TB Epidemiology Journey

: Implications for TB program Interventions, activities, Strategy

Dr. P.K. Sen TAI Gold Medal Oration

Dr Vineet K Chadha

National Expert Committee

Sub-national TB prevalence surveys in India, 2006-2012: Results of uniformly conducted data analysis

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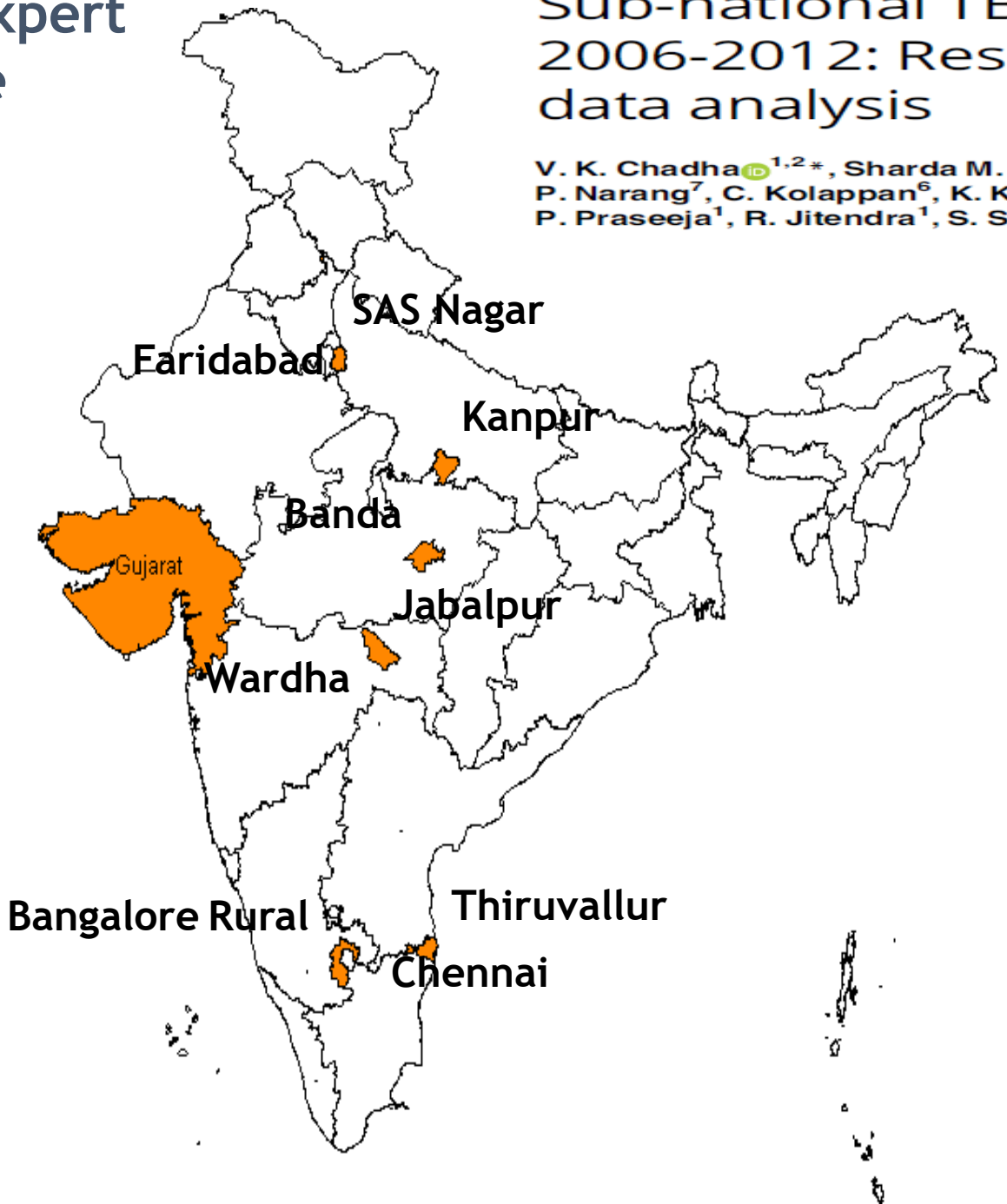
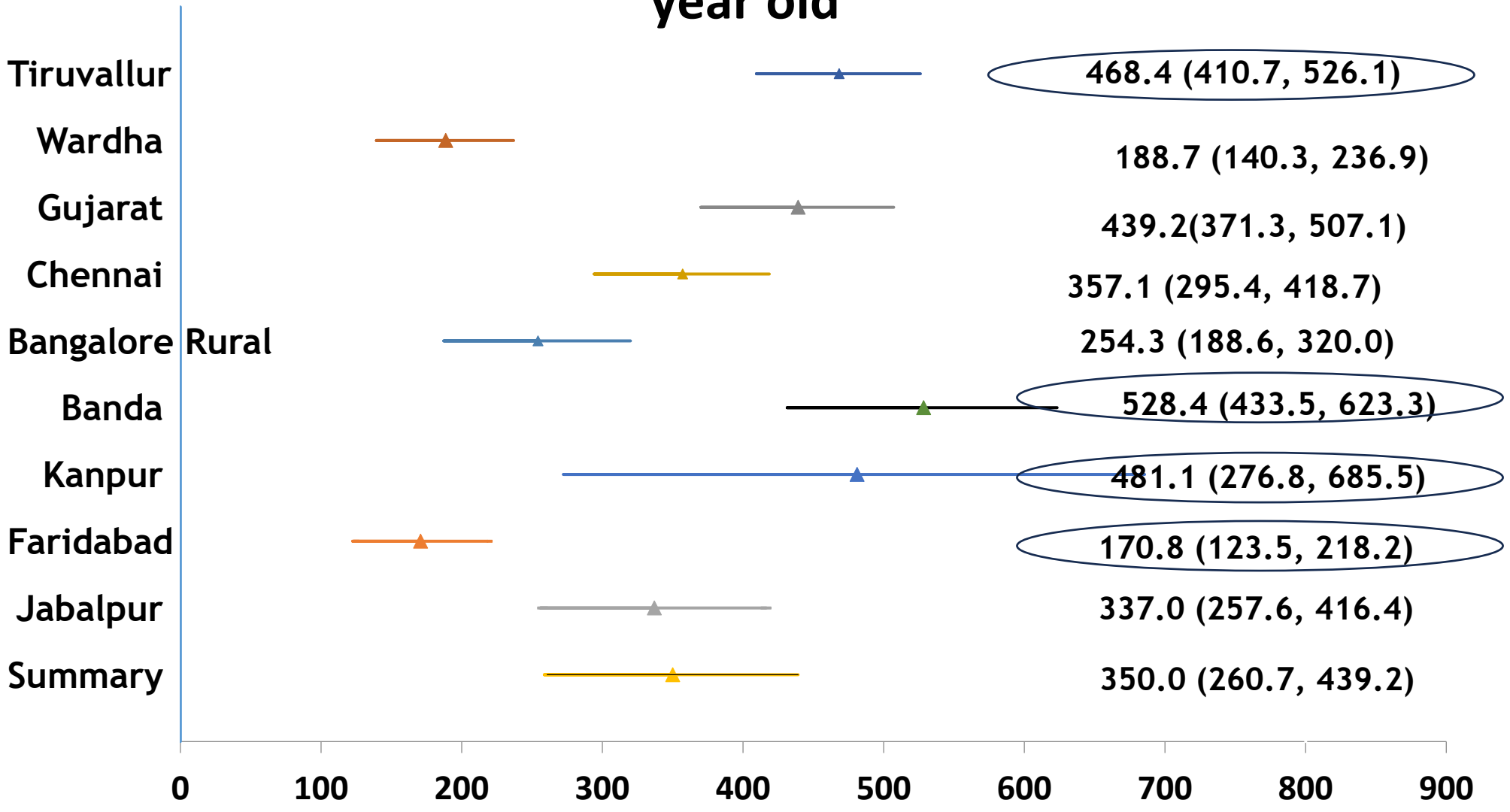


N=7,15,989

	Sample Size	Screening methods
Rural Bangalore	68400	PTB Symptoms, CXR
Thiruvallur	82000	
Wardha	47828	
Chennai	52142	
Gujarat	96900	
Jabalpur	90000	Symptoms
Faridabad	90000	
Kanpur Banda	90000	
SAS Nagar	90000	

State level-1, District level-7, Sub-district level-2

Prevalence of Bacteriologically Positive PTB Cases among >14 year old



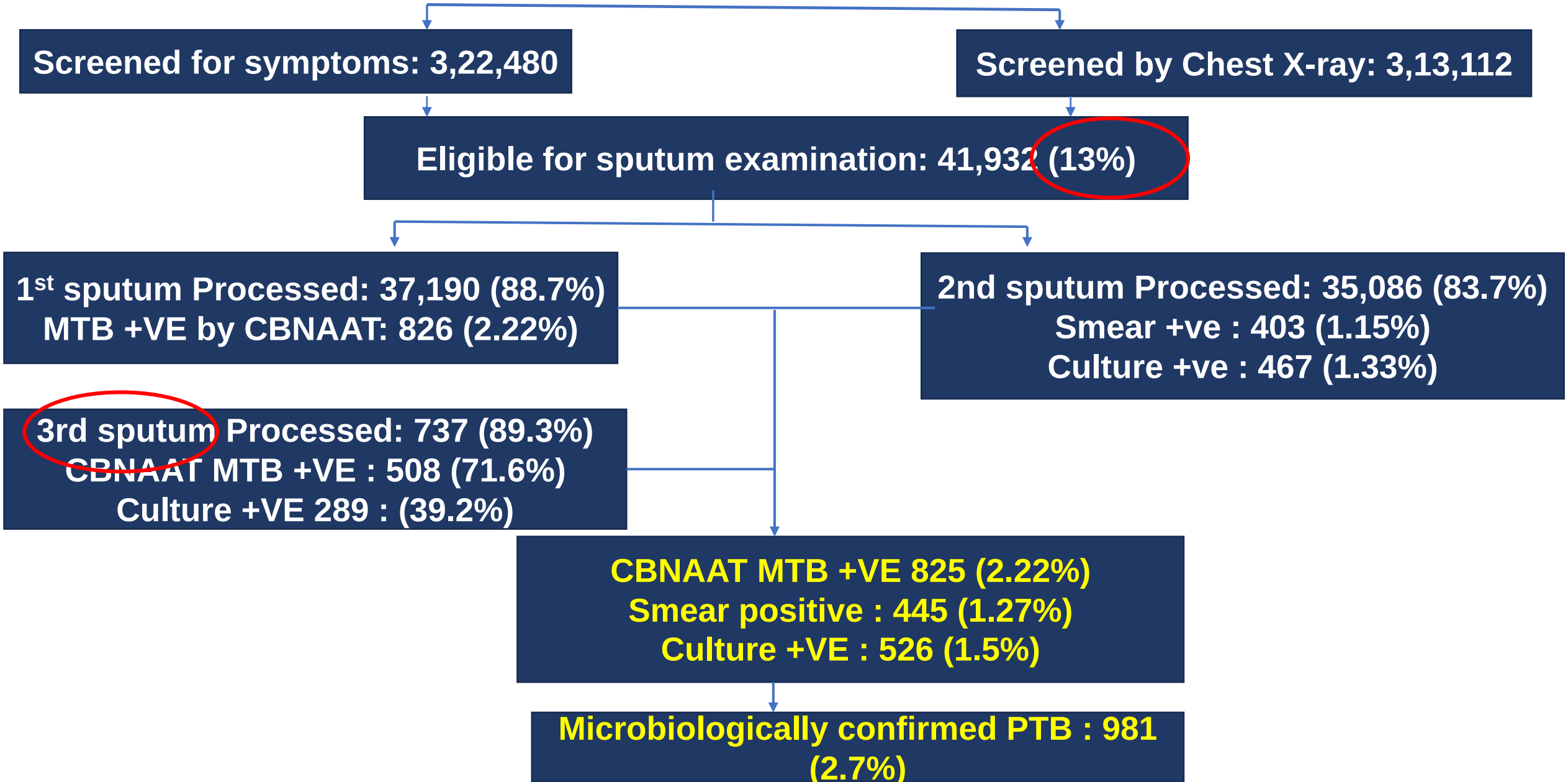
31% asymptomatic TB patients: definition of presumptive PTB, CXR screening in provider initiated Case finding.

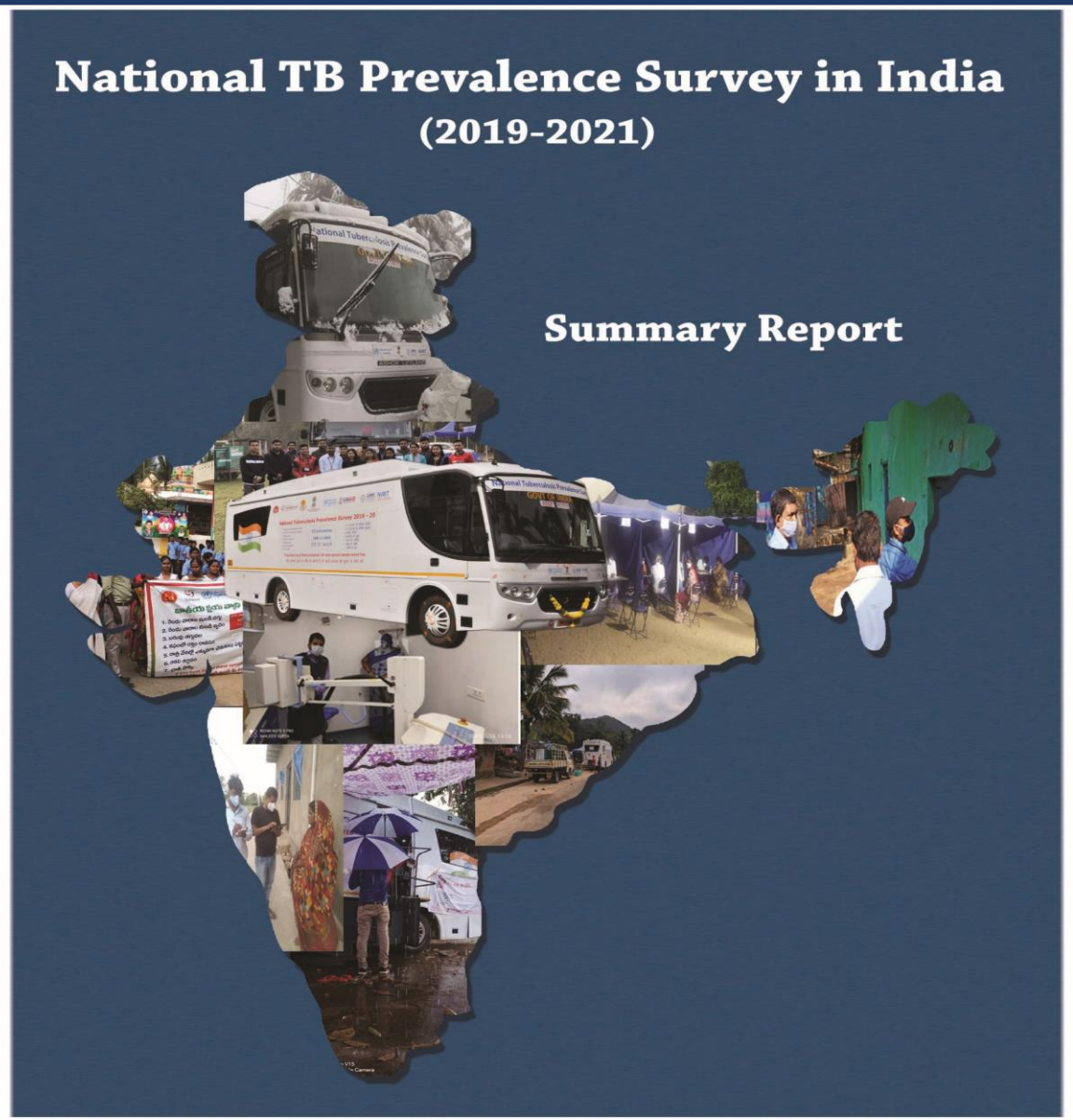
Sensitivity and specificity of screening tools duirng ACF

Screening criteria	Sensitivity (%)
Cough ≥ 2 weeks	56.2 (46.7, 65.4)
Any symptom*	66.0 (56.3, 74.5)
Any symptom / h/o ATT	71.2 (64.8, 76.75)
Any pulmonary abnormality on X-ray	76.6 (70.8, 81.6)
Cough ≥ 2 weeks / Any pulmonary abnormality on X-ray	94.3 (91.1,96.4)
Any symptom / h/o ATT / Any CXR pulmonary abnormality	100

**Persistent cough for ≥2 weeks/Fever for ≥1 month/Chest pain for ≥1 month/History of hemoptysis in last 6 months*

National TB Prevalence survey

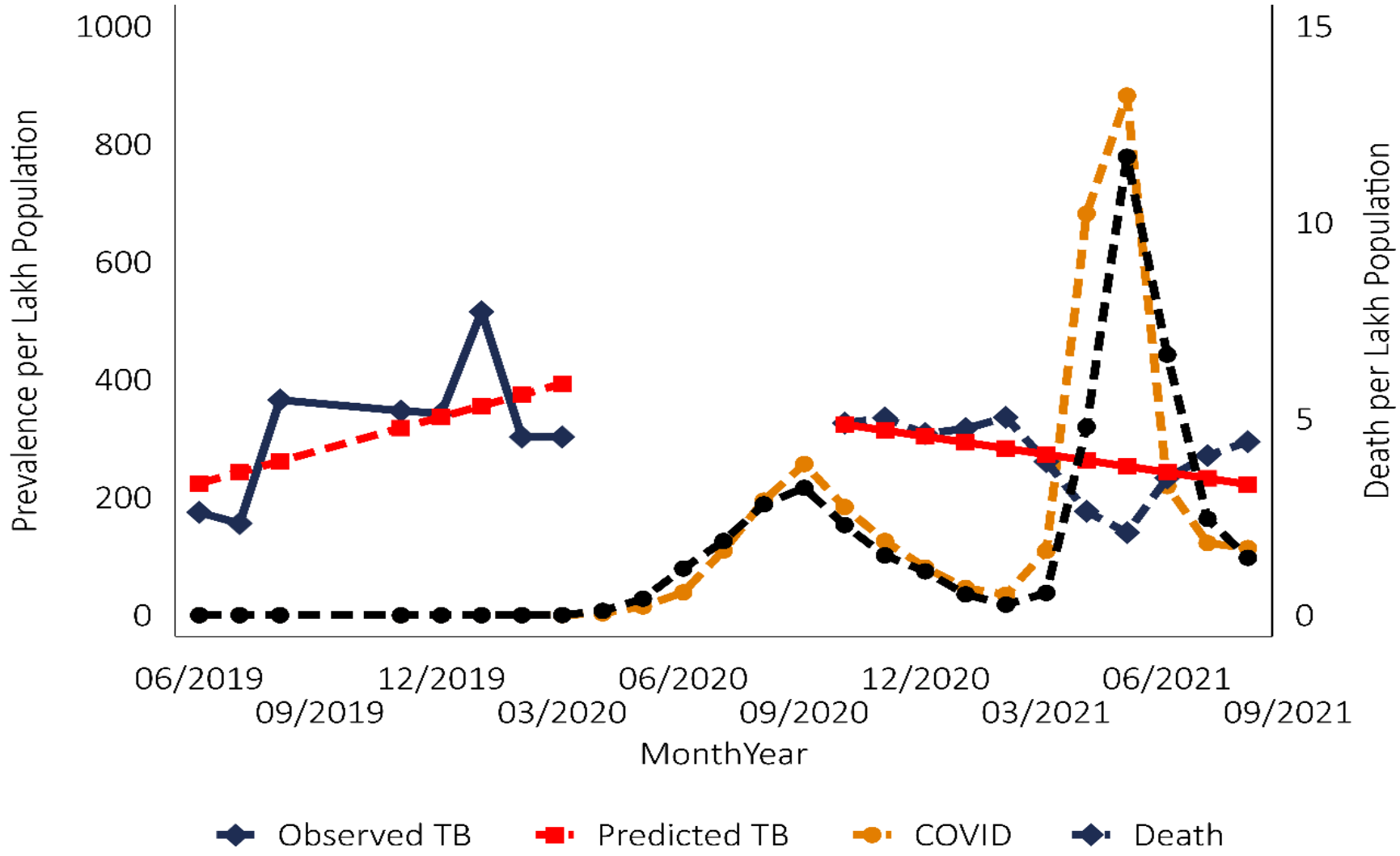




Prevalence of microbiologically confirmed PTB, ≥15 years
= 316 (290-342) / lakh population

Prevalence of all forms of TB, all ages (corrected for EPTB & Pediatric TB)
= 312 (286-227) / Lakh population

Prev. of Infection
= 31% (27.2-33.5)



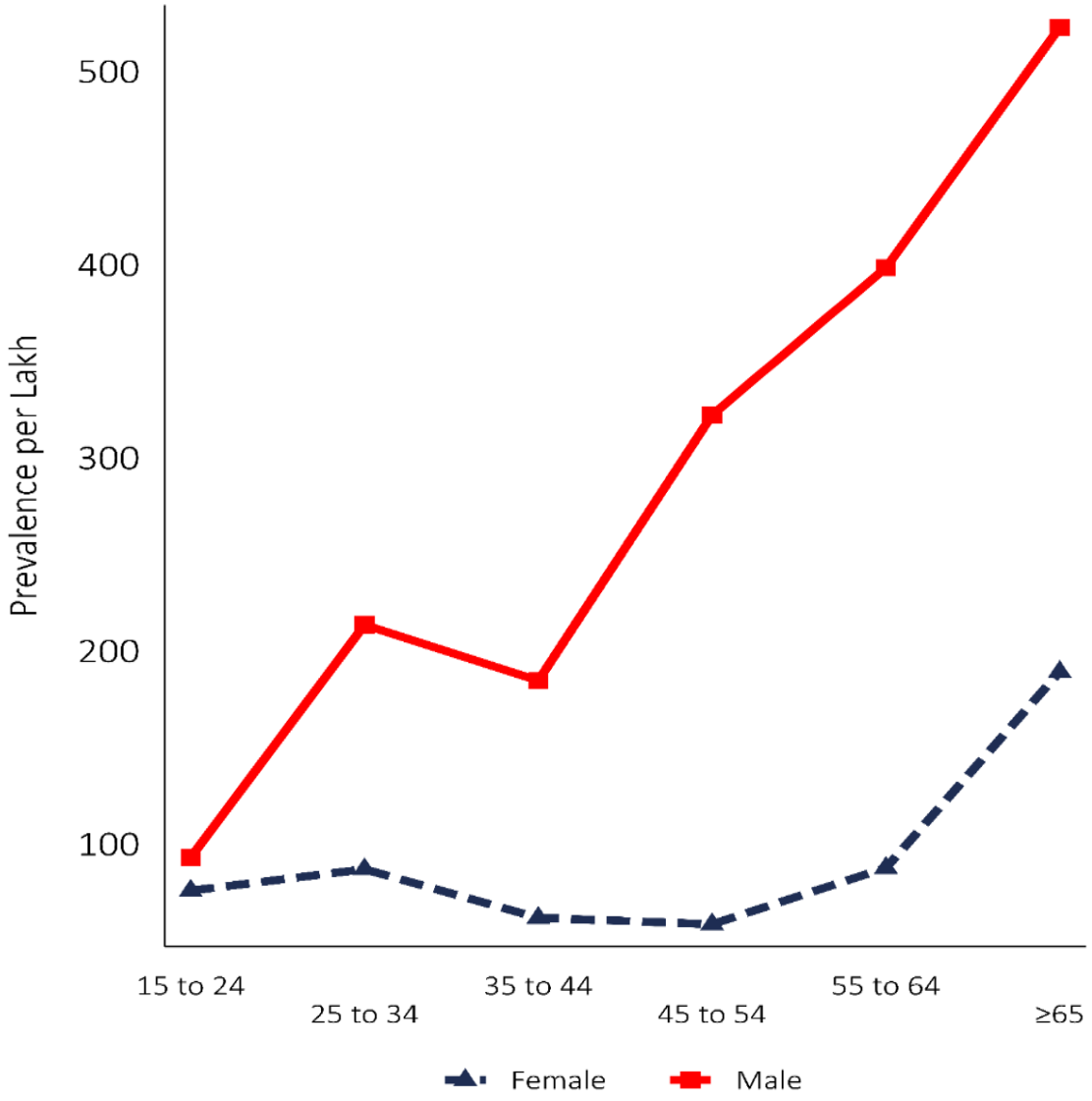
TB Positives- 981; Correlation [Observed TB vs COVID:-40.9 (p=0.082); Observed TB vs Death:-44.4 (p=0.057)]

Covid induced mortality : under-estimation of TB prevalence

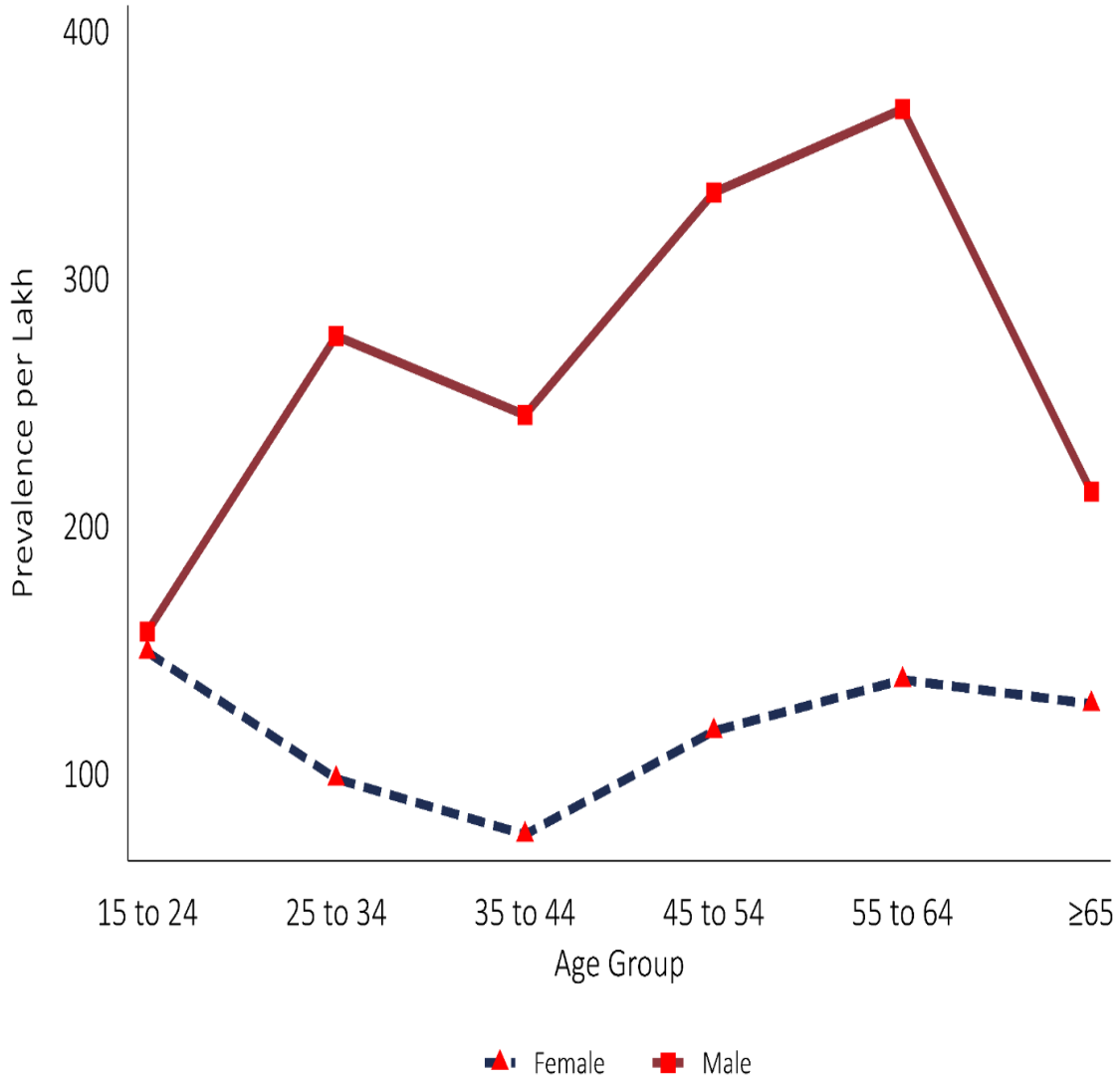
Other Implications of Prevalence Survey findings

- No decline in prevalence between 2009 to 2020 : possible increase?
  - ~Age-structure, size of KVPs?
- TB situation does not change rapidly: Periodicity between surveys *(Expert group :17 surveys)*
- 10 persons infected /sm+ve PTB = Pre-chemotherapeutic area (Kolin study)
  - ➢delay in diagnosis: promote awareness, active case finding (ACF)
- High proportions of untreated prevalent cases: Role of ACF

Prevalence



Currently on anti-TB treatment



Elderly : a KVP (NATBPS)

Implications..

- Benchmarks Presumptive PTB (general population): 5-13%
  Sputum positivity rate: 2.3-3.7%
  NNS/Case : 300-500/L

- Sharath et al : **ACF by states** (supposedly among KVPs)
  - Presumptive TB: <1-67%
  - NNS : 31-11000 KVP listing?
    - ➢ quality of screening?
    - ➢ quality of sputum specimen?
    - ➢ Positive Predictive Vale of diagnostic algorithms actually implemented

. Trop. Med. Infect. Dis. **2021**, 6, 206.

Implications for Active tuberculosis case finding

- **High proportion of false +ve**
  - *NAAT = 40% (NATBPS, Phillipines) after single screen+ve*
  - *Smear : Sub-national surveys-33%; NATBPS -45%*
  - *Model: 90% (1/10 false positive) at prevalence ≥1500/lakh population*

➢ **Confirm diagnosis by a +ve test result on another sp. specimen/ CXR suggestive of active TB**

{WHO assessment of National surveys in 17 countries: concern about false +ve cases, 15% of Smear+ve NTM}.

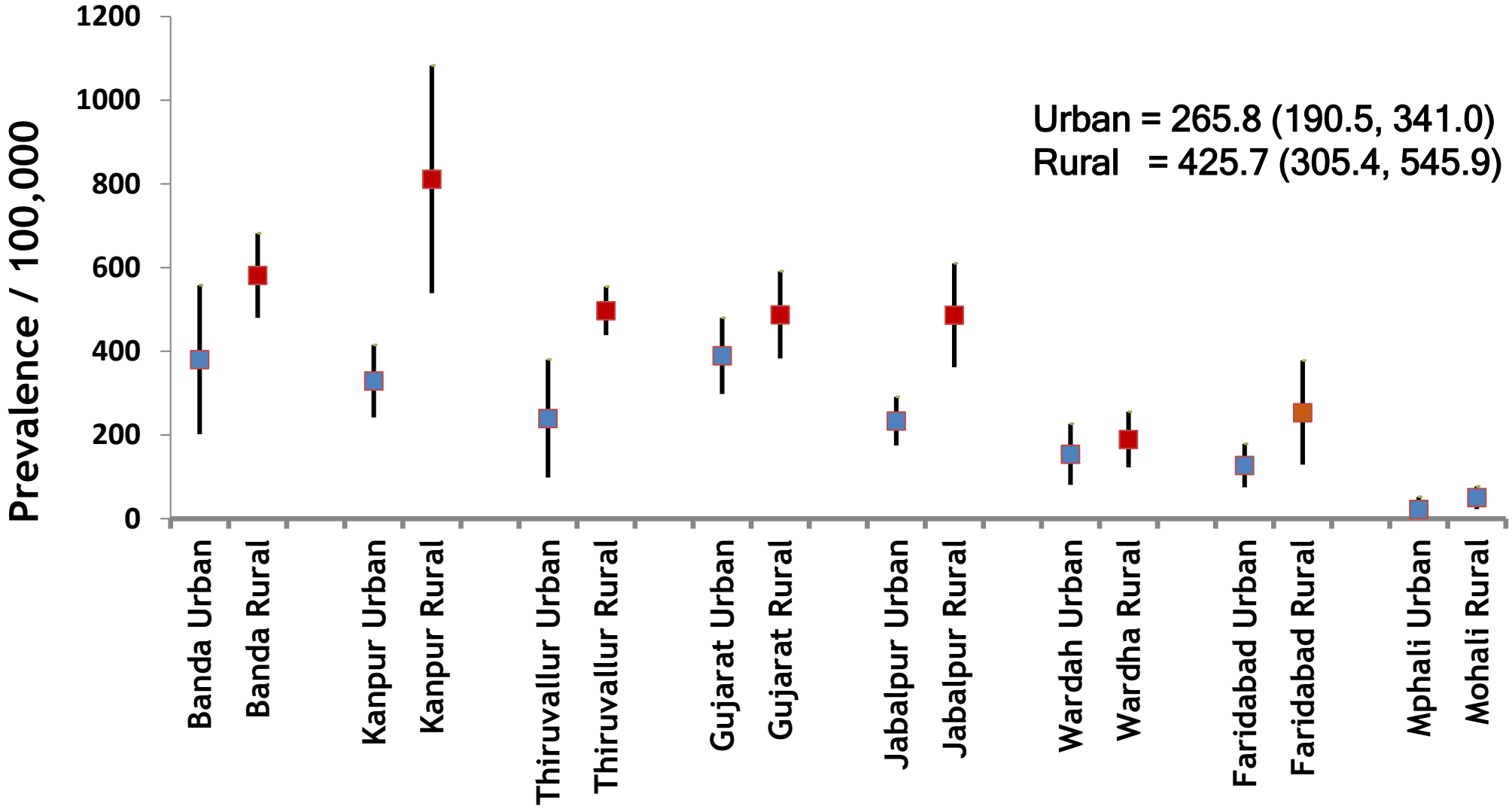
- CXR as a secondary screening tool : high Diagnostic accuracy

- **PPV of CXR based TB diagnosis** in absence of a sputum +ve result
  - *<20% at prevalence ≤500/L*
  - *55% at prevalence is 2500/L*

Lot of false +ve in community based case detection: Choose algorithm

Sub-national surveys

Urban: Rural prevalence ratio=1:1.6 (1.2-2.5:1)



- 17 National surveys in other countries: Higher prevalence in Urban areas

Risk of Infection

Disease prevalence, 2009

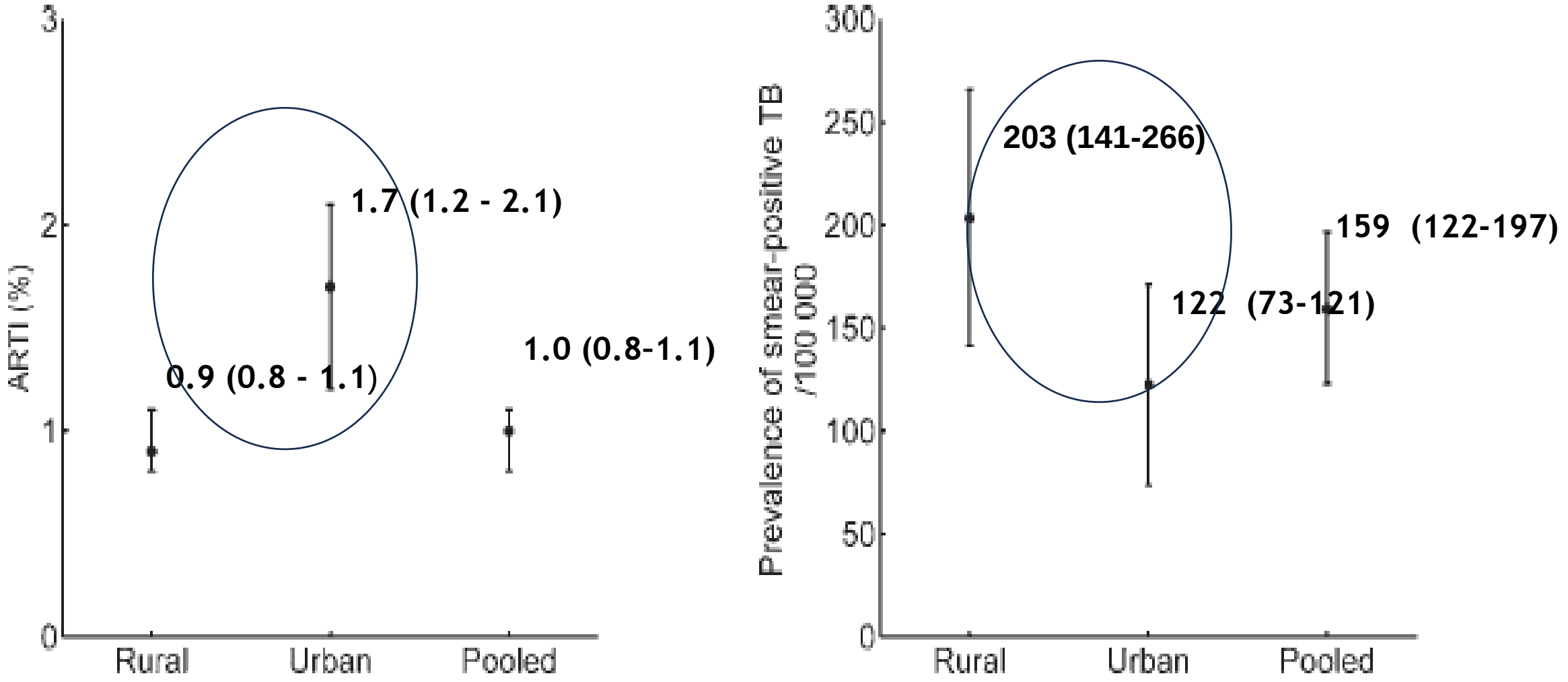
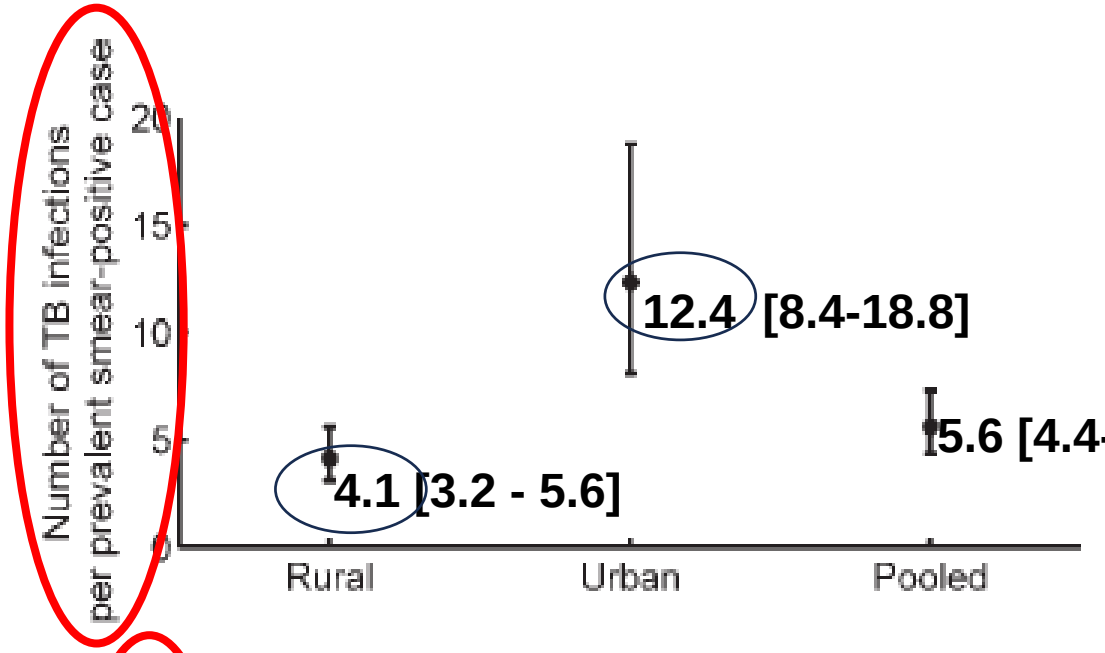
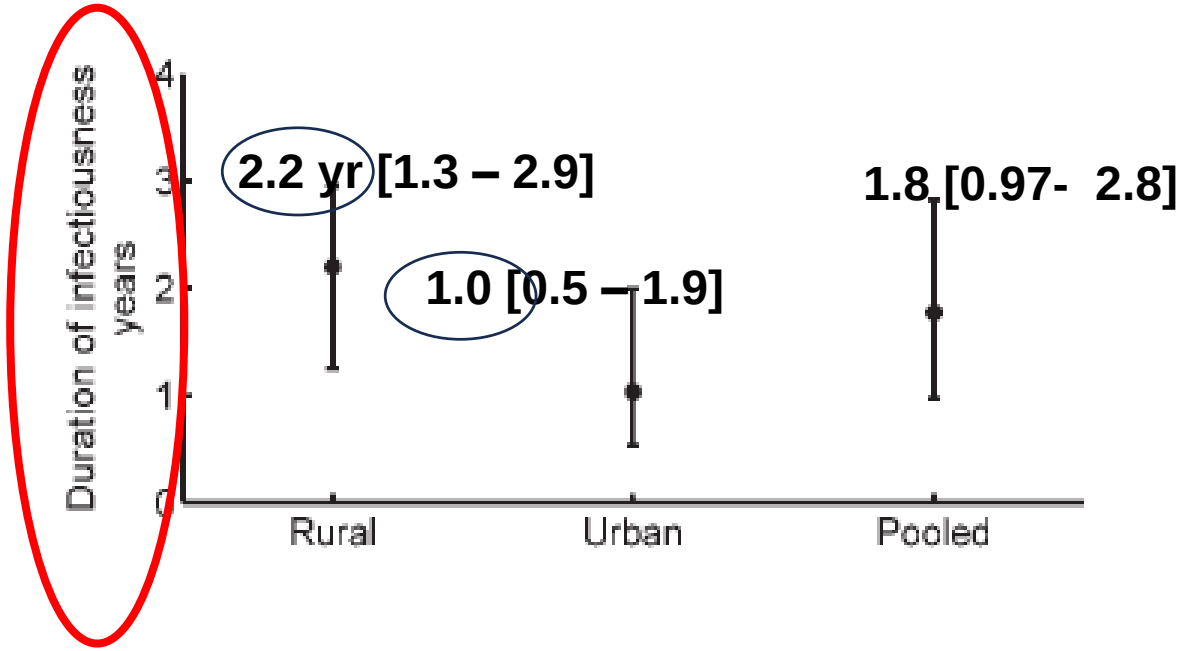
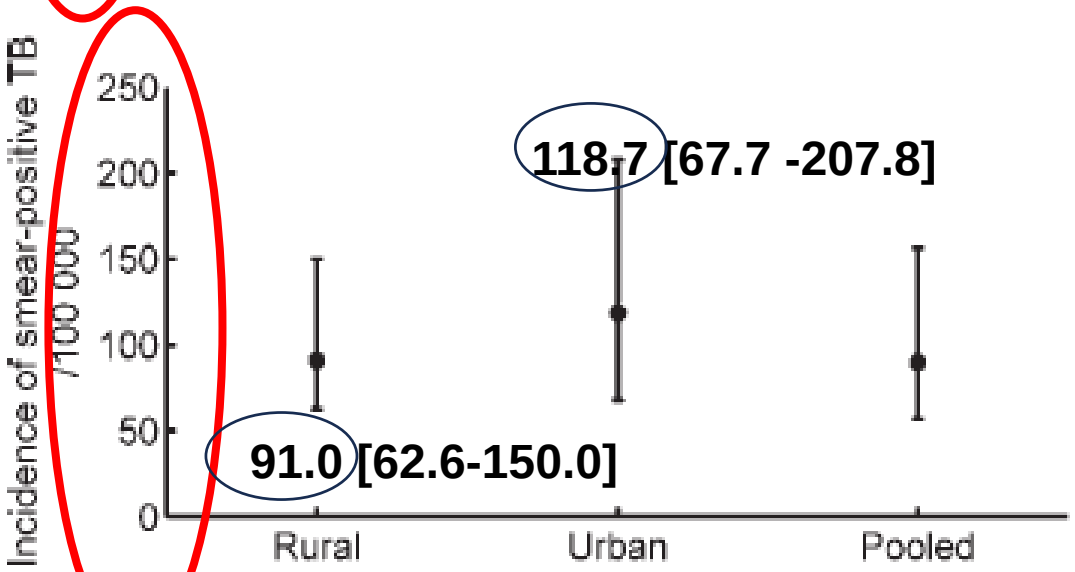


Figure 2 Results of pooled prevalence surveys, showing contrasting epidemiology between urban and rural tuberculosis in India. ARTI = annual risk of tuberculous infection.







Setting specific focus:

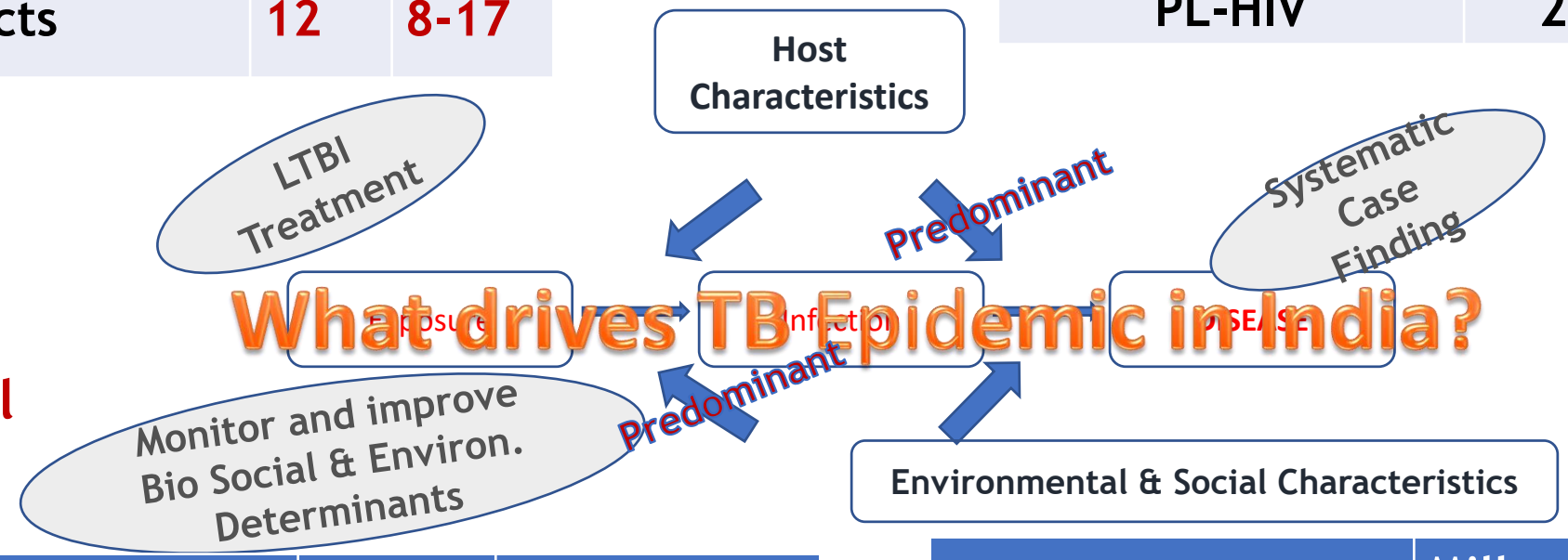
- *urban areas: decrease transmission*
- *Rural areas: reduce delay*

Figure 4 Application of the model to prevalence survey data from India. Owing to different TB epidemics in urban and rural settings, estimates for these settings are shown separately. TB = tuberculosis.

TB Key & Vulnerable populations

Proximity of contact & duration of exposure		
	Mill.	R.R
HH Contacts	12	8-17

Co-factors		
	Mill.	R.R
UND	173.6	4.5
PL-DM	101.5	4.5
PL-HIV	2.1	18



PAF

Incidence & Prevalence estimates

Multisectoral response

	Mill.	RR
Regular Alcohol use	104.6	3.3
Tobacco Use	240.7	2.3
Miners & Silica Exposed	20	4
Textile	20	10
HCW	2.2	3-15

	Mill.	RR
Cooking by solid fuel	580	1.5-2.5
BPL	372	
Slum dwellers	65	
Homeless	1	37-450
Prisoners	0.5	33

Scientific Research Publishing

Journal of Tuberculosis Research, 2016, 4, 213-219
http://www.scirp.org/journal/jtr
ISSN Online: 2329-8448
ISSN Print: 2329-843X

Relationship between Nutritional Support and Tuberculosis Treatment Outcomes in West Bengal, India

Blesson Samuel[1*], Tyson Volkmann[2], Sushma Cornelius[1], Sugata Mukhopadhay[1], MejoJose[1], Kaushik Mitra[3], Ajay M. V. Kumar[4], John E. Oeltmann[2], Sidhajyoti Parija[5], Aslesh Ottapura Prabhakaran[6], Patrick K. Moonan[2], Vineet K. Chadha[7]

- Smear+ve PTB patients (BPL) in 2 districts of Bengal, 2012–2013.

Characteristic	Successful	Unsuccessful	Total	P-value
No nutritional support	316 (79%)	84 (21%)	400	<0.001
Nutritional support	158 (91%)	15 (9%)	173	

- RR of unfavourable outcome when not provided nutritional support = 2.4
  - ➢ **First evidence for nutritional support during treatment**

Nutritional support for adult patients with microbiologically confirmed pulmonary tuberculosis: outcomes in a programmatic cohort nested within the RATIONS trial in Jharkhand, India

Anurag Bhargava, Madhavi Bhargava, Ajay Meher, G Sai Teja, Banurekha Velayutham, Basilea Watson, Andrea Benedetti, Ganesh Barik, Vivek Pratap Singh, Dhananjay Singh, Adarsh Kibballi Madhukeshwar, Ranjit Prasad, Rajeev Ranjan Pathak, Vineet Chadha, Rajendra Joshi

Major finding	Implications
UND- 82%; severe-50%, very severe -17%	Reducing prevalence of determinants of TB incidence, mortality crucial to End TB
Low BMI, DM, Anaemia ~ fatality risk	
Weight gain cf NTEP data: 1.5 times	Relevance of Nikshay Mitra, other initiatives
>5% weight gain by 2mo ~ 60% reduced fatality	
Per unit BMI increase ~ 12% reduced fatality	
UND at end of TTT: 55%	Need for longer Nutr support

Lancet Glob Health 2023; 11: 1402–11

Nutritional supplementation to prevent tuberculosis incidence in household contacts of patients with pulmonary tuberculosis in India (RATIONS): a field-based, open-label, cluster-randomised, controlled trial

Anurag Bhargava, Madhavi Bhargava, Ajay Meher, Andrea Benedetti, Banurekha Velayutham, G Sai Teja, Basilea Watson, Ganesh Barik, Rajeev Ranjan Pathak, Ranjit Prasad, Rakesh Dayal, Adarsh Kibballi Madhukeshwar, Vineet Chadha, Madhukar Pai, Rajendra Joshi, Dick Menzies, Soumya Swaminathan

	Control Group	Intervention Group
N	4712	5621
Incidence cases (all forms)	2.6%	1.7%
Incidence/100 person years	1.27	0.78
Incidence Rate Ratio	**0.62**	
Incidence cases (Micro+	90	62
Incidence/100 person years	0.94	0.51
Incidence Rate Ratio	**0.54**	

Family centric Nutritional supplementation in TB:

- ✓ Reduces TB mortality
- ✓ Reduces incidence in HHC

Lancet 2023: 19;402(10402):627-640

State level Disease burden study

Leading causes of DALYs Lost		
1990		**2016**
1. Diarrheal Diseases		1.Ischaemic Heart Disease
2. LRTIs		2 COPD
3. Neonatal pre-term birth		3, Diarrheal Diseases
4. TB		4. LRTIs
5. Measles		5. Cerebrovascular disease
6. ischemic heart disease		6. Iron-deficiency Anemia
7. Other neonatal		7. Neonatal pre-term birth
8. COPD		**8. TB**

TB YLLs (years of Life lost) :rank 7

TB YLDs (Years of Life lived with disability) : rank >30

Highest DALY rates in Bihar, UP, Jharkhand. Raj., Assam, Chhattisgarh, MP, Odisha, Uttarakhand: highest DALY Rates/L, majorly attributed to mortality

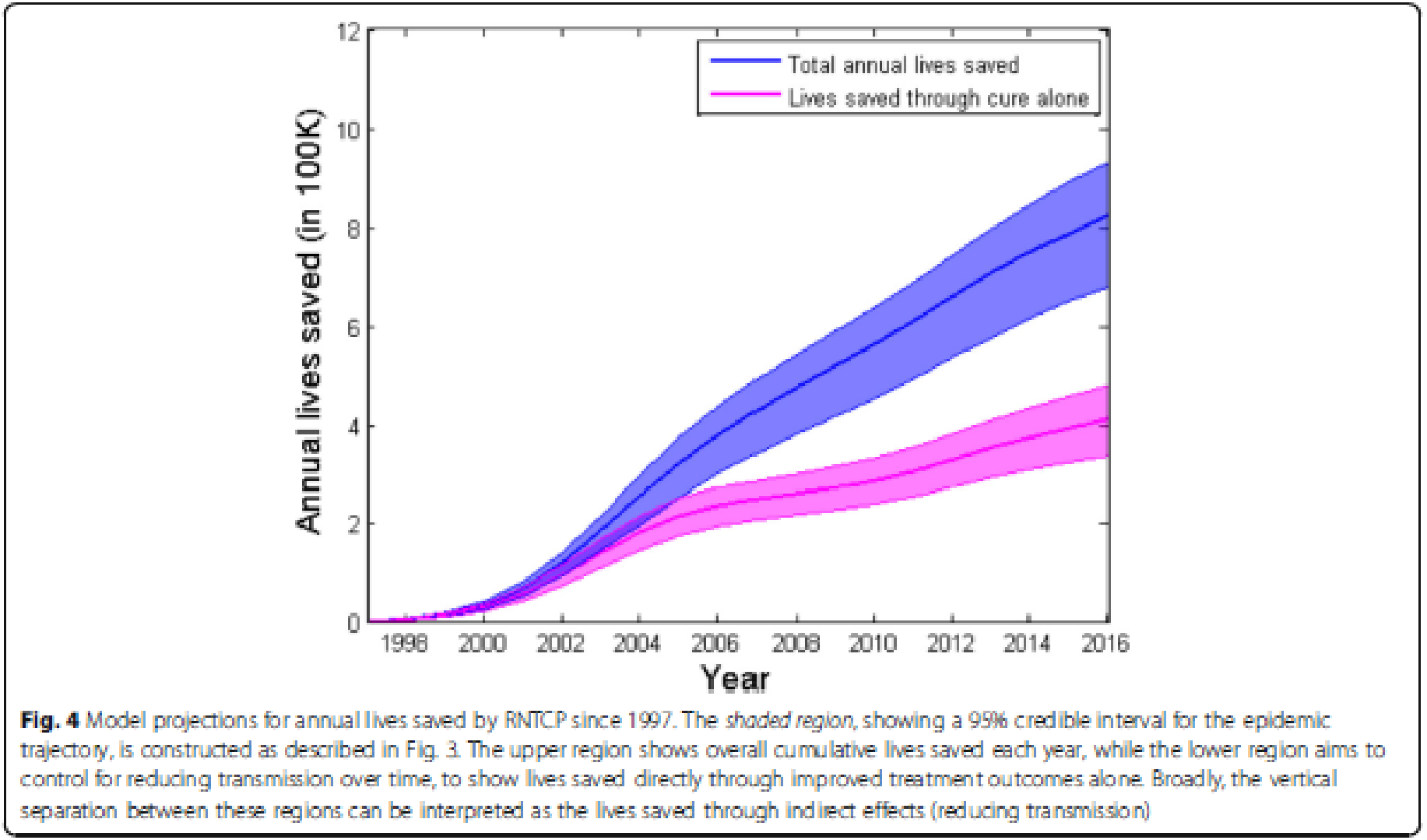


Fig. 4 Model projections for annual lives saved by RNTCP since 1997. The *shaded region*, showing a 95% credible interval for the epidemic trajectory, is constructed as described in Fig. 3. The upper region shows overall cumulative lives saved each year, while the lower region aims to control for reducing transmission over time, to show lives saved directly through improved treatment outcomes alone. Broadly, the vertical separation between these regions can be interpreted as the lives saved through indirect effects (reducing transmission)

	Direct effect	Indirect effect	Total
Lives saved (million)	4.2	3.3	7.5
Of above, MDRTB deaths saved	0.7	0.8	1.5

Lancet. 2014 September 13; 384(9947): 1005–1070. doi:10.1016/S0140-6736(14)60844-8.

Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

- Prevalence to incidence ratio = 1.6
- Average duration of disease= 20 months
- Globally, CFR 1990-2000:36%, 2000-2013: 18%; 2.9% per year decline

Annualized rate of change				
	1990-2000		2000-2013	
	Incidence	Mortality	Incidence	Mortality
Worldwide	+0.03	-3.3	-0.6	-3.7
India	-1.1	-5.2	-1.1	-4.0

Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models

Rein M G J Houben, Nicolas A Menzies, Tom Sumner, Grace H Huynh, Nimalan Arinaminpathy, Jeremy D Goldhaber-Fiebert, Hsien-Ho Lin, Chieh-Yin Wu, Sandip Mandal, Surabhi Pandey, Sze-chuan Suen, Eran Bendavid, Andrew S Azman, David W Dowdy, Nicolas Bacaër, Allison S Rhines, Marcus W Feldman, Andreas Handel, Christopher C Whalen, Stewart T Chang, Bradley G Wagner, Philip A Eckhoff, James M Trauer, Justin T Denholm, Emma S McBryde, Ted Cohen, Joshua A Salomon, Carel Pretorius, Marek Lalli, Jeffrey W Eaton, Delia Boccia, Mehran Hosseini, Gabriela B Gomez, Suvanand Sahu, Colleen Daniels, Lucica Ditiu, Daniel P Chin, Lixia Wang, Vineet K Chadha, Kiran Rade, Puneet Dewan, Piotr Hippner, Salome Charalambous, Alison D Grant, Gavin Churchyard, Yogan Pillay, L David Mametja, Michael E Kimerling, Anna Vassall, Richard G White

- to assess whether End TB targets of reduction in incidence by 50% & mortality by 75% achievable by 2025?
- what interventions, and at which level of scale-up needed to meet targets?
  - Increasing access to high quality care
  - Improved diagnostics
  - Improve quality of post-diagnosis care
  - ACF in general population
  - ACF followed by TPT
  - All simultaneously

Key findings & implications

- baseline level of interventions : 0–19% reduction in incidence
- improving access to high-quality care crucial
  - 20% additional reduction achievable
- Improving quality of tuberculosis care in private sector essential

❑Reduction achieved: 18% (2015-2023)

- Stop TB Strategy scale up plans of specified interventions
  - targets appear unfeasible
  - avert 3.1 million (1.2 -5.8) incidence cases averted
  - avert 1.1 million (0.8 million–2.1 million) deaths averted

➢Higher levels of scale-up needed

Menzies et al. **Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa:** a combined analysis of nine models, The Lancet Global Health, 2016, ISSN 2214-109X, http://dx.doi.org/10.1016/S2214-109X(16)30265-0.

- Expanding access : most attractive of single intervention strategies
- Improving treatment averts more DALYs at lower cost than mWRDs or ACF
- Early identification, effective treatment and prevention of TB: Reduced costs to patients-direct, indirect
- Service costs to double base case levels
- Net savings in societal costs
- Cost per DALY averted falls below per capita GDP, even before patient cost-savings are considered

Chadha VK, Praseeja P, Srivastava R, et al. **Pre-treatment delay and out of pocket expenses by notified new tuberculosis patients in an Indian mega city.** Indian J Tuberc. 2022; 69:446-452.

	2017	2005
PP as first provider	75%	75%
Avg. No of HFs visited pre- diagnosis	3 (1-7)	3 (1-7)
Patient delay- Median (Mean)	5 (15)	7(21)
Doctor delay-Median (Mean)	33 (53)	34 (52)
Total delay- Median (Mean)	44 (68)	53 (72)
Mean pre-diagnostic expenditure	402$^	145$^
Direct medical Expenditure	54%	50%
Non-medical Direct exp.	5%	12%
Indirect expenditure	41%	38%
Catastrophic expenses: % Households		20%

- Relevance of private sector
- No reduction in system delay

➢ to reduce system delay & % HHs with catastrophic expenditure

- Pvt sector skill upgradation
- linkage to free diagnostic services

Conversion rate: 2005-45; 2017: 67

Right Care for every TB patient every time

Improving Quality of TB Care

Thank You