Optimizing the Allocative Efficiency of TB Case Detection Interventions: What are the Key Considerations ?

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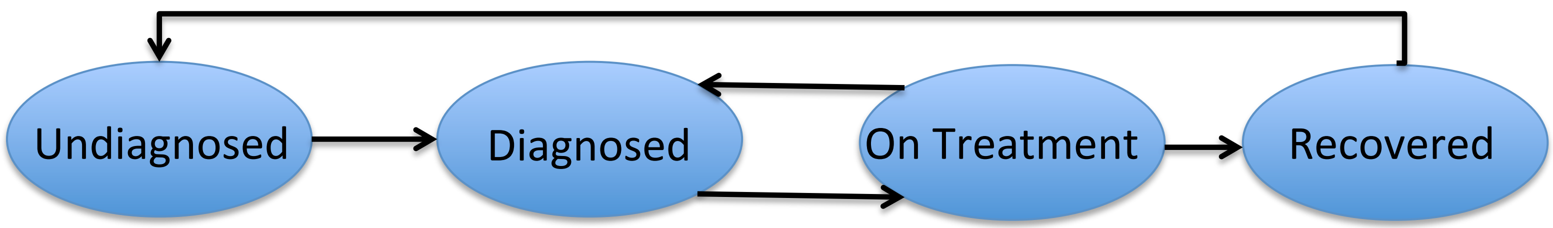
Case detection: what are the hurdles?

Undiagnosed compartments are the denominator for all screening and diagnosis services/interventions



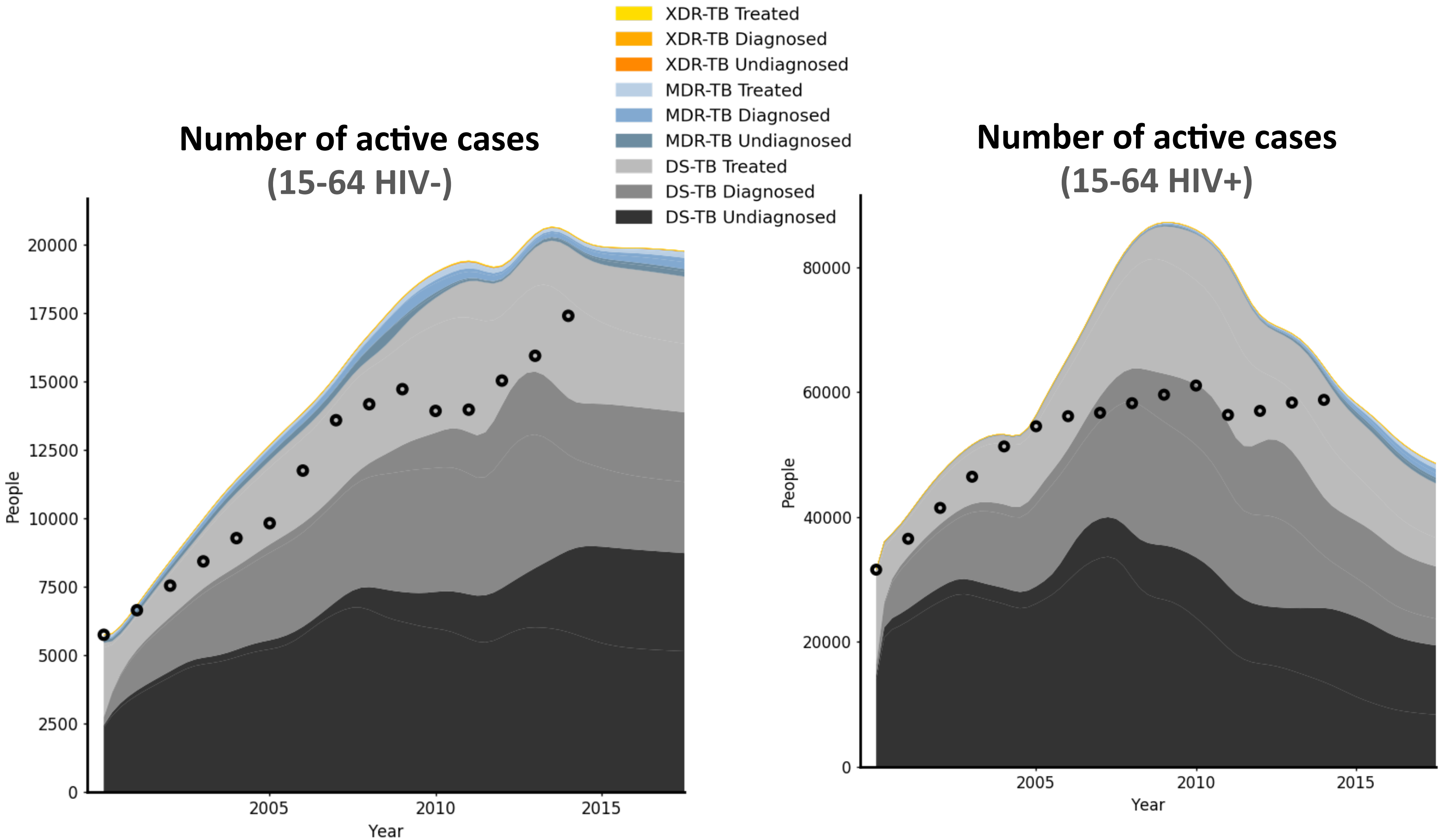
Three significant hurdles exist for the analysis of screening interventions:

1. Estimating the undiagnosed cases
2. Estimating the number TB cases targeted by an intervention
3. Triangulating programmatic data (coverage and impact) to epidemiological data

- Analysis requires workable estimates for evaluating program cost-effectiveness
- Estimates of these considerations becomes *vital* when applying optimizations to optimally allocate amongst different interventions

Estimating the Number of Undetected Cases – Gauteng

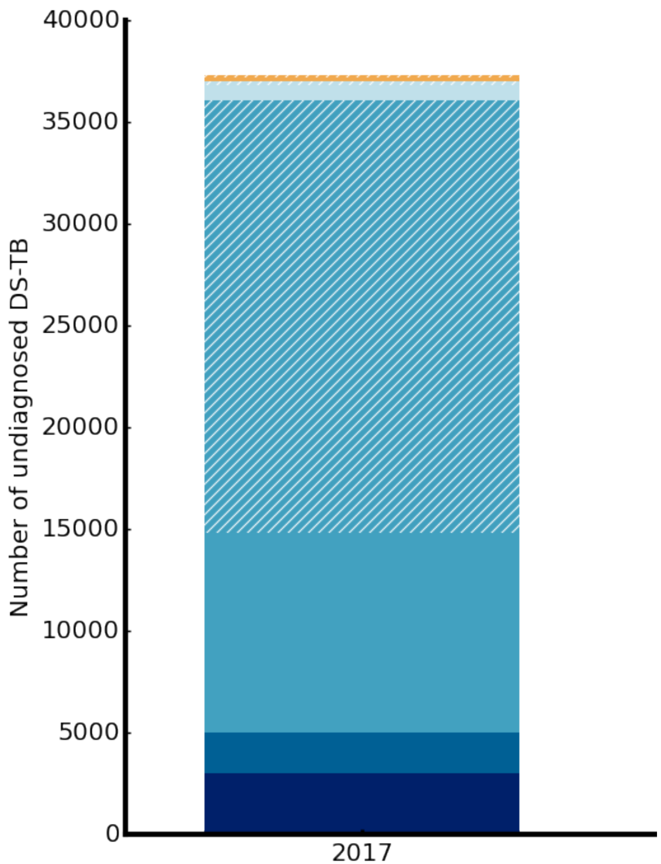
Varying diagnosis rates observed depending on population groups, and co-morbidities



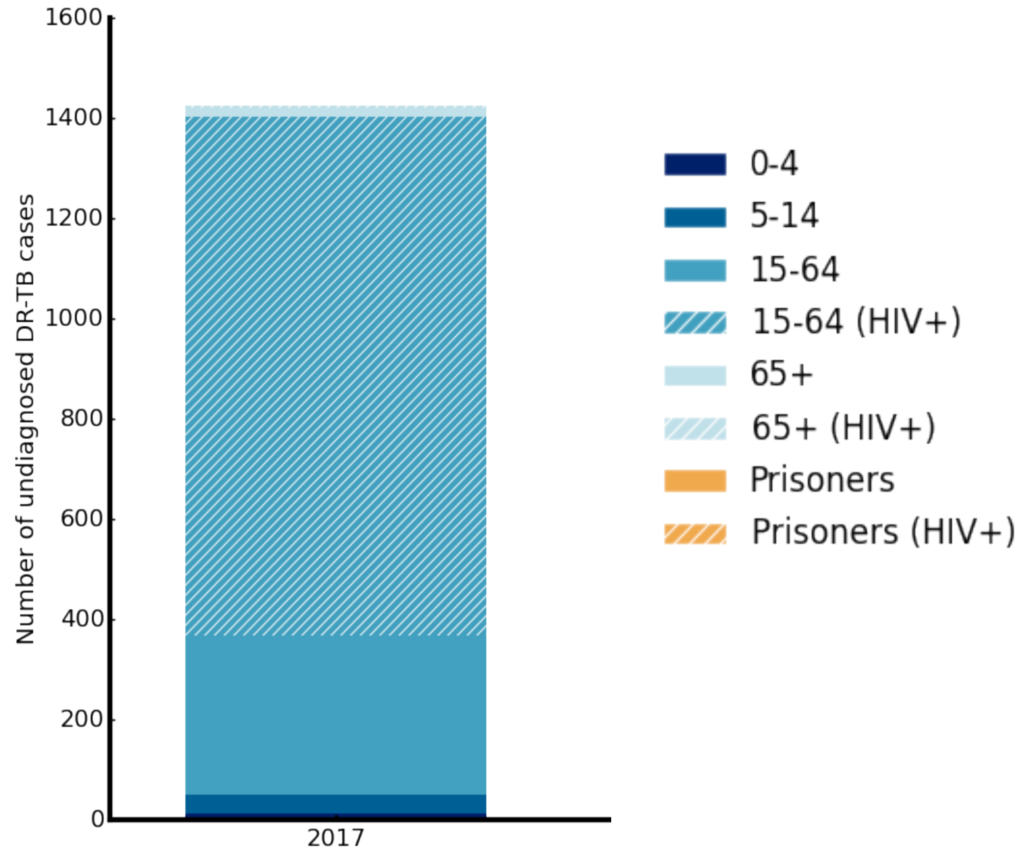
Profile of Undetected Cases for 2017 – Gauteng

Majority of undetected cases in HIV positive adults, especially for DR-TB

Number of undiagnosed
DS-TB cases



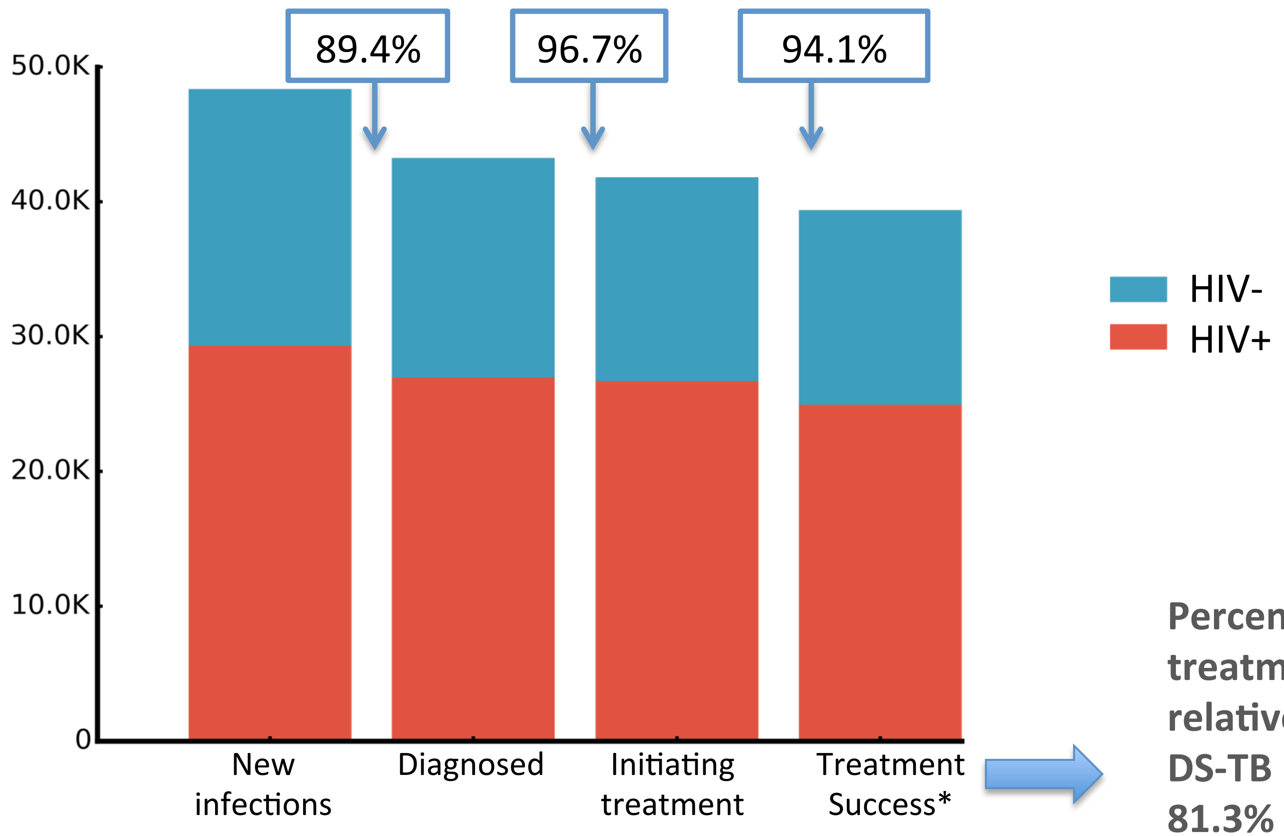
Number of undiagnosed
DR-TB cases



DS-TB Care Cascade

- Varying diagnosis rates observed by population group and TB drug-resistance
- Case detection is a vital step, underpinning all following points of care along the cascade

Total modeled number of new DS-TB cases by HIV-status



Percentage of treatment success relative to all new DS-TB infections is 81.3%

*Treatment success includes cure and completion

DR-TB Care Cascade

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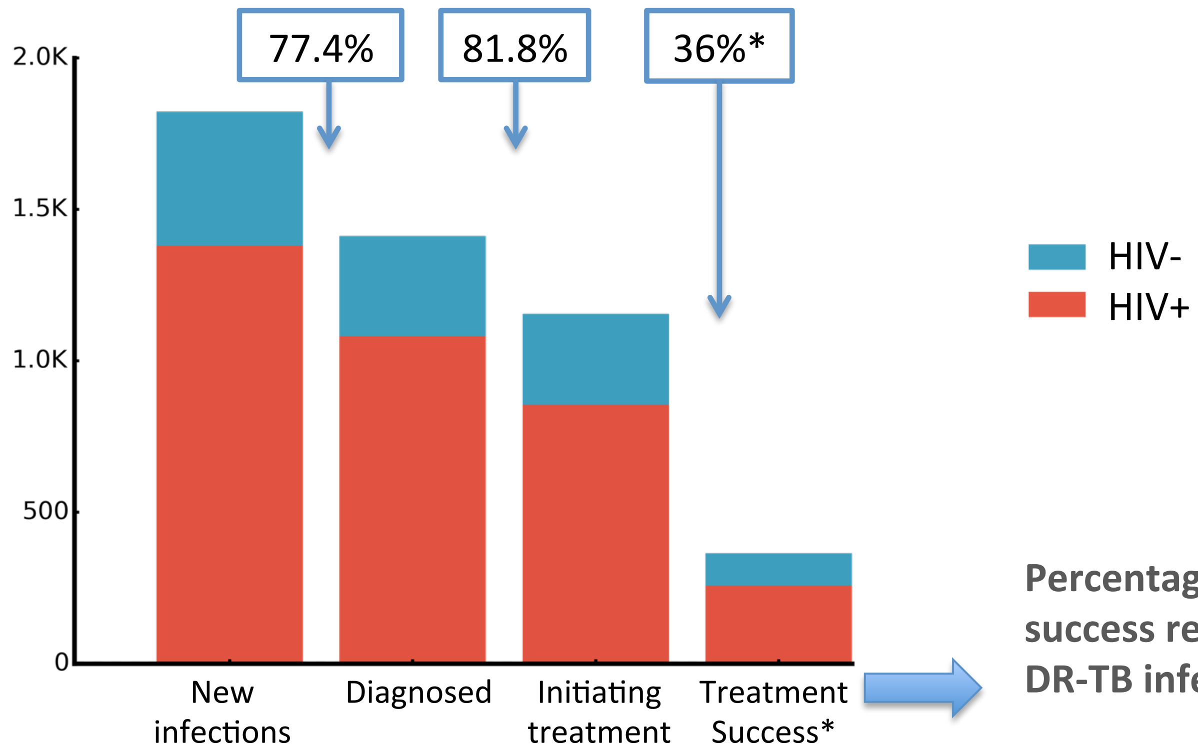
Total modeled number of new DR-TB cases by HIV-status



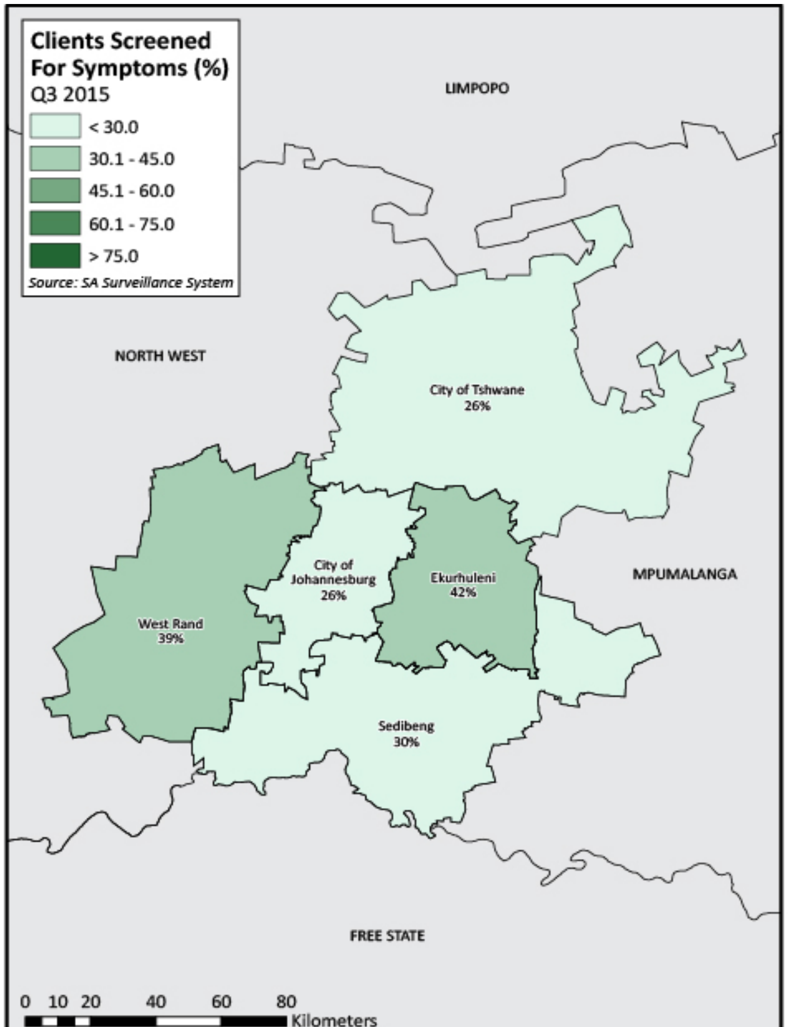
Percentage of treatment success relative to all new DR-TB infections is 22.8%

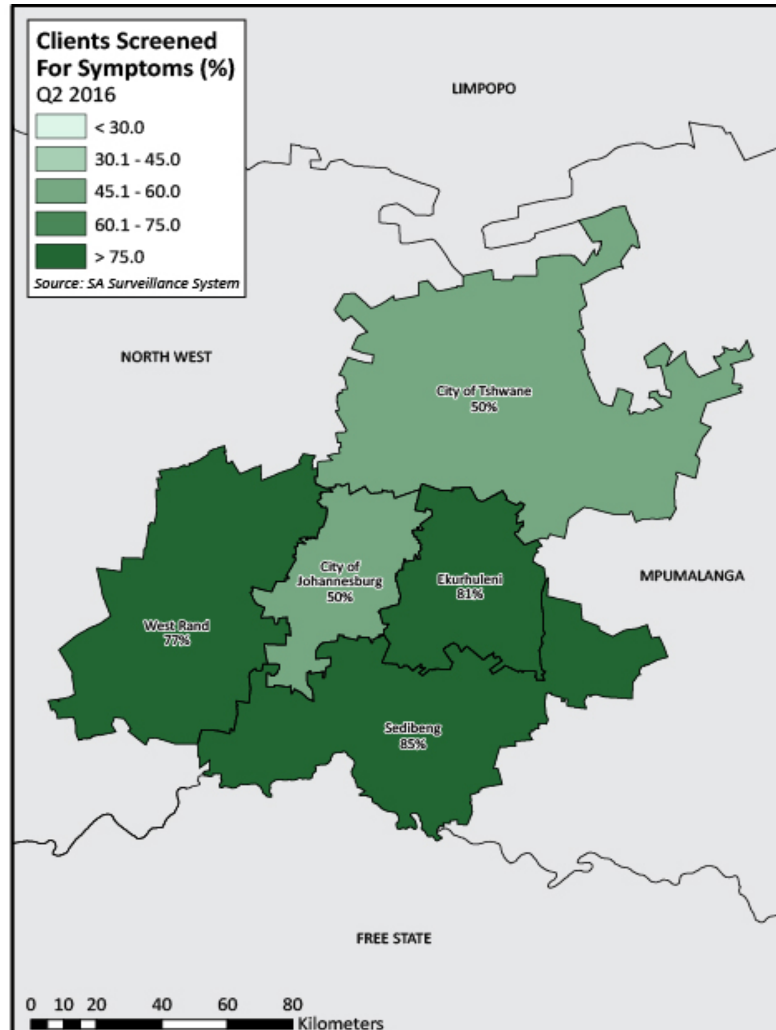
**The 36% treatment success rate is informed by 2014 MDR-TB outcomes data. This was only used in the historical calibration and not to inform future projections after optimization modeling*

Varying screening intensity across space and time (symptom screen coverage by district in Gauteng)

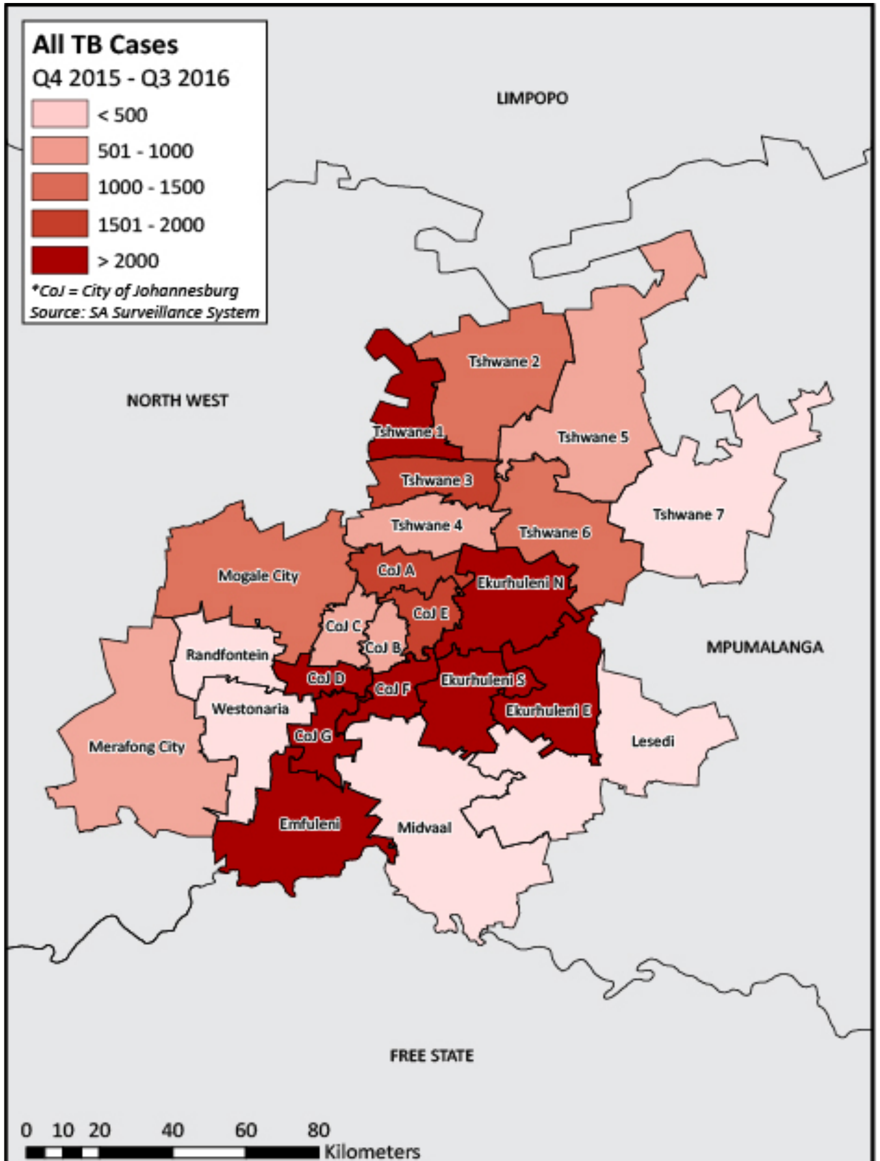
Geographic heterogeneity of screening coverage and protocol adherence

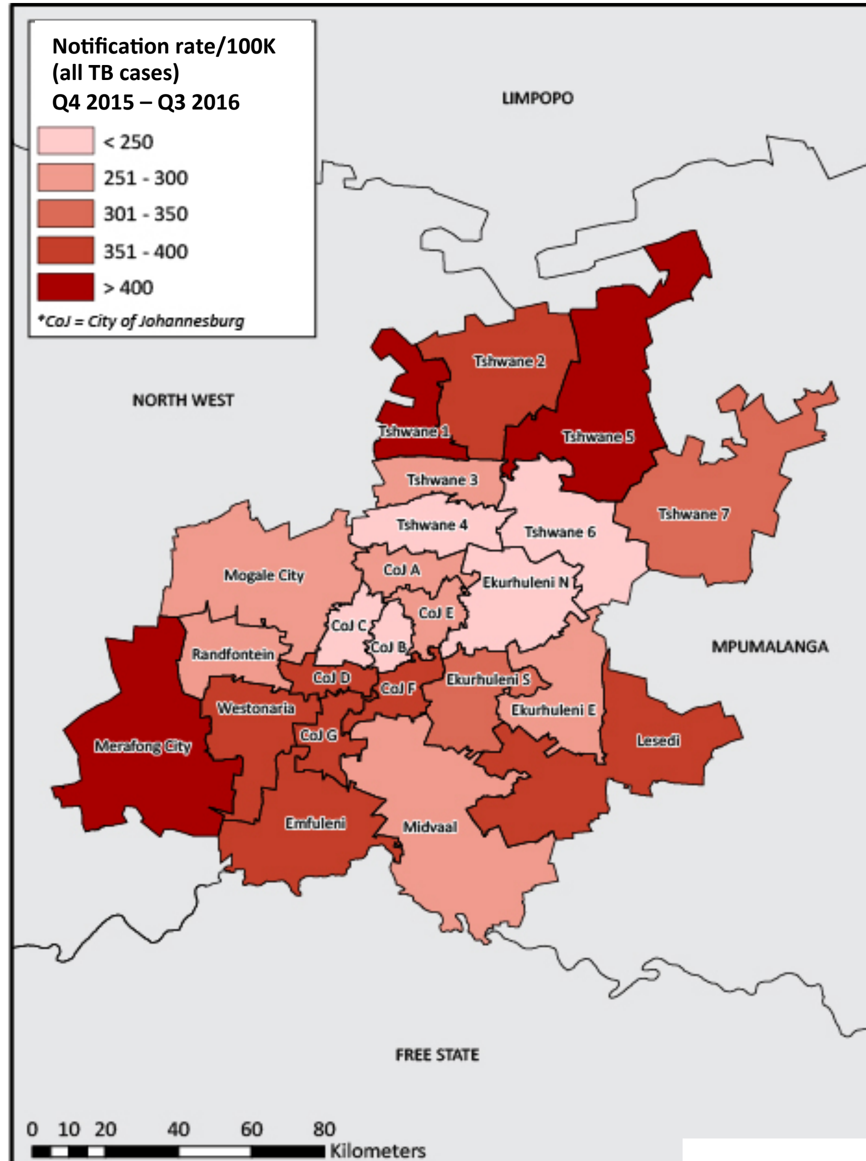
Q3 2015 → 1 year scale-up → Q2 2016





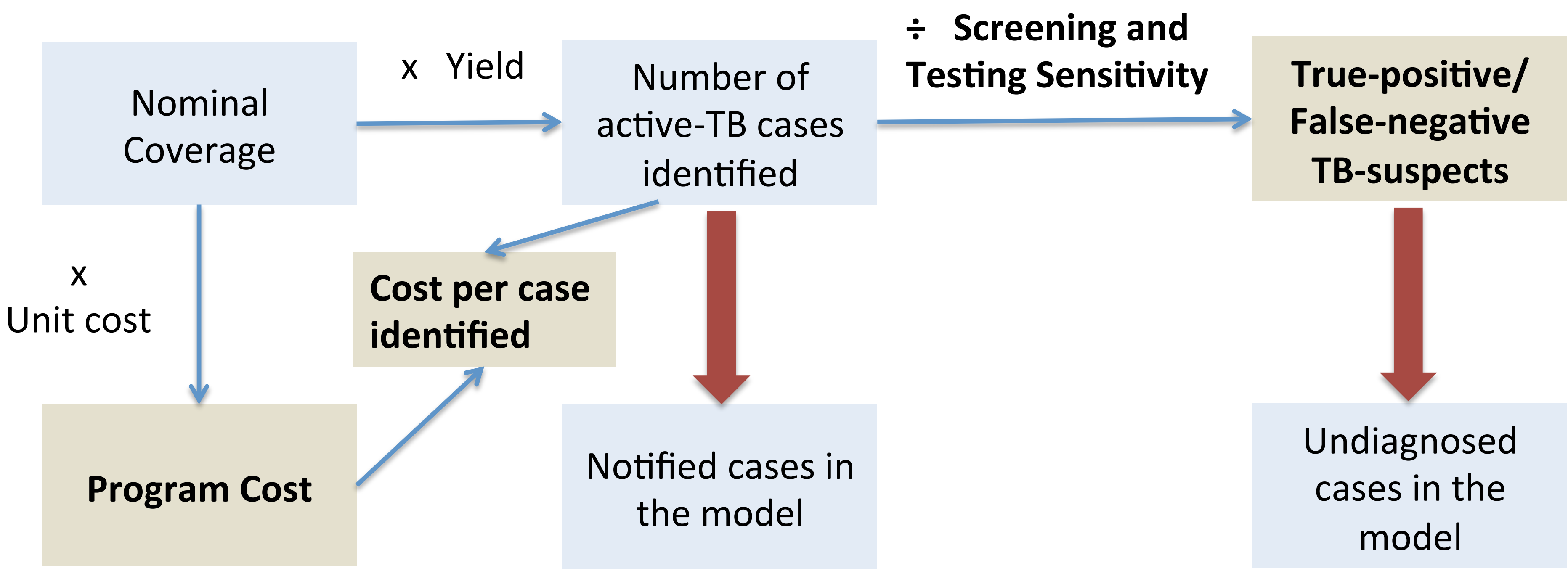
Varying burden across sub-districts in Gauteng





Main Data Considerations for Case-Finding Programmes

- Nominal Coverage
- Yield
- Screening and testing sensitivity
- Costs
- Programmatic saturation levels



Examples of Main Data Considerations (based on Gauteng)

Screening Programme	Population Targeted	Nominal Coverage	Number of Active Cases Identified	Number of Cases Tested by Xpert	Number of True Positives/False-negatives Screened
Mass-Screening at PHC	All HIV- populations	5,596,086	*6,141*	*11,631*	*56,460*
Active Case Finding for PLHIV at PHC	All HIV+ populations	707,613	*28,305*	*32,164*	*77,132*
Enhanced Mass-Screening at PHC	All HIV- populations	0 - Prospective	*7676*	*10904*	*26148*
Mobile Outreach Screening	High risk groups	0 - Prospective	*138*	*158*	*378*
Contact Tracing for DS-TB cases	All populations	*34,020*	*919*	*1,044*	*2,503*
Contact Tracing for DR-TB cases	All populations	*5,330*	*144*	*164*	*392*

Symptom Screening SA, Claassens et al. 2017	Sensitivity
Only cough question	21%
Four standard	38%
Only cough question (HIV-)	24%
Four standard (HIV-)	42%

Screening programs	Yield	Unit Costs	Yielded Costs
Mass screening at PHC	0.40%	*6.55*	*$9,545*
Enhanced Mass screening at PHC	0.50%	*13.1*	*$9,491*
Mobile units/outreach	2.20%	*1089.03*	*$46,432*
Contact tracing for DR cases	2.70%	*129.28*	*$8,258*
Contact tracing for DS cases	2.70%	*129.28*	*$8,207*
ACF among PLHIV	4.00%	*78.6*	*$5,802*

Focus on Mass-Screening at Gauteng PHCs

- Differences in yield or sensitivity can therefore have significant effects on the cost per case found
- Practical implications of this are that some small improvements in protocol are greatly preferred by the optimisation algorithm

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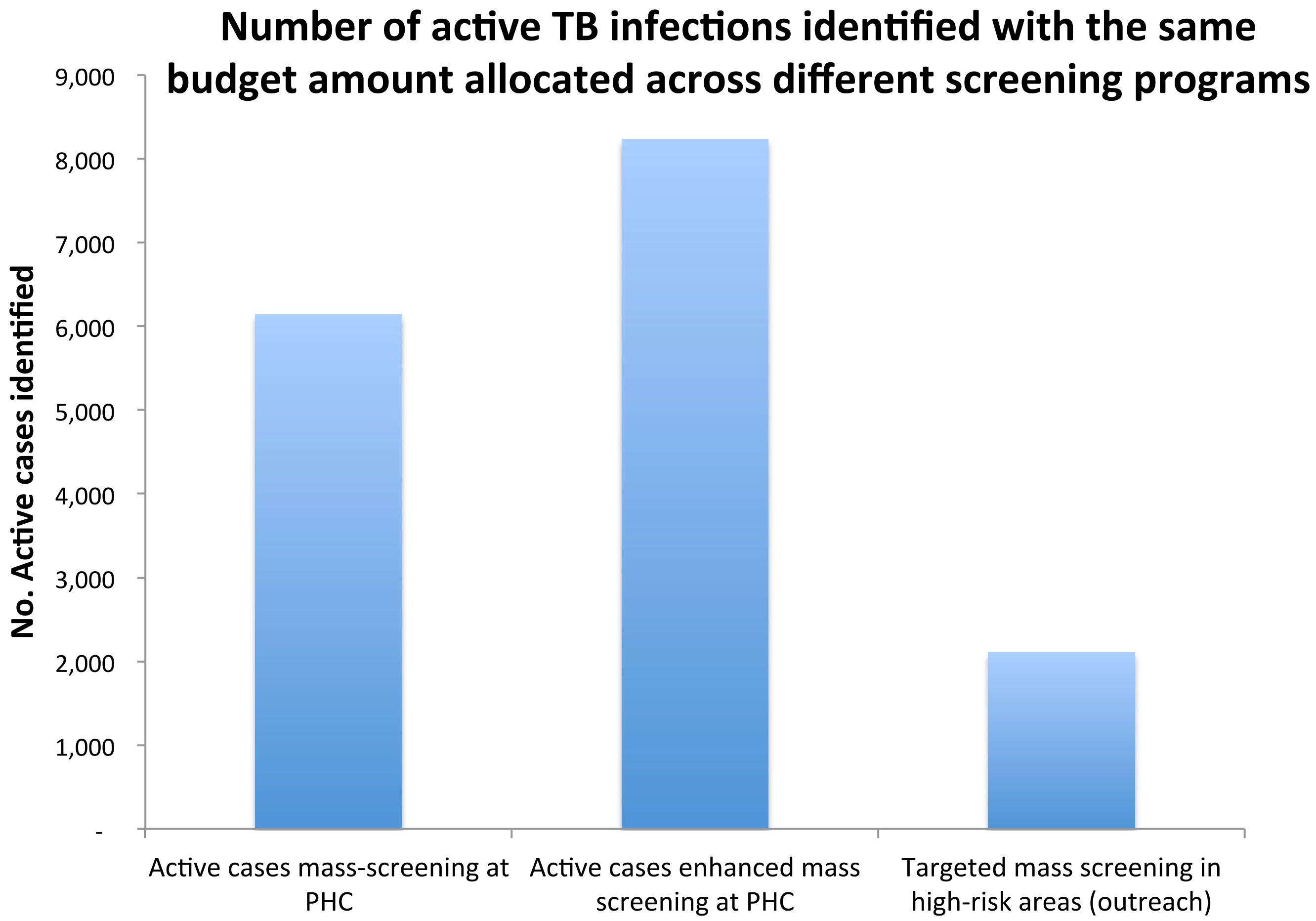
Four standard	38%



Summary so far

- Estimating number of undiagnosed cases necessary - denominator for all case detection interventions
- Capacity to model profiles of undetected cases essential - when data is available can inform targeting and impact of case detection strategies
- Lack of appropriate programmatic data, at times even nominal coverage and unit costs not known
- Number of cases detected by intervention is unavailable – issues of routine monitoring and integrated data systems
- Until vital programmatic data are accurately and routinely collected, there will be greater uncertainty when modeling the impact and best resource allocation of case detection for sub-populations

Optimisation

Aim: For a given amount of money, what's the best outcome we can achieve for a fixed budget?

Typically, for the entire care cascade, "Best" could mean:

- Fewest infections / deaths / DALYs as objective
- A combination of the above (combined objective, weighted)

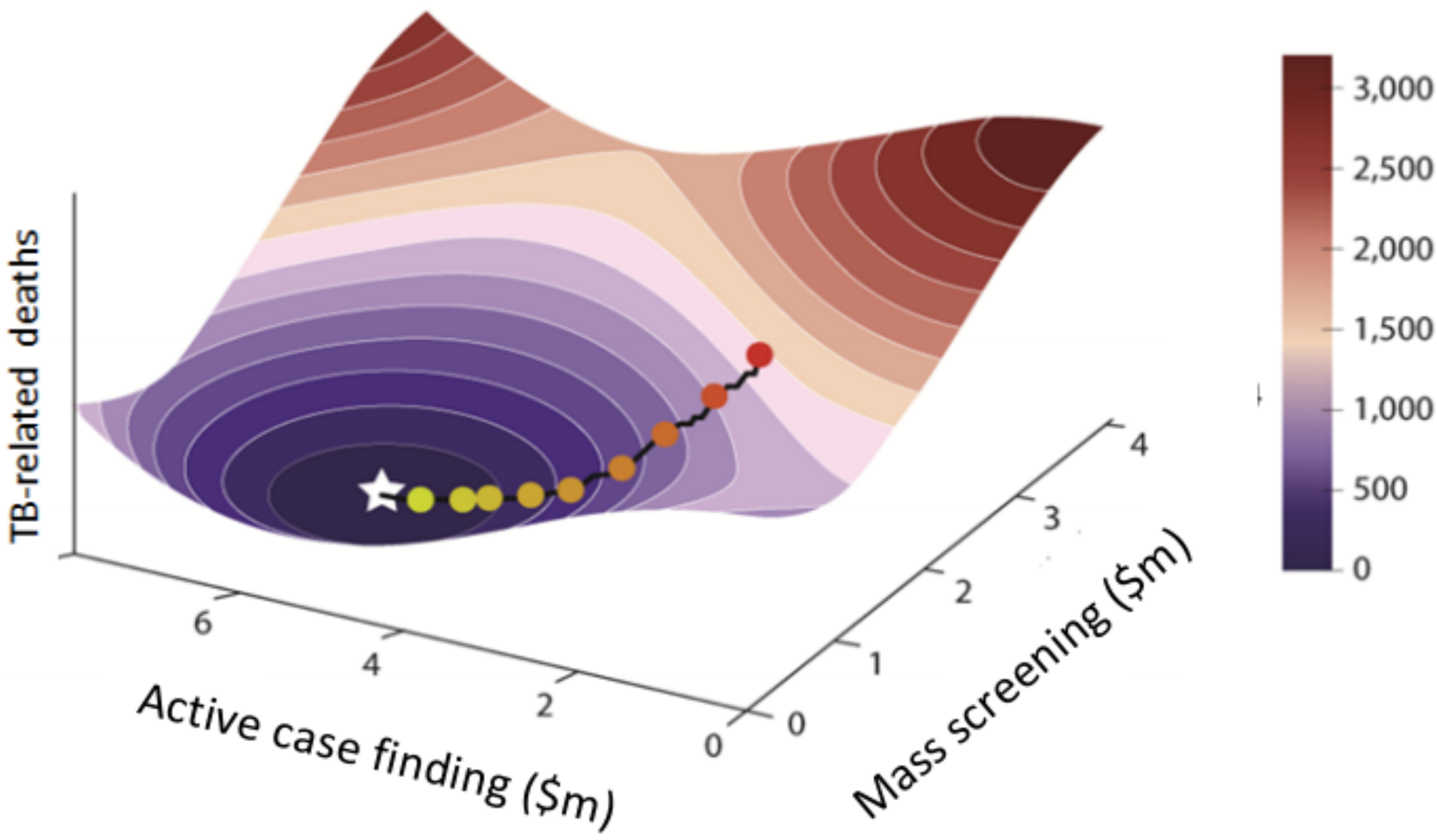
In this instance, we could instead define best:

- Increasing the number of cases detected
- Reducing the number of false positives and false negatives

For the entire population – or for high-risk groups

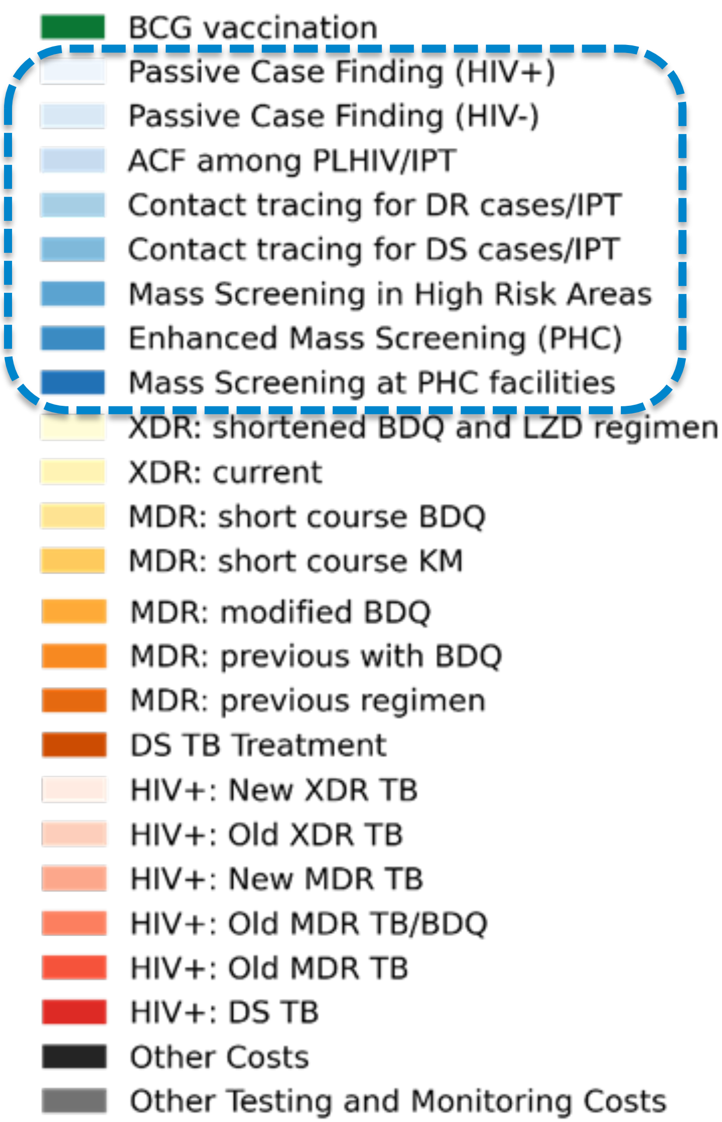
However, these are implicitly included in the above example, as typically identifying cases and linking them to treatment will reduce new infections and TB-related deaths

An example of the objective landscape: Two case finding interventions



Optimisation Step

- For each TB intervention/modality:
  - one set of logistic curves relating funding to coverage level
  - one set of curves (generally linear relationships) between coverage levels and clinical or behavioral outcomes
- Outcomes expected from changes in funding assumed by interpolating and extrapolating available data using a fitted logistic curve
- Limitation: all changes in outcomes assumed to be due to changes in intervention funding
- Computing capacity need driven by number of interventions to optimise across



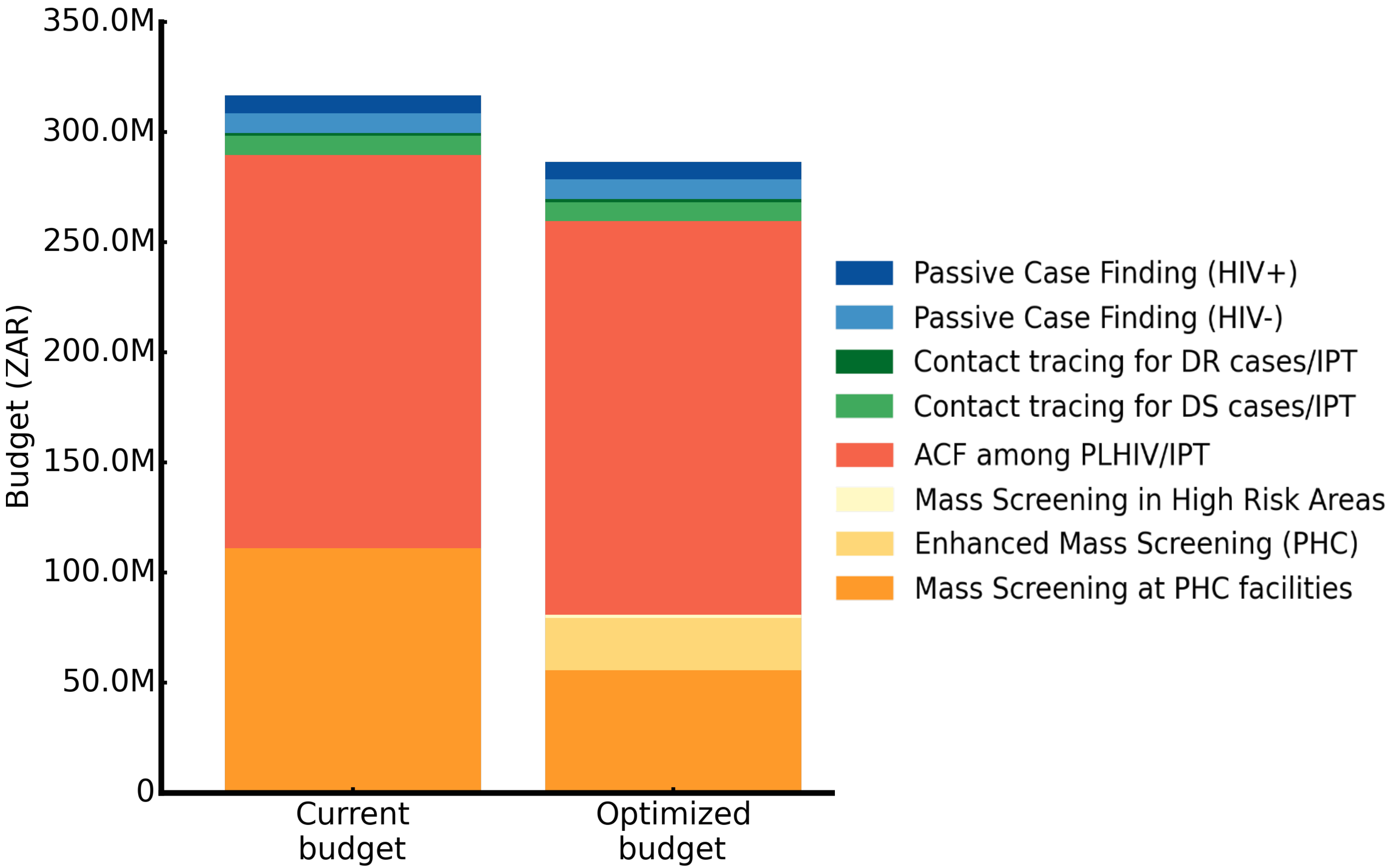
Constraining the Optimisation: Examples

- Given the patient- and provider-side barriers (such as clinical, behavioural, logistical, financial, and political), constraints for certain interventions were set alongside key stakeholders from the country in order to reflect these

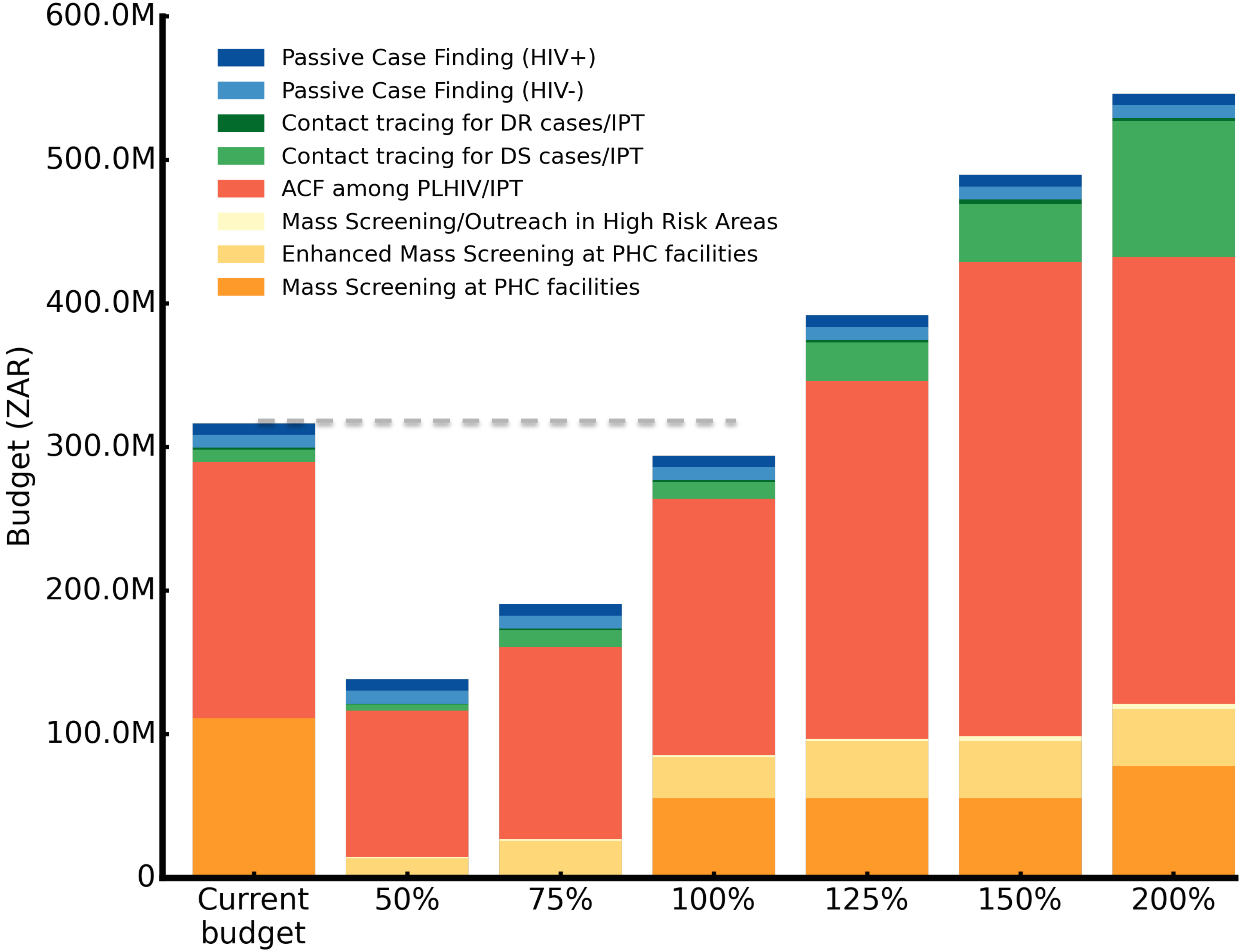
	Min % of current budget	Max % of current budget
Mass-Screening at PHC /IPT	50%	70%
Enhanced Mass-Screening at PHC (Prospective)/IPT	30%	50%
Outreach in High-Risk Areas (Prospective)/IPT	20%	50%
Contact Tracing for DS-TB/IPT	100% (as currently underfunded)	Unconstrained
Contact Tracing for DR-TB/IPT	100% (as currently underfunded)	Unconstrained
Active Case Finding for PLHIV in PHC/IPT	100% (as part of ART care)	Unconstrained
Old MDR Regimen	10%	20%
Current XDR Regimen	20%	60%
HIV+: Old MDR TB	10%	20%
HIV+: Current XDR TB	20%	60%

*These constraints can also be considered in terms of coverage, as well as relative or absolute terms

Optimisation Results: All Gauteng Case-Detection Programmes



Optimisation Results: Gauteng Budget Scale-Up



Conclusions

- Model estimates of undiagnosed cases are vital for optimising investments into case detection interventions
  - Understanding the profiles of undetected cases is useful for guiding detection efforts and allocation of funding
- Nominal coverage, unit or program costs, yield and sensitivity are necessary for optimising different case finding interventions
  - A concerted effort is required to routinely collect programmatic data to improve modelling accuracy, particularly given the difficulty of triangulating programmatic and epidemiological data
  - Balance between more & better routine data and "reporting overload"
- In optimisation step, constraints are required to reflect real world considerations and provide feasible and policy-relevant recommendations

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