



# **Internal Migration and Transmission of Tuberculosis in China**

Socio-demographic factors in TB prevention

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Sept.13, 2018, Washington D.C.  
TB-MAC/WHO Annual Meeting

# Internal migration in China

- One of the most extensive internal migration in the world.
- The economic boom in China has drawn rural Chinese to mega cities in search of higher incomes
  - 20% of total population (282 million in 2016)
- The household registration system (*Hukou*)
  - Health insurance (not feasible in urban health system)
  - Social security welfares, etc.

***Due to the household registration system, migrant workers have previously not enjoyed the same benefits in healthcare, pensions and other social benefits as city residents***

Wednesday, March 15, 2017, 09:13

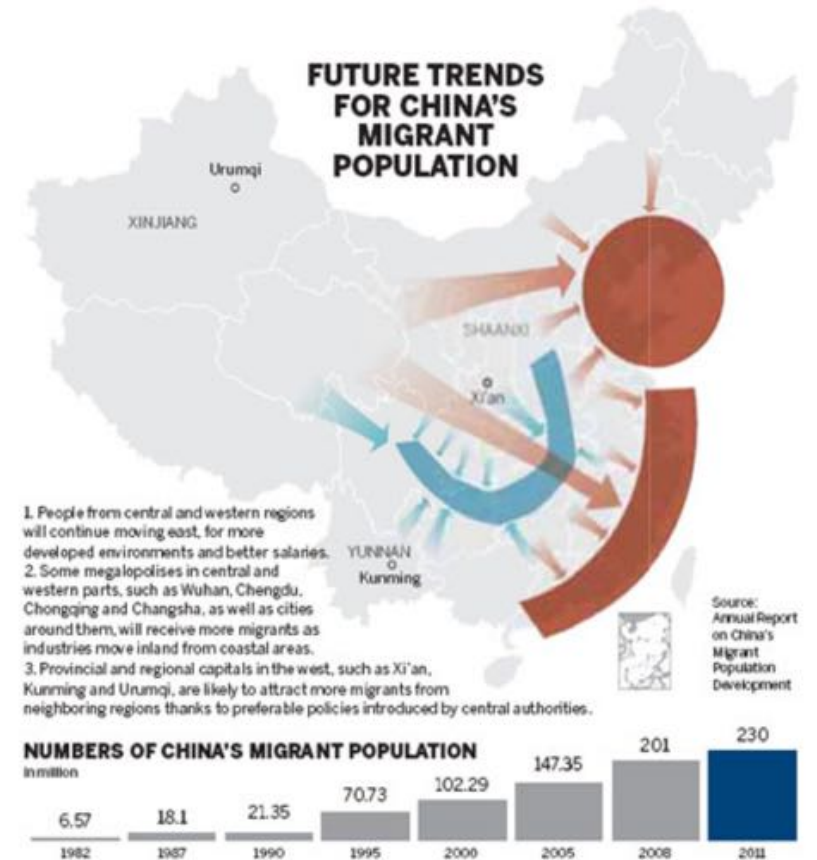
## **282m rural Chinese migrant workers in 2016**

By Xinhua



Migrant workers wait at Zhengzhou Railway Station in Zhengzhou, capital of central China's Henan Province, Feb 15, 2013. The number of rural migrant workers in China hit 282 million at the end of 2016, an increase of 4.24 million from a year before, according to the Ministry of Human Resources and Social Security (MHRSS) March 14. (Photo / Xinhua)

Source: [www.chinadaily.com.cn](http://www.chinadaily.com.cn)



Young population  
Low education level  
Low socioeconomic status  
Vulnerable to communicable diseases  
(e.g. HIV, TB...)

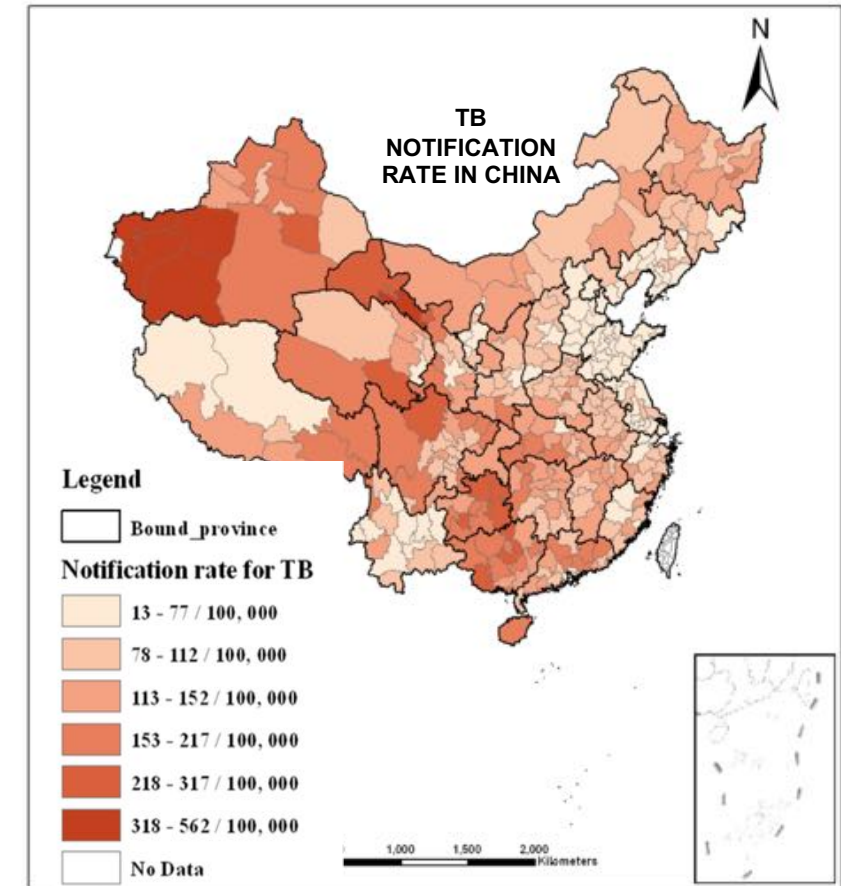
Hu X., et al. Lancet 2008

Peng, X., et al. Science 2011

Annual Report on China's Migrant Population Department

# TB among internal migrants

- Massive internal migration has been associated with the increased TB notification in urban areas
- > 4.5 million prevalent TB cases, 80% in rural China.
- Risk factors with TB infection and care
  - Heavy working load, malnutrition
  - Overcrowding living condition
  - Low knowledge of TB
  - Delay to diagnosis and treatment
  - Non-adherence to treatment
  - Low economic status
- However, the role of migrants in local tuberculosis epidemics is unclear



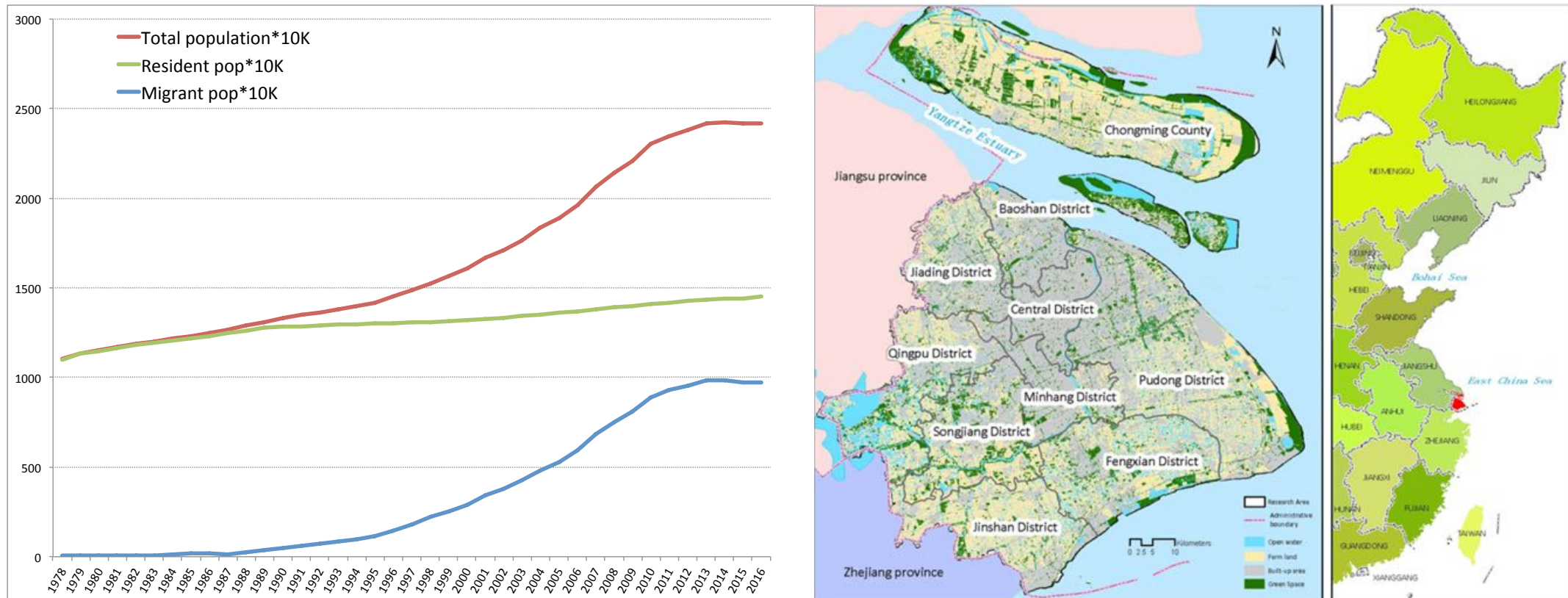
Sun., et al; Int. J. Environ. Res. Public Health 2015

# Study Design and Objectives

- Population-based study from 2009 to 2016
- Use spatial, genomic, and epidemiological analysis to evaluate the role of internal migration in local TB epidemics and the transmission dynamics of tuberculosis among both migrants and residents in Shanghai, China

# Study setting and population

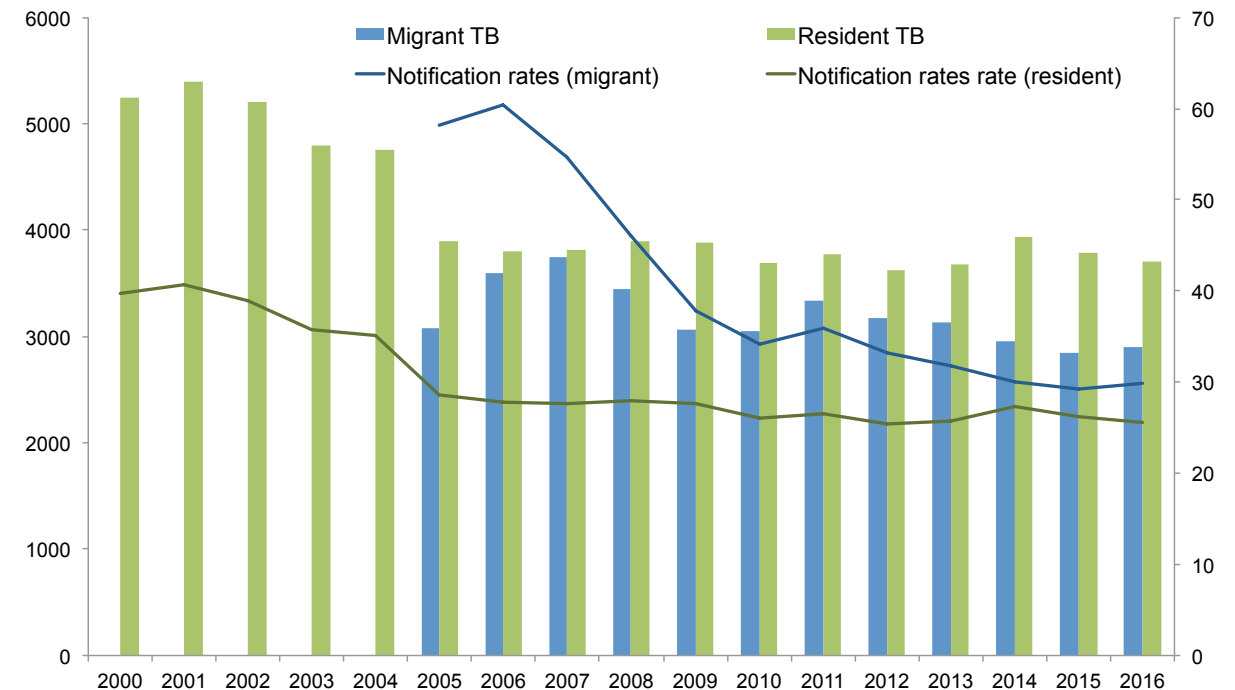
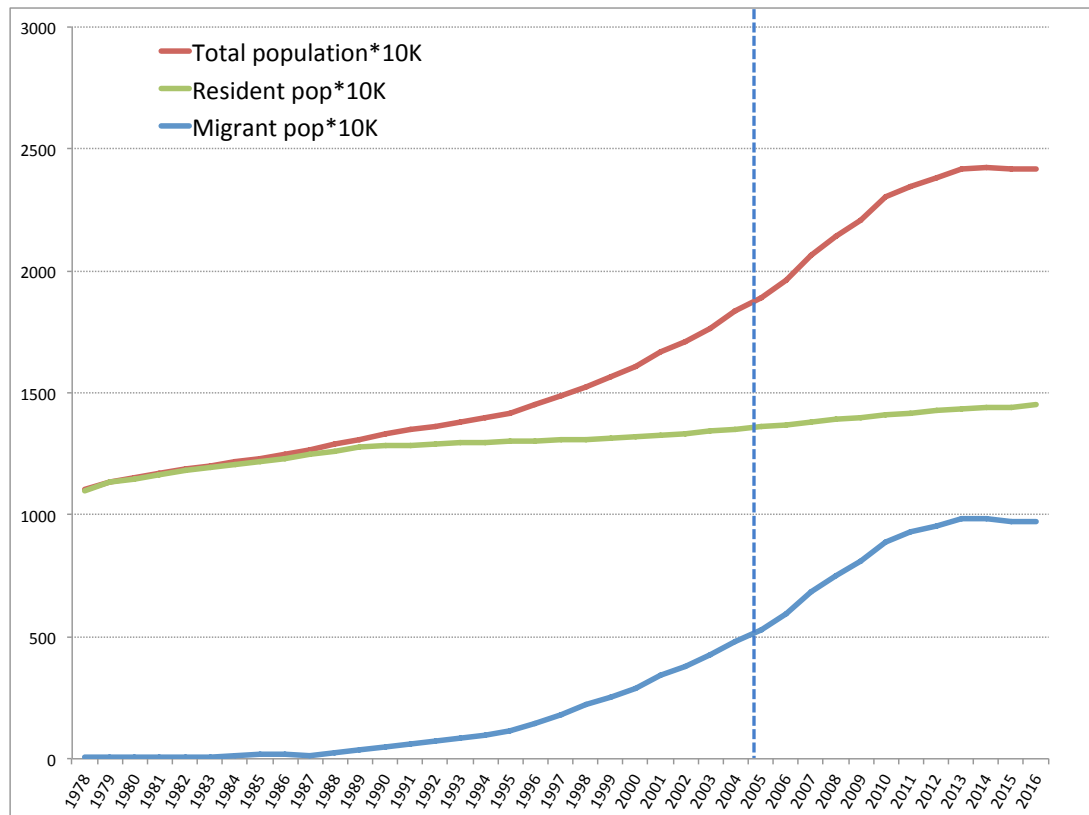
- Shanghai is the largest metropolis city in China (also most populous city)
- 23 millions in 2010 and 40% were migrant population (2010 national census)





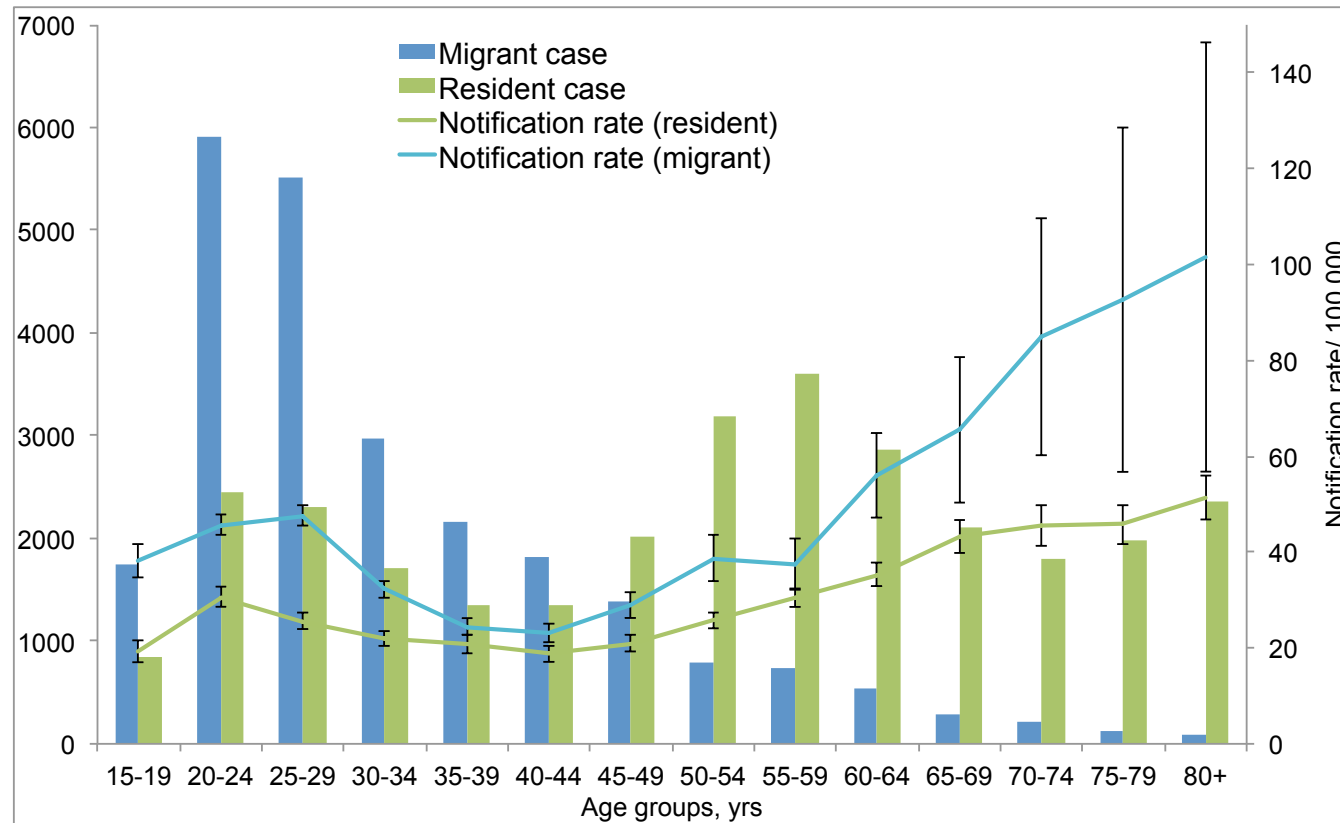
# Study setting and population

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- 23 millions in 2010 and 40% were migrant population (2010 national census)



# Notification rate of pulmonary TB in Shanghai

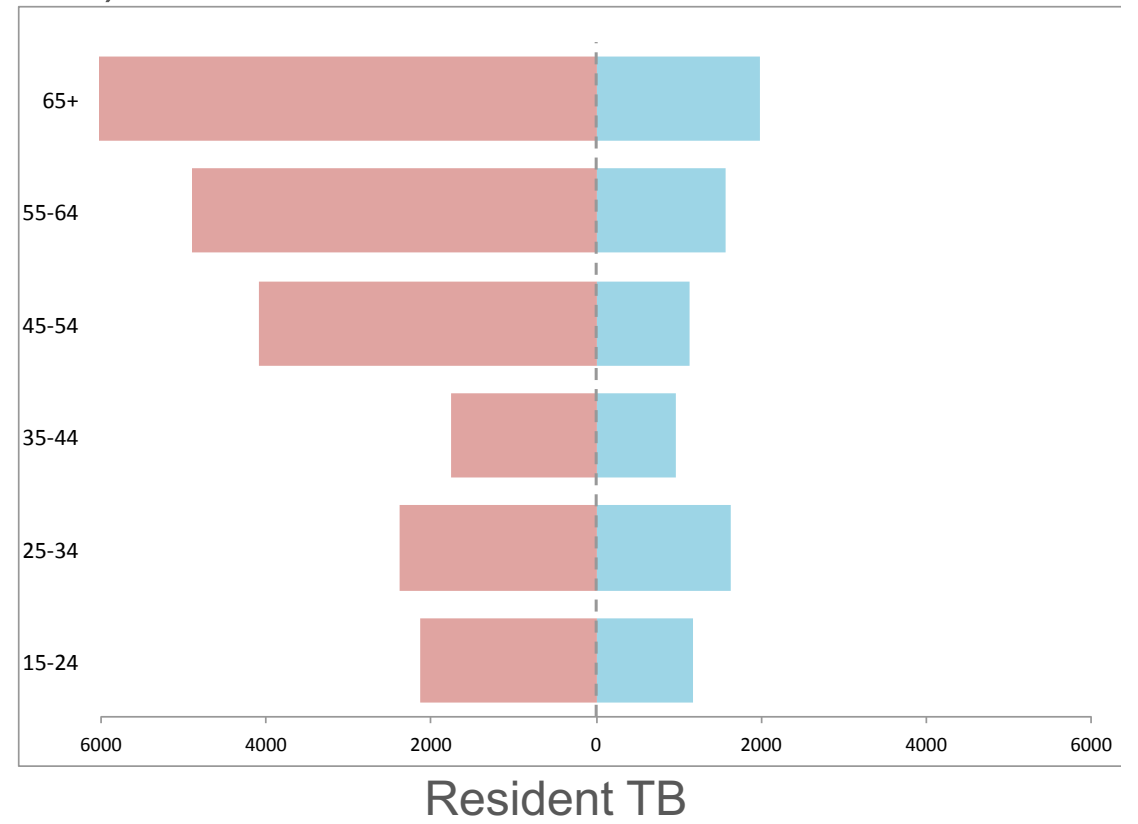
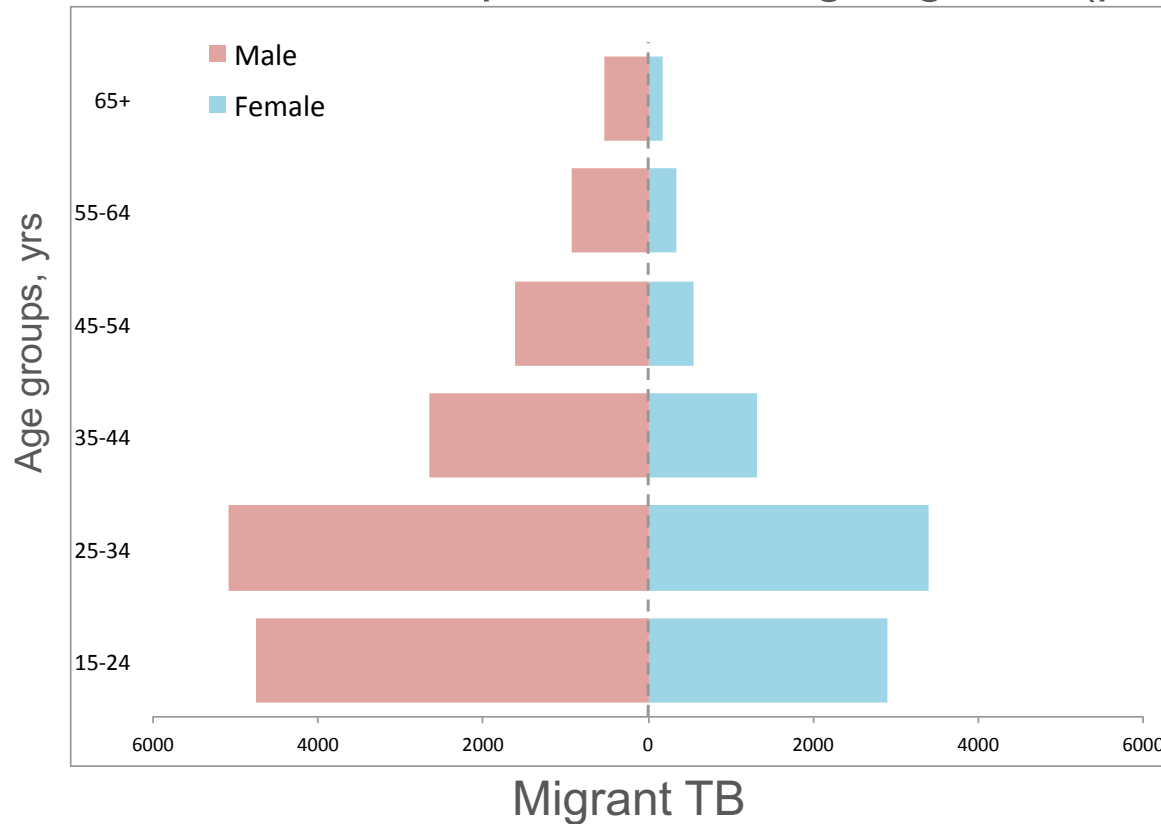
Migrant population has higher TB notification rate than resident population.



<http://www.wsjsw.gov.cn> Shanghai Health Bureau  
<http://www.stats-sh.gov.cn/> Shanghai Statistical Yearbook

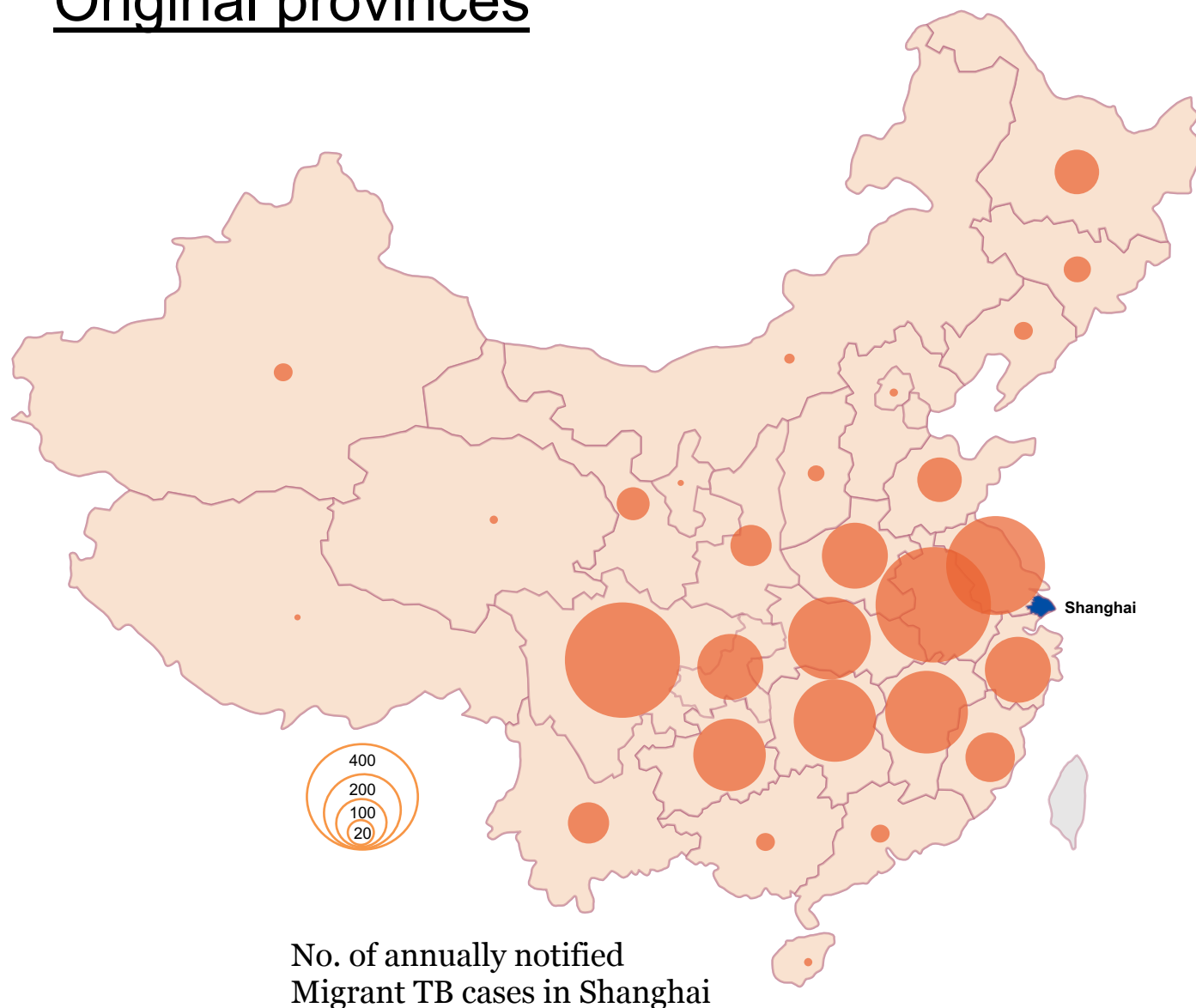
# Population structure of TB patients by Household status

- Migrants account for 44% of the notified pulmonary TB cases
- Young migrant patients vs. Aging local resident patients
- More female TB patients among migrants ( $p < 0.001$ )



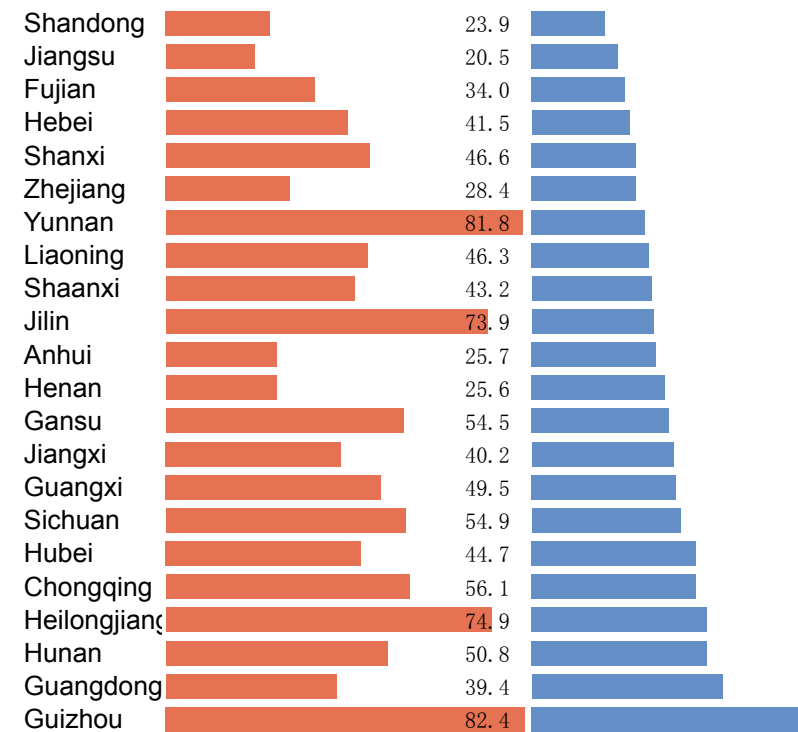


# Original provinces

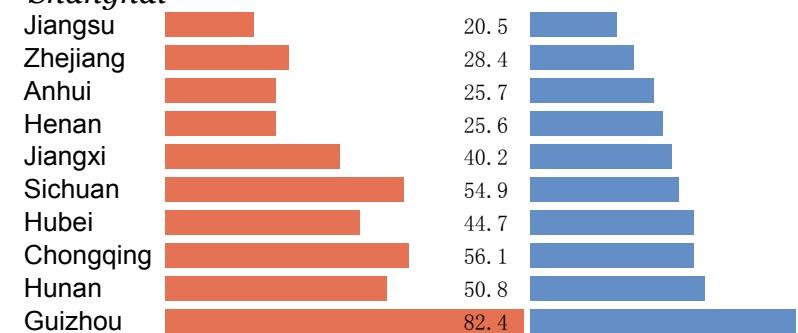


## TB Notification rate by provinces

Estimated in Shanghai National estimated rate/100 000



Provinces with at least 100 TB cases reported annually in Shanghai

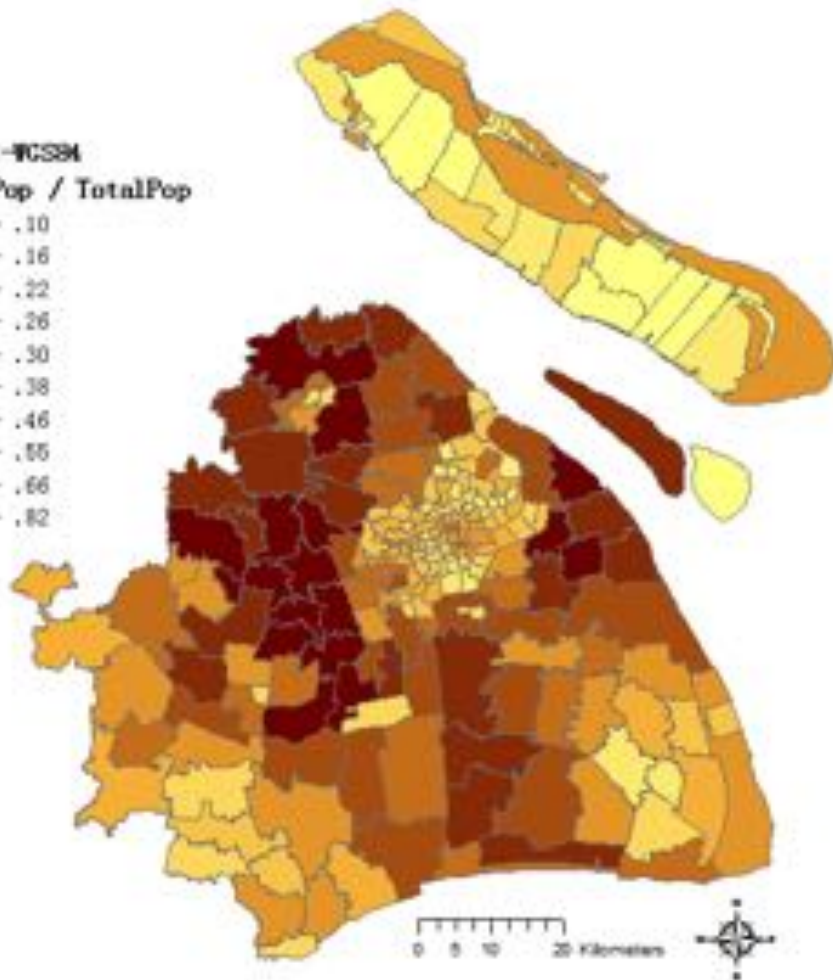


- Q.1:
- What impact do migrants have on residential TB/MDR-TB risk?

# Spatial distribution of population and TB cases

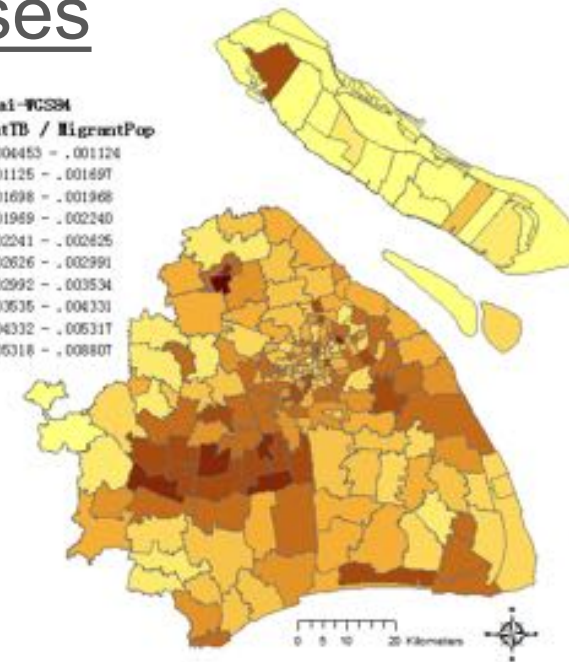
shanghai-WCSM  
MigrantPop / TotalPop

Yellow	.05 - .10
Light Yellow	.10 - .16
Light Orange	.16 - .22
Orange	.22 - .26
Dark Orange	.26 - .30
Brown	.30 - .38
Dark Brown	.38 - .46
Very Dark Brown	.46 - .55
Black	.55 - .66
Dark Red	.66 - .82



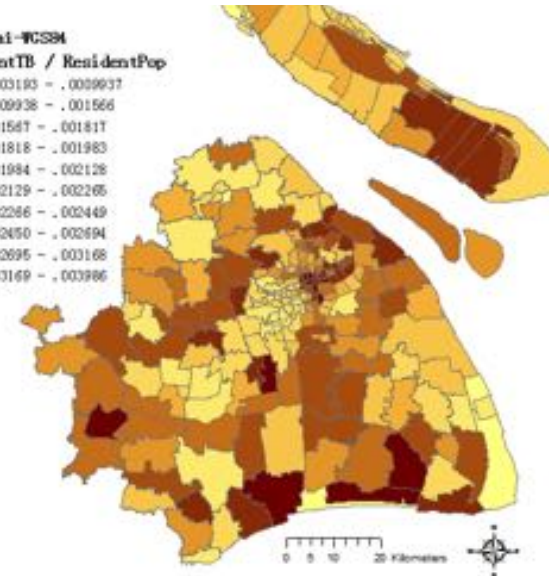
shanghai-WCSM  
MigrantTB / MigrantPop

Yellow	.0004453 - .001124
Light Yellow	.001125 - .001697
Light Orange	.001698 - .001968
Orange	.001969 - .002240
Dark Orange	.002241 - .002425
Brown	.002426 - .002991
Dark Brown	.002992 - .003534
Very Dark Brown	.003535 - .004331
Black	.004332 - .005317
Dark Red	.005318 - .008807



shanghai-WCSM  
ResidentTB / ResidentPop

Yellow	.0003193 - .0009937
Light Yellow	.0009938 - .001566
Light Orange	.001567 - .001817
Orange	.001818 - .001983
Dark Orange	.001984 - .002128
Brown	.002129 - .002265
Dark Brown	.002266 - .002449
Very Dark Brown	.002450 - .002694
Black	.002695 - .003168
Dark Red	.003169 - .003986

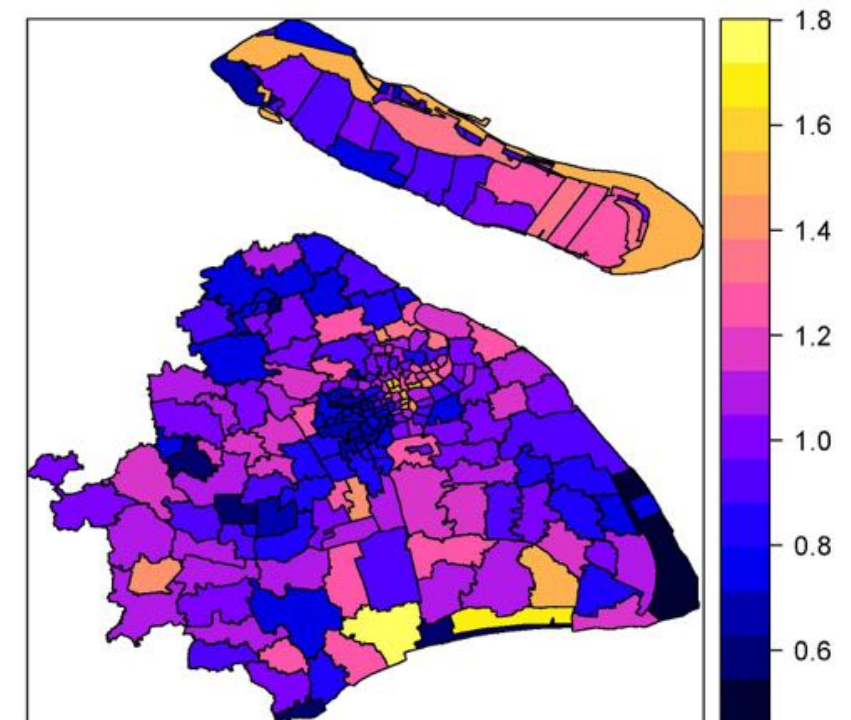


# Spatial Disease mapping of TB

- Main question: What impact do migrants have on residential TB risk?

Parameter	Posterior Mean (SD)	Quantile-Based Credible Interval
Industrial Park	0.988 (0.050)	(0.894, 1.088)
% of Population Migrant	1.032 (0.018)	(0.997, 1.067)
Population Density	1.003 (0.002)	(0.999, 1.007)
Per Capita GDP	0.999 (0.004)	(0.992, 1.006)
Household Size	1.472 (0.233)	(1.059, 1.989)
Rooms per Household	0.802 (0.084)	(0.647, 0.977)
Migrant Sex Ratio	1.005 (0.009)	(0.987, 1.022)
Resident Sex Ratio	1.063 (0.042)	(0.981, 1.148)
% of Resident Population Elderly (65+)	1.341 (0.076)	(1.199, 1.494)
% Migrants with Low Education level	1.108 (0.032)	(1.047, 1.173)

Spatial Poisson model  
Modeled Relative Risks: TB



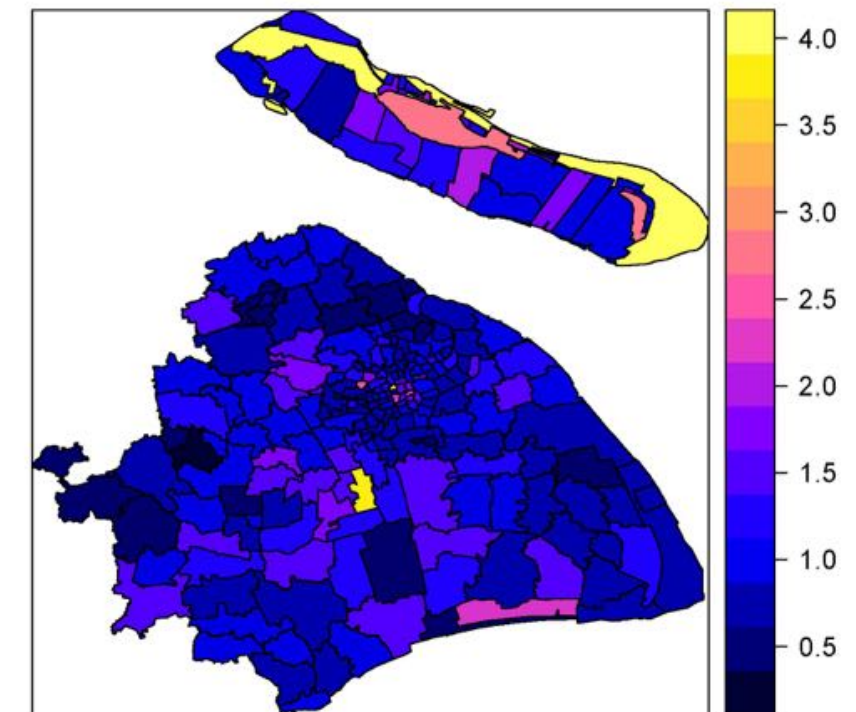
Preliminary results  
Provided by Joshua Warren

# Spatial Disease mapping of MDR-TB

- Main question: What impact do migrants have on residential MDR-TB risk?

Parameter	Posterior Mean (SD)	Quantile-Based Credible Interval
Industrial Park	0.889 (0.164)	(0.607, 1.248)
% of Population Migrant	1.110 (0.068)	(0.982, 1.249)
Population Density	1.011 (0.008)	(0.996, 1.025)
Per Capita GDP	1.008 (0.012)	(0.985, 1.031)
Household Size	1.665 (1.062)	(0.457, 4.461)
Rooms per Household	0.958 (0.323)	(0.463, 1.722)
Migrant Sex Ratio	1.002 (0.038)	(0.927, 1.075)
Resident Sex Ratio	1.142 (0.166)	(0.849, 1.492)
% of Resident Population Elderly(65+)	1.615 (0.352)	(1.045, 2.406)
% Migrants with Low Education level	1.065 (0.101)	(0.884, 1.280)

Spatial Poisson model  
Modeled Relative Risks: MDR-TB



Preliminary results  
Provided by Joshua Warren



# Did the spatial risk mapping capture the signal of MDR-TB transmission? (Work in progress...)

- Main question: What impact do migrants have on residential TB/MDR-TB risk?

MDR-TB clusters from 2009 to 2012

-32% genomic clustered

-73% combined new and clustered MDR cases

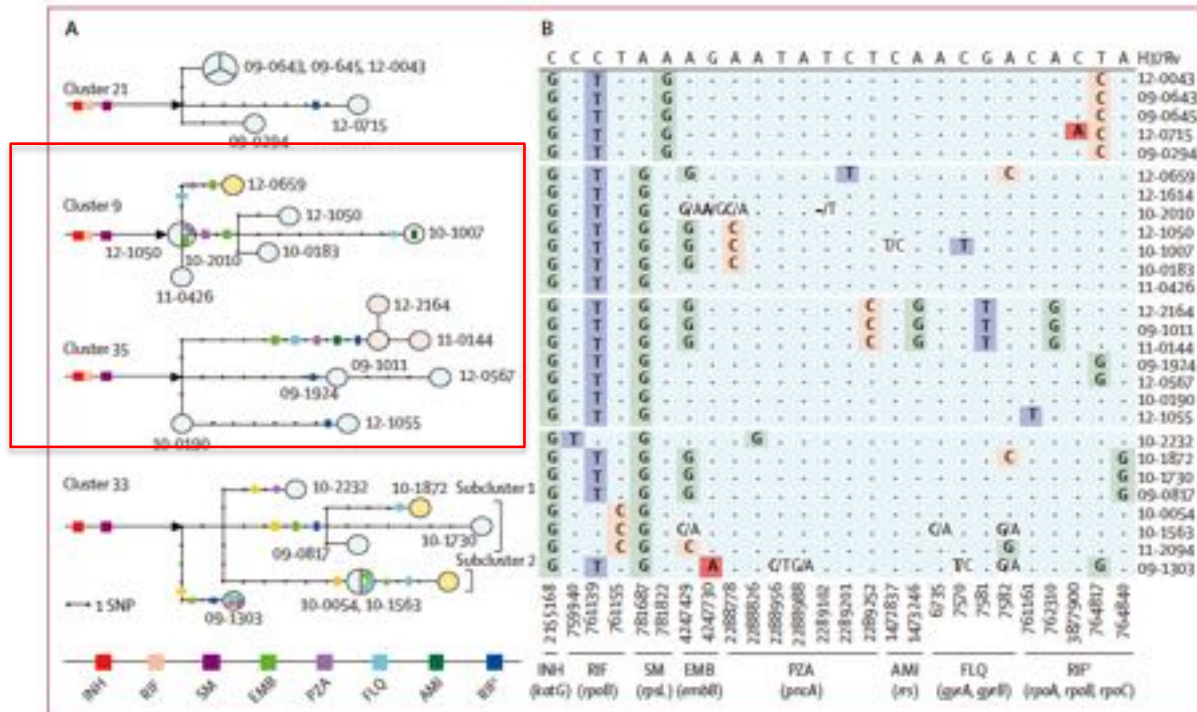
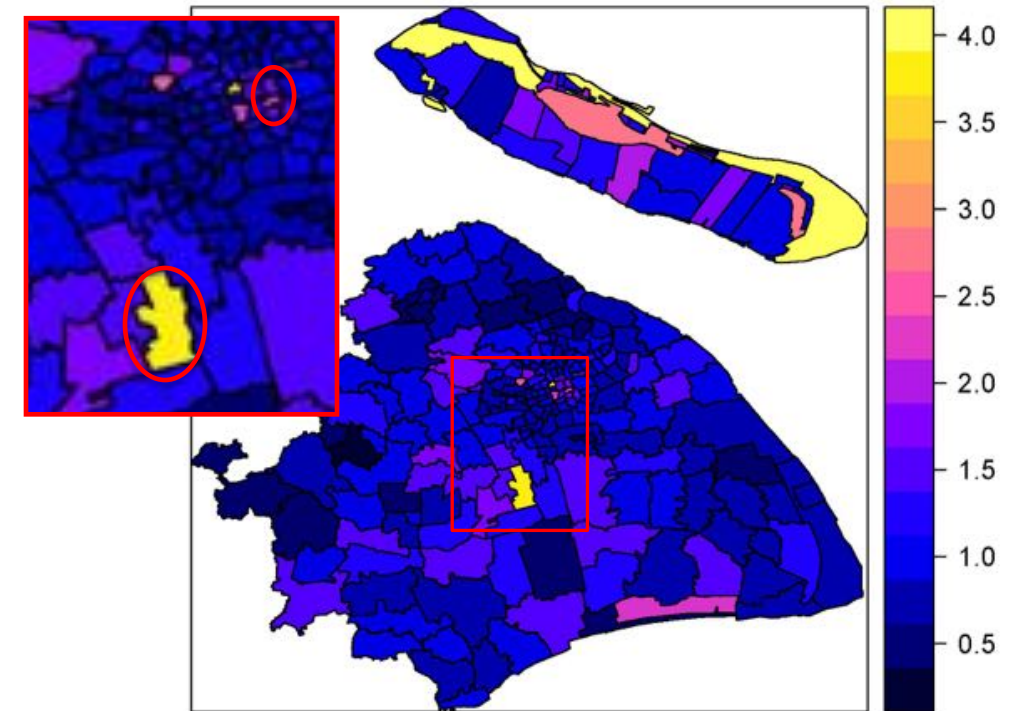


Figure 4: Transmission networks of multidrug-resistant tuberculosis based on genetic distances and drug-resistance mutations

Modeled Relative Risks: MDR-TB



Yang, C., et al. Lancet Infect Dis 2017; 17(3): 275-84

- Q.2:
- The role of migrants in local *M. tuberculosis* transmission is unclear
  - Importation and reactivation cases, or
  - Locally transmitted cases ?



# Transmission of *M. tb* between migrants and residents

- Population-based study in Songjiang, Shanghai
  - All notified culture-confirmed adult (>15 yo) TB patients
  - Jan. 2009 -Dec. 2015
- Demographics
  - 1.75 mil, 62% of the population were migrants
  - Migrants: increased from 0.6 to 1.2 mil (2008-14)
  - Residents: kept steady around 0.6 mil
- Methods
  - Whole-genome sequencing and transmission inference
  - Correlation between spatial and genomic distance

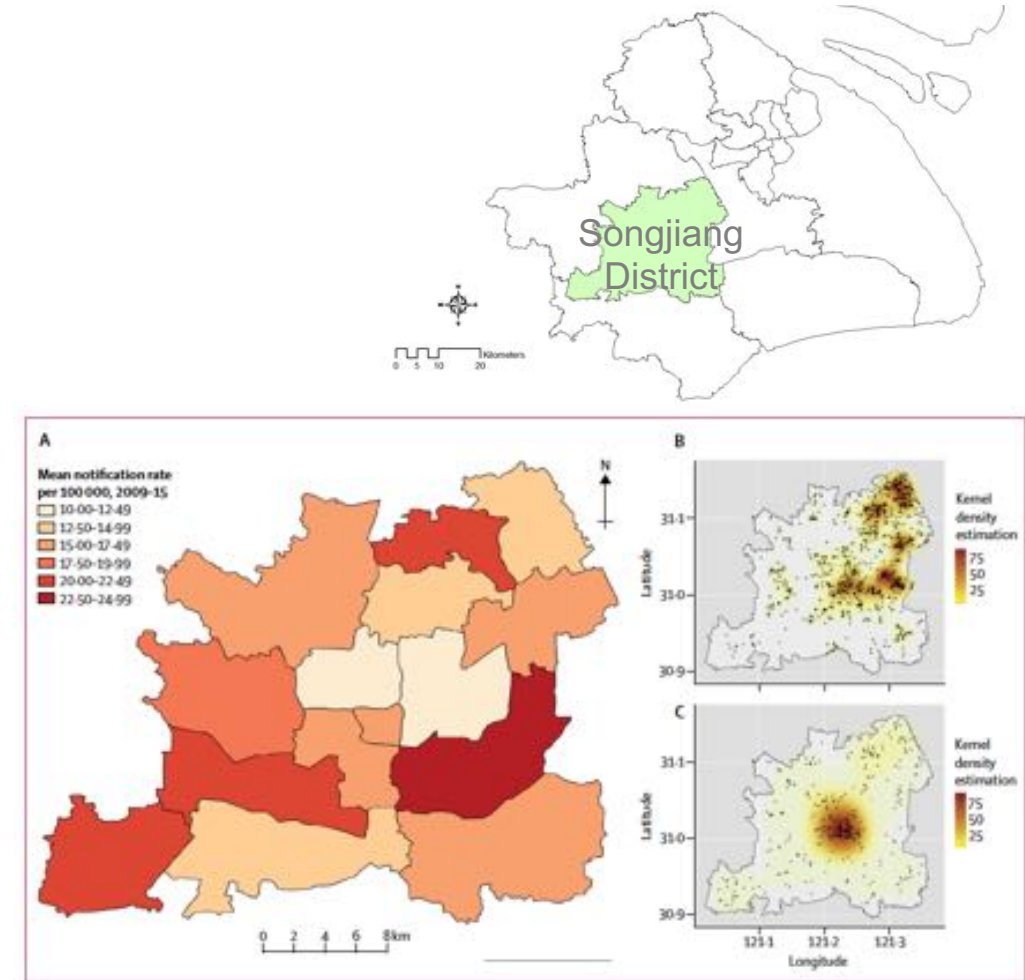


Figure 3: Overall culture-positive tuberculosis notification rate by sub-district (A), and kernel density estimation for migrants (B) and residents (C) in Songjiang, Shanghai, 2009-15

Yang C, et al. Lancet Infect Dis 2018; 18(7): 788-95

# Genotypic clustering analysis

- VNTR genotyping
- 1607 isolates had genotypic data
  - 488(30%) were in genotypic clusters
- WGS analysis
- 218 VNTR-based clustered strains with cluster size  $\geq 3$  patients
  - 150 within 10 SNPs of at least one other case in a cluster
  - Resident-only clusters had larger genetic distance than migrant-only and mixed clusters

## Pair-wise comparisons of SNPs within clusters

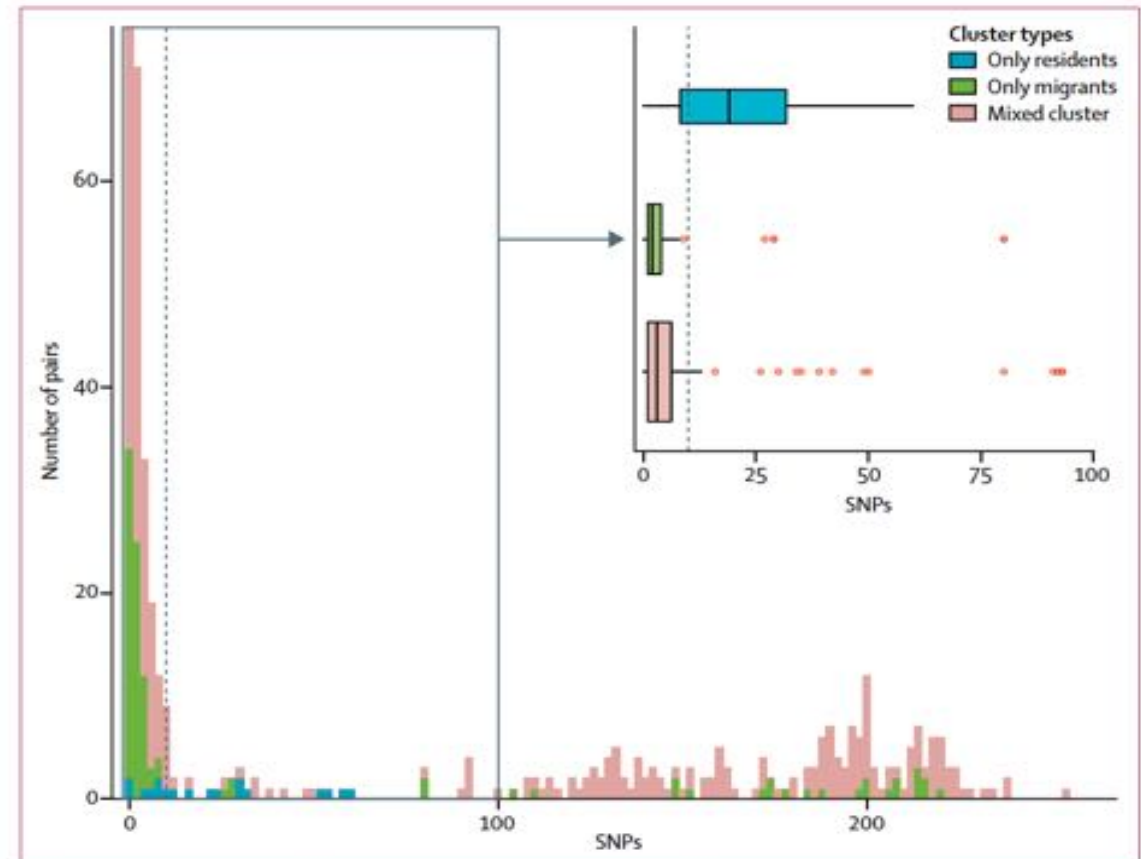


Figure 2: Distribution of pair-wise genetic distances (number of SNPs) within VNTR-based clusters. SNP=single-nucleotide polymorphism. VNTR=variable number of tandem repeats. The dashed lines show the ten SNP threshold.

Yang C, et al. Lancet Infect Dis 2018; 18(7): 788-95

# Genomic clustering was associated with Spatial proximity

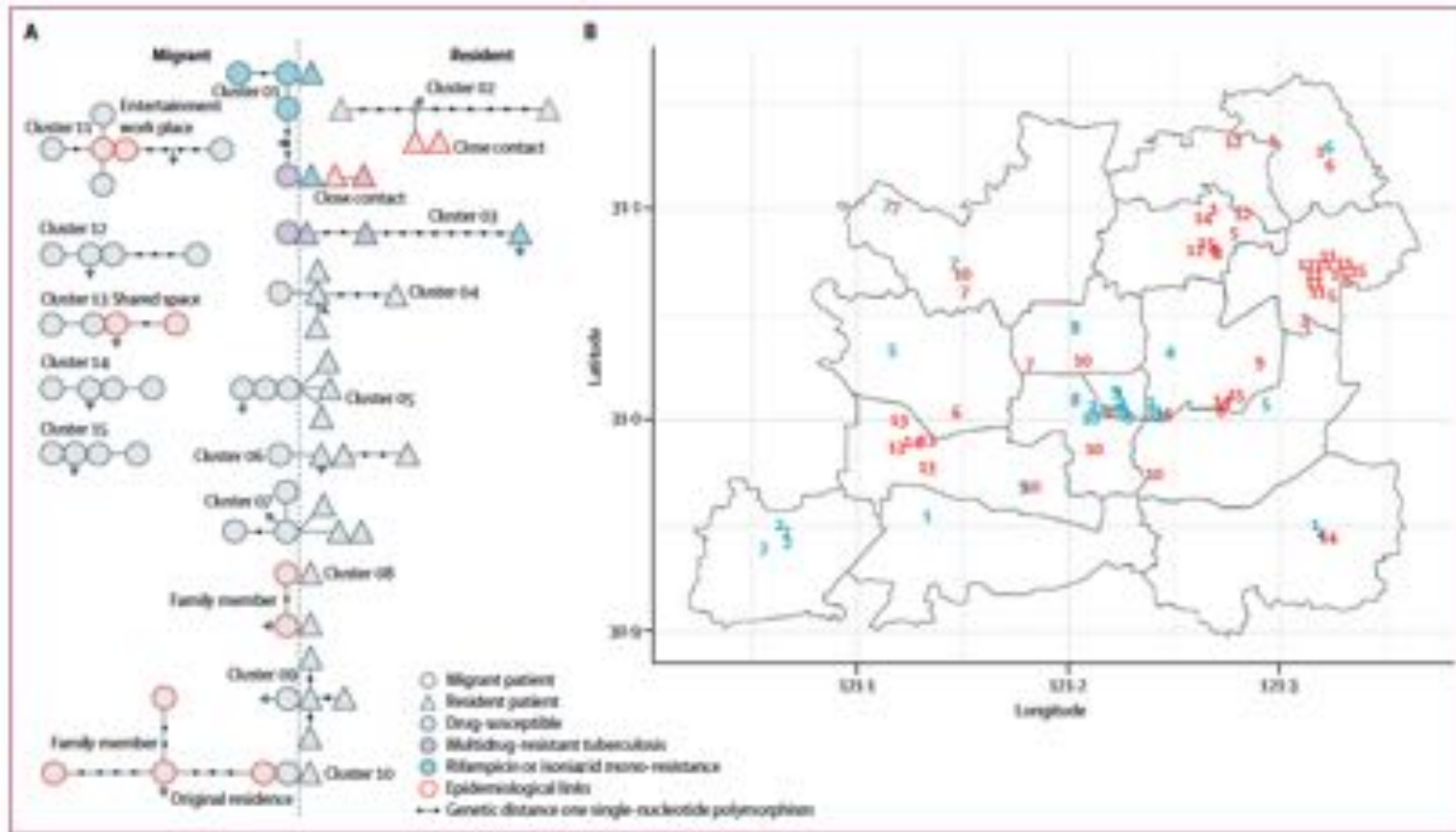


Figure 4: Genetic clusters with at least four patients (A), and spatial distribution of genetic clusters (B). In (A), *Mycobacterium tuberculosis* isolates are separated by lines with length (as suggested by the dots) representing genetic distance. Arrows show the next closest isolate in the sequenced collection. In (B), orange numbers represent migrant patients and blue numbers represent resident patients.

	Distance between homes (per each additional km)		p value	Akaike information criterion
	Odds ratio*	95% CI		
3	0.90	0.87–0.93	<0.0001	1516
5	0.89	0.87–0.92	<0.0001	1792
10	0.89	0.87–0.91	<0.0001	2020
50	0.90	0.87–0.92	<0.0001	2189
100	0.93	0.91–0.95	<0.0001	3188

SNP=single-nucleotide polymorphism. \*Adjusted for covariates including household registration status (ie, migrant or resident) and genetic sub-lineages.

Table 2: Logistic regression of association between spatial distance and genetic relatedness, by genetic distance of genomic cluster (SNPs)

- The odds of two patients being genomically clustered increases as the spatial distance between the patients decreases
- 84%** of migrant within a WGS cluster migrated from different provinces

# Summary

- The influx of internal migrants has contributed to increased TB notification in an urban area in China
  - Not solely due to importation and reactivation of latent infections acquired elsewhere
  - Locally transmission between migrants and residents is not uncommon
- Migrants appear to be contributing to TB and MDR-TB risk for residents
  - Being in a region with poorly educated migrants contributes to TB risk for residents, but not MDR-TB risk
- **Interpretation**
  - More common and prompt active case-finding strategies to ensure the early detection of TB among migrants to provide treatment to interrupt and minimize the transmission

# Challenges...

- Like many developed countries where immigration is the main reason for stagnation or increasing in TB incidence, the resurgence of TB in many parts of China occurs mainly because of the huge population mobility of migrants.
  - What is the major drivers of flattening of TB incidence in Shanghai? **Migration or Aging population?**
- What is the impact of **latent-infected** new migration on the local TB incidence rate and the importance of **cross-infection** (e.g. recent transmission) between migrants and residents population in Shanghai and other mega cities in China?
- Could reinforced **active case screening** be efficient in detecting TB cases among migrant population? How? When? And Where?
  - What is the impact of TB control interventions **targeting hotspot/migrant** vs. general community?
- Effective interventions to reduce the **social and economic barriers** in seeking TB health care among migrants

# Thank you

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