# Yield, NNS and prevalence of screening for DM and hypertension among pulmonary tuberculosis index cases and contacts through single time screening: A contact tracing-based study 

Shengqiong Guo ${ }^{1,2}$, Virasakdi Chongsuvivatwong ${ }^{2 *}$, Min Guo ${ }^{3}$, Shiguang Lei ${ }^{1 *}$, Jinlan Li ${ }^{1 *}$, Huijuan Chen ${ }^{1}$, Jiangping Zhang ${ }^{4}$, Wen Wang ${ }^{4}$, Cui Cai ${ }^{5}$<br>1 Guizhou Center for Disease Control and Prevention, Guiyang, Guizhou, China, 2 Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand, 3 Anshun People's Hospital, Anshun, Guizhou, China, 4 Yunyan Center for Disease Control and Prevention, Guiyang, Guizhou, China, 5 Guiyang Public Health Clinical Center, Guiyang, Guizhou, China<br>* cvirasak@medicine.psu.ac.th (VC); 948488961 @qq.com (SL); 740820442@qq.com (JL)

Citation: Guo S, Chongsuvivatwong V, Guo M, Lei S, Li J, Chen H, et al. (2022) Yield, NNS and prevalence of screening for DM and hypertension among pulmonary tuberculosis index cases and contacts through single time screening: A contact tracing-based study. PLoS ONE 17(1): e0263308. https://doi.org/10.1371/journal.pone.0263308

Editor: Chaisiri Angkurawaranon, Chiang Mai University, THAILAND

Received: August 22, 2021
Accepted: January 18, 2022
Published: January 28, 2022
Copyright: © 2022 Guo et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Funding: 1. The Guizhou Science and Technology project (S.G., grant number [2020]1Y355); 2. The Post-subsidy Fund Project of National Natural Science Foundation of China in 2019: Special project for the cultivation of novel academic seedlings and innovative exploration of Guizhou Provincial Center for Disease Control and


#### Abstract

\section*{Introduction}

Diabetes mellitus (DM), hypertension and pulmonary tuberculosis (PTB) are catastrophic illnesses that collectively lead to increased mortality and premature death. However, the size of the problem and the appropriate approach to deal with the burden is still unclear. We aimed to evaluate the yield, number needed to screen (NNS) to prevent one death or adverse event for screening DM and hypertension and assess the prevalence and contributors to DM and/or hypertension.

\section*{Methods}

Based on PTB contact tracing, a cross-sectional study was conducted among 801 PTB index cases and 972 household contacts from April 2019 to October 2020 in Guizhou, China. All the participants were screened for DM and hypertension. The yield was calculated as the proportion of newly detected cases among the study subjects, excluding known cases. The NNS was computed by dividing the number needed to treat for risk factors by the prevalence of the unrecognized diseases. The univariate and multivariate logistic regression analyses were applied to determine the independent predictors of DM and/or hypertension.

\section*{Results}

Of the 1,773 participants, the prevalence of DM and hypertension was $8.7 \%$ ( $70 / 801$ ) and $15.2 \% ~(122 / 801)$ in the PTB patients, $3.2 \%$ (31/972) and $14.0 \%$ (136/972) in the contacts, respectively. The prevalence of DM and/or hypertension was $21.2 \%$ (170/801) among the PTB patients and $15.4 \%$ (150/972) among their contacts. The screening yields to detect


Prevention 2019 (S.L., grant number 2019); 3. Thailand's Education Hub for ASEAN Countries (TEH-AC) Scholarship (S.G., grant number TEH-AC 054/2017); 4. The research reported in this publication was partially supported by the Fogarty International Center and the National Institute of Allergy and Infectious Diseases, of the National Institutes of Health (V.C., grant number D43 TW009522). The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding agencies. The sponsors or funders did not play any roles in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: Enter: The authors have declared that no competing interests exist.
new cases of DM and hypertension among PTB patients were $1.9 \%$ and $5.2 \%$, and that in the contacts were $0.8 \%$ and $4.8 \%$, respectively. The NNS for DM was 359 for the PTB cases and 977 for the contacts, 299 for PTB cases and 325 for hypertension, respectively. Older age, under or overweight and obesity, family history hypertension and earlier diagnosis of other chronic conditions were the independent predictors for DM and/or hypertension among both PTB cases and their contacts.

## Conclusion

Screening for DM and hypertension should be mandated in PTB patients and their household contacts to disclose undetected cases of these two conditions during TB contact tracing, which might reduce the potential cardiovascular disease deaths.

## Introduction

Diabetes mellitus (DM), hypertension and pulmonary tuberculosis (PTB) are still catastrophic illnesses that collectively lead to increased mortality and premature death. These chronic conditions exacerbate the progress of PTB diseases, such as delaying sputum-culture conversion from positive to negative, which has caused an obstacle in the control of PTB [1].

The prevalence of DM and hypertension is consistently found to be higher among PTB patients than among the general population. In India, the prevalence of diabetes was $7.5 \%$ for PTB patients and $4.5 \%$ for non-PTB patients and that of hypertension was $24.5 \%$ and $17.3 \%$, respectively [2]. In South Africa, $26.9 \%$ of people with PTB had one and $25.3 \%$ had at least two chronic diseases [3]. In a community-based study in China, the prevalence of DM in PTB patients ( $6.3 \%$ ) was higher than that in the non-PTB controls (4.7\%) with a 3 -fold higher odds ratio (OR) [4].

DM and hypertension are usually considered as twin diseases with substantial overlap. They are frequently concurrent, which share a common pathway and risk factors such as obesity, physical inactivity, and unhealthy lifestyle [5]. In addition, some studies reported that substantial undiagnosed cases with the comorbidity of hypertension and DM were observed [6, 7], which indicates some patients are undiagnosed and untreated, probably leading to a lot of complications, even premature deaths. However, little is known about the precise size of the problem and the appropriate approach to deal with the burden is still unclear.

Disease screening is considered to produce yields both in the clinical field and public health. Yield is the measure of previously unrecognized disease, diagnosed as the result of screening and brought to treatment [8]. According to the World Health Organization (WHO), the number needed to screen (NNS) is the number of persons that need to undergo screening in order to diagnose TB among people at-risk on TB [9]. However, a more public health intensive criteria previously proposed by Rembold was the number of people that needed to screen for a given duration to prevent one death or adverse event [10].

In this article, we analyzed and adopted Rembold's concept of NNS. If the yield is of high value and the NNS is small, the screening is supposed to add value to the resources spent in regular monitoring. Both the yield and NNS of screening for DM and hypertension were rarely evaluated in the settings of PTB control programs. Screening activities for diabetes and hypertension in the general population have increased as health systems continue to evolve [11-13]. That for diabetes and hypertension in PTB patients has also grown recently [6, 14, 15]. It is
significant to document the magnitude of yield and NNS of DM and hypertension screening among the two populations.

It is challenging to directly compare PTB patients and the general populations due to the limited actual conditions. Due to the above reasons, we conducted a large-scale PTB household contact tracing to find the magnitude of undetected NCDs. We aimed to 1) evaluate the yield of screening for DM and hypertension; 2) explore the NNS for DM and hypertension to prevent premature death from these two conditions; and 3) assess the prevalence and contributors to DM and/or hypertension. Our results would provide an insight into assessing the strategies for routine screening and control of related diseases for policymakers.

## Materials and methods

## Study design and sample size

This was a cross-sectional study based on a PTB contact-trace program conducted in Guizhou, China from April 1, 2019 to October 30, 2020.

Totally, 116 villages/communities with high PTB incidence in Guizhou were drawn as the study sites. We considered that the chances of having DM or hypertension were more similar among the household members than among the general population. This required adjusting of the sample size with design effect (Deff) [16-18], the value of which was assumed as 2.0 in this study. Eventually, the minimum sample size was computed using the infinite population proportion formula with a continuity correction as shown below.

$$
\mathrm{N}=\left[\mathrm{Z}_{1-\mathrm{a} / 2}^{2} * \mathrm{P} *(1-\mathrm{P})\right] * \text { Deff } / d^{2}
$$

where p is the prevalence of DM and hypertension of the epidemiology survey with $7.6 \%$ and $27.8 \%$, respectively in Guizhou in 2010 [19], Deff $=2.0, d=25 \% \times$ P, and the type I error rate $(\alpha)=0.05$.

The formula resulted in a sample size for DM of 1,495 and 409 for hypertension. With the consideration of a $10 \%$ rate of non-response, 1661 people were planned to be recruited for DM screening and 454 for hypertension screening.

## Relevant definitions

Yield. In different kinds of literature, the yield has different meanings. Firstly, it can be the measure of previously unrecognized disease, diagnosed as the result of screening and brought to treatment. Other forms of yield are provided by persons with known disease who have previously lapsed from treatment [8, 20, 21]. Since we ran this screening to detect the unrecognized cases of DM and hypertension, we confine our interest to the first definition. Our yield was calculated from the number of newly detected diseases among the screened population that excluded those known to be diseased. Note that the yield was calculated in other papers by positive predictive value (PPV) [22,23]. This was, however, not relevant to the purpose of our study.

Number needed to screen (NNS). The number of people that need to be screened to prevent one death or one adverse event [10]. To calculate the NNS, we added three more terms, the number needed to treat (NNT), absolute risk reduction (ARR) and the prevalence of interested disease ( PrC ). NNT is the reciprocal of the ARR, defined as the number of people that need to be treated for a given duration, such as five or ten years, to prevent one death or one adverse event [10]. ARR is the number of percentage points the risk goes down if something protective has been done to stop it [24]. The PrC is the prevalence of an interested disease that
is unrecognized $[10,25]$. Eventually, the NNS is one divided by AAR multiply one divided by PrC.

PTB index case. At least two positive results of sputum smear, or positive result of one sputum smear with chest X-ray positive subsequent to two weeks of antibiotic medication, or Xpert MTB/RIF cartridges assay positive [26], or one sputum sample cultured containing bacilli. Household contact: Lived in the same house with an index PTB patient for more than 6 hours per week [27] between 3 months earlier than the diagnosis of the PTB index case and 14 days after the PTB index case initiating anti-tuberculosis treatment.

DM. Fasting plasma glucose (FPG) $\geq 126 \mathrm{mg} / \mathrm{dl}$ or random plasma glucose (RPG) $\geq 200$ $\mathrm{mg} / \mathrm{dl}$ or a previous diagnosis of DM.

Prediabetes. FPG at least 110 but below $126 \mathrm{mg} / \mathrm{dl}$ [28] according to the parameters set by the American Diabetes Association (2016).

Hypertension. Systolic blood pressure (SBP) $\geq 140 \mathrm{mmHg}$ and/or diastolic blood pressure $(\mathrm{DBP}) \geq 90 \mathrm{mmHg}$ or with a history of previously known disease as per WHO criteria. Prehypertension: SBP 130~139 mmHg and/or DBP $85 \sim 89 \mathrm{mmHg}$ [29].

Salt-intake limit. Over 6 grams/day/adult according to the Dietary Guidelines for Chinese Residents (2016) [30].

Oil-intake limit. Over 30 grams/day/adult according to the Dietary Guidelines for Chinese Residents (2016) [30].

Smoking. Smoking in the past 12 months, including both daily and non-daily smoking.
Drinking. Drinking in the past 12 months, including both daily and non-daily drinking.

## Ethical consideration and guidelines and regulations statement

This protocol was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand (No: 61-335-18-1) and the Ethics Committee of Guizhou Centre for Disease Control and Prevention (No: Q2019-01) before this study was conducted. We confirm that all the methods were carried out in accordance with the relevant human guidelines and regulations.

## Consent to participate

Before the study was conducted, written informed consent was obtained from each study participant. For participants aged under 18 years, the information sheet was sent to their parents or legal guardians. All investigations related to them were initiated with the written informed consent of their parents or legal guardians.

## Study procedure and data collection

Initially, newly diagnosed PTB cases aged 15 years or more and currently on treatment for a duration of 0-6 months and notified to the National Tuberculosis Program from the study site were consecutively retrieved. Pregnant women, mentally disabled persons, and those living alone were excluded from the analysis.

During the patients' monthly visits to the hospital to obtain their medications, PTB medical staff would approach the patients to obtain informed consent and make an appointment with them for a home visit.

During the home visits, we surveyed up to three contacts aged 15 years or more. The simple random sampling method was used to select respondents when there were more than three adult contacts in any study household.

The presence of DM and hypertension were screened by assessing SBP/DBP and FPG/RPG among all participants following the standard criteria. The participants with different diseases
identified from the study were transferred to their local clinics to get appropriate treatment. Those with known diseases who have previously lapsed from treatment were suggested to access their local hospitals to continue medical services.

## Statistical analysis

Data obtained from the questionnaires and medical records reviewing were entered into EpiData version 3.1 (http://www.epidata.dk/). R language and environment version 3.6 .3 (https:// cran.r-project.org/) was employed for the statistical analysis. Student's t-test or ANOVA was used to compare age, FPG/RPG and SBP/DBP among groups as appropriate and summarized using the mean and standard deviation. The nonparametric Mann-Whitney $U$ test was performed for continuous variables when data were not normally distributed. Chi-square or Fisher exact tests were applied for categorical variates where appropriate.

The yield was calculated by dividing the number of newly detected diseases by the number of subjects screened, excluding those known to be diseased. The NNS was computed by dividing the NNT for risk factors by PrC. The NNT was computed through one divided by the ARR of the interested disease, which equals the risk off treatment minus the risk on treatment [31]. We obtained the estimates for ARR of DM [31] and hypertension [32] for our study from the previous studies.

The univariate analysis was applied for the risk factors contributing to DM and/or hypertension that were regarded as twin diseases. The considered variables included socio-demographic, behavioral and clinical characteristics, such as gender, age, occupation, monthly income, smoking, drinking, exercising, staying-up-late, meat-eating frequency, and family history of DM and hypertension and other non-communicable diseases (NCDs), presence of other NCDs and the knowledge of edible oil and salt intake limits.

We fitted a multivariate logistic regression model to determine the associated factors. For the outcome variable in the model, we used the subjects who were normal as the referent group and those with DM or hypertension or both of DM \& hypertension as the positive group. The independent variables were those having a $P$ value $<0.2$ in the univariate analysis. The ORs of associated factors to DM and/or hypertension from the final model were demonstrated through two forest plots [33], one for the PTB patients and another for their household contacts.

## Investigation quality control

This study mainly referred to the previous exposure of the research subjects, so recall bias might be caused by the distortion or vague memory of the respondents. We trained the investigators to collect the data with a blind method and investigate skillfully to reduce recall bias. Besides, we addressed missing data via a multiple imputation technique.

## Results

## Sampling and general characteristics

Initially, 809 index PTB cases were recruited, and 1,016 related adult household contacts were selected. Six neither responded nor participated in the disease screening test and were excluded during the in-home visits. Similarly, 39 contacts were excluded as they did not respond and therefore did not participate in the screening process. Later, two PTB index cases and their five household contacts were also excluded due to unqualified information. Eventually, 801 ( $45.2 \%$ ) PTB index cases and 972 (54.8\%) household contacts were included in the study (Fig 1).

# Consecutive sampling for pulmonary index $\mathbf{T B}$ cases $(\mathbf{n}=\mathbf{8 0 9}$ ) 



6 did not respond and 2 unqualified questionnaires excluded

Index TB cases with sputum culture $(+/-)(\mathrm{n}=801)$


Screening for DM \& HTN among 801 index TB cases and 972 household contacts through FPG/RPG test + SBP + DBP + anthropometry test + questionnaire interview including other NCDs characteristics with self-report ( $\mathrm{n}=1773$ )

Fig 1. Flowchart of study on yield, NNS and prevalence of DM/hypertension screening, 2020. PTB: tuberculosis. DM: diabetes. HTN: hypertension. NCDs refer to DM, hypertension, dyslipidemia, malignant neoplasm, chronic obstructive pulmonary disease, heart attack and chronic renal disease.
https://doi.org/10.1371/journal.pone.0263308.g001
Of the 1,773 participants, aged between 15 and 99 years, the mean (standard deviation, SD) age of PTB patients was 47.6 (19.3) years, with $62.8 \%$ males. The family contact group's mean (SD) age was 46.6 (15.7) years, with $42.8 \%$ males. Table 1 compares the background characteristics of the respondents. The PTB cases were significantly older, more likely to be male and had a lower income. The household contacts were more likely to be married or cohabitating than PTB cases. Both groups were primarily peasants and not significantly different in terms of their levels of education attained.

## Prevalence, yield and NNS of DM and hypertension

Table 2 displays the prevalence, the yield and the NNS of screening for DM and hypertension. The prevalence of DM among PTB patients was $(56+14) / 801=8.7 \%$. This was statistically significantly higher than among the contact of $(23+8) / 972=3.2 \%$ ( $P$ value of Chi-square test $<0.01)$. Similarly, the yield or newly detected rate in the PTB group $(14 / 745=1.9 \%)$ was significantly higher than that in the contact group $(8 / 949=0.8 \%)$ with $P$ value $<0.01$. On the contrary, the NNS of the former (359) is lower than that of the latter (977).

Table 1. Socio-demographic characteristics of study participants (n, \%).

| Demographic Characteristics |  | Total | Patient | Contact | $P$ value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Total |  | 1773 | 801 | 972 |  |
| Age group (years) | 15~34 | 503(28.4) | 254(50.5) | 249(49.5) | $<0.001$ |
|  | 35~59 | 814(45.9) | 298(36.6) | 516(63.4) |  |
|  | 60~100 | 456(25.7) | 249(54.6) | 207(45.4) |  |
| Gender | Female | 854 (48.2) | 298 (37.2) | 556 (57.2) | $<0.001$ |
|  | Male | 919 (51.8) | 503 (62.8) | 416 (42.8) |  |
| Education | Below primary | 833 (47.0) | 368 (45.9) | 465 (47.8) | 0.148 |
|  | Middle school | 784 (44.2) | 351 (43.8) | 433 (44.5) |  |
|  | University and above | 156 (8.8) | 82 (10.2) | 74 (7.6) |  |
| Occupation | Clerk | 79 (4.5) | 38 (4.7) | 41 (4.2) | 0.002 |
|  | Student | 90 (5.1) | 56 (7) | 34 (3.5) |  |
|  | Peasant | 987 (55.7) | 418 (52.2) | 569 (58.5) |  |
|  | Migrant-laborer | 617 (34.8) | 289 (36.1) | 328 (33.7) |  |
| Marriage | Single | 105 (5.9) | 68 (8.5) | 37 (3.8) | $<0.001$ |
|  | Married/cohabitating | 1398 (78.8) | 559 (69.8) | 839 (86.3) |  |
|  | Separated/divorced/widowed | 270 (15.2) | 174 (21.7) | 96 (9.9) |  |
| Monthly income (CNY) | 0~999 | 688 (38.8) | 365 (45.6) | 323 (33.2) | $<0.001$ |
|  | 1,000~2,999 | 660 (37.2) | 254 (31.7) | 406 (41.8) |  |
|  | 3,000~4,999 | 302 (17) | 124 (15.5) | 178 (18.3) |  |
|  | 5,000~ | 123 (6.9) | 58 (7.2) | 65 (6.7) |  |

## Note CNY: Chinese yuan.

https://doi.org/10.1371/journal.pone.0263308.t001

There was no significant difference in hypertension prevalence between the two groups $(15.2 \%$ vs. $14.0 \%)$. So was the difference in the yield ( $5.2 \%$ vs. $4.8 \%$ ). Consequently, the NNSs for hypertension of both groups were close ( 299 vs. 325).

Overall, with many times that the screening yield of hypertension was higher than DM, the NNS for hypertension was consistently lower than that for DM in all groups.

Table 2. Prevalence, percent yield and NNS of DM/hypertension screening, 2020 ( $\mathrm{n}, \%$ ).

| Subject group | Non-diabetes (a) | Prediabetes (b) | Diabetes |  | $\begin{aligned} & \text { Yield }=[(\mathbf{d}) /(\mathbf{a}+\mathrm{b} \\ & +\mathrm{d})] \times \mathbf{1 0 0}(\%) \end{aligned}$ | $\begin{gathered} \text { Prevalence }(\text { PrC })=[(c+d) /(a \\ +b+c+d)] \times \mathbf{1 0 0}(\%) \end{gathered}$ | $\mathbf{A R R}^{\#}$ | $\text { NNT }^{\# \#}$ | $\mathbf{N N S}^{\# \# \#}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | Previously known (c) | Newly detected (d) |  |  |  |  |  |
| Total | 1,218 | 454 | 79 | 22 | 1.3 | 5.7 | 0.032 | 31 | 548 |
| Patient | 523 | 208 | 56 | 14 | 1.9* | 8.7* | 0.032 | 31 | 359 |
| Contact | 695 | 246 | 23 | 8 | 0.8 | 3.2 | 0.032 | 31 | 977 |
| Subject group | Nonhypertension (a) | Prehypertension <br> (b) | Hypertension |  | $\begin{aligned} & \text { Yield }=[(\mathbf{d}) /(\mathrm{a}+\mathrm{b} \\ & +\mathrm{d})] \times \mathbf{1 0 0}(\%) \end{aligned}$ | $\begin{gathered} \text { Prevalence }(\text { PrC })=[(\mathrm{c}+\mathrm{d}) /(\mathrm{a} \\ +\mathrm{b}+\mathrm{c}+\mathrm{d})] \times \mathbf{1 0 0}(\%) \end{gathered}$ | $\mathbf{A R R}^{\#}$ | $\mathbf{N N T}^{\# \#}$ | $\mathrm{NNS}^{\# \# \#}$ |
|  |  |  | Previously known (c) | Newly detected (d) |  |  |  |  |  |
| Total | 1,220 | 295 | 179 | 79 | 5.0 | 14.6 | 0.022 | 45 | 311 |
| Patient | 554 | 125 | 85 | 37 | 5.2 | 15.2 | 0.022 | 45 | 299 |
| Contact | 666 | 170 | 94 | 42 | 4.8 | 14.0 | 0.022 | 45 | 325 |

Note ${ }^{\#}$ ARR: Absolute risk reduction $\left(A R R_{D M}=0.032, A R R_{\text {hypertension }}=0.022\right) .{ }^{\# \#}$ NNT: Number needed to treat (NNT $\left.=1 / A R R\right) .{ }^{\# \# \#}$ NNS: Number needed to screen to save one life (NNS $=\mathrm{NNT} / \operatorname{PrC}) .{ }^{*} P$ value $<0.05$ compared to the contact group.
https://doi.org/10.1371/journal.pone.0263308.t002

Table 3. Prevalence of DM and/or hypertension and DM \& hypertension, 2020 ( $\mathrm{n}, \%$ ).

| Variable |  | Total | Gender |  |  | Age (year-old) |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Female | Male | $P$ value | 15~34 | 35~59 | 60~100 | $P$ value |
| Diabetes or hypertension | patient |  | 170(21.2) | 56 (18.8) | 114 (22.7) | 0.23 | 9 (3.5) | 57 (19.1) | 104 (41.8) | $<0.001$ |
|  | contact | 150(15.4) | 83 (14.9) | 67 (16.1) | 0.68 | 9 (3.6) | 65 (12.6) | 76 (36.7) | $<0.001$ |
|  | $P$ value | 0.002 |  |  |  |  |  |  |  |
| Diabetes and Hypertension | patient | 22(2.7) | 6 (2.0) | 16 (3.2) | 0.451 | 0 (0.0) | 7 (2.3) | 15 (6.0) | $<0.001$ |
|  | contact | 17(1.7) | 9 (1.6) | 8 (1.9) | 0.807 | 1 (0.4) | 7 (1.4) | 9 (4.3) | 0.006 |
|  | $P$ value | 0.207 |  |  |  |  |  |  |  |
| Prediabetes or prehypertension | patient | 302(37.7) | 98 (32.9) | 204 (40.6) | 0.037 | 75 (29.5) | 121 (40.6) | 106 (42.6) | 0.005 |
|  | contact | 371(38.3) | 199 (35.8) | 172 (41.3) | 0.09 | 76 (30.5) | 207 (40.1) | 88 (42.5) | 0.013 |
|  | $P$ value | 0.879 |  |  |  |  |  |  |  |
| Prediabetes and Prehypertension | patient | 31(3.9) | 8 (2.7) | 23 (4.6) | 0.25 | 4 (1.6) | 16 (5.4) | 11 (4.4) | 0.061 |
|  | contact | 45(4.6) | 21 (3.8) | 24 (5.8) | 0.191 | 4 (1.6) | 34 (6.6) | 7 (3.4) | 0.006 |
|  | $P$ value | 0.504 |  |  |  |  |  |  |  |

https://doi.org/10.1371/journal.pone.0263308.t003

## Breakdown of prevalence of DM and/or hypertension

Table 3 displays the prevalence of DM and/or hypertension and DM comorbid with hypertension. The prevalence of DM and/or hypertension was $21.2 \%$ (170/801) among the PTB patients and $15.4 \%$ (150/972) among their household contacts. The prevalence of DM comorbid with hypertension was $2.7 \%(22 / 801)$ among the former and $1.7 \%$ (17/972) among the latter. High proportions of prediabetes and prehypertension were detected in PTB patients and their families. Except for prediabetes and prehypertension in PTB cases, the prevalence of the other identified diseases of the two groups increased significantly with increasing age.

## Univariate analysis for DM and/or hypertension

Taking the presence of DM and/or hypertension as the dependent variable, the univariate analysis was conducted using the Chi-square test or Fisher test. Older age, less education, underweight or obesity, being separated/divorced/widowed, family history of hypertension and other NCDs and an earlier diagnosis of other NCDs were the associated factors of DM and/or hypertension according to the univariate analysis.

Among the PTB patients, DM and/or hypertension was more likely to occur among peasants and those individuals with a family history of DM or with sputum-smear positive results.

In the household contacts, those with a lower monthly income, or knew the limit of saltintake, or were depressed and cared for their PTB patients were more likely to have DM and/ or hypertension ( $P$ values are available in the S1 Table).

## Forest plots of multivariate logistic regression analysis

With the presence of DM and/or hypertension as the dependent variable, the variables with a $P$ value $<0.2$ got from the univariate analysis as the independent variables, a multivariate logistic regression model was applied to determine the independent predictors.

Figs 2 and 3 display the forest plots of the independent predictors of DM and/or hypertension among PTB index cases and their household contacts. Older age, under or overweight and obesity, hypertension family history, and earlier diagnosis of other NCDs were the collectively independent predictors of DM and/or hypertension for both PTB index cases and their household contacts. Having a family history of DM was the positively associated factor of DM

# Odds Ratios of Predictors to Presence of DM and/or HTN (VS Normal Subjects) 



Fig 2. Adjusted odds ratios of association to DM and/or hypertension among the PTB patients, 2020. Blueline refers to $95 \% \mathrm{CI}$. * Stands for $P$ values, ${ }^{* * * * '}<0.001^{* * * *}$ $<0.01^{* \prime}<0.05$. DM: diabetes mellitus. HTN: hypertension. NCDs refer to DM, hypertension, dyslipidemia, malignant neoplasm, chronic obstructive pulmonary disease, heart attack, chronic renal disease. Diagnosed NCDs refer to been diagnosed as NCD patients mentioned above except for DM and hypertension. Other marital statuses: Separated/divorced/widowed.
https://doi.org/10.1371/journal.pone.0263308.g002
and/or hypertension among the PTB cases (Fig 2). Lower-income and smoking were significantly associated with DM and/or hypertension in the household contacts (Fig 3).

## Discussion

The prevalence of DM was more than two times higher among the index PTB cases than their household contacts, whereas the prevalence of hypertension in the two groups was close. Undetected hypertension was more common than undetected DM in both groups. As a result, the yield of screening for hypertension is higher and the NNS was lower than that for DM.

Our prevalence of DM or hypertension is slightly lower than in a survey conducted in the general population in 2010 of Guizhou ( $7.6 \%$ and $27.8 \%$, respectively) [19]. The lower prevalence might be because the participants in our study were younger than those in the survey in 2010 ( $\geq 15$ years vs. $\geq 18$ years). In the current study, DM and hypertension co-existed in $2.2 \%$

# Odds Ratios of Predictors to Presence of DM and/or HTN (VS Normal Subjects) 



Fig 3. Adjusted odds ratios of association to DM and/or hypertension among the household contacts, 2020. Blueline refers to 95\%CI. * Stands for $P$ values, ${ }^{* * * * ' ~}<$ $0.001^{\text {(**) }}<0.01^{\text {(*) }}<0.05$. DM: diabetes mellitus. HTN: hypertension. NCD refers to DM, hypertension, dyslipidemia, malignant neoplasm, chronic obstructive pulmonary disease, heart attack, chronic renal disease. Diagnosed NCD refers to been diagnosed as NCD patient mentioned above except for DM and hypertension. Other marital statuses: Separated/divorced/widowed.
https://doi.org/10.1371/journal.pone.0263308.g003
(2.7\% among the PTB cases and $1.7 \%$ in the contacts), slightly lower than $4.5 \%$ in the general population of an Indian study [34], while the DM prevalence among PTB cases was higher than $6.0 \%$ reported in a study from Angola [6]. PTB patients comorbid with DM have a lower concentration of anti-tuberculosis drugs and a higher risk of drug toxicity than tuberculosis patients without DM [35], indicating that PTB patients should be remained a priority group for medical services on chronic conditions. However, chronic diseases in their family contacts
also should be properly managed because we observed a significant proportion of prediabetes and prehypertension in these participants who were considered a substitute for the general population. Furthermore, the household contacts might carry similar susceptible genes with their index cases, such as speckle 110 (SP110), or human leukocyte antigen (HLA), which might be the possibly susceptible genes to the occurrence of DM or TB disease [36-38].

Just like PTB, early detection of DM and hypertension is of value in preventing related complications. In our study, the NNS for detecting DM was 359 in PTB patients and 977 in the household contacts. The respective numbers for hypertension were 299 and 325. The values of NNS in PTB cases were lower than that in their family in both DM and hypertension; especially for DM, the difference even reached three times. The NNS indicates how many persons needed to screen for a given duration to prevent one death or adverse event. The lower the NNS is, the more pivotal the screening would be. Therefore, in our sampled participants, 359 PTB index cases, or 977 household contacts, are needed to be screened for DM to prevent one death or adverse event for a given duration if the detection was followed by a routine treatment for the patients [10]. The number of contacts is 3-fold over that of PTB cases, which might be because the risk of developing DM is higher in the PTB group than in their household contacts. In other words, the TB patients' screening of DM and hypertension should not be missed, and their contacts must be investigated during the contact tracing activities. Our NNS number of hypertension (311) is similar to 274 in a study of Rembold [10]. Note that the NNS numbers were lower for hypertension than that for DM as hypertension is known to have an immense contribution to cardiovascular disease death in the population.

The NNS matters and so does the yield. The yield reflects the importance of these sample screenings among the PTB cases and their families. The greater the yield is, the more probability of the interesting disease the screened people would have. The estimated percent yield in the PTB cases was almost three times (1.9\%) over their family ( $0.8 \%$ ) for DM addition to the known DM cases, which had further addressed the more priority of medical service related to DM the PTB cases should have [10]. The yield values of screening hypertension in the PTB cases and household contacts were similar. However, our data point out that neglected or undetected hypertension is more common. The yield of hypertension was 3 to 6 times higher than that of DM. More importantly, blood pressure screening can save more lives than DM screening. Thus, hypertension screening should always accompany DM screening, and chronic conditions should be investigated as routine screening programs. This approach is particularly justified in some countries with obtaining the high yield of newly detected cases [11-13].

In our study, older age, under or overweight and obesity, family history of hypertension and earlier diagnoses of other NCDs were identified as the contributors to DM and/or hypertension. Disease screening among critical populations is suggested regarding these risk factors since it may bring more benefits [39-41].

Our study is in line with the previous studies on yield and NNS for screening DM and hypertension in PTB patients and their families [11-14]. The values of NNS and yield were not directly comparable due to the difference in definitions of the two terms. Yet, our study posts an insight into the chronic conditions among households with a PTB case, which makes significant implications in the control programs for TB and NCDs.

## Limitations

There were some limitations in this study. First, it is challenging to address which appeared first between PTB and DM and/or hypertension due to the cross-sectional design and the nature of the three illnesses. Second, the subjects included only index PTB patients and their
household contacts. Although household contacts are considered a substitute for the general population, the two populations might have different socio-demographic characteristics.
Therefore, the study was unable to directly compare the prevalence data of DM and hypertension, prediabetes and prehypertension between PTB cases and the general population. Prudence should be observed when the results of this study are generalized.

## Conclusion

Screening for DM and hypertension should be mandated in PTB patients and their household contacts to disclose undetected cases of these two conditions during the TB contact tracing, which might reduce the potential cardiovascular disease deaths.

## Supporting information

S1 Checklist. STROBE statement-checklist of items that should be included in reports of observational studies.
(DOCX)
S1 Table. Univariate analysis for DM and/or hypertension.
(PDF)
S1 File. Study protocol \& questionnaire for study on yield, NNS and prevalence of screening for diabetes mellitus and hypertension.
(PDF)
S1 Data. Original data for study on yield, NNS and prevalence of screening for diabetes mellitus and hypertension.
(XLSX)

## Acknowledgments

This study is a part of the first author's thesis to fulfill the requirement of a Ph.D. degree in Epidemiology, Prince of Songkla University, Thailand. Doctor Angkana Chaiprasert and Assistant Professor Edward McNeil are acknowledged for their comments and revisions in the preparation of the protocol and manuscript. The authors acknowledge the contribution of the Centers for Disease Control and Prevention and the Designated TB Hospitals in Guizhou Province.

## Author Contributions

Conceptualization: Shengqiong Guo, Virasakdi Chongsuvivatwong.
Data curation: Shengqiong Guo, Virasakdi Chongsuvivatwong.
Formal analysis: Shengqiong Guo, Virasakdi Chongsuvivatwong.
Funding acquisition: Shengqiong Guo, Virasakdi Chongsuvivatwong, Shiguang Lei.
Investigation: Shengqiong Guo, Min Guo, Shiguang Lei, Jinlan Li, Huijuan Chen, Jiangping Zhang, Wen Wang, Cui Cai.

Methodology: Shengqiong Guo, Virasakdi Chongsuvivatwong.
Project administration: Shengqiong Guo.
Resources: Shengqiong Guo.
Software: Shengqiong Guo, Virasakdi Chongsuvivatwong.

Supervision: Shengqiong Guo, Virasakdi Chongsuvivatwong, Shiguang Lei.
Validation: Shengqiong Guo, Virasakdi Chongsuvivatwong, Shiguang Lei.
Visualization: Shengqiong Guo, Virasakdi Chongsuvivatwong.
Writing - original draft: Shengqiong Guo, Virasakdi Chongsuvivatwong.
Writing - review \& editing: Shengqiong Guo, Virasakdi Chongsuvivatwong.

## References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Research and Clinical Practice. 2019; 157:107843. https://doi.org/10.1016/j. diabres.2019.107843 PMID: 31518657
2. Marak B, Kaur P, Rao SR, Selvaraju S. Non-communicable disease comorbidities and risk factors among tuberculosis patients, Meghalaya, India. Indian Journal of Tuberculosis. 2016; 63(2):123-125. https://doi.org/10.1016/j.ijtb.2015.07.018 PMID: 27451823
3. Peltzer K. Tuberculosis non-communicable disease comorbidity and multimorbidity in public primary care patients in South Africa. Afr j prim health care fam med. 2018; 10(1). https://doi.org/10.4102/ phcfm.v10i1.1651 PMID: 29781683
4. Wang Q, Ma A, Han X, Zhao S, Cai J, Ma Y, et al. Prevalence of Type 2 Diabetes among Newly Detected Pulmonary Tuberculosis Patients in China: A Community Based Cohort Study. PLoS Study. PLoS One. 2013; 8(12). https://doi.org/10.1371/journal.pone. 0082660 PMID: 24367535
5. Sharma B, Khanal VK, Jha N, Pyakurel P, Gurung GN. Study of the magnitude of diabetes and its associated risk factors among the tuberculosis patients of Morang, Eastern Nepal. BMC Public Health. 2019; 19. https://doi.org/10.1186/s12889-019-7891-x PMID: 31752802
6. Segafredo G, Kapur A, Robbiati C, Joseph N, Sousa JR de, Putoto G, et al. Integrating TB and noncommunicable diseases services: Pilot experience of screening for diabetes and hypertension in patients with Tuberculosis in Luanda, Angola. PLOS ONE. 2019; 14:e0218052. https://doi.org/10.1371/ journal.pone. 0218052 PMID: 31276500
7. Ogbera AO, Kapur A, Chinenye S, Fasanmade O, Uloko A, Odeyemi K. Undiagnosed diabetes mellitus in tuberculosis: A Lagos report. Indian J Endocrinol Metab. 2014; 18(4):475-479. https://doi.org/10. 4103/2230-8210.137488 PMID: 25143901
8. Wilson J, Jungner G. The Principles and Practice of Screening for Disease. World Health Organization Public Health Papers \#34. 1967;22.
9. WHO consolidated guidelines on tuberculosis Module 2: Screening-Systematic screening for tuberculosis disease. Accessed November 8, 2021. https://www.who.int/publications-detail-redirect/ 9789240022676.
10. Rembold C. Number needed to screen: Development of a statistic for disease screening. BMJ (Clinical research ed). 1998; 317:307-312. https://doi.org/10.1136/bmj.317.7154.307 PMID: 9685274
11. Pastakia SD, Ali SM, Kamano JH, Akwanalo CO, Ndege SK, Buckwalter VL, et al. Screening for diabetes and hypertension in a rural low income setting in western Kenya utilizing home-based and commu-nity-based strategies. Global Health. 2013; 9:21. https://doi.org/10.1186/1744-8603-9-21 PMID: 23680083
12. Kubiak RW. Prevalence and risk factors for hypertension and diabetes among those screened in a refugee settlement in Uganda. 2021; 15(1): 1-8. https://doi.org/10.1186/s13031-021-00388-z PMID: 34225741
13. Heianza Y, Arase Y, Saito K, Hsieh SD, Tsuji H, Kodama S, et al. Development of a Screening Score for Undiagnosed Diabetes and Its Application in Estimating Absolute Risk of Future Type 2 Diabetes in Japan: Toranomon Hospital Health Management Center Study 10 (TOPICS 10). The Journal of Clinical Endocrinology \& Metabolism. 2013; 98(3):1051-1060. https://doi.org/10.1210/jc.2012-3092 PMID: 23393174
14. Byrne AL, Marais BJ, Mitnick CD, Garden FL, Lecca L, Contreras C, et al. Feasibility and yield of screening for non-communicable diseases among treated tuberculosis patients in Peru. The International Journal of Tuberculosis and Lung Disease. 2018; 22(1):86-92. https://doi.org/10.5588/ijtld.17. 0381 PMID: 29297431
15. Kumpatla S, Aravindalochanan V, Rajan R, Viswanathan V, Kapur A. Evaluation of performance of A1c and FPG tests for screening newly diagnosed diabetes defined by an OGTT among tuberculosis
patients—A study from India. Diabetes Research and Clinical Practice. 2013; 102(1):60-64. https://doi. org/10.1016/j.diabres.2013.08.007 PMID: 24035281
16. Aamir AH, Ul-Haq Z, Mahar SA, Qureshi FM, Ahmad I, Jawa A, et al. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA 1 c : a popula-tion-based survey from Pakistan. BMJ Open. 2019; 9(2):e025300. https://doi.org/10.1136/bmjopen-2018-025300 PMID: 30796126
17. Basit A, Fawwad A, Qureshi H, Shera AS. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016-2017. BMJ Open. 2018; 8(8): e020961. https://doi.org/10.1136/bmjopen-2017-020961 PMID: 30082350
18. Organization WH. World Health Organization vaccination coverage cluster surveys: reference manual. World Health Organization; 2018.
19. Liu Tao, Wang Dingming, Sun Liangxian. Status of Chronic Disease and Associated Factors in Guizhou. Guizhou science and technology press, Guiiyang, 2015. https://www.amazon.cn/dp/ B06XCS8BZS.
20. Zhang C, Ruan Y, Cheng J, Zhao F, Xia Y, Zhang H, et al. Comparing yield and relative costs of WHO TB screening algorithms in selected risk groups among people aged 65 years and over in China, 2013. PLoS ONE. 2017; 12. https://doi.org/10.1371/journal.pone.0176581 PMID: 28594824
21. Basic Epidemiology for Tuberculosis Program Staff, 2nd Edition | National Prevention Information Network | Connecting public health professionals with trusted information and each other. Accessed November 1, 2021. https://npin.cdc.gov/publication/basic-epidemiology-tuberculosis-program-staff-2nd-edition.
22. Molinaro A. Diagnostic tests: How to estimate the positive predictive value. Neuro-Oncology Practice. 2015; 2:npv030. https://doi.org/10.1093/nop/npv030 PMID: 31386059
23. Parikh R, Mathai A, Parikh S, Chandra Sekhar G, Thomas R. Understanding and using sensitivity, specificity and predictive values. Indian J Ophthalmol. 2008; 56(1):45-50. https://doi.org/10.4103/03014738.37595 PMID: 18158403
24. Absolute vs. Relative Risk: What Does Percentage Risk Really Mean?. Breastcancer.org. 2016. Accessed November 1, 2021. https://www.breastcancer.org/risk/understand/abs_v_rel.
25. Porta M. A Dictionary of Epidemiology. Oxford University Press; 2014. 377 p. https://play.google.com/ books/reader?id=vEZmAwAAQBAJ\&pg=GBS.PA200.
26. Kenaope L, Ferreira H, Seedat F, Otwombe K, Martinson N, Variava E. Sputum culture and drug sensitivity testing outcome among X-pert MTB/Rif positive, rifampicin resistant sputa: A retrospective studyNot all rifampicin resistance is MDR. Journal of Global Antimicrobial Resistance. 2019; 21. https://doi. org/10.1016/j.jgar.2019.11.008 PMID: 31733411
27. A household-level score to predict the risk of tuberculosis among contacts of patients with tuberculosis: a derivation and external validation prospective cohort study | Elsevier Enhanced Reader. Reader. https://doi.org/10.1016/S1473-3099(19)30423-2.
28. Kerner W, Brückel J. Definition, Classification and Diagnosis of Diabetes Mellitus. Experimental and Clinical Endocrinology \& Diabetes. 2014; 122(07):384-386. https://doi.org/10.1055/s-0034-1366278 PMID: 25014088
29. WHO | Implementation tools. WHO. Accessed September 28, 2018. http://www.who.int/ cardiovascular_diseases/publications/implementation_tools_WHO_PEN/en/.
30. Zhang N, Du SM, Ma GS. Current lifestyle factors that increase risk of T2DM in China. European Journal of Clinical Nutrition. 2017; 71(7):832-838. https://doi.org/10.1038/ejcn.2017.41 PMID: 28422119
31. Kaasenbrood L, Poulter NR, Sever PS, Colhoun HM, Livingstone SJ, Boekholdt SM, et al. Development and Validation of a Model to Predict Absolute Vascular Risk Reduction by Moderate-Intensity Statin Therapy in Individual Patients With Type 2 Diabetes Mellitus. Circulation: Cardiovascular Quality and Outcomes. 2016; 9(3):213-221. https://doi.org/10.1161/CIRCOUTCOMES.115.001980 PMID: 27174798
32. Ho C, Breslin M, Doust J, Reid C, Nelson M. Effectiveness of blood pressure-lowering drug treatment by levels of absolute risk: Post hoc analysis of the Australian National Blood Pressure Study. BMJ Open. 2018; 8:e017723. https://doi.org/10.1136/bmjopen-2017-017723 PMID: 29555790
33. Codewar. How draw forestplot for regression in R. csdnCSDN: https://blog.csdn.net/tm_ggplot2/article/ details/113705379. Available from: https://blog.csdn.net/tm_ggplot2/article/details/113705379?ops_ request_misc=\%257B\%2522request\%255Fid\%2522\%253A\%2522162753384816780366575335\% 2522\%252C\%2522scm\%2522\%253A\%252220140713.130102334.pc\%255Fblog.\%2522\% 257D\&request_id=162753384816780366575335\&biz_id=0\&utm_medium=distribute.pc_search_ result.none-task-blog-2~blog~first_rank_v2~rank_v29-1113705379.pc_v2_rank_blog_default\&utm_ term=\%E6\%A3\%AE\%E6\%9E\%97\&spm=1018.2226.3001.4450.
34. Tripathy JP, Thakur JS, Jeet G, Jain S. Prevalence and determinants of comorbid diabetes and hypertension: Evidence from non communicable disease risk factor STEPS survey, India. Diabetes \& Metabolic Syndrome: Clinical Research \& Reviews. 2017; 11:S459-S465. https://doi.org/10.1016/j.dsx. 2017.03.036 PMID: 28395951
35. Riza AL, Pearson F, Ugarte-Gil C, Alisjahbana B, van de Vijver S, Panduru NM, et al. Clinical management of concurrent diabetes and tuberculosis and the implications for patient services. Lancet Diabetes Endocrinol. 2014; 2(9):740-753. https://doi.org/10.1016/S2213-8587(14)70110-X PMID: 25194887
36. Chang S-Y, Chen M-L, Lee M-R, Liang Y-C, Lu T-P, Wang J-Y, et al. SP110Polymorphisms Are Genetic Markers for Vulnerability to Latent and Active Tuberculosis Infection in Taiwan. Disease Markers. 2018;1-12. https://doi.org/10.1155/2018/4687380 PMID: 30627224
37. Hindi K, Khazal N. Human leukocyte antigen-genotyping according to sex in extrapulmonary tuberculosis patients in Iraq. Reviews in Medical Microbiology. 2021; 32:124-7. https://doi.org/10.1097/MRM. 0000000000000240
38. Kust SA, Streltsova MA, Panteleev AV, Karpina NL, Lyadova IV, Sapozhnikov AM, et al. HLA-DR-Positive NK Cells Expand in Response to Mycobacterium Tuberculosis Antigens and Mediate Mycobacte-ria-Induced T Cell Activation. Frontiers in Immunology. 2021; 12:1531. https://doi.org/10.3389/fimmu. 2021.662128 PMID: 34012446
39. Shiferaw DA, Mekonnen HS, Abate AT. House-hold contact tuberculosis screening adherence and associated factors among tuberculosis patients attending at health facilities in Gondar town, northwest, Ethiopia. BMC Infect Dis. 2019; 19. https://doi.org/10.1186/s12879-019-4695-7 PMID: 31852545
40. Workneh MH, Bjune GA, Yimer SA. Prevalence and associated factors of tuberculosis and diabetes mellitus comorbidity: A systematic review. PLoS One. 2017; 12(4). https://doi.org/10.1371/journal. pone. 0175925 PMID: 28430796
41. Sarker M, Barua M, Guerra F, Saha A, Aftab A, Latif AHMM, et al. Double Trouble: Prevalence and Factors Associated with Tuberculosis and Diabetes Comorbidity in Bangladesh. PLoS One. 2016; 11(10). https://doi.org/10.1371/journal.pone. 0165396 PMID: 27798659
