

# Mobilising community networks for the early identification of tuberculosis and treatment initiation in Cambodia: an evaluation of a seed-and-recruit model

## Supplementary Materials

### Contents

Measurement of TB stigma and psychological distress.....	2
Stratified analyses on the effect of case finding strategies on the time from onset of TB symptoms to treatment initiation .....	2
Stratified analyses on the effect of case-finding strategies on the detection of bacteriologically confirmed TB.....	2
Supplementary Table 1: Effect of one-off roving ACF on the time from the onset of symptoms (in days) to treatment initiation among people with TB in Cambodia .....	3
Supplementary Table 2: Stratified analysis for the effect of one-off roving ACF on the time from the onset of symptoms (in days) to treatment initiation among people with TB in Cambodia .....	4
Supplementary Table 3: Effect of one-off roving ACF on the detection of bacteriologically confirmed TB in Cambodia .....	4
Supplementary Figure 1: Community-based active case finding using a seed-and-recruit model. ....	5
Supplementary Figure 2: One-off roving active case finding.....	6
Supplementary Figure 3: Time from the onset of symptoms to TB treatment initiation by case-finding strategies.....	7
Supplementary Figure 4: Flow diagram of the types of tuberculosis and the diagnostics used. ....	8
Supplementary Figure 5: Kernel-density plot distribution of the total delay in days.....	9
References .....	10

### **Measurement of TB stigma and psychological distress**

We measured the thoughts and feelings of people with TB (e.g., people with TB feel alone, lose friends when they share their TB diagnosis and are afraid to tell others their TB diagnosis because others may assume that they have HIV) using validated TB stigma scales developed by Van Rie and colleagues.[1, 2] Patient perspectives toward TB were elicited using 12 questions in the stigma scale[1, 2], and they were measured on a Likert scale (0 to 3), with 0 being “*strongly disagree*” and 3 being “*strongly agree*”. The minimum score was 0, and the maximum possible score was 36. The Cronbach’s alpha for this scale was 0.878.

We measured psychological distresses from the day that the study participants experienced TB symptoms until TB was diagnosed based on the total score of the 6 negative items in the General Health Questionnaire (GHQ)-12.[3] Each item was measured on a Likert scale (0 to 3), with 0 being “*not at all*” and 3 being “*much more than usual*”. We coded responses of 0 and 1 as 0 and responses of 2 and 3 as 1 according to the 0-0-1-1 scoring method.[4] The median score of 3 was used as a cut-off. The Cronbach’s alpha for GHQ-12 in this study was 0.747.

### **Stratified analyses on the effect of case finding strategies on the time from onset of TB symptoms to treatment initiation**

Comparing the effect of community-based ACF using a seed-and-recruit model with one-off roving ACF (model 1) and PCF (model 2) on total delay, we did not find significant heterogeneity in both models in the estimates by age (model 1:  $P$  for interaction = 0.086; model 2:  $P$  for interaction = 0.403), sex (model 1:  $P$  for interaction = 0.820; model 2:  $P$  for interaction = 0.158), TB knowledge (model 1:  $P$  for interaction = 0.733; model 2:  $P$  for interaction = 0.111), operational districts (model 1:  $P$  for interaction = 0.606; model 2:  $P$  for interaction = 0.208) and education levels (model 1:  $P$  for interaction = 0.745).

### **Stratified analyses on the effect of case-finding strategies on the detection of bacteriologically confirmed TB**

We found significant heterogeneity in the estimates by operational districts (model 1:  $P$  for interaction = 0.001; model 2:  $P$  for interaction = 0.011) and sex (model 1:  $P$  for interaction = 0.036). The results of the stratified analyses were presented in Table 4.

**Supplementary Table 1: Effect of one-off roving ACF on the time from the onset of symptoms (in days) to treatment initiation among people with TB in Cambodia**

	Crude HR	95% CI	p-value	Adjusted HR	95% CI	p-value
Case finding strategies						
PCF	1.00			1.00		
One-off roving ACF	1.47	1.14 - 1.90	0.003	1.15	0.87 - 1.53	0.335
Operational districts						
Urban	1.00			1.00		
Rural	1.42	1.17 - 1.73	<0.001	1.27	1.02 - 1.59	0.036
Sex						
Male	1.00			1.00		
Female	1.03	0.85 - 1.23	0.786	0.88	0.72 - 1.07	0.196
Education level						
Primary and lower	1.00			1.00		
Above primary	0.71	0.55 - 0.91	0.008	0.78	0.59 - 1.04	0.091
Presence of other known medical conditions						
Yes	1.00			1.00		
No	1.22	0.99 - 1.50	0.062	1.30	1.04 - 1.61	0.020
Cough <sup>a</sup>						
Yes	1.00			1.00		
No	1.53	1.17 - 2.00	0.002	1.47	1.11 - 1.94	0.006
Dyspnea <sup>a</sup>						
Yes	1.00			1.00		
No	0.74	0.61 - 0.90	0.003	0.70	0.56 - 0.86	0.001
TB knowledge <sup>b</sup>						
Poor	1.00			1.00		
Good	0.81	0.66 - 1.00	0.053	0.78	0.63 - 0.97	0.025
Age, in years	1.00	0.99 - 1.01	0.658	1.00	0.99 - 1.01	0.831
Distance from home to health facility, in kilometers	1.00	0.97 - 1.02	0.786	0.99	0.96 - 1.01	0.300
Patient perspectives toward TB <sup>c</sup>	1.06	1.03 - 1.08	<0.001	1.05	1.03 - 1.08	<0.001

HR, hazards ratio; CI, confidence interval; ACF, active case finding; PCF, passive case finding; TB, tuberculosis

<sup>a</sup>Symptoms prior to TB diagnosis self-reported by study participants

<sup>b</sup>Evaluated based on the answers from 8 questions regarding the characteristics, symptoms of TB, route of transmission, prevention, and treatment of TB with a total score of 13 (median = 9). Respondents were regarded as having poor TB knowledge if they scored the median and below and good TB knowledge if they scored above the median.

<sup>c</sup>Evaluated based on the answers from 12 questions, measured on a Likert scale (0 to 3), with 0 being strongly disagree and 3 being strongly agree. Minimum score is 0 and the maximum score is 36

**Supplementary Table 2: Stratified analysis for the effect of one-off roving ACF on the time from the onset of symptoms (in days) to treatment initiation among people with TB in Cambodia**

	Age <55			Age ≥ 55		
	Adjusted HR <sup>a</sup>	95% CI	p-value	Adjusted HR <sup>a</sup>	95% CI	p-value
Case finding strategies						
PCF	1.00			1.00		
One-off roving						
ACF	2.43	1.27 - 4.65	0.007	0.96	0.68 - 1.36	0.814
	Age <63			Age ≥ 63		
	Adjusted HR <sup>a</sup>	95% CI	p-value	Adjusted HR <sup>a</sup>	95% CI	p-value
Case finding strategies						
PCF	1.00			1.00		
One-off roving						
ACF	1.89	1.28 - 2.79	0.001	0.69	0.41 - 1.16	0.165

HR, hazards ratio; CI, confidence interval; PCF, passive case finding; ACF, active case finding

<sup>a</sup>Adjusted for operational districts, operational districts, gender, education levels, presence of other known medical conditions, TB symptoms (cough and dyspnea), TB knowledge, age, distance from place of residence to public health facilities, and TB stigma

**Supplementary Table 3: Effect of one-off roving ACF on the detection of bacteriologically confirmed TB in Cambodia**

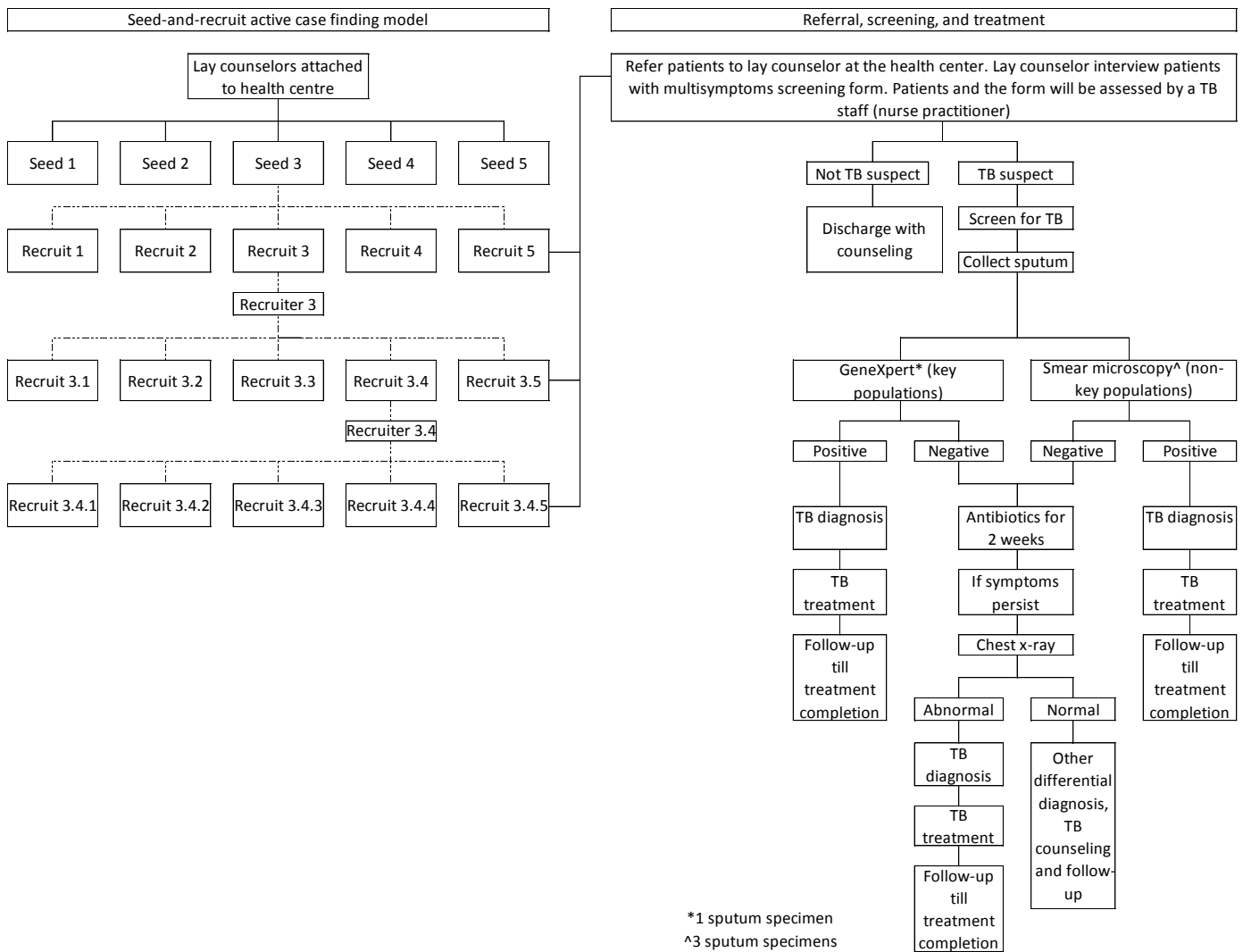
	Crude PR	95% CI	p-value	Adjusted PR	95% CI	p-value
Case finding strategies						
PCF	1.00			1.00		
One-off roving ACF	0.85	0.60 - 1.19	0.338	0.68	0.46 - 0.99	0.043
Operational districts						
Urban	1.00			1.00		
Rural	1.50	1.09 - 2.06	0.014	1.94	1.34 - 2.80	<0.001
Sex						
Male	1.00			1.00		
Female	0.73	0.56 - 0.95	0.022	0.77	0.58 - 1.03	0.080
Ever smoked <sup>a</sup>						
Ever	1.00			1.00		
Never	0.77	0.59 - 1.01	0.061	0.83	0.60 - 1.14	0.244
Alcohol use <sup>b</sup>						
Non-drinker	1.00			1.00		
Drinker	1.25	0.95 - 1.66	0.110	1.05	0.75 - 1.45	0.790
Fever <sup>c</sup>						
Yes	1.00			1.00		
No	1.28	0.98 - 1.66	0.068			
Age, in years	0.99	0.98 - 1.00	0.033	0.99	0.98 - 1.00	0.049

PR, prevalence ratio; CI, confidence interval; ACF, active case finding; PCF, passive case finding

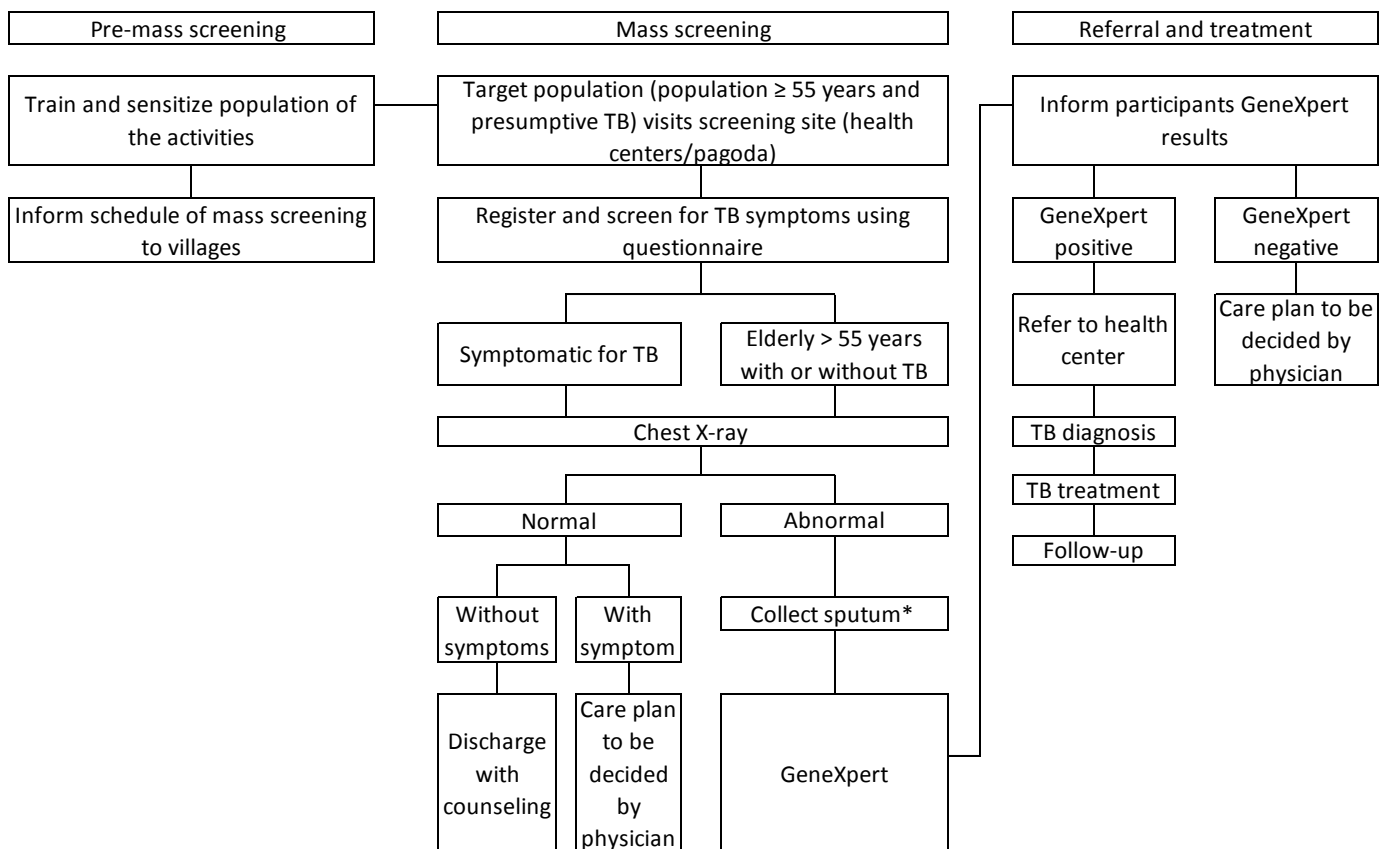
<sup>a</sup>Ever smoked included current and ex-smokers

<sup>b</sup>Drinkers reported frequency of alcohol use that ranges from once a month or less to 4 times or more per week. Non-drinkers refer to teetotalers.

<sup>c</sup>Symptoms prior to TB diagnosis self-reported by study participants

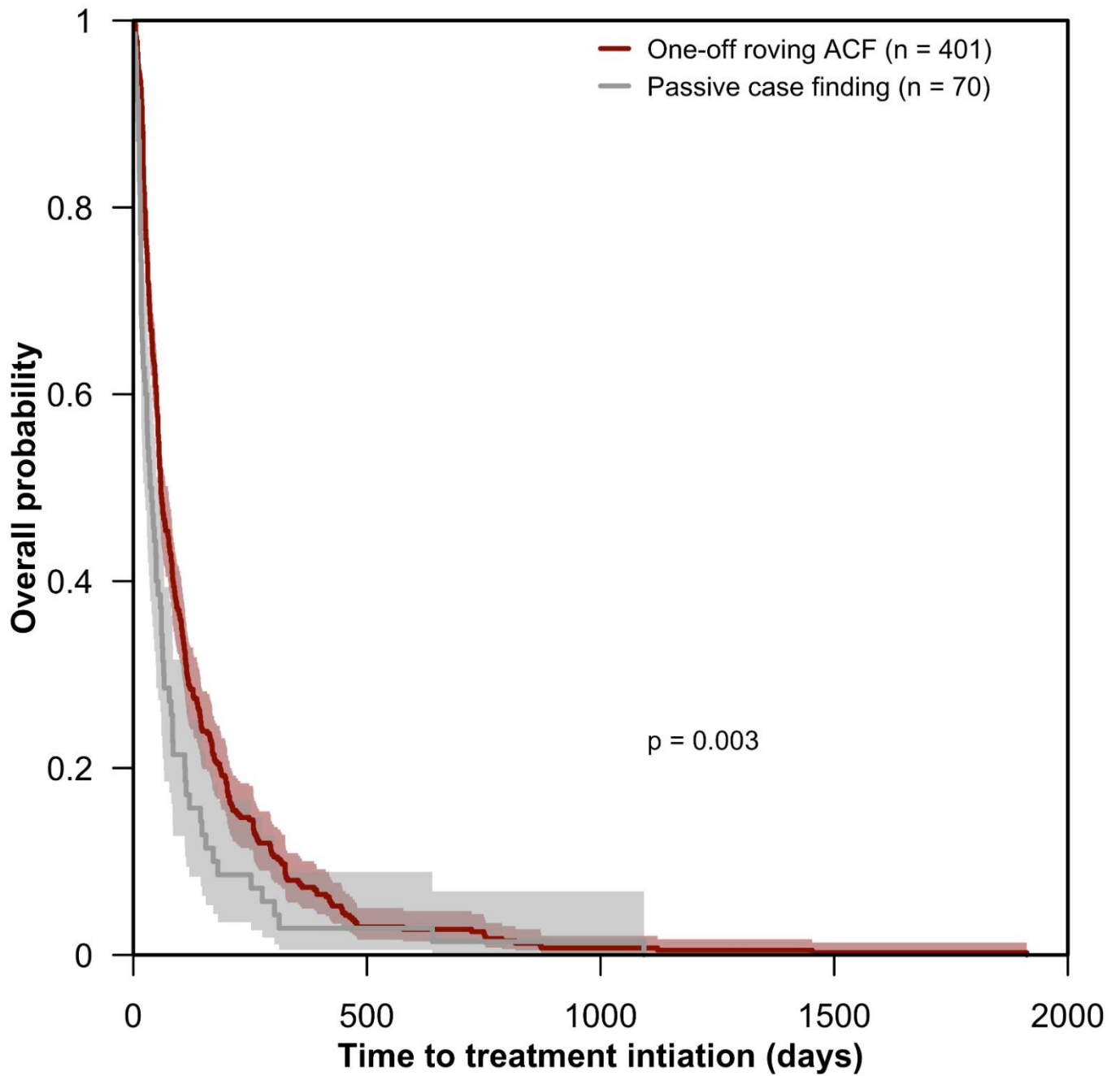


**Supplementary Figure 1: Community-based active case finding using a seed-and-recruit model.** Dotted lines illustrated a network that seed, and recruiter could potentially build to find and refer presumptive TB to care in snowball manner. Recruits who met the criteria of a recruiter were trained to recruit other people who might have TB in the community. The key populations in this context referred to people aged 55 and above, people with diabetes, people living with HIV, household contacts of TB patients, and people who use and inject drugs. For the GeneXpert test, one sputum specimen was collected. For smear microscopy, three sputum specimens were collected at three different times, over two days.

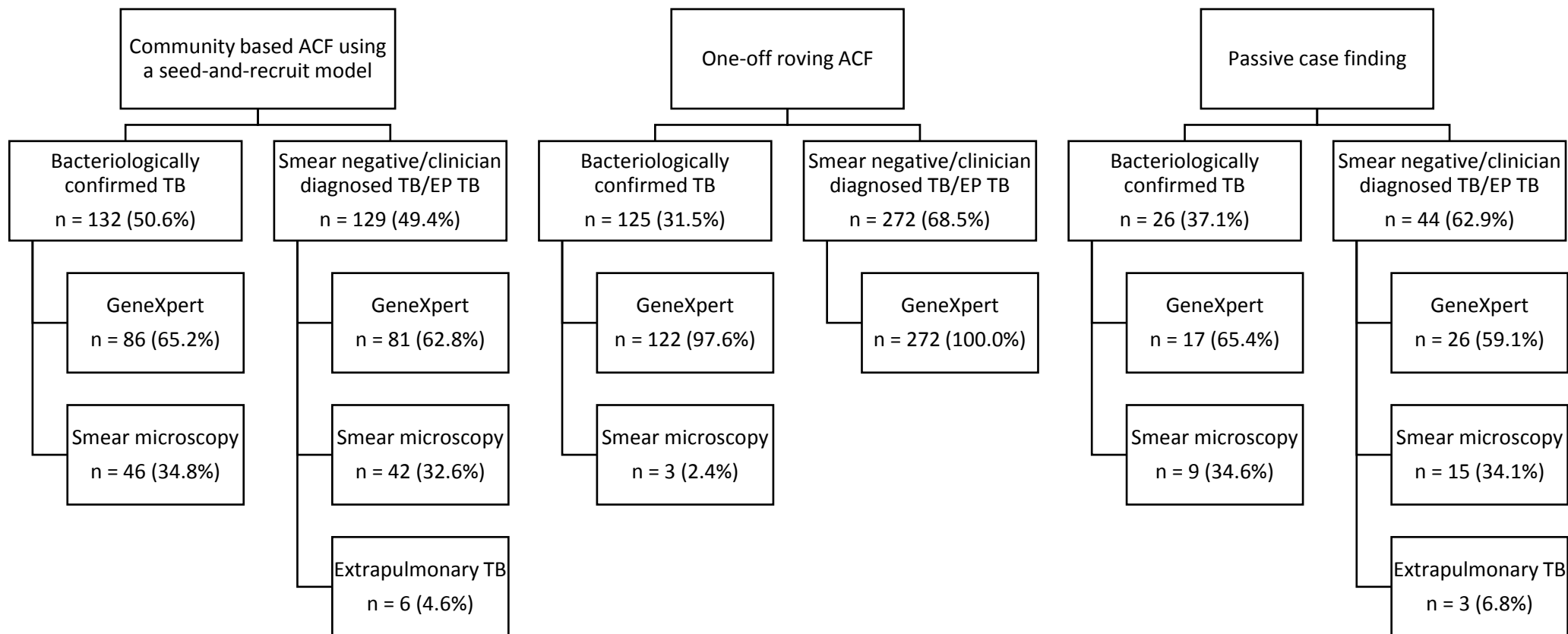


\*1 sputum specimen

**Supplementary Figure 2: One-off roving active case finding.** In the pre-mass screening stage, program staff invited the target population (people aged 55 and above) and other presumptive TB cases in the community to a roving, one-off active case finding day at the health centres or other public sites in the community such as the pagoda. For the GeneXpert test, one sputum specimen was collected.

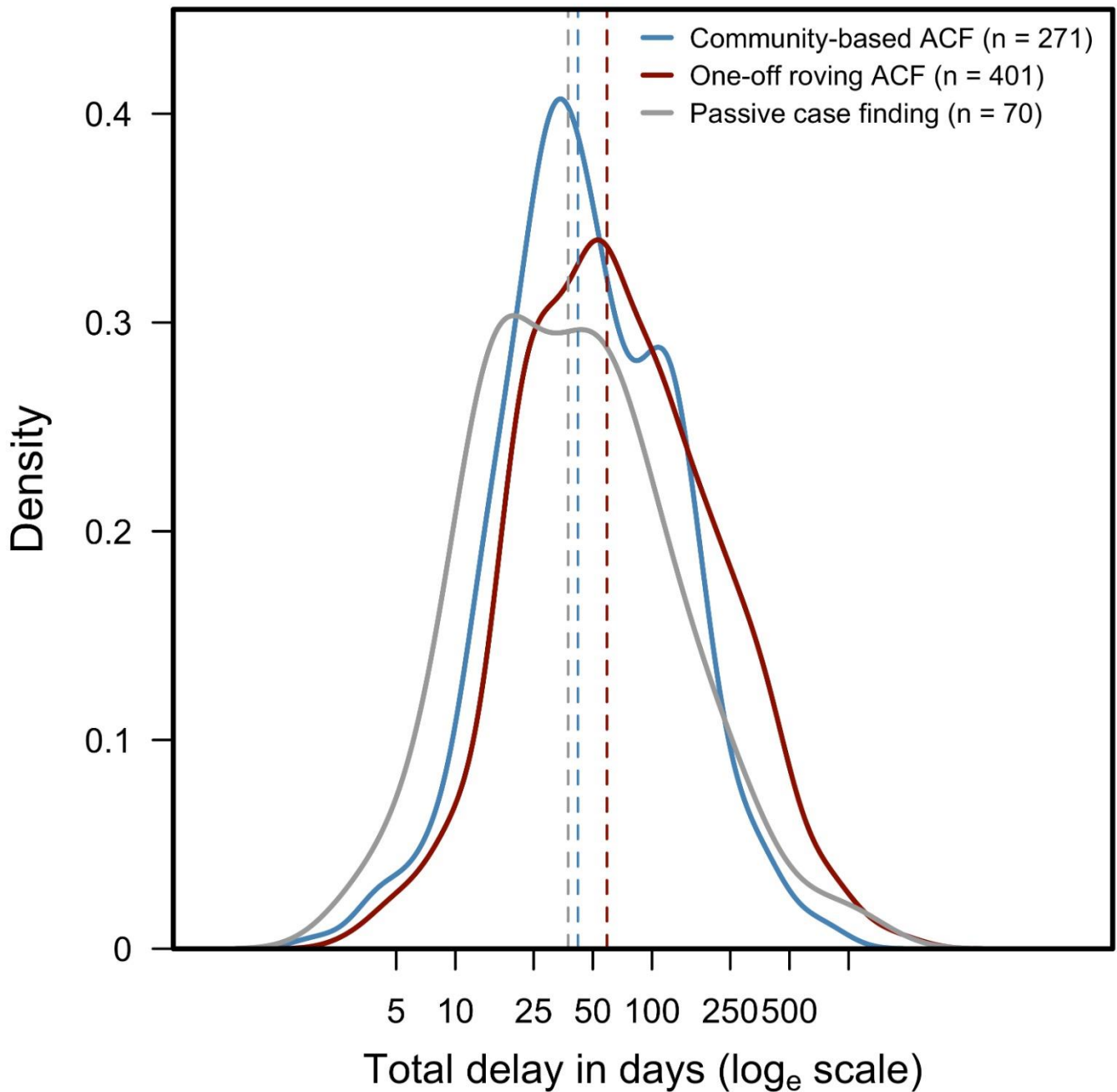


**Supplementary Figure 3: Time from the onset of symptoms to TB treatment initiation by case-finding strategies.** The Kaplan-Meier curves for the time from onset of symptoms to TB treatment initiation comparing one-off roving ACF and passive case finding. The overall probability denotes  $\Pr(T \geq t)$ , where  $T$  is the time to treatment initiation in days.



**Supplementary Figure 4: Flow diagram of the types of tuberculosis and the diagnostics used.** The flow diagram illustrates the proportions of participants identified through the three models by the types of TB and TB diagnostics tests. The bacteriological status of presumptive TB was determined at the health centres by either smear microscopy—for members of the general population—or GeneXpert MTB/RIF—for TB KAP in accordance with the national guideline. For the one-off roving ACF, the mass screening event was made known to the member of the community, especially among the target population (people aged  $\geq 55$ ). Individuals who visited the event were screened using TB symptoms questionnaire and chest x-ray. The bacteriological status of individuals with an abnormal chest x-ray was determined using GeneXpert MTB/RIF modalities on-site during the screening session.





**Supplementary Figure 5: Kernel-density plot distribution of the total delay in days.** We examined the distribution of total delay in days (logarithmic scale) among three case-finding models. The dotted lines in blue, red, and grey indicate the median total delay for community-based ACF using a seed-and-recruit model, one-off roving ACF, and passive case finding, respectively. We compared the difference in median time from onset of symptoms to TB treatment initiation (total delay, in days) between community ACF using a seed-and-recruit model and one-off roving ACF ( $p < 0.001$ ), community ACF using a seed-and-recruit model and passive case finding ( $p = 0.157$ ), and one-off roving ACF and passive case finding ( $p < 0.001$ ) using Wilcoxon rank-sum test with continuity correction.

## References

1. Van Rie A, Sengupta S, Pungrassami P, Balhip Q, Choonuan S, Kasetjaroen Y, Strauss RP, Chongsuivatwong V. Measuring stigma associated with tuberculosis and HIV/AIDS in southern Thailand: exploratory and confirmatory factor analyses of two new scales. *Trop. Med. Int. Health* 2008; 13: 21–30.
2. Meershoek A, Zwerling A, Daftary A, Citro B, Smyth C, Lewis D, Cheallaigh DN, Byrne E, Mitchell EMH. TB stigma measurement guidance. Den Haag: KNCV Tuberculosis Foundation; 2018.
3. Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinelli M, Gureje O, Rutter C. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. *Psychol Med* 1997; 27: 191–197.
4. Goldberg D, Williams P. A user's guide to the general health questionnaire. NFER-NELSON; 1988.