Tobacco, diabetes, HIV, and Tuberculosis: The importance of dynamic modeling when chronic and infectious diseases interact

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Overview

- Tuberculosis control policy context
- Key risk factors
- TB and tobacco -- illustrating approach and lessons learned
- TB and diabetes -- work in progress

Tuberculosis (TB)

- TB is an airborne communicable disease
- TB is a leading cause of death worldwide
- 1/3 of the world's population is infected
- 10-15% of those infected will progress to disease in their lifetime
- Inexpensive and effective treatment available

Traditional TB control

- "Prevention starts with cure"
- Five core principles of DOTS
  - Clear and sustained political commitment
  - Accurate case detection through quality assured technology
  - Standardized treatment including patient support and supervision
  - Reliable and effective drug supply
  - Capable monitoring and evaluation system

Global TB goals

- Millennium Development Goals
  - To reverse the increasing trend in TB incidence rates
  - To halve TB prevalence and death rates between 1990 and 2015
- Process goals
  - To diagnose 70% of new TB cases
  - To successfully treat 85% of these

Global TB Control

- Stop TB Strategy (2006)
  - Continue DOTS expansion
  - Address drug resistance
  - Address TB-HIV coinfection
  - Strengthen health systems
  - Engage all health care providers in TB control (public and private)
  - Enable and encourage research to advance TB diagnosis, treatment, and prevention

Current policy issues

- In 2007 an estimated 94% of people lived in areas covered by DOTS programs
- Many countries have reached (or are close to reaching) treatment targets
  - But many are NOT on track for meeting corresponding outcome goals
  - WHY?
- New policy focus emerging: TB elimination
  - Reduce TB incidence rate to 1/100,000 in the next 50 years
  - HOW?

Key TB Risk Factors

- On the “policy radar screen”
  - HIV infection
- Missing
  - Diabetes
  - Tobacco exposure (active and SHS)
  - Malnutrition
  - Alcohol or drug abuse
  - Indoor air pollution
  - Spending time in a prison, a health care setting, a country with high TB prevalence
  - …. (MANY OTHERS!)

Big picture questions…

- Why aren't we seeing projected decreases in TB incidence rates -- what's missing from our model?
- What are feasible TB control options including, but looking beyond, pharmacological solutions? What are the constraints to which each might work in particular environments? Consider targeted use…
- Recognizing that resources are limited and given that what is feasible and sustainable in one community may not be in another -- what should TB control look like (and how does "where" affect this answer)?
- What will happen to TB outcomes if one of these missing risk factors becomes more prevalent?
- What would it take to get us to TB elimination targets?

Research questions…

- Which risk factors are most important?
- We must care about this…
  - Because we can't do everything
  - To motivate the general population (or providers, or funders, etc)

The association between smoking and TB

Relative risk for ever versus never-smokers:	
Being infected	1.7 (1.3-2.0)
Developing TB disease	2.7 (2.0-3.9)
Dying from TB	2.4 (1.3-4.2)
Relative risk for smokers compared to non-smokers:	
Treatment default	2.0 (1.5-2.5)
Smear conversion	0.6 (0.4-0.8)
Cavitary TB	1.9 (1.6-2.2)

Impact assessment

Population Attributable Risk % (PAR%)

$$PAR\% = \frac{p*(RR-1)}{p*RR+(1-p)*1}*100$$

$$= \frac{p*(RR-1)}{p*(RR-1)+1}*100$$

where p=prevalence of exposure;
RR=Relative Risk

Impact assessment

	RR	PAR%*
Developing TB	2.7	34%
Dying of TB	2.4	29%

* 29% ever-smoking prevalence
(Source: Mackay, Eriksen, Shafey 2006. *The Tobacco Atlas, 2nd edition.*)

Impact assessment

	RR	PAR%*	Model estimate*
Developing TB (Uncertainty in mechanisms) (Uncertainty in TB parameters)	2.7	34%	60% (59-72%) (56-65%)
Dying from TB (Uncertainty in mechanisms) (Uncertainty in TB parameters)	2.4	29%	57% (55-69%) (52-62%)

* 29% ever-smoking prevalence
(Source: Mackay, Eriksen, Shafey 2006. *The Tobacco Atlas, 2nd edition.*)

Impact of smoking, by smoking status

	Overall*	Ever-smokers*	Never-smokers*
Developing TB (Uncertainty in mechanisms) (Uncertainty in TB params.)	60% (59-72%) (56-65%)	78% (78-84%) (75-81%)	42% (39-59%) (36-48%)
Dying from TB (Uncertainty in mechanisms) (Uncertainty in TB params.)	57% (55-69%) (52-62%)	74% (74-83%) (71-78%)	42% (38-58%) (36-48%)

* 29% ever-smoking prevalence

(Source: Mackay, Eriksen, Shafey 2006. *The Tobacco Atlas, 2nd edition.*)

Research questions (cont)…

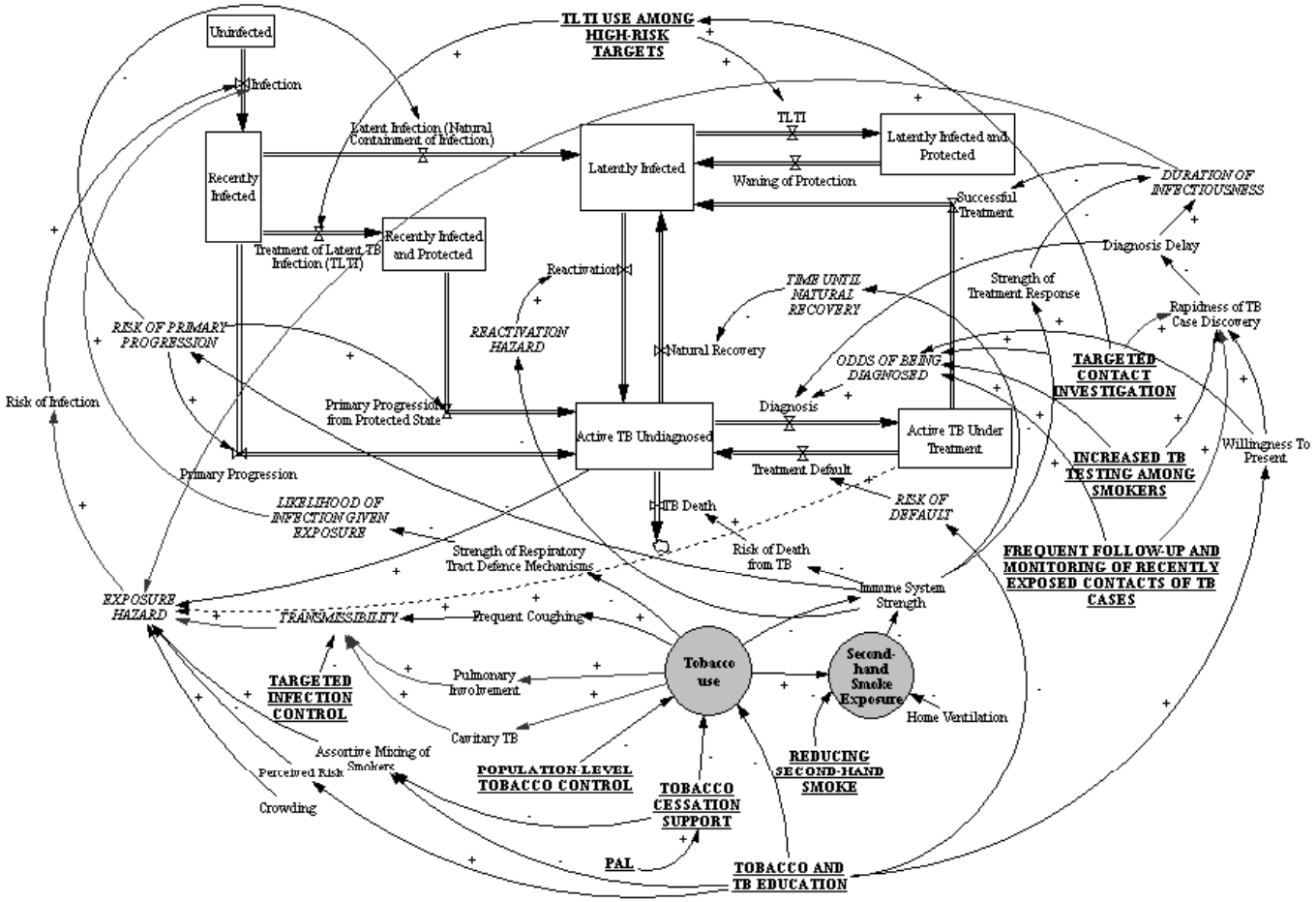
- How specifically does each risk factor affect TB dynamics?

- We must care about this…
  - To get the model right
  - To accurately prioritize leverage points
  - To inspire innovative thoughts about intervention

Effects of tobacco exposure on TB dynamics

- Smoking:
  - causes structural changes in the respiratory tract
  - impairs immune response
  - increases risk of transmission
  - alters treatment rate
  - increases non-TB death rate
  - is social

Effects of tobacco exposure on TB dynamics -- and interventions



Smoking is a modifiable risk factor…

- Potential tobacco control policies: taxation, education, warning labels, restrictions on supply, ad bans, smoking bans in public places
- We can:
  - Prevent initiation
  - Encourage cessation
  - Support cessation
  - Encourage harm reduction strategies

Smoking is an identifiable risk factor…

- Encourage PAL approach
- Screen smokers for TB infection and disease
- Use chemoprophylaxis among recently infected smokers
- Intensify measures to make sure smokers comply with TB treatment

Policy modeling: India

Case study: India

- Substantial TB epidemic
  - >20% of new TB cases globally
- Close to reaching treatment targets
- No evidence of meeting corresponding outcome targets
- <5% of TB cases co-infected with HIV, 0.5% of population HIV+ overall

Tobacco use in India

- Average age of initiation 20-25
- Adult smoking prevalence (25+)
  - 38% among men
  - 3% among women
- Focus on smoked tobacco, though smokeless tobacco widely used
- May be on the rise (need more data)

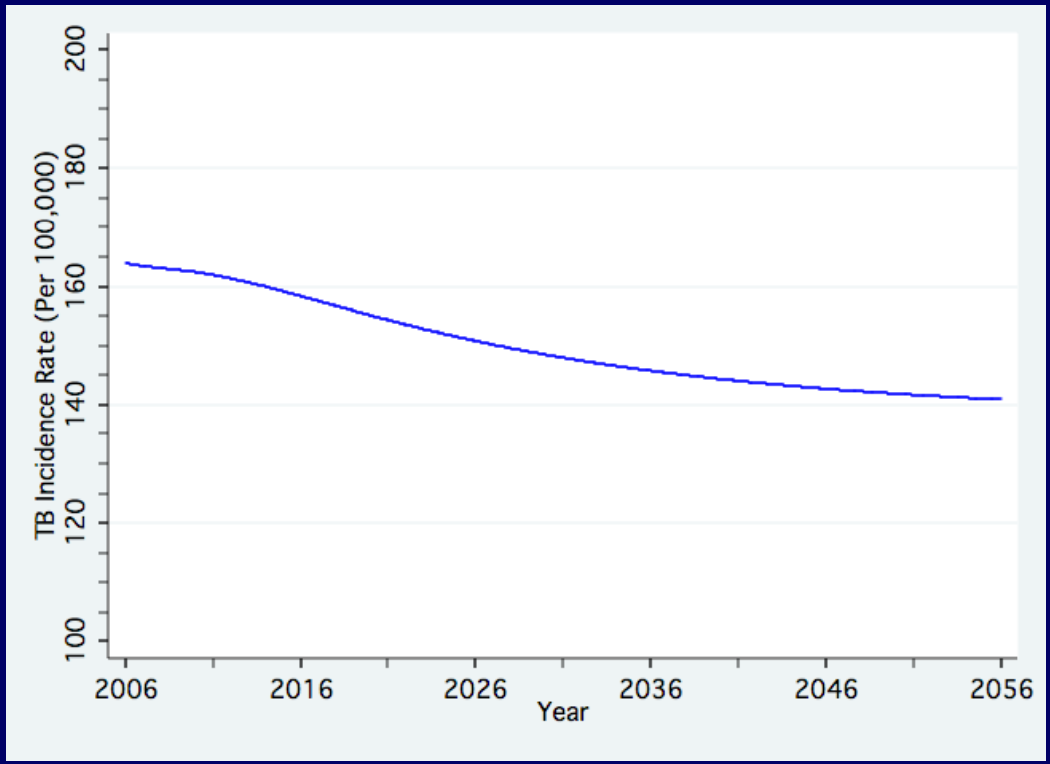
Tobacco control in India

- In 2003, established comprehensive tobacco-control policy
  - Increased tobacco taxation
  - Restrictions on smoking in public places
  - Advertising ban
- Need to strengthen existing policies, and add
  - Information/counter-advertising
  - Support for successful cessation
- GOAL: to reduce smoking prevalence by 15-25% by 2020

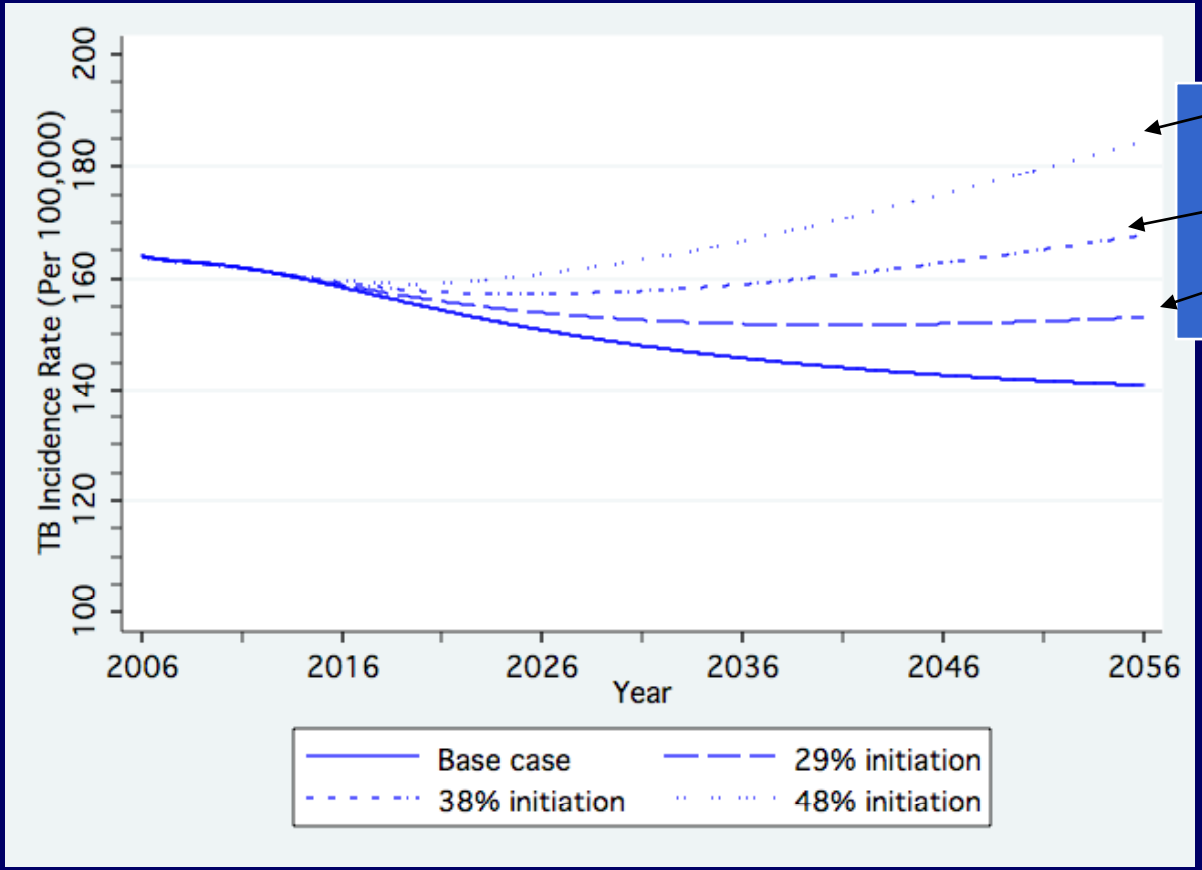
So…

- What will happen if tobacco-control policy is not enhanced (and smoking prevalence increases)?
- What will happen to population-level TB outcomes if tobacco-control targets are met?

Policy implications: India



Policy implications: India

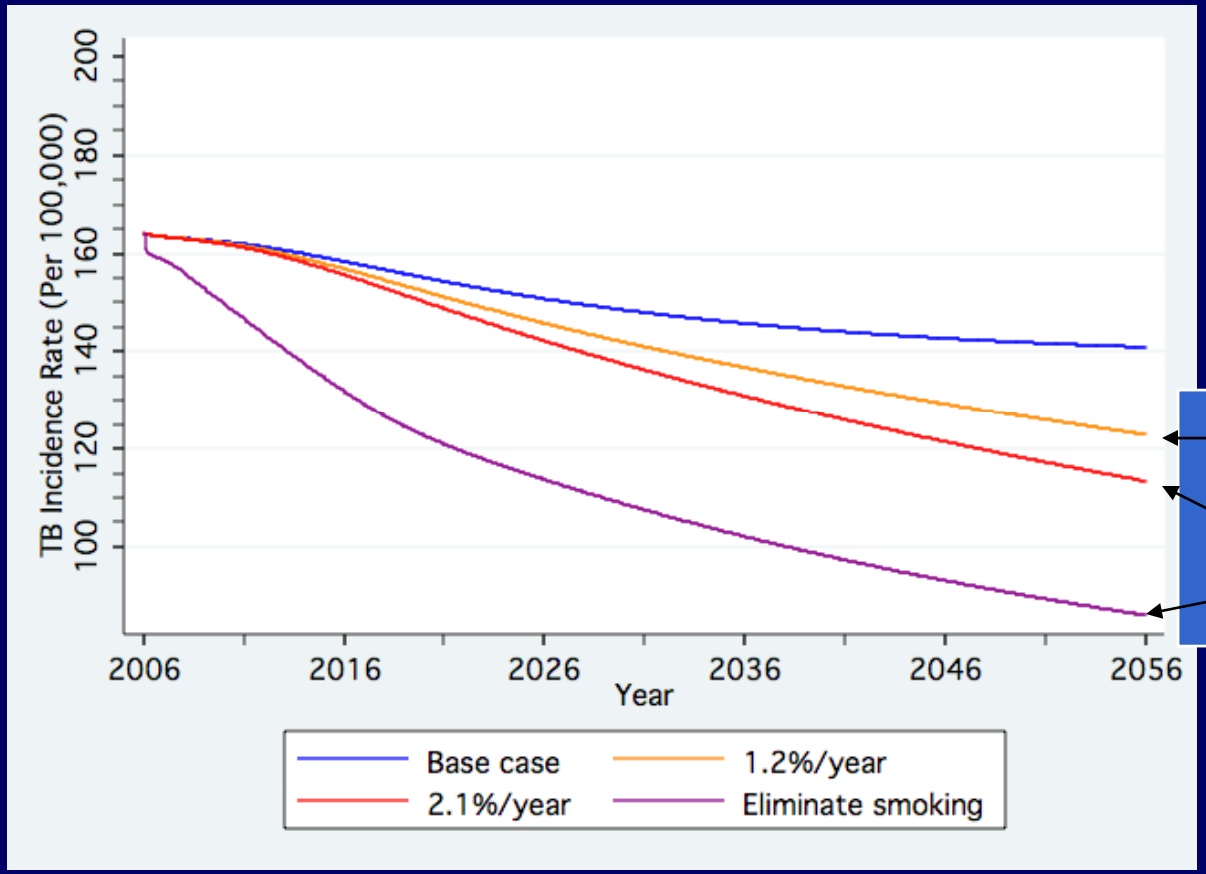


31% higher

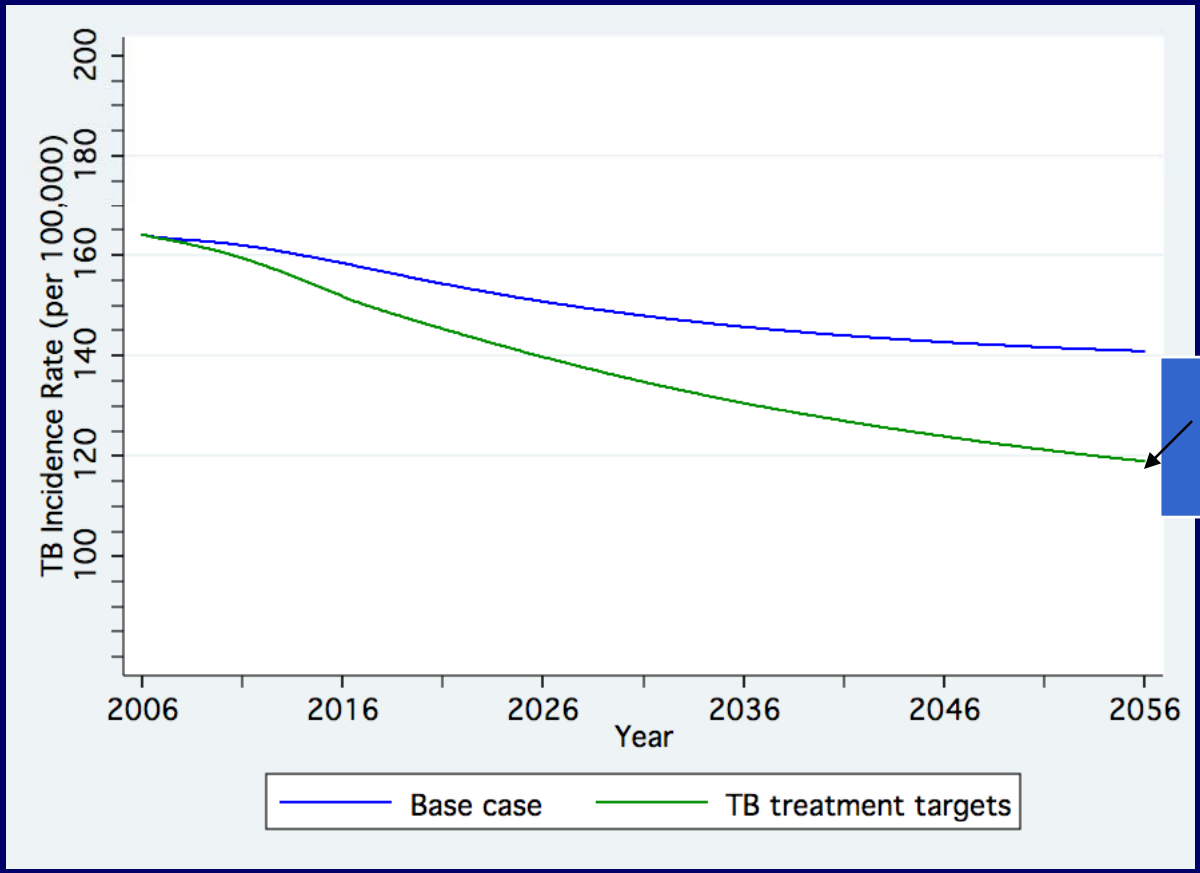
19% higher

9% higher

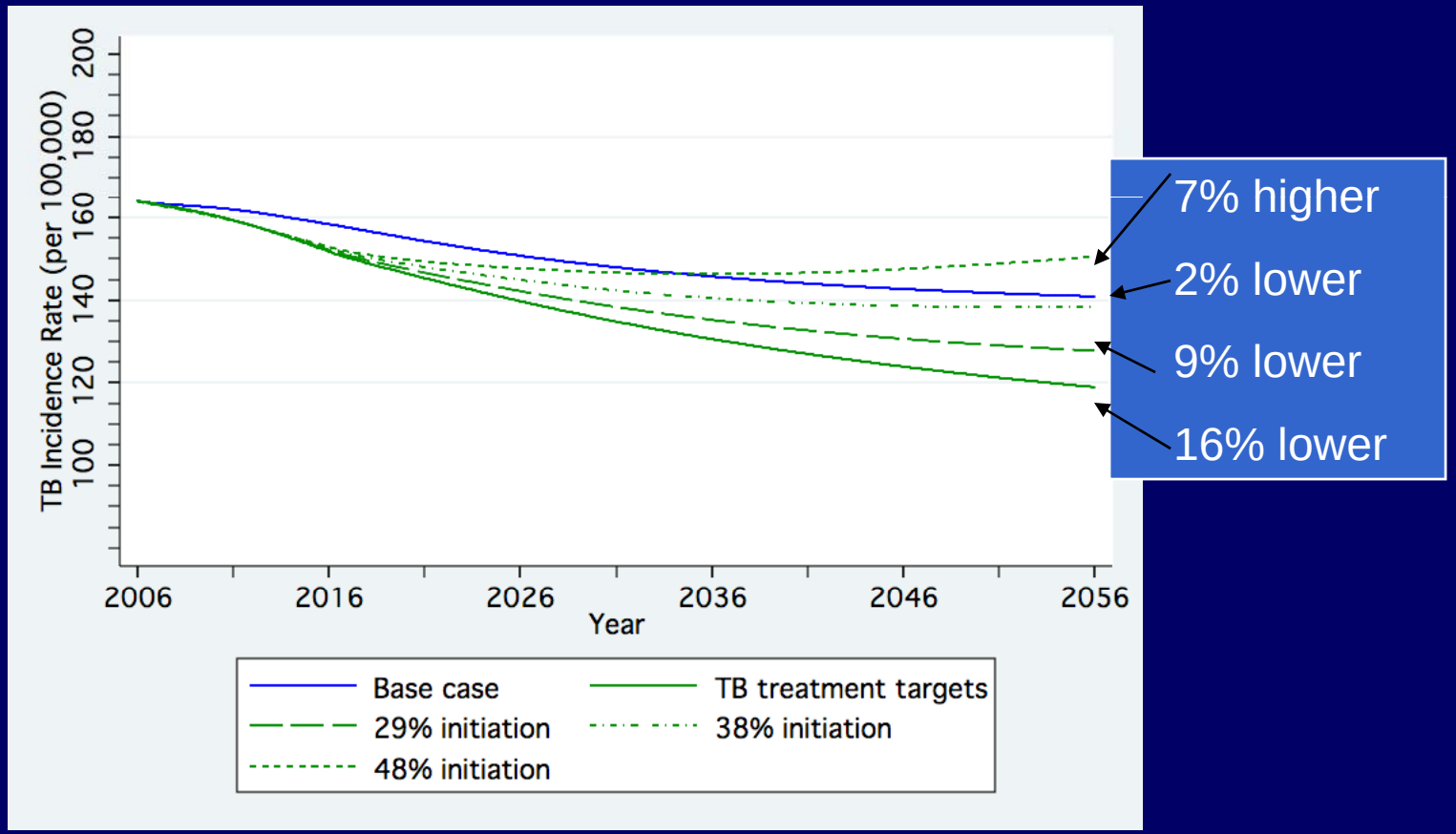
Policy implications: India



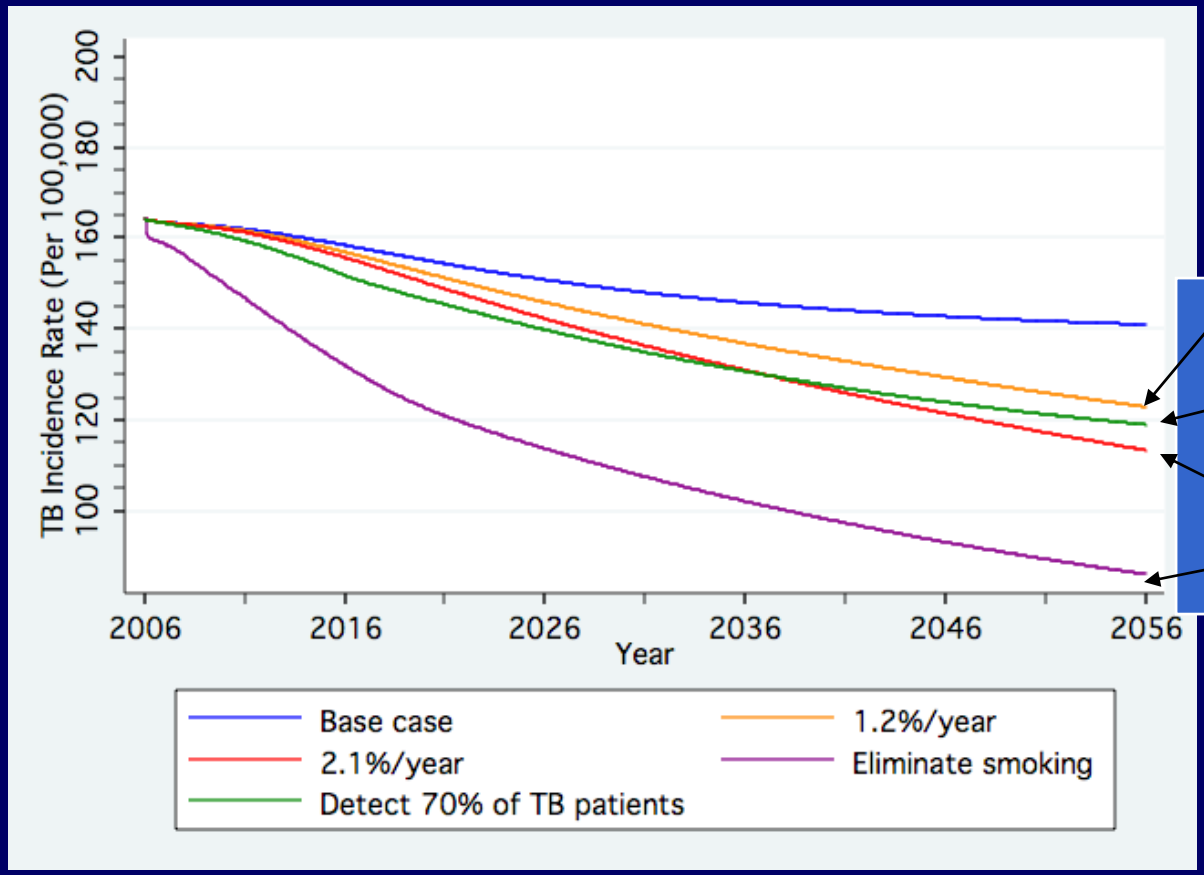
Policy implications: India



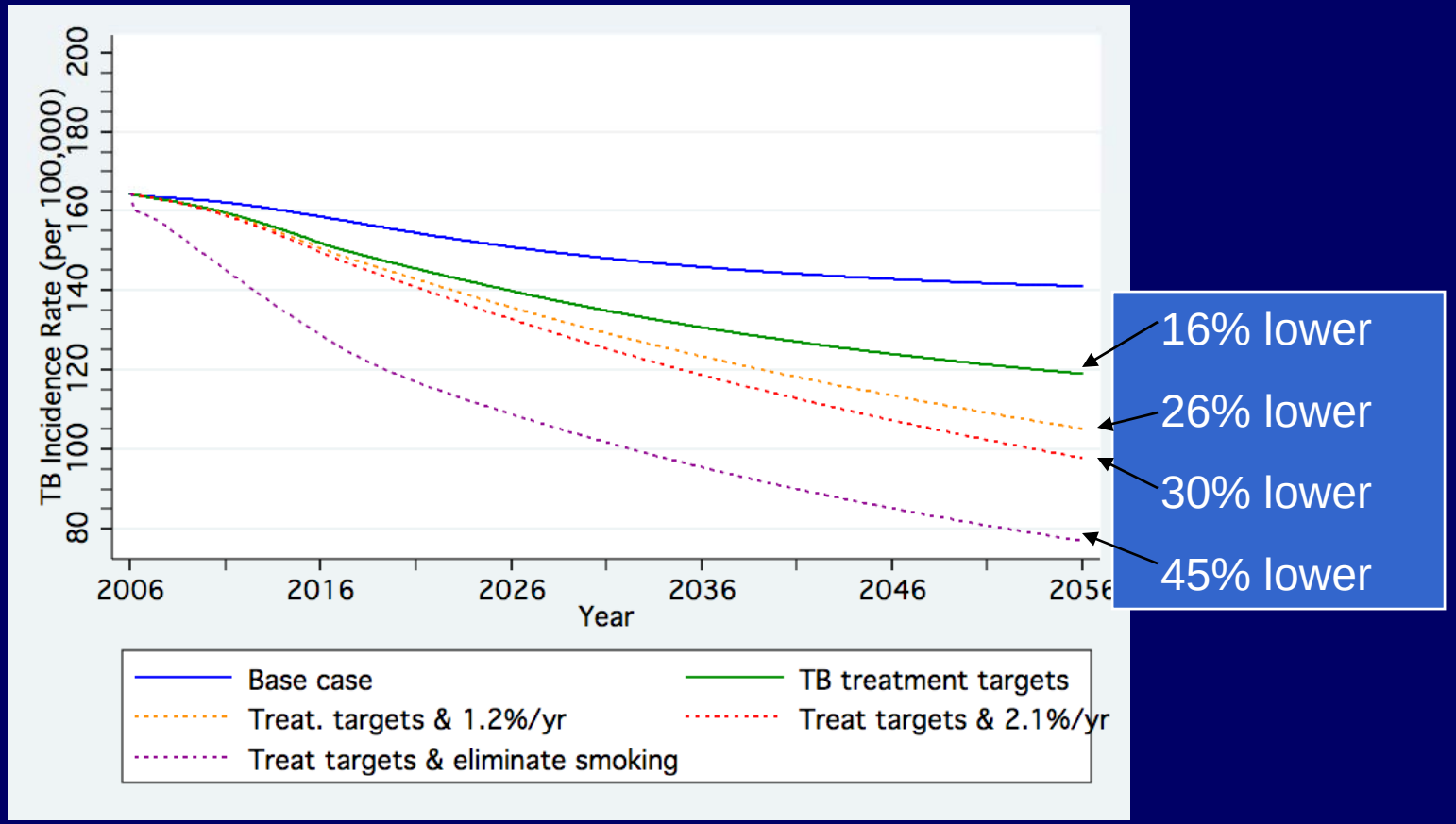
Policy implications: India



Policy implications: India



Policy implications: India



Diabetes and TB…

The association between diabetes and TB

- Less is known…
- Diabetes is associated with risk of developing TB disease (estimated odds ratios range from 1.15 to 8)
- Limited evidence suggests immune effects at play
- Diabetics who develop pulmonary TB are more likely to develop smear-positive and cavitary disease
- Diabetics are sometimes more likely to default from treatment programs
- Diabetics on TB treatment are less likely to experience smear conversion within 2 months of treatment
- Diabetics with TB may be more likely to die
  - » (Source: Stevenson et al (2007) in Chronic Illness 3:228)

Diabetes and TB

- Evidence is more varied than for tobacco exposure
- Less evidence about causality (more of a puzzle remains)
- How much of the increased risk is driven by late-stage diabetes?
- What specific mechanisms are at play?

Work in progress in Saskatchewan…

- Objectives…
  - To learn more about mechanisms and the magnitude of TB effects
  - To learn more about interactions between risk factors
  - To identify powerful, feasible, and locally-tailored intervention packages
  - To begin to understand how power of policies varies by environment

Why build simulation models?

- Systems are complex
- Make *mental models* explicit, develop shared understanding
- Virtual world in which to test and compare intervention strategies at population level and identify key leverage points
- Tool for engaging stakeholders and policy makers to identify the most cost effective and locally acceptable interventions (foundation for discussing trade-offs)
- Help identify most important gaps in our understanding of the system

Thank you!

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