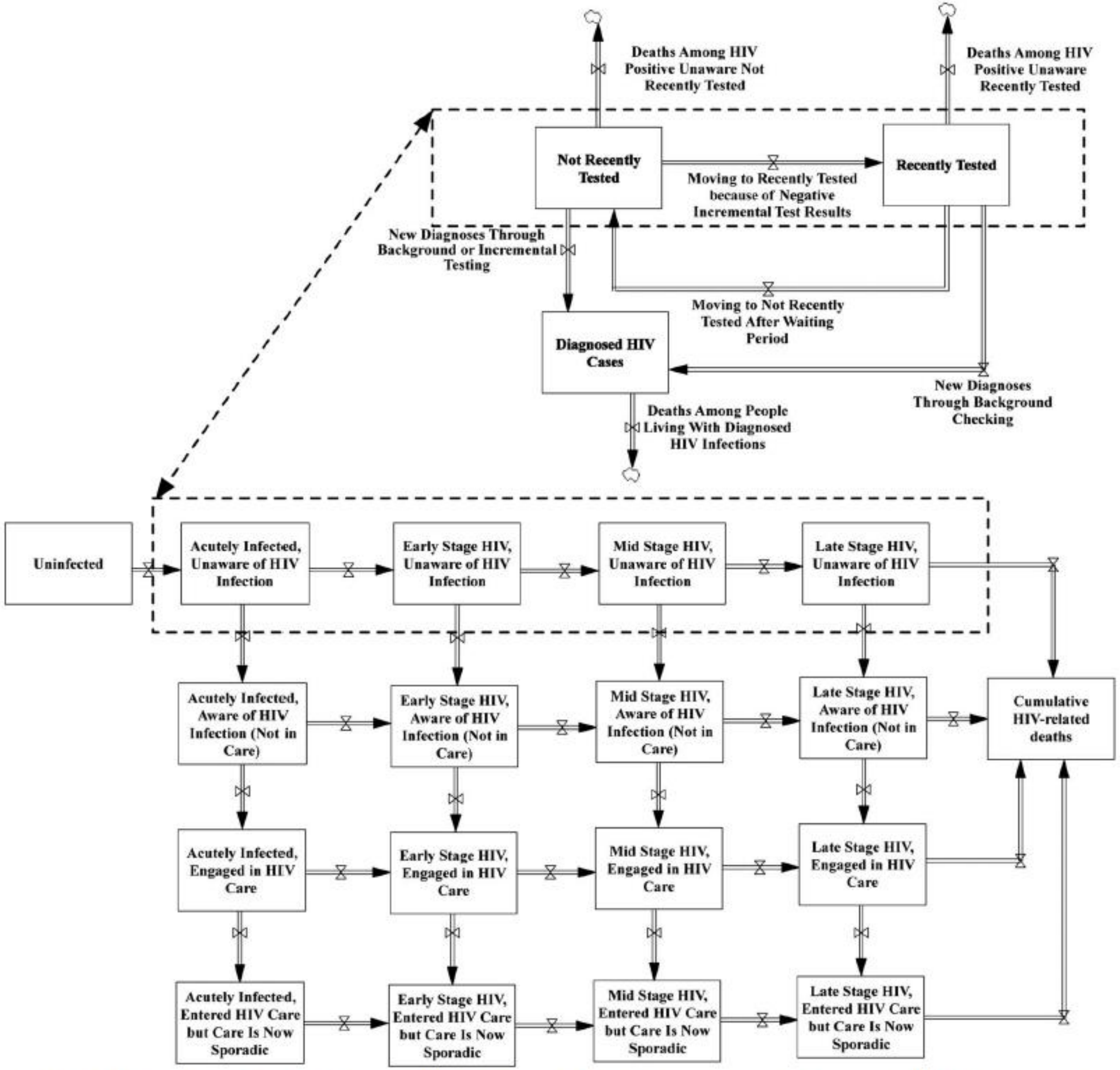


FIGURE 1. Stock-and-flow diagram of the New York system of HIV testing and care (bottom), HIV testing structure (top), and their relationship.

Optimising under (non-budget) constraint

Martin (2011)

- Objective: assess how constraints (max annual budget) and policy objectives (minimise prevalence and health utility losses) affect optimal timing and scale-up, and the subsequent costs and impact of an antiviral treatment intervention among IDUs
- Methods: constrained optimisation scenarios

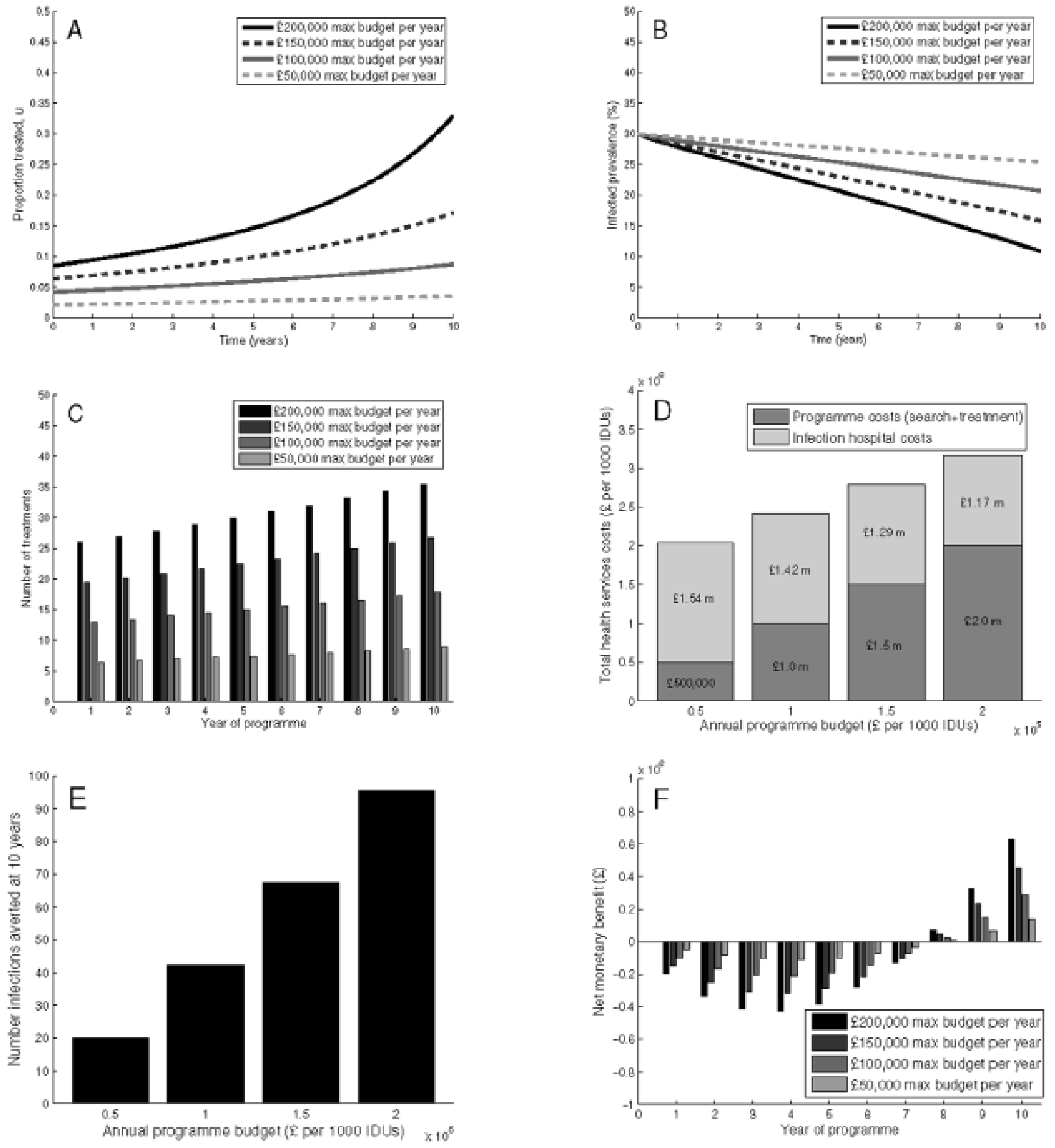


Figure 1. Scenario A: Minimising health service costs and HCV health utility losses. Simulations are with a 30% baseline prevalence, showing (A) programme coverage, (B) prevalence reductions, (C) number of treatments, (D) total health service costs (comprised of programme costs and infection costs), (E) infections averted, and (F) net monetary benefit. Parameters used are as shown in Tables 1–2, with $\zeta_{20}=3{,}800$, $\beta_{20}=5{,}800\times(1/\omega)$, $\tau_f=50$, and with no final time prevalence constraint.
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