TRENDS IN THE GLOBAL TB EPIDEMIC AND THE IMPACT ON LOCAL TB ELIMINATION EFFORTS

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GOALS

- Describe the the global and US burden of Tuberculosis (TB) disease

- Describe how the global TB epidemic is currently impacting the TB epidemic in the US

- Identify the challenges of TB elimination in the US

- Outline why continued efforts towards TB elimination are important for our community

- Identify strategies for optimizing TB services in communities

THE GLOBAL TB REPORT 2016
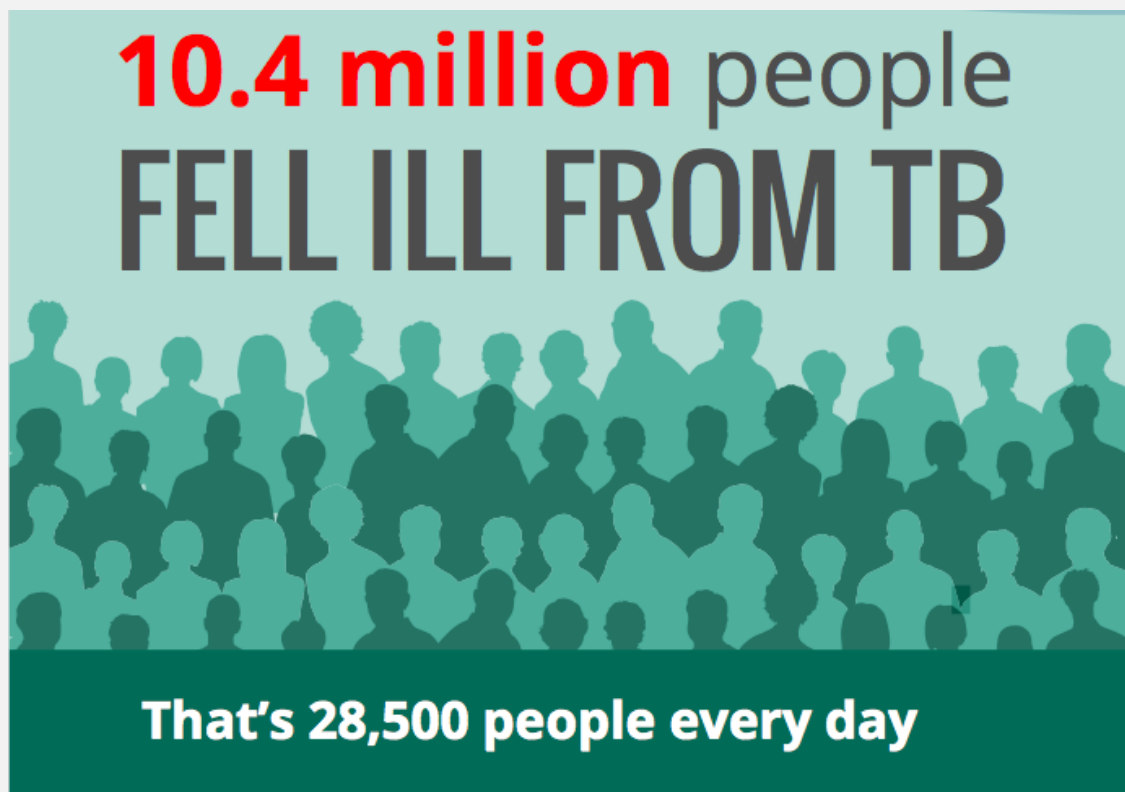
10.4 million people
FELL ILL FROM TB

That's 28,500 people every day

- **1 million children**
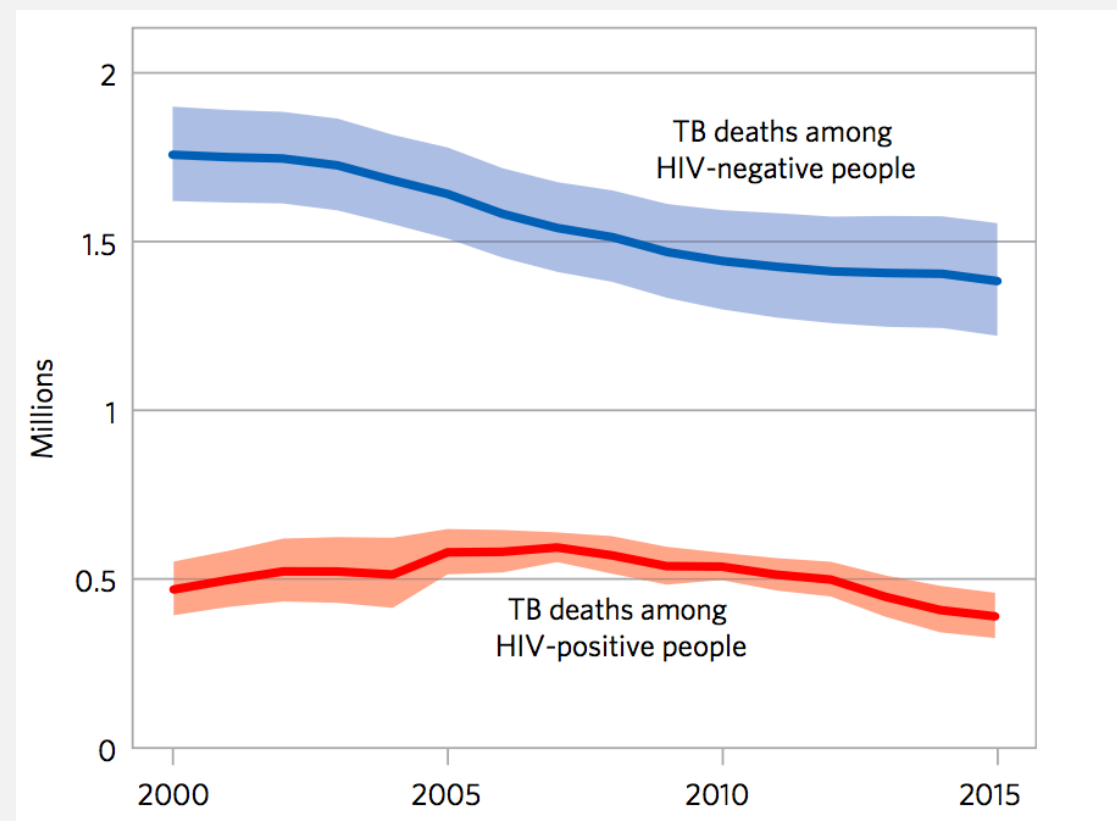
TB CAUSES MORE DEATHS THAN ANY OTHER INFECTION GLOBALLY

49 million lives saved between 2000-2015

TB deaths fell by 22% in the same period

1.8 MILLION TB DEATHS
INCLUDING 0.4 MILLION TB DEATHS AMONG PEOPLE WITH HIV*

TB was one of the top ten causes of death worldwide

TB was responsible for more deaths than HIV and malaria

DRUG RESISTANT TB

- **580,000 with drug-resistant TB disease (DR-TB)**
  - Estimated 38% mortality
  - **<50% of estimated DR-TB burden was actually detected**
 - **Estimated 39,000 waiting to start treatment**

DRUG RESISTANCE

Only 1 in 5 people needing treatment for **multidrug-resistant TB in 2015** ACTUALLY RECEIVED IT

Only half of those who started MDR-TB treatment **WERE CURED**

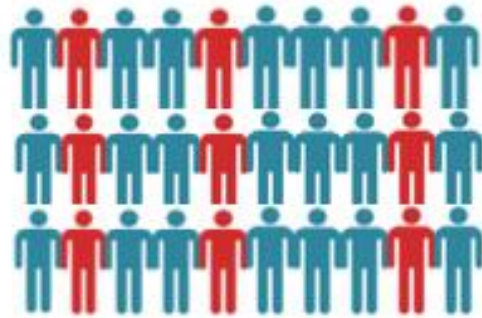# DRUG RESISTANT TB: A SUPERBUG WHICH DESERVES MORE ATTENTION

Estimated incidence of MDR/RR-TB in 2015, for countries with at least 1000 incident cases. Areas that are not applicable are in grey.
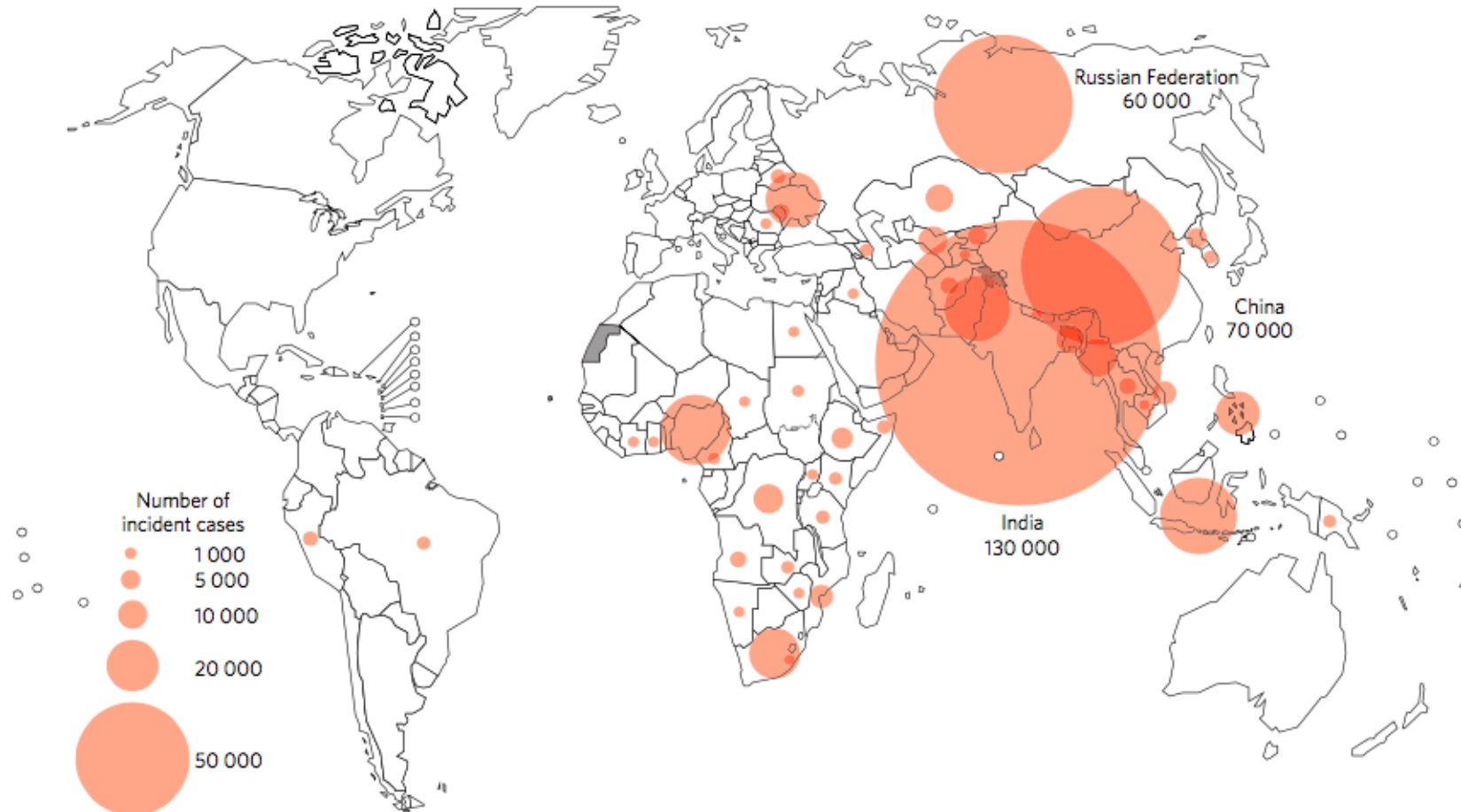
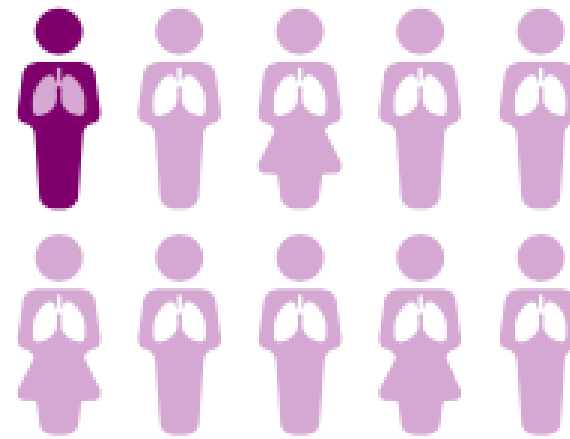# TB INFECTION (LATENT TB) IS VERY COMMON GLOBALLY

2-3 billion

persons with LTBI globally

About one in three persons

RISK FACTORS

Exposure → LTBI → Active TB

RISK FACTORS

1 in 10

Without treatment, 1 in 10 people with latent TB infection will develop TB disease.

Guidelines on the management of latent tuberculosis infection

THE END TB STRATEGY

World Health Organization

www.who.int
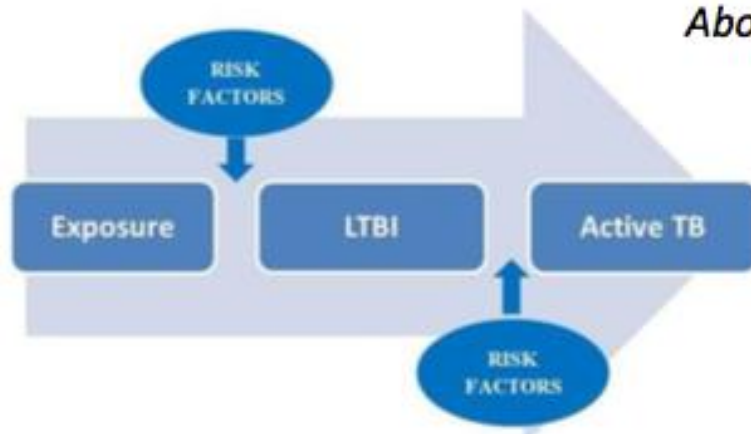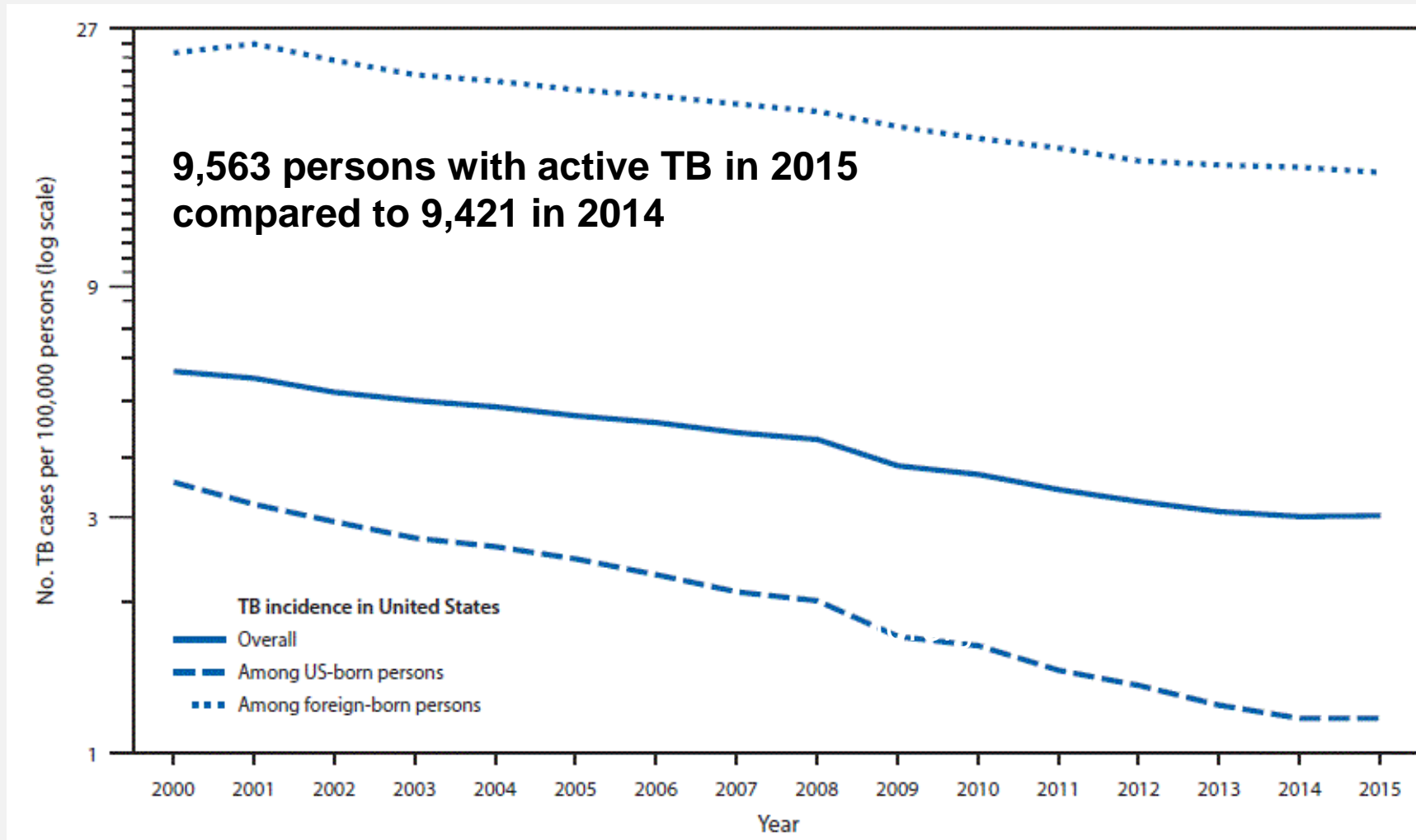
POOL OF LATENT DRUG-RESISTANT TB

- Recent estimates of the number of children with latent drug-resistant TB:
  - 5 million with isoniazid monoresistance
  - 2 million with multi-drug resistant (MDR) TB
  - 100,000 with extremely drug resistant (XDR)
- Number if individuals with DR-latent TB in the U.S is not well characterized

Dodd, PJ et al. Lancet Infect Dis2016

FOR THE FIRST TIME IN 2 DECADES, OVERALL TB INCIDENCE REMAINED FLAT IN THE US

9,563 persons with active TB in 2015 compared to 9,421 in 2014

Y-axis: No. TB cases per 100,000 persons (log scale)
X-axis: Year

TB incidence in United States
— Overall
- - - Among US-born persons
······ Among foreign-born persons

Salinas JL, et al. MMWR Morb Mortal Wkly Rep

FOR THE FIRST TIME IN 2 DECADES, OVERALL TB INCIDENCE REMAINED FLAT IN THE US

- Estimated 80-86% of those with active TB are due to reactivation in the U.S.

- Incidence among US-born persons was flat, with a slight total increase in the absolute number

- Among foreign born persons, incidence decreased from 15.4 to 15.1/100,000 with a slight increase in the absolute number

Salinas JL, et al. MMWR Morb Mortal Wkly Rep 2016
Shea KM, et al. Am J Epidemiol. 2014

RECENT TRANSMISSION OF TB: PATIENT CHARACTERISTICS

- Analysis from Jan 2011-Sept 2014
  - n=26,586 genotyped cases
  - Evidence for recent transmission in 14%
- 91% among individuals born in the US
- After multivariable analysis, adjusted prevalence ratio (aPR) was higher for:
  - Children <4 years of age
  - People of color
 - Individuals reporting homelessness

Characteristic	Value	Limited recent transmission		Extensive recent transmission	
		aPR	Wald 95% CI	aPR	Wald 95% CI
Sex	Female	Reference		Reference	
	Male	1.1	1.0–1.2	1.1	1.0–1.3
Age (years)	≤4	2.8	2.4–3.3	1.9	1.4–2.6
	5–14	1.5	1.1–2.0	1.3	0.8–1.9
	15–24	1.4	1.3–1.6	1.2	1.1–1.5
	25–44	Reference		Reference	
	45–64	0.9	0.8–1.0	1.0	0.9–1.1
	≥65	0.5	0.4–0.6	0.5	0.4–0.6
Origin	Foreign-born	0.4	0.3–0.4	0.2	0.2–0.2
	U.S.-born	Reference		Reference	
Race and ethnicity*	Hispanic	1.5	1.3–1.7	2.0	1.7–2.4
	American Indian /Alaska Native	1.5	1.2–2.0	3.6	2.9–4.4
	Asian	1.1	0.9–1.3	2.4	1.9–3.0
	Black	1.6	1.4–1.8	3.0	2.6–3.5
	Native Hawaiian / Pacific Islander	1.5	1.1–2.2	3.2	2.3–4.5
	White	Reference		Reference	

*Persons of Hispanic ethnicity might be of any race; non-Hispanic persons are categorized as Asian, black, white, American Indian/Alaska Native, Native Hawaiian or other Pacific Islander, or of multiple races. Bold text indicates statistically significant result.
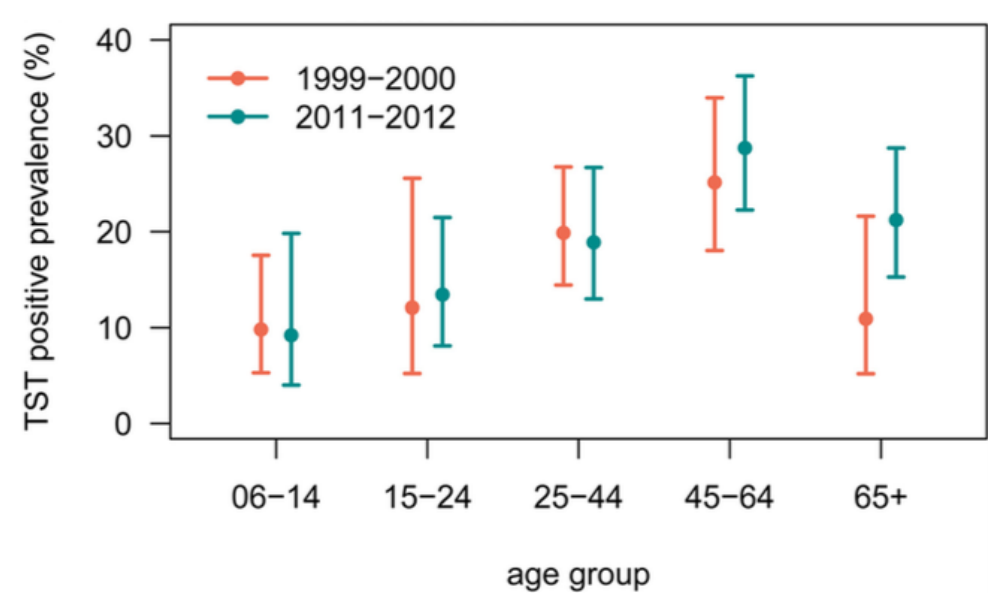
Yuen CM, et al. PLoS ONE 11(4): 2016
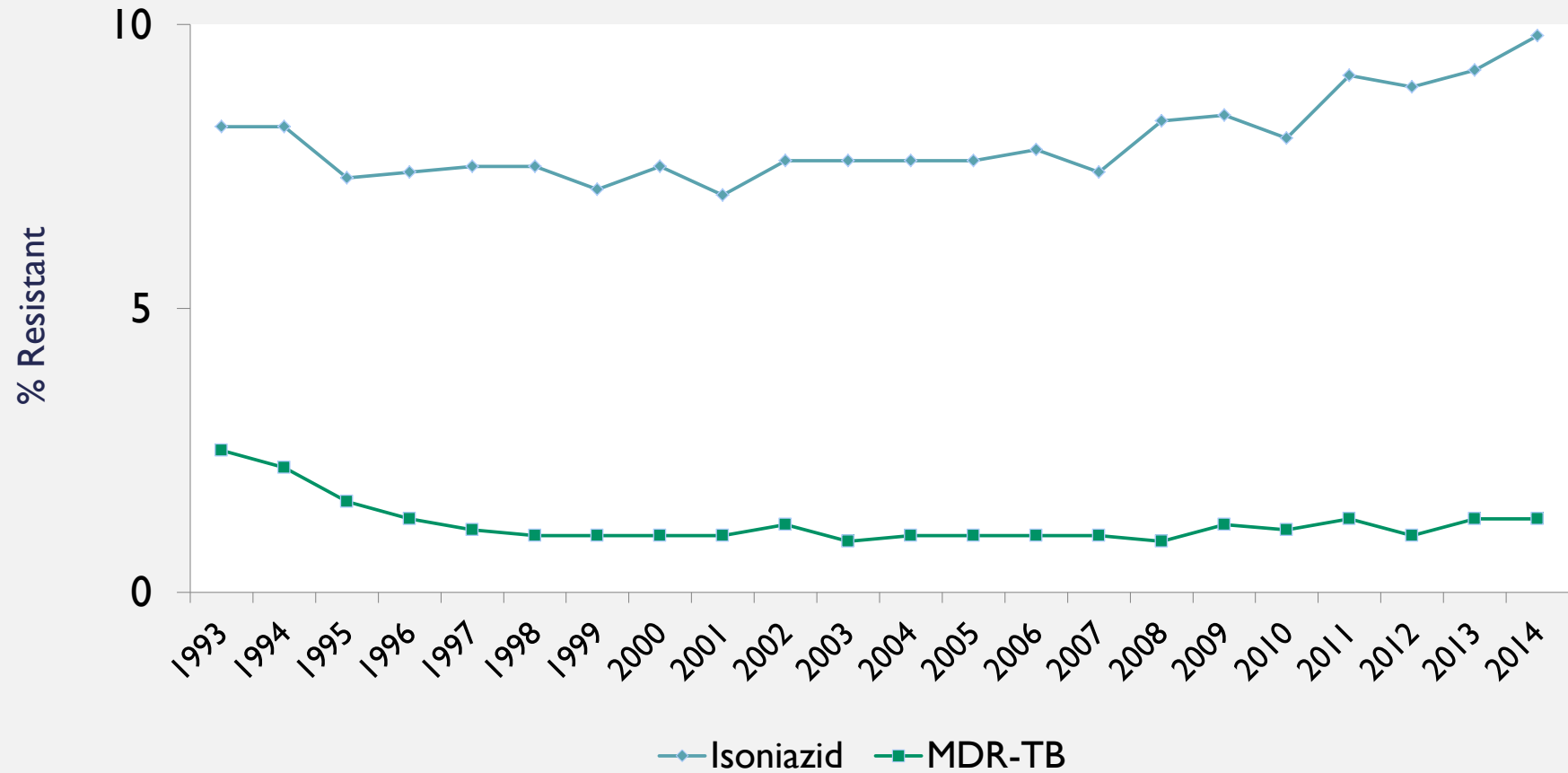
TST prevalence: no travel to TB endemic area
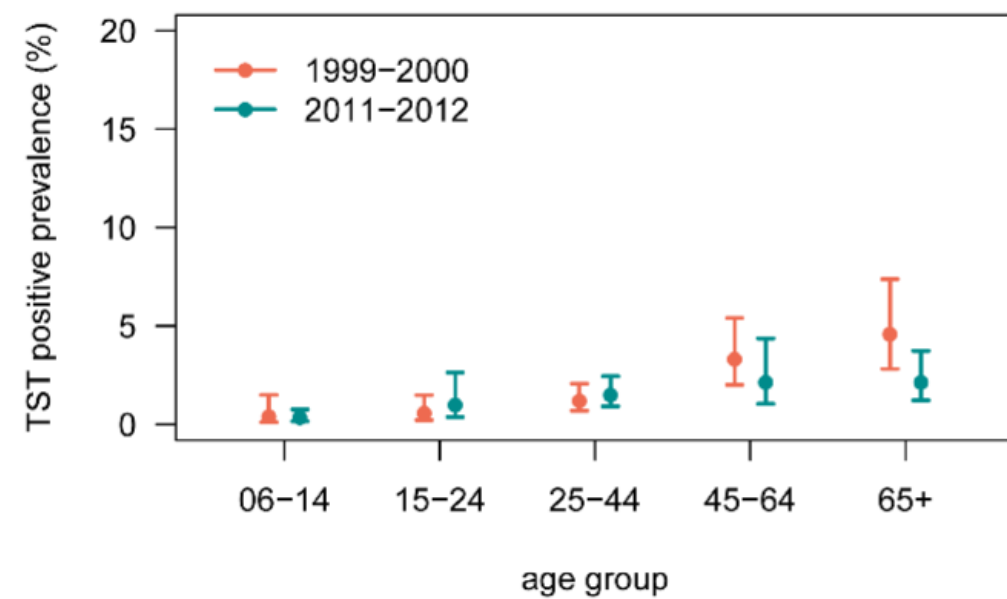
TST prevalence: lived in TB endemic area

THERE ARE AN ESTIMATED 13 MILLION INDIVIDUALS WITH LATENT TB IN THE US

Miramontes, PLoS One, 2015

TB IN THE US IS LARGELY A REFLECTION OF THE GLOBAL TB EPIDEMIC

- Shifts in the global TB epidemic impact the US epidemic

  - The number of individuals with latent and active drug-resistant TB is worrisome

- Recent transmission does not appear to be driven by individuals who were born or who lived outside of the US

- The prevalence of latent TB is higher among individuals who were born or who lived outside of the US

STRATEGIES FOR TB ELIMINATION: GETTING TO AN INCIDENCE OF 1/MILLION

- Collaborating with other countries to reduce the global burden of TB
  - *"recognizing the fact that tuberculosis is not constrained by national boundaries"*
- Mobilizing and sustaining public support and commitment for elimination of tuberculosis
- Accelerating the rate of decline of tuberculosis
- Developing new diagnostic tools
- Monitoring progress

Ending Neglect

The Elimination of Tuberculosis in the United States

INSTITUTE OF MEDICINE
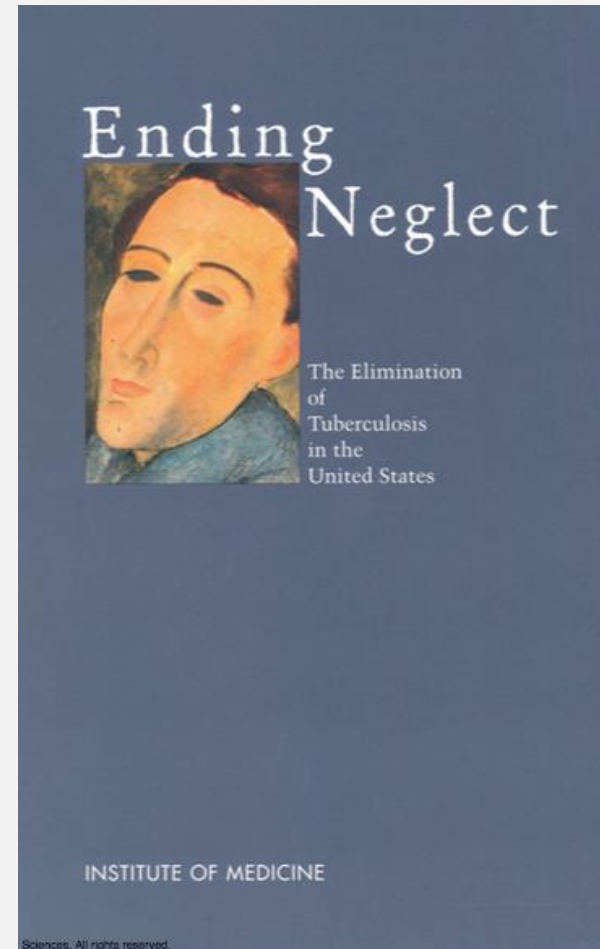
TB ELIMINATION PLAN FOR COLORADO: FOCUSING ON THE TB INFECTION CARE CONTINUUM

- Goal 1: Find and engage individuals and populations at-risk for TB infection

- Goal 2: Test those at-risk for TB infection and progression to TB disease so individuals know their status

- Goal 3: Ensure completion of treatment of those diagnosed with TB infection

- Goal 4: Create systematic support for TB prevention

- Goal 5: Tailor communication messages to key groups

- Goal 6: Integrate emerging technologies/Report and track with on-going evaluation of programmatic effectiveness

The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis
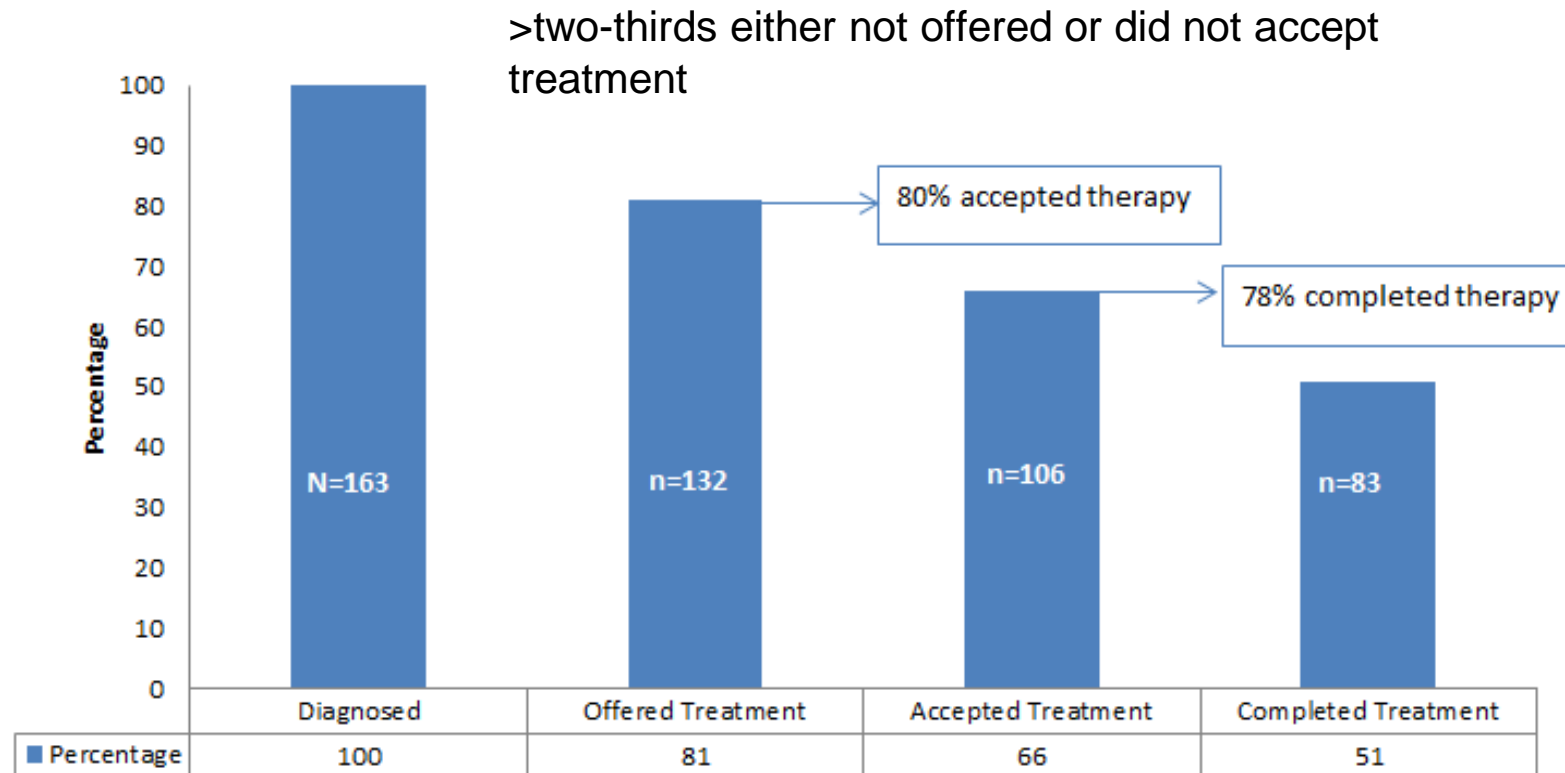
Hannah Alsdurf, Philip C Hill, Alberto Matteelli, Haileyesus Getahun, Dick Menzies

- Higher treatment completion with rifampin (50%) compared to isoniazid (19%)

- Completion rates for non-contacts/refugees: 9.7%

- Reasons for not completing:
  - Toxicity
  - Health systems issues
  - Social situation
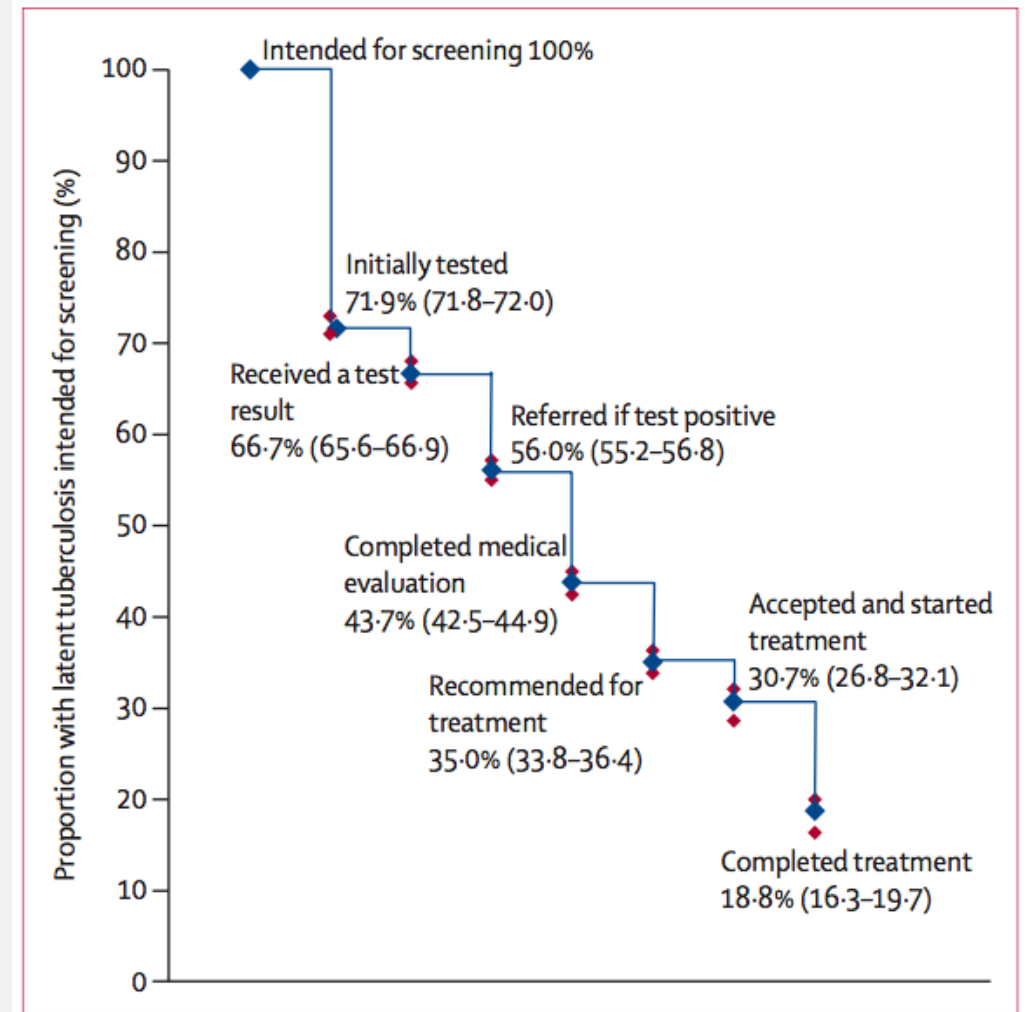
IDENTIFYING GAPS IN TUBERCULOSIS PREVENTION AMONG ADULTS AT AN URBAN, PUBLIC HEALTH CLINIC: AN LTBI CARE CONTINUUM

TB Continuum of Care for a sample cohort of patients diagnosed with Class 2 LTBI at DMTBC (N=163)

>two-thirds either not offered or did not accept treatment

80% accepted therapy

78% completed therapy

	Diagnosed	Offered Treatment	Accepted Treatment	Completed Treatment
Percentage	100	81	66	51

N=163, n=132, n=106, n=83

# At least 44% of individuals with active TB in the Denver Metro area could have avoided developing TB disease

Preventable cases of reported active TB from 2009-2014, Denver Metro Area	N	%
Total Cases	307	-
Foreign-born	246	80
Report date > 6 months from arrival	187	61
TST or QFT positive at diagnosis	**135**	**44**

Foreign-born

45%   55%

■ Preventable
■ Not preventable
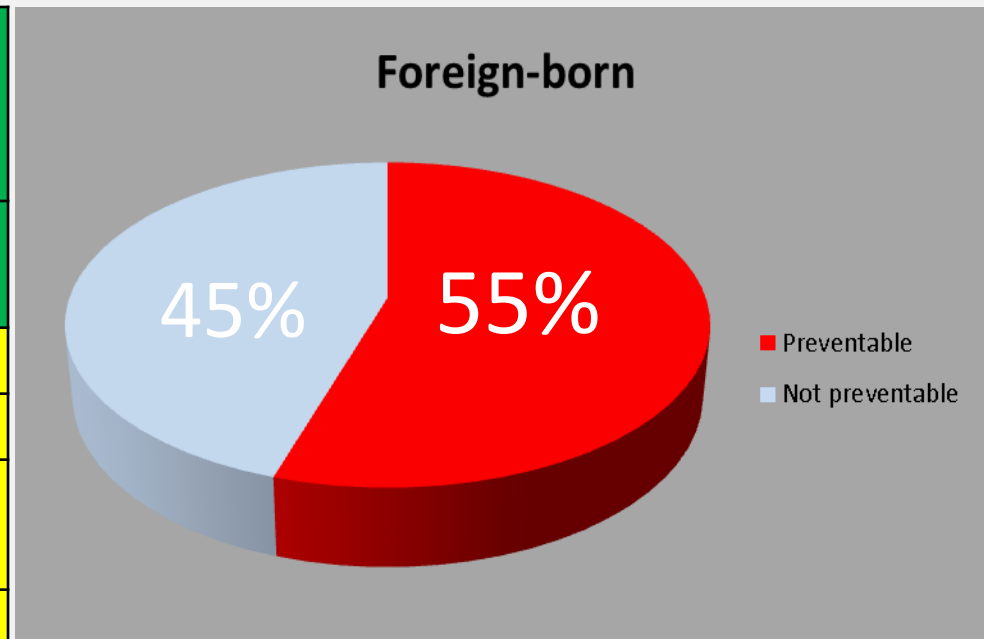
Median years in US until diagnosis=7.5

Colorado's incidence in 2015 was 13/million; thus could potentially get to 7/million

PROJECTED TIME TO TB ELIMINATION IN THE US
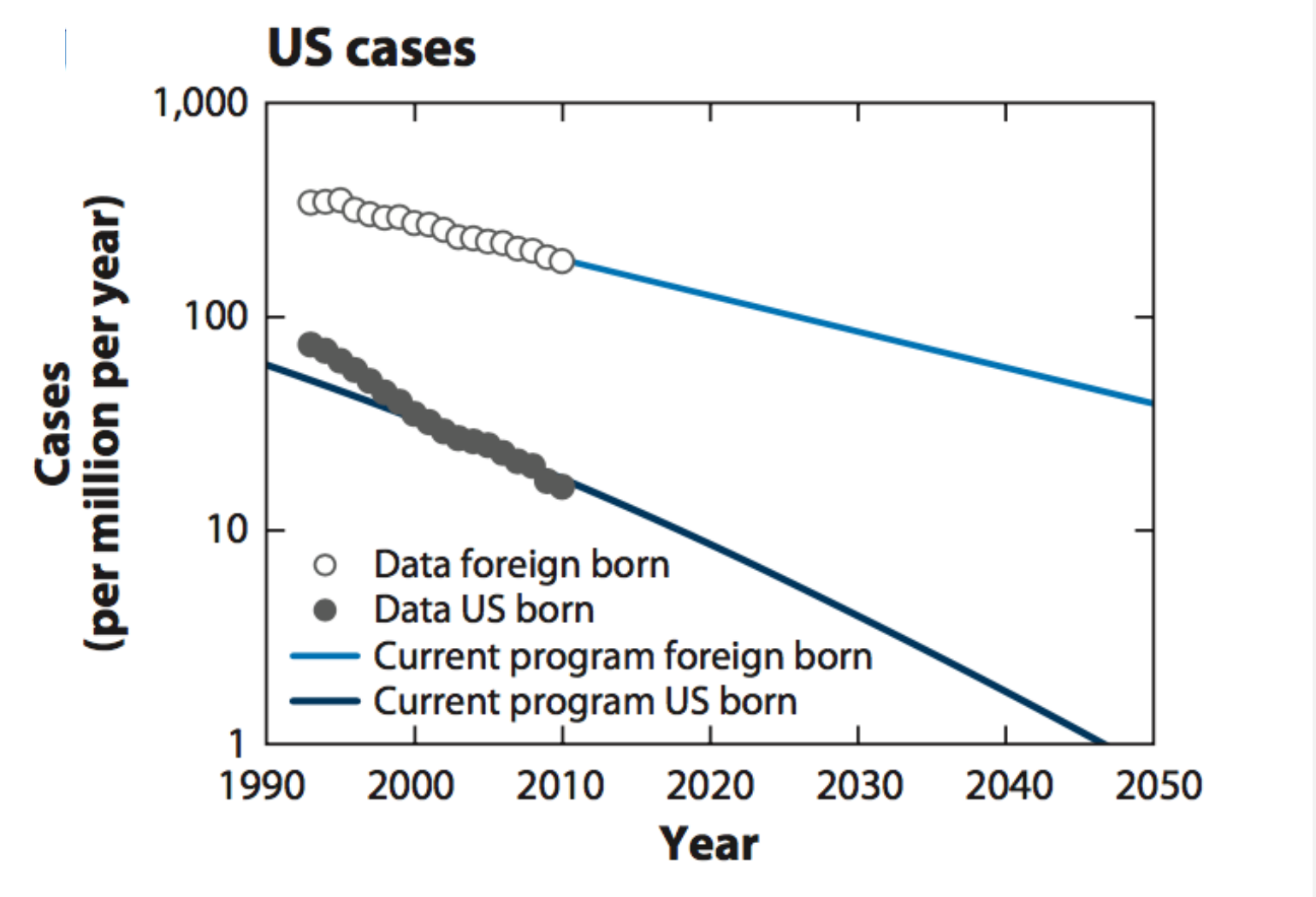
PROJECTED TIME TO TB ELIMINATION IN THE US—THE CHALLENGES

- Few people who need TB infection testing have received it

- Of those who are tested, many are lost to follow-up before they are ever offered treatment or they decline

- Acceptance rates can vary

- Completion rates impacted by adverse effects, and differences in ability to remain in care

- IGRAs and TSTs can miss up to 20% of individuals with TB infection/disease

- Public health resources are limited

KEEP CALM AND BANG YOUR HEAD AGAINST THE WALL

http://occupyme.net/2014/03/12/silver-platter-of-frustration/

WHY SHOULD WE TRY TO ACHIEVE TB ELIMINATION?

PREVENT COMPLICATIONS FROM TB DISEASE

- Treatment side effects
- Loss of job/income
- Loneliness
- Feelings of self-blaming
- Anger/frustration
- Anxiety over transmission to friends/family
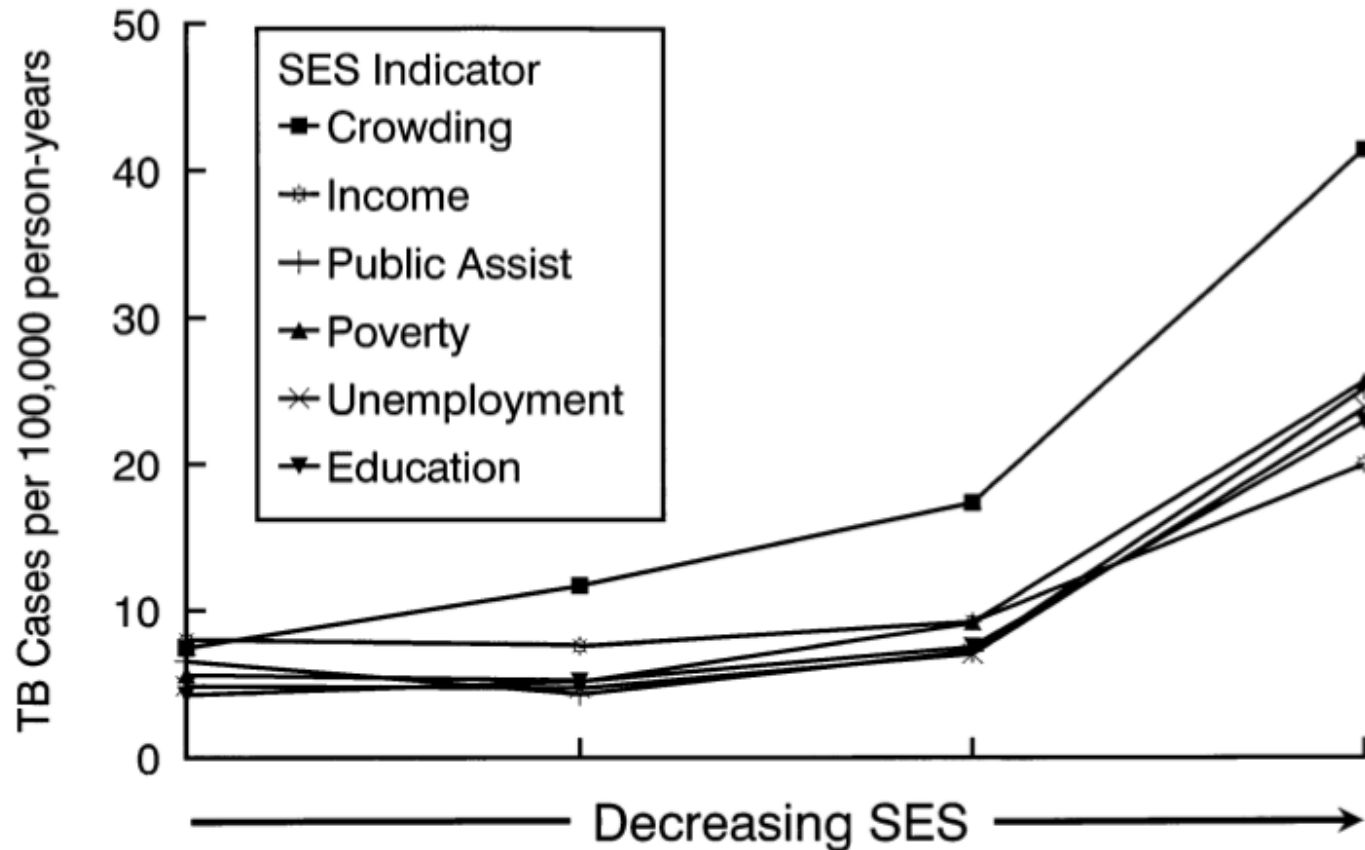- Fear of "re-entering" society and embracing a normal life

TB DISPROPORTIONATELY AFFECTS INDIVIDUALS EXPERIENCING POOR LIVING CONDITIONS AND MALNUTRITION

Ortblad KF et al. Lancet 2015; 386: 2354–62
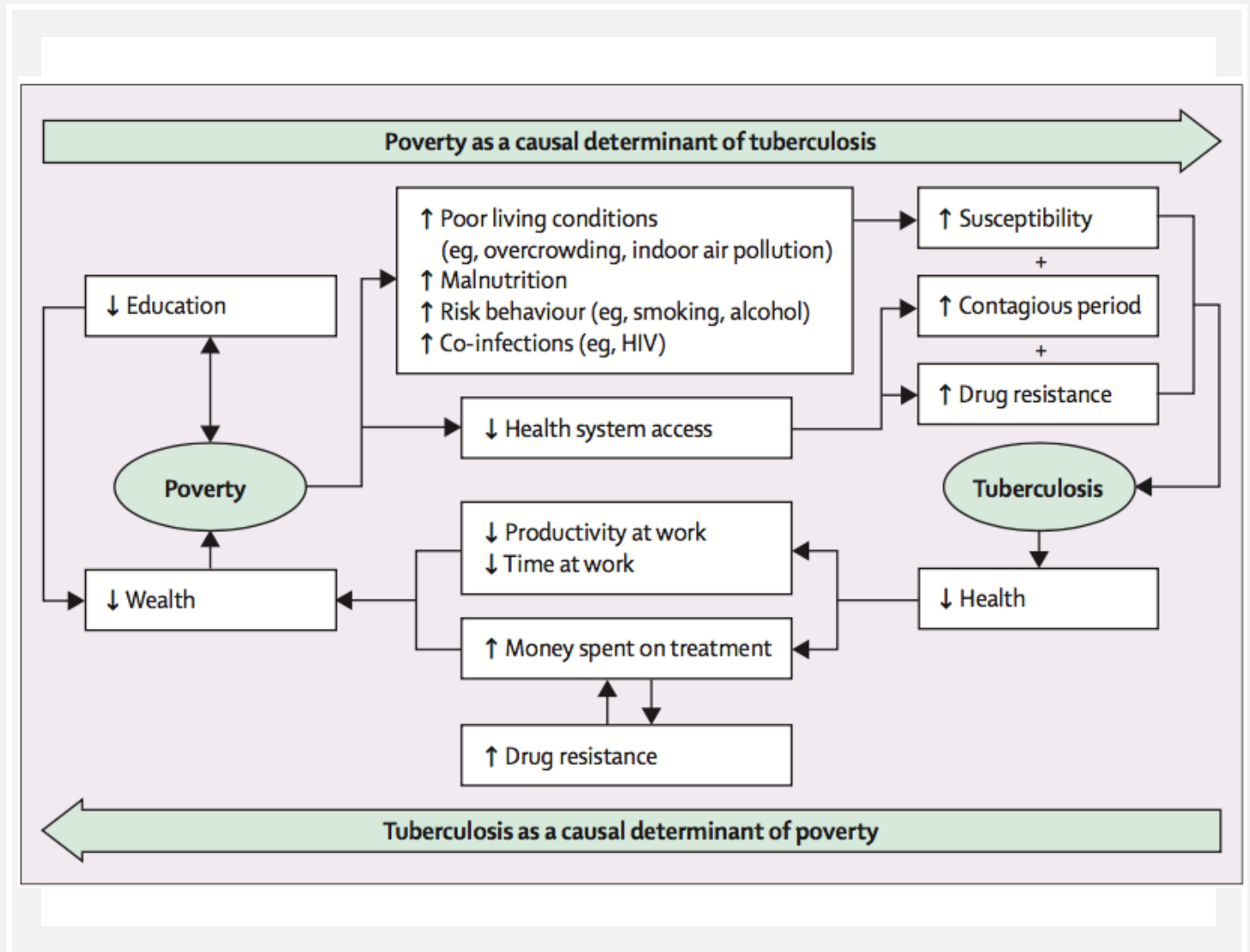
HIGHER TB INCIDENCE AS SOCIO-ECONOMIC STATUS *DECREASES*

TB RATE RATIOS BY SES INDICATOR AND SES QUARTILE

SES Indicator	Simple SES Models			Combined SES Model		
	2nd	3rd	4th	2nd	3rd	4th
Crowding	1.0	1.3*	2.2*	0.9	1.1	1.7*
Income	1.4*	1.6*	2.1*	1.0	1.0	1.0
Poverty	1.2*	1.6*	2.3*	1.2*	1.3*	1.5*
Public Assistance	1.0	1.2*	1.8*	0.9	1.0	1.2*
Unemployment	1.2*	1.4*	2.0*	1.1*	1.1*	1.2*
Education	1.5*	2.0*	2.5*	1.3*	1.4*	1.5*

TB Rate Ratios by SES Quartile (*compared to 1st SES quartile*)

* Denotes statistical significance, based on a 95% CI not including 1.0.

Cantwell MF, et al. AJRCCM 1997

TB CASE RATES BY RACE/ETHNICITY, UNITED STATES, 2003–2014

Salinas JL, et al. MMWR Morb Mortal Wkly Rep 2016
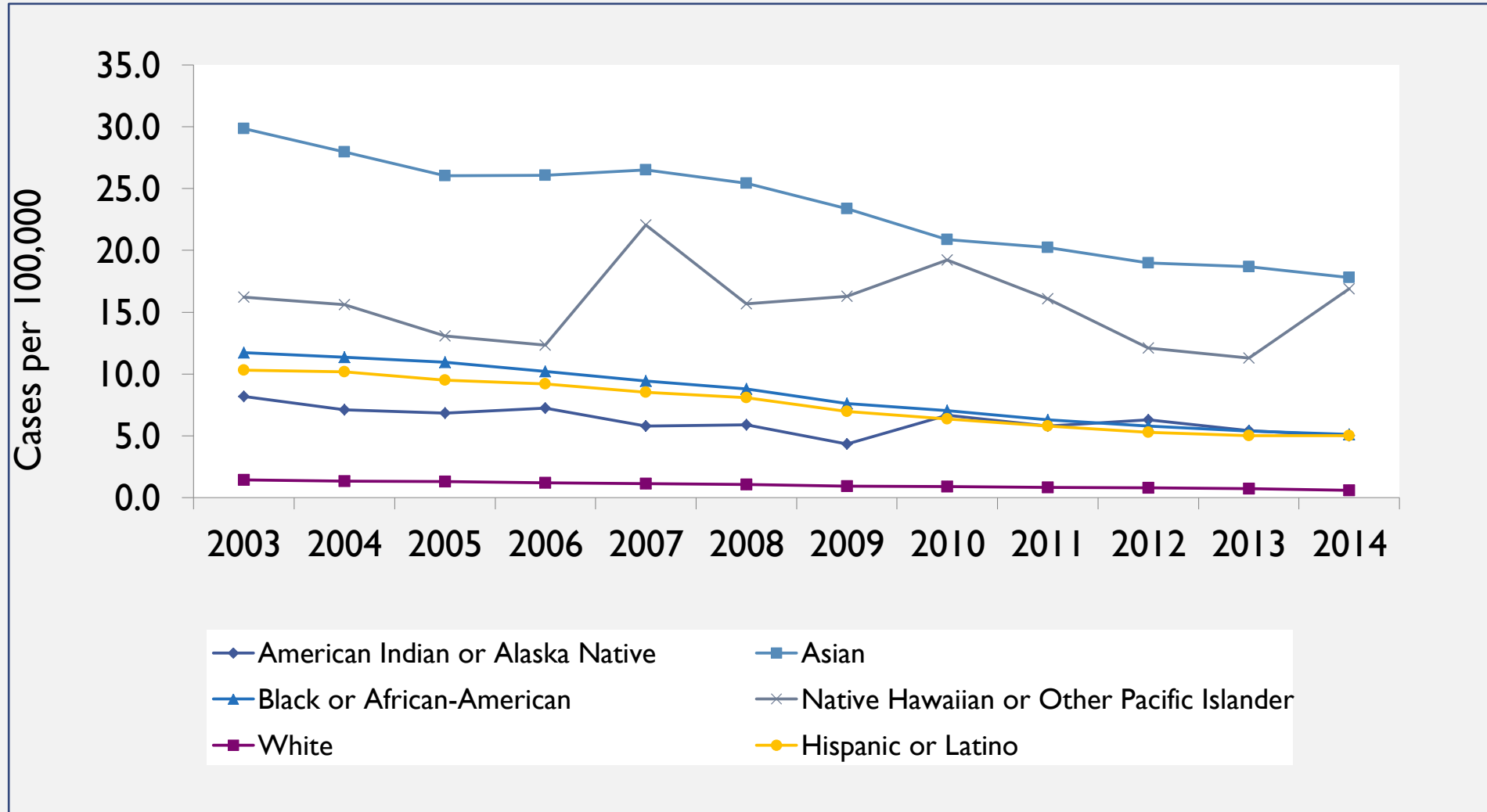
INSTITUTE OF MEDICINE, 2002:

- "A large body of published research reveals that racial and ethnic minorities experience a lower quality of health services, and are less likely to receive even routine medical procedures than are white Americans."
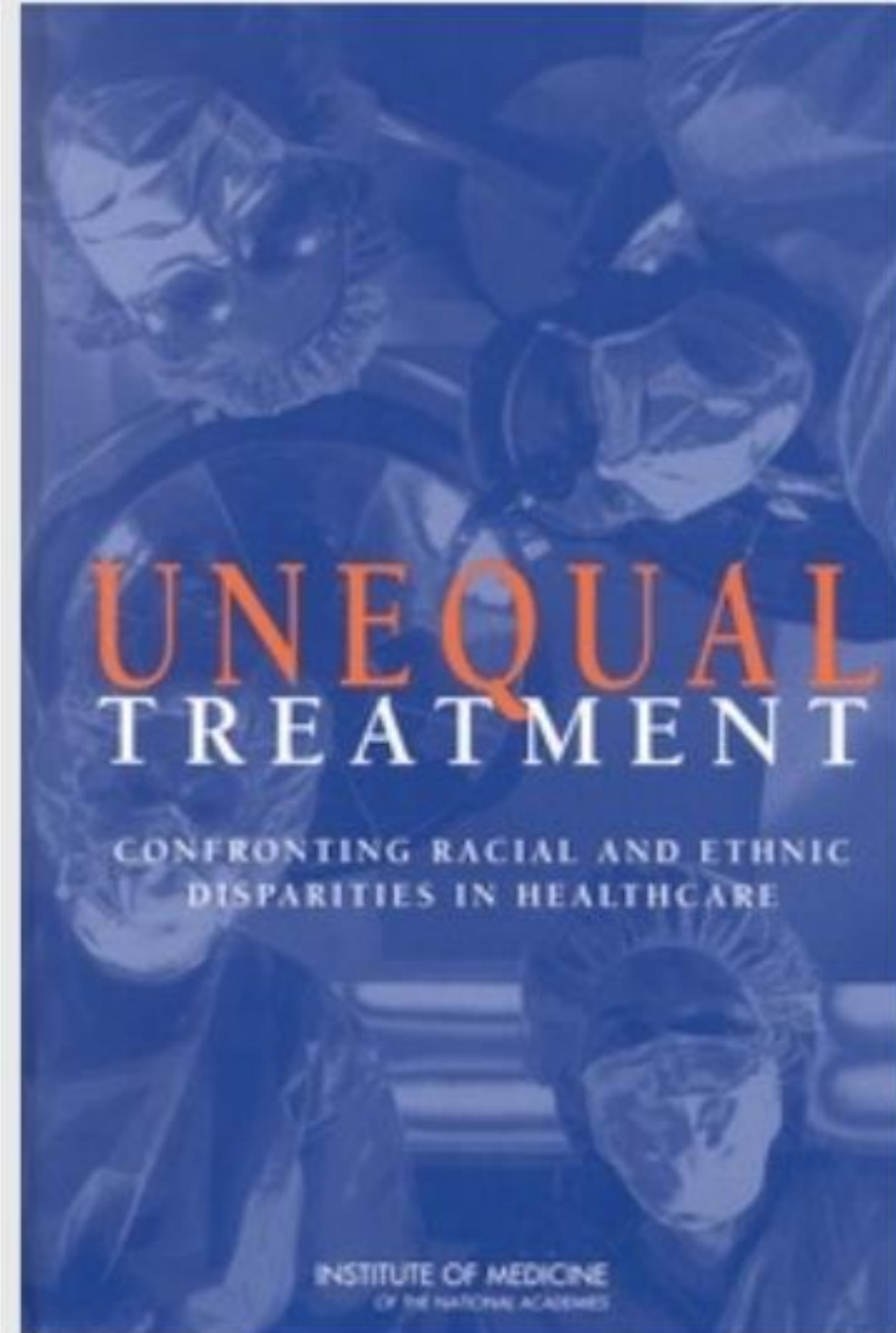
WHY SHOULD WE TRY TO ACHIEVE TB ELIMINATION?

- Eliminate the need for someone to undergo treatment for active TB and what can be the near complete disruption of their lives

- Improve the health of our community through addressing health inequities associated with income inequality, and ethnic/racial biases

WHAT DO YOU NEED TO ACHIEVE ELIMINATION?

IMPROVED POPULATION HEALTH ASSOCIATED WITH DECREASED TB INCIDENCE

| Indicator	Adjusted estimate of effect on change in TB incidence rate/100 000 between 1990 and 2005 (from MLR model)[†]
Change in life expectancy (1990–2005)	−7.8
Change in under-5 mortality (1990–2005) rate, per 1000	+1.0
Change in measles immunization coverage (1990–2005)	−1.3
Percent change in per capita GDP (1990–2005)	−0.05
HIV prevalence in 2005*	+20.9
Change in treatment success DOTS (1990–2005)	−0.9

* Value reported for HIV prevalence in 2005 should be similar to that for change in HIV prevalence between 1990 and 2005 (see Methods for explanation).
[†] As change in life expectancy, under-5 mortality and measles vaccination coverage were run in three separate models, the adjusted estimates presented represent estimates adjusted for change in GDP, HIV, change in treatment success and baseline 1990 estimates only. Estimates were obtained in three different models for change in per capita GDP, HIV prevalence in 2005 and change in treatment success. Estimates presented for these three parameters in this table were taken from Model 2.
TB = tuberculosis; GDP = gross domestic product; HIV = human immunodeficiency virus; MLR = multi-linear regression.

INCREASED SOCIAL PROTECTION IS ASSOCIATED WITH DECREASED TB INCIDENCE

- Social protection spending
  - 21 European countries 1995, 2012:
    - increase in social protection spending of US$100 per person was associated with:
      - 1.5% decrease in # TB case notifications
      - 1.7% decrease in estimated TB incidence

(r= –0.65; p=0.0003)

Reeves A, et al. Lancet Infect Dis 2011
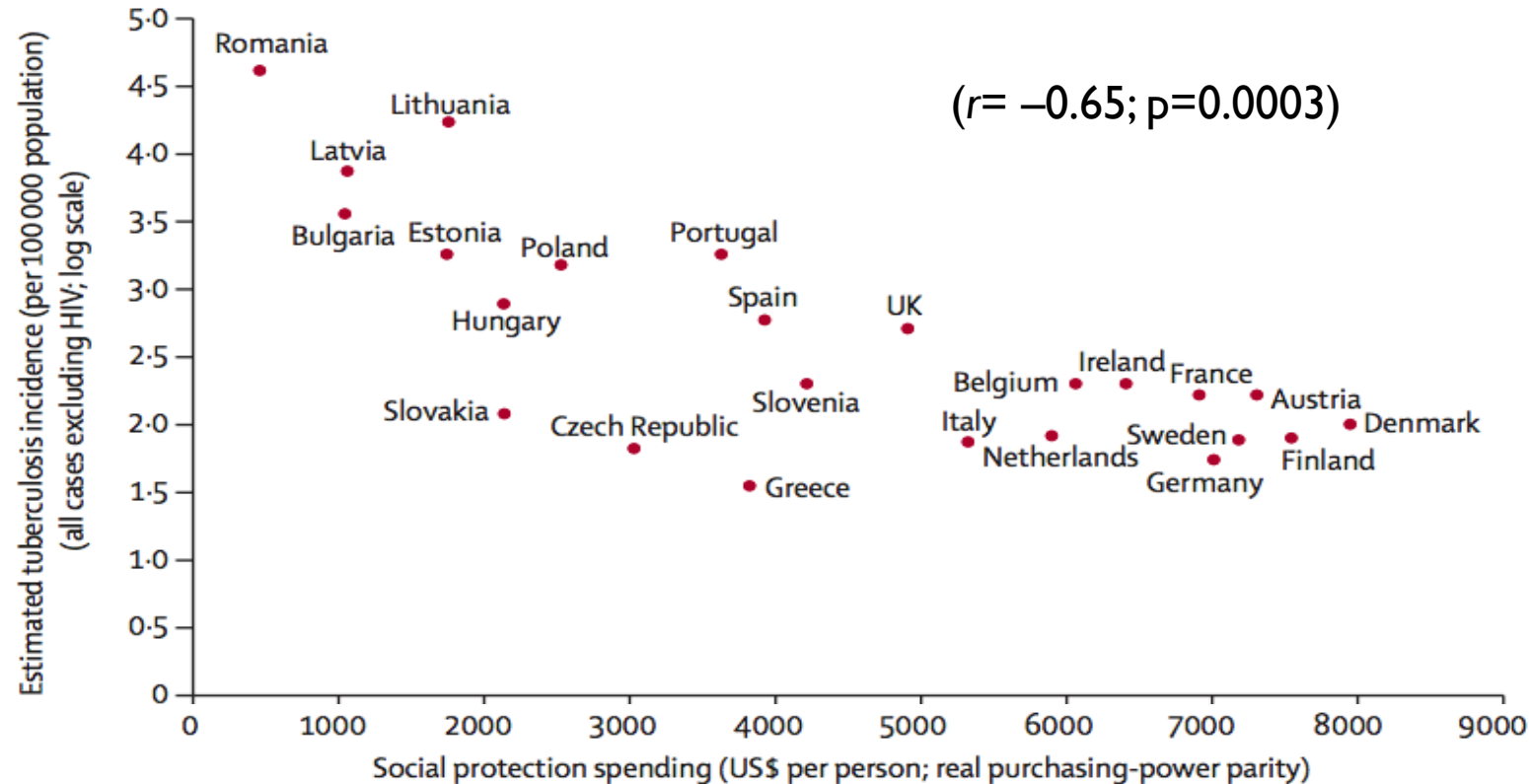
INTEGRATED HEALTH PROMOTION AND POVERTY REDUCTION INTERVENTIONS: IMPACT ON TB IN A COMMUNITY

- Peru: Innovative Socio-economic Interventions Against TB (ISIAT) project

  - socio-economic interventions to reduce TB burden

  - aims to increase use of TB care/prevention services

    - Mitigate poverty-related TB risk in households of active TB patients

  - Baseline: years 2003-2007

  - Intervention commenced in 12/2007

Rocha C, et al. *Int J Tuberc Lung Dis* 2011
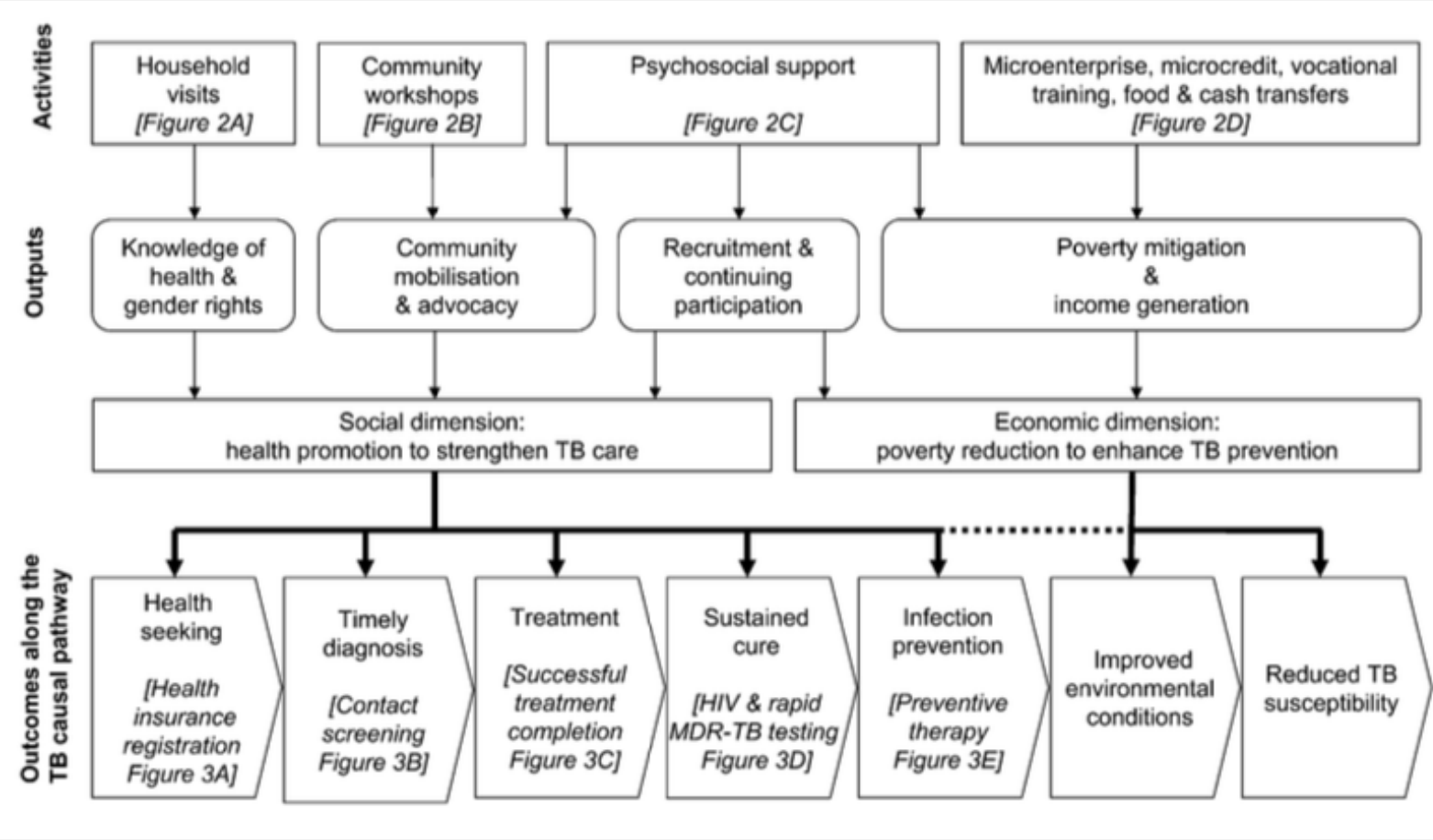
RESULTS

Interim analysis of 2078 individuals, 336 with active TB
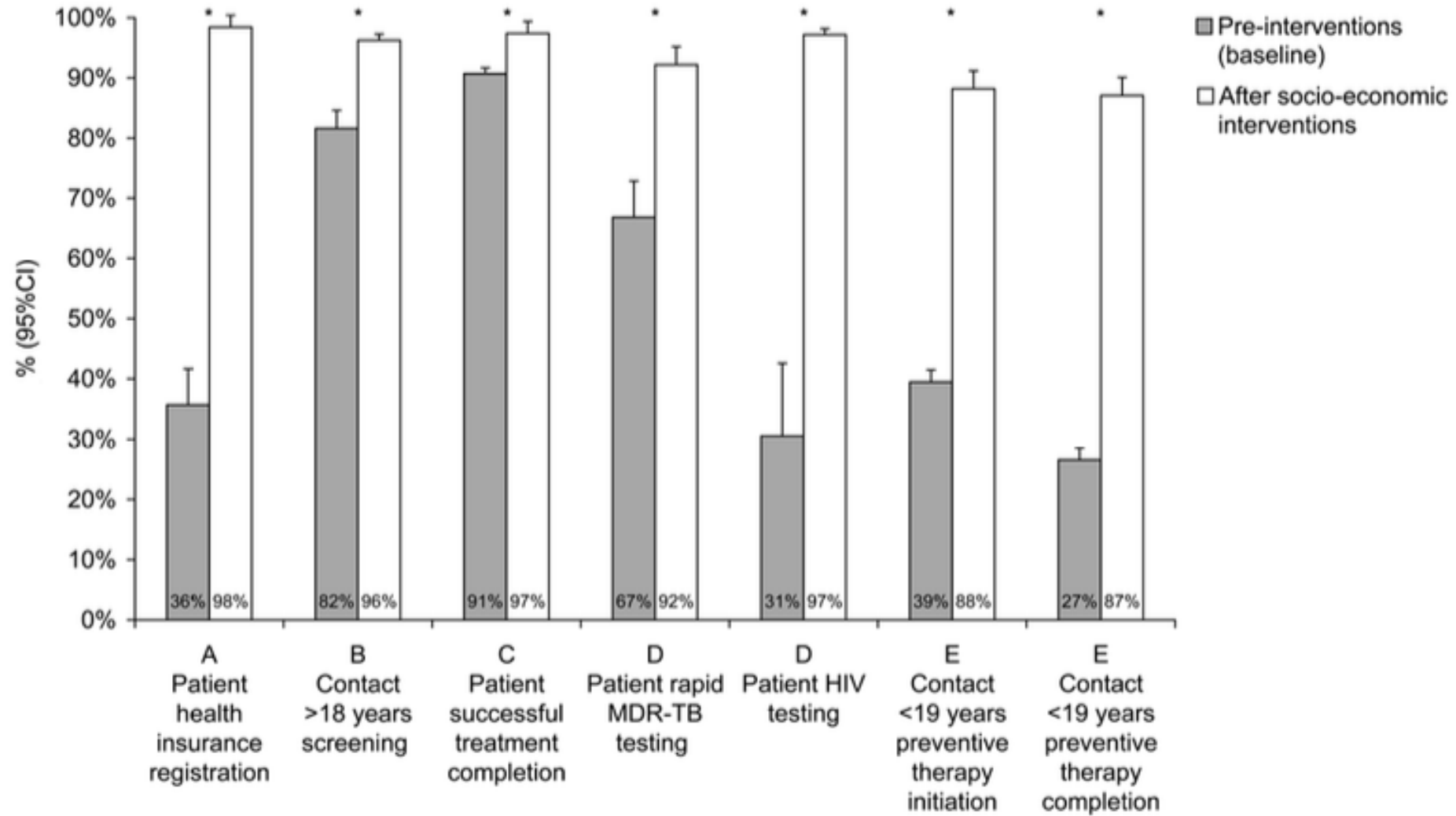
Pre-interventions: A) 216 patients; B) 642 contacts; C) 1554 patients; D) 190 MDR-TB patients testing, 72 for HIV testing E) 2829 contacts initiated LTBI therapy; n=1116 contacts with treatment completion.
Post intervention: :A) 318 patients; B) 748 household contacts; C) 307 patients; D) 307 MDR- TB patients testing, 318 for HIV testing; E) 542 contacts for LTBI therapy; 441 contacts with treatment completion. * Indicates P < 0.00001 for pre-interventions vs. post-interventions

TUBERCULOSIS AMONG THE HOMELESS — PREVENTING ANOTHER
# OUTBREAK THROUGH COMMUNITY ACTION

- Challenges in extending LTBI treatment among Seattle's homeless:

  - Stigma

  - Side effects

  - Need to avoid alcohol use

- Partnered with local businesses to create meal vouchers:

  - Met with widespread approval: vouchers made treatment feasible, not perceived as a bribe

    - .."incentives demonstrated the clinic's awareness of their difficult lives and a willingness to adapt a holistic approach to effective health care delivery"

<div align="right">Gupta V, et al. NEJM 2015</div>

FINDING TB EARLIER TO LIMIT TRANSMISSION, DECREASE TIME TO EFFECTIVE TREATMENT: GENE XPERT MTB/RIF

Xpert": nucleic acid or genetic amplification test (NAAT) to detect *M. tuberculosis* in sputum samples

Can tell you if there is drug resistance to rifampin

New Gene Xpert Omni model is battery powered, wireless, internet connectivity

9 in.

Boehme, C et al. N Engl J Med 2010;363:1005-15.
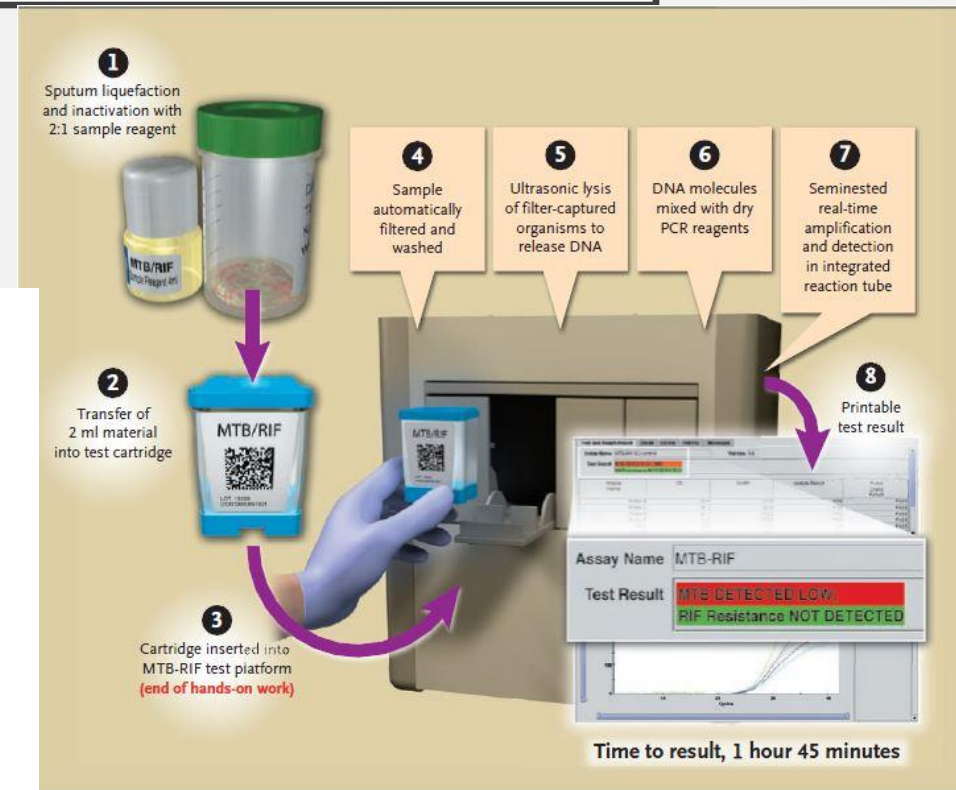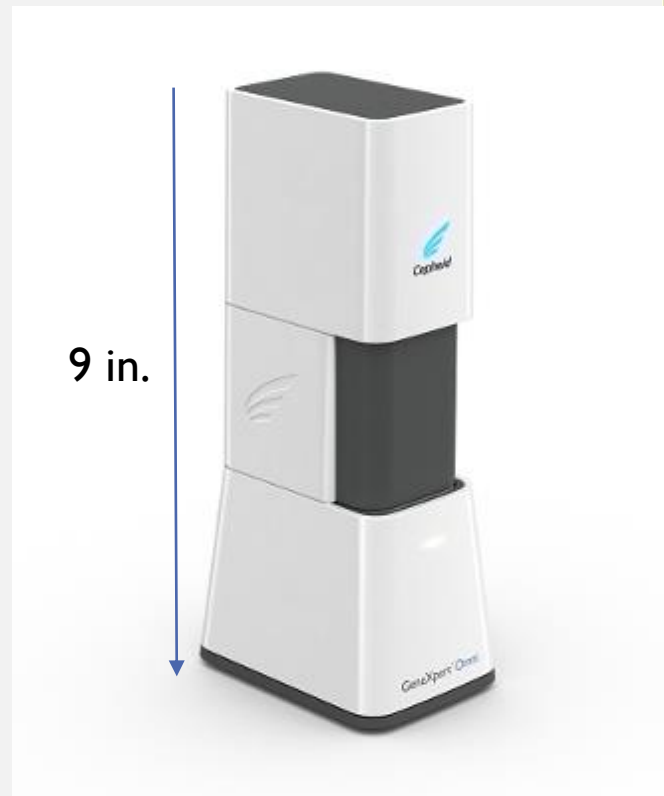
Evaluation of Xpert MTB/RIF Versus AFB Smear and Culture to Identify Pulmonary Tuberculosis in Patients With Suspected Tuberculosis From Low and Higher Prevalence Settings

|		Sensitivity		Specificity	
Characteristic	TB Culture Positive	AFB Smear Positive/ TB Culture Positive	AFB Smear Negative/ TB Culture Positive	TB Culture Negative	NPV
All participants, first Xpert assay	81.4% (175/215) [75.7%–86.0%]	98.5% (129/131) [94.6%–99.6%]	54.8% (46/84) [44.1%–65.0%]	98.7% (735/745) [97.5%–99.3%]	94.8% (735/775) [93.0%–96.2%]
HIV status					
HIV infected	73.6% (64/87)[b] [63.4%–81.7%]	100.0% (39/39) [91.0%–100.0%]	52.1% (25/48) [38.3%–65.5%]	98.3% (339/345) [96.3%–99.2%]	93.6% (339/362) [90.6%–95.7%]
HIV uninfected	86.7% (111/128)[b] [79.8%–91.5%]	97.8% (90/92) [92.4%–99.4%]	58.3% (21/36) [42.2%–72.9%]	99.0% (396/400) [97.5%–99.6%]	95.9% (396/413) [93.5%–97.4%]
Region					
Low TB Prevalence (United states)	85.2% (75/88) [76.3%–91.2%]	96.7% (59/61) [88.8%–99.1%]	59.3% (16/27) [40.7%–75.5%]	99.2% (526/530)[c] [98.1%–99.7%]	97.6% (526/539) [95.9%–98.6%]
Higher TB prevalence (Brazil & South Africa)	78.7% (100/127) [70.8%–85.0%]	100.0% (70/70) [94.8%–100.0%]	52.6% (30/57) [39.9%–65.0%]	97.2% (209/215)[c] [94.0%–98.7%]	88.6% (209/236) [83.9%–92.0%]
Sputum collection					
Induced	86.8% (59/68) [76.7%–92.9%]	100.0% (50/50) [92.9%–100.0%]	50.0% (9/18) [29.0%–71.0%]	99.2% (254/256) [97.2%–99.8%]	96.6% (254/263) [93.6%–98.2%]
Expectorated	77.4% (103/133) [69.6%–83.7%]	97.2% (69/71) [90.3%–99.2%]	54.8% (34/62) [42.5%–66.6%]	98.2% (429/437) [96.4%–99.1%]	93.5% (429/459) [90.8%–95.4%]
Sputum processing					
Unprocessed	78.0% (32/41) [63.3%–88.0%]	92.6% (25/27)[d] [76.6%–97.9%]	50.0% (7/14) [26.8%–73.2%]	99.1% (233/235) [97.0%–99.8%]	96.3% (233/242) [93.1%–98.0%]
Concentrated	82.2% (143/174) [75.8%–87.2%]	100.0% (104/104)[d] [96.4%–100.0%]	55.7% (39/70) [44.1%–66.8%]	98.4% (502/510) [96.9%–99.2%]	94.2% (502/533) [91.9%–95.9%]
All participants, 2 Xpert assays[e]	88.1% (192/218) [83.1%–91.7%]	100.0% (133/133) [97.2%–100.0%]	69.4% (59/85) [59.0%–78.2%]	97.9% (746/762) [96.6%–98.7%]	96.6% (746/772) [95.1%–97.7%]

DOMESTIC RETURNS FROM INVESTMENT IN THE CONTROL OF TUBERCULOSIS IN OTHER COUNTRIES

Modelling Cost-effectiveness of investing in TB services in other countries:

Expansion of DOTS in Mexico through allocation of $34.9 million:

2591 fewer cases of tuberculosis in the US

Net savings of $108 million over 20 years
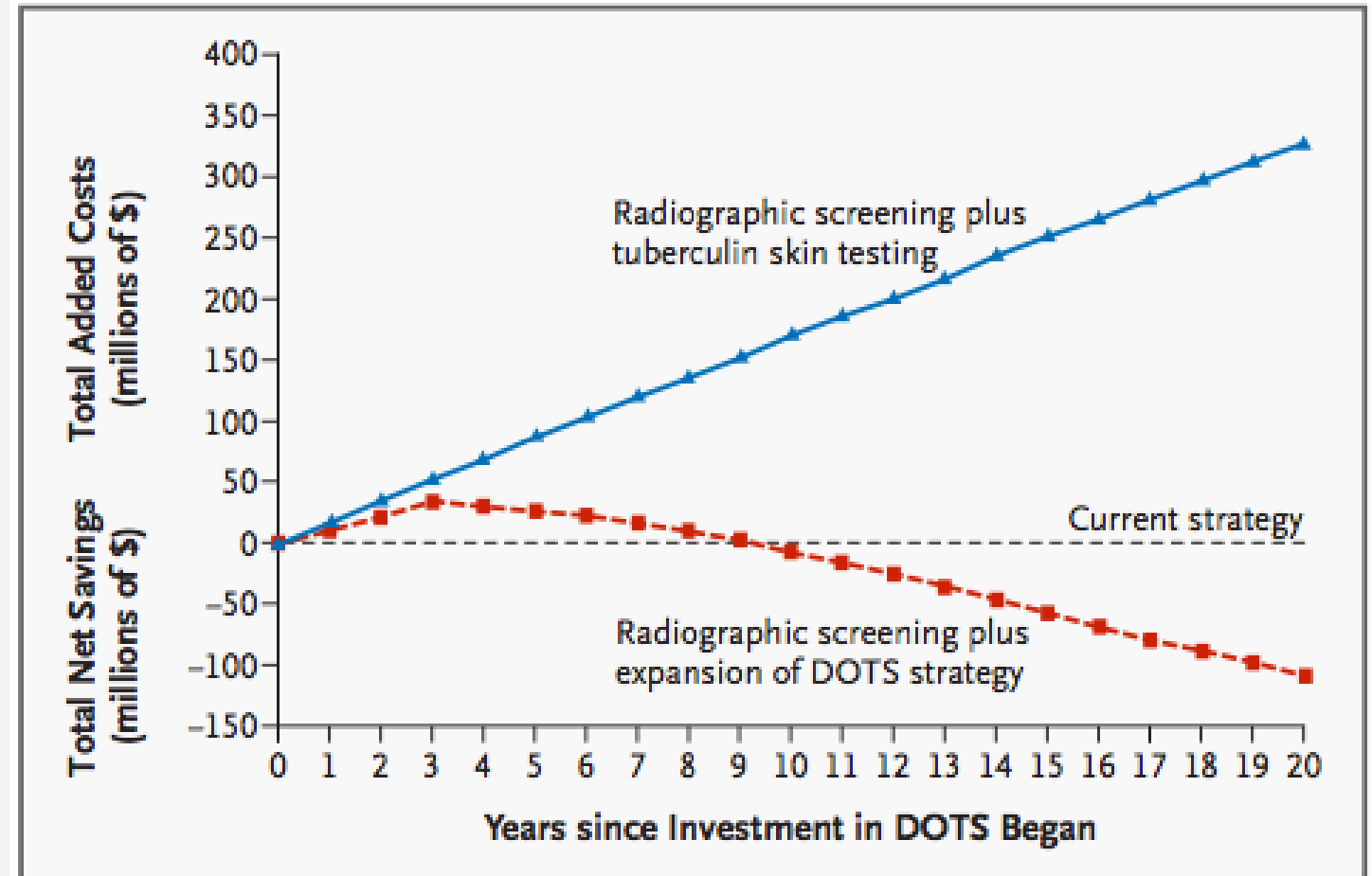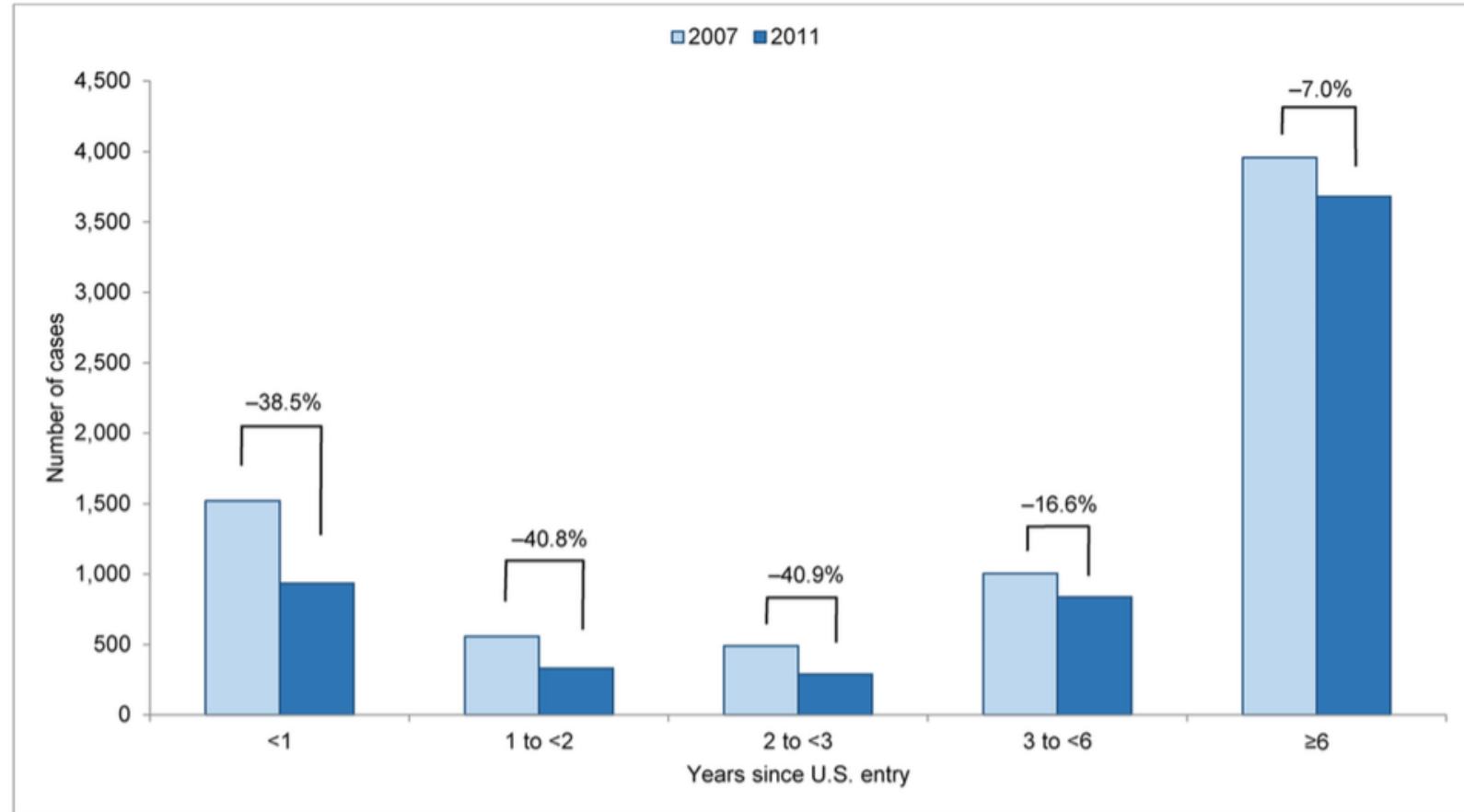

Schwartzman K N Engl J Med 2005;

Among recent entrants (<3 years):

From Mexico, decline was due to decreases in total population.

From Philippines, India, Vietnam and China, decline was due to decreases in TB case rates

Among non-recent entrants (> 3 years:

decrease entirely due to decreased TB case rate

- Light shaded bars= TB case counts in 2007; dark shaded bars= TB case counts counts in 2011. Percentages indicate the percent decline in case count for each group during 2007–2011

Screening for Latent Tuberculosis Infection in Adults
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

Population	Asymptomatic adults at increased risk for infection
Recommendation	Screen for latent tuberculosis infection (LTBI). Grade: B

Risk Assessment	Populations at increased risk for LTBI include persons who were born in, or are former residents of, countries with increased tuberculosis prevalence and persons who live in, or have lived in, high-risk congregate settings (eg, homeless shelters and correctional facilities). Local demographic patterns may vary across the United States; clinicians can consult their local or state health departments for more information about populations at risk in their community.
Screening Tests	Screening tests include the Mantoux tuberculin skin test and interferon-gamma release assays; both are moderately sensitive and highly specific for the detection of LTBI.
Treatment and Interventions	The CDC provides recommendations for the treatment of LTBI at http://www.cdc.gov/tb/topic/treatment/ltbi.htm.
Balance of Benefits and Harms	The USPSTF concludes with moderate certainty that the net benefit of screening for LTBI in persons who are at increased risk for tuberculosis is moderate.

JAMA, 2016

DECENTRALIZE PREVENTATIVE TB INFECTION SCREENING AND CARE

- Breathe Easy South Texas (BEST) Project Partnership

  - Outreach to 75 providers; 15 community providers offering preventative TB services

    - Nearly 1800 individuals tested

    - Plans for further scale-up

- TB Project ECHO® in Washington to increase TB preventative services expertise in Washington State

DECENTRALIZE PREVENTATIVE TB INFECTION SCREENING AND CARE

- Partnering with health systems to use electronic medical record reminders and best practices alerts for the USPSTF

  - Addition of country of risk to demographics collected at registration

- Scaling up LTBI therapy in primary care clinics through use of pharmacists and nurses for refills on stable patients

MAXIMIZING RESOURCES

- Use of video-recorded DOT to free up resources for outreach staff:
  - Partner with community based organizations
  - Patient education
  - Partner with other public health programs to bundle services
    - Immunization programs, maternal-child health programs

WHAT ELSE IS NEEDED?

- **Addressing racial/ethnic disparities in health**
  - Incorporating Health Equity goals into TB programmatic goals
    - Training for staff on recognizing and mitigating unconscious bias
    - Improving cultural competency
- **Address stigma**
  - Normalization of TB preventative services at the primary care level
- Trials to evaluate novel agents for LTBI
- Further optimization of TB diagnostics

US$ 2 BILLION GAP

Funding shortfall for TB implementation

Gap of over US$1 billion per year for TB research

QUESTIONS? THANK YOU!