BMJ Open

Tuberculosis infection and hypertension: Prevalence estimates from the US National Health and Nutrition Examination Survey

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-075176
Article Type:	Original research
Date Submitted by the Author:	28-Apr-2023
Complete List of Authors:	Salindri, Argita; Stanford University School of Medicine, Department of Medicine Auld, Sara; Emory University School of Medicine, Division of Pulmonary and Critical Care Medicine; Emory University School of Public Health, Department of Epidemiology Gujral, Unjali; Emory University School of Public Health, Hubert Department of Global Health Urbina, Elaine; University of Cincinnati College of Medicine, Department of Pediatrics Andrews, Jason R; Stanford University School of Medicine, Division of Infectious Diseases and Geographic Medicine, Department of Medicine Huaman, Moises; University of Cincinnati College of Medicine, Department of Internal Medicine Magee, Matthew J.; Emory University School of Public Health, Hubert Department of Global Health; Emory University School of Public Health, Department of Epidemiology
Keywords:	Hypertension < CARDIOLOGY, Tuberculosis < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title Page

Prepared according to manuscript instructions for *BMJ Open* (original research)

Version: April 13, 2023

Title: Tuberculosis infection and hypertension: Prevalence estimates from the US National Health and Nutrition Examination Survey

Authors:

Argita D. Salindri[1], Sara C. Auld[2,3], Unjali P. Gujral[4], Elaine M. Urbina[5], Jason R. Andrews[1], Moises A. Huaman[6*], Matthew J. Magee[3,4*]

Affiliations:

1. Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, CA, USA
2. Division of Pulmonary and Critical Care Medicine, Emory University School of Medicine, Atlanta, GA, USA
3. Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
4. Hubert Department of Global Health, Emory University Rollins School of Public Health, Atlanta, GA, USA
5. Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH, USA
6. Department of Internal Medicine, College of Medicine, University of Cincinnati, Cincinnati, OH, USA

*Equal contribution

Main Article word count: 3179

Abstract count: 250/250

Key points: 37/40

Tables & Figures: 5/Not specified

References: 38/40

Keywords: latent tuberculosis infection, interferon-γ response, hypertension

Summary:

The prevalence of hypertension was high (59%) among adults with tuberculosis infection in the U.S. In addition, we found that the prevalence of hypertension was significantly higher among adults with positive QFT without established hypertension risk factors.

Corresponding Author:

Argita Salindri, PhD, MPH

Division of Infectious Diseases and Geographic Medicine

Department of Medicine

Stanford University School of Medicine

Biomedical Innovations Building, Stanford, CA 94304

Email: adsalind@stanford.edu

Phone: +1 404 490 5906

ABSTRACT

Objectives: Latent Tuberculosis infection (LTBI) is marked by dynamic host-pathogen interactions with persistent low-grade inflammation and is associated with increased risk of cardiovascular diseases (CVD) including acute coronary syndrome, myocardial infarction, and stroke. However, few studies assess the relationship between LTBI and hypertension, an intermediate of CVD. We sought to determine the association between LTBI and hypertension using data representative of the adult US population.

Methods: We performed cross-sectional analyses using data from the 2011–2012 US National Health and Nutrition Examination Survey (NHANES). Eligible participants included adults with valid QuantiFERON-TB Gold In-Tube (QFT-GIT) test results who also had blood pressure measures and no history of TB disease. LTBI was defined by a positive QFT-GIT. We defined hypertension by either elevated measured blood pressure levels (i.e., systolic ≥130mmHg or diastolic ≥80mmHg) or known hypertension indications (i.e., self-reported previous diagnosis or use of antihypertensive medications). Analyses were performed using robust quasi-Poisson regressions and accounted for the stratified probability sampling design of NHANES.

Results: The overall prevalence of LTBI was 5.7% (95%CI 4.7–6.7) and hypertension was present among 48.9% (95%CI 45.2–52.7) of participants. The prevalence of hypertension was higher among those with LTBI (58.5%, 95%CI 52.4–64.5) than those without LTBI (48.3%, 95%CI 44.5–52.1) (prevalence ratio [PR]=1.2, 95%CI 1.1–1.3). However, after adjusting for confounders, the prevalence of hypertension was similar for those with and without LTBI (adjusted PR=1.0, 95%CI 0.9 –1.1). Among individuals without CVD risk factors of elevated BMI ($PR_{normal\ BMI}$=1.6, 95%CI 1.2–2.0), hyperglycemia ($PR_{euglycemia}$=1.3, 95%CI 1.1–1.5), or cigarette smoking ($PR_{non\text{-}smokers}$=1.2, 95%CI 1.1–1.4), the unadjusted prevalence of hypertension was higher among those with LTBI vs. no LTBI (Figure 1).

Conclusions: More than half of adults with LTBI in the US had hypertension. Importantly, we observed a relationship between LTBI and hypertension among those without established CVD risk factors.

Strengths and limitations

Strengths:

- These analyses were conducted using data representative of civilian, non-institutionalized US adults, and thus, provide a robust population estimate of the prevalence of latent tuberculosis infection and hypertension in the US
- Comprehensive definitions and different cut-offs of hypertension were used (i.e., measured blood pressure level, previous diagnosis hypertension by healthcare providers) to model the association between latent tuberculosis infection and hypertension

Limitations:

Our findings may not be representative to other regions with higher burdens of tuberculosis

- The cross-sectional study design of NHANES prevented us from assessing the temporal relationship between latent tuberculosis infection and hypertension

INTRODUCTION

About one-quarter of the world's population (~2 billion) has been infected to *Mycobacterium tuberculosis* (*Mtb*). [1] Among individuals infected with the bacteria, 5-10% are at risk of developing TB disease at some point in their life. [2 3] Tuberculosis infection (TBI), or most commonly known as latent tuberculosis infection or LTBI, is increasingly recognized as a heterogenous clinical state in which some individuals have dynamic host-pathogen interactions with persistent low-grade inflammation. This immune dysregulation has been associated with an increased risk of cardiovascular diseases (CVD) including acute coronary syndromes, myocardial infarction, and stroke. [1 4-12] This convergence of TBI and CVD risk poses a particular challenge for low- and middle-income countries where TBI is most prevalent and incidence of chronic non-communicable diseases, including CVD, is increasing rapidly. [13 14] Improved understanding of the impact of TBI on CVD risk is vital in settings where TBI and CVD are highly co-prevalent in order to design public health intervention programs aiming to reduce the burden of two diseases.

Epidemiologic data from observational cohort studies support an increased risk of CVD among people with TB disease. [8-12] Several studies also indicated that hypertension, an established intermediate of CVD, may be more common among patients with TB disease compared to non-TB controls [8 11 15-17]. Furthermore, CVD was the leading contributor to post-TB mortality, accounting for 15 – 26% of deaths among TB survivors in a recent systematic review and meta-analysis. [18] In addition to these associations between TB disease and CVD, recent observational studies have found an association between TBI and various CVDs including acute myocardial infarction and coronary artery disease. [9 19 20]. However, studies assessing the association between TBI and hypertension remain limited.

To date, few studies have evaluated the relationship between TBI and hypertension. One cohort study from a large metropolitan healthcare system in the U.S. reported that

individuals with TBI had greater incidence of hypertension compared to those without TBI and that rates were highest among those untreated for TBI. [5] Furthermore, it is unknown whether the quantitative measures of IGRA, which may indicate the underlying mycobaterial burden and has been associated with increased risks of progression to TB disease [21-24], is associated with hypertension. Improved understanding of the association between TBI, quantitative measures of IGRA, and and hypertension may clarify the role that TB prevention efforts in reducing the burden of CVD, both in the U.S. and globally.

Given existing knowledge gaps, we aimed to estimate the association between TBI and hypertension prevalence. We also investigated whether the magnitude of host immune responses to *Mtb* was associated with hypertension among those with positive IGRA test results.

METHODS

Study Design and Eligible Participants

We performed an analysis of cross-sectional data from the 2011 – 2012 US National Health and Nutrition Examination Survey (NHANES), the most recent NHANES cycle released that includes measures of TBI. NHANES is a study led by the US Centers for Disease Control and Prevention (CDC) which aims to assess the health and nutritional status of non-institutionalized civilians representative of the US population. NHANES collects demographic and health information using questionnaires administered by trained interviewers and standardized physical examinations performed in mobile examination centers. Eligible NHANES participants for our analyses were adults (≥18 years) with valid TBI test results and blood pressure measurements, and no history of TB disease (Figure 1).

Study Measures and Definitions

Our primary study outcome, any hypertension, was defined as having either (1) "measured hypertension," defined as an average systolic blood pressure level of ≥130 mmHg or diastolic blood pressure level of ≥80 mmHg across three consecutive measurements, or (2) a self-reported previous hypertension diagnosis by a health care provider or current use of antihypertensive medications (i.e., known hypertension). We categorized measured blood pressure levels into "normal" (i.e., systolic <120mmHg and diastolic <80mmHg), "borderline hypertension" (i.e., systolic 120-129mmHg and diastolic <80mmHg), "stage 1 hypertension" (i.e., systolic 130 – 139mmHg or diastolic 80-89mmHg), and "stage 2 hypertension" (i.e., systolic ≥140mmHg or diastolic ≥90mmHg) according to American College of Cardiology/American Heart Association guidelines. [25] Among participants with a prior diagnosis of hypertension, we classified blood pressure as "controlled" (systolic <130 mmHg and diastolic <80 mmHg) or "uncontrolled" (systolic ≥130mmHg or diastolic ≥80mmHg) with or without a self-reported use of antihypertensive medications.

Our primary study exposure, TBI, was defined by a positive QuantiFERON-TB Gold In Tube or QFT test. Individuals with indeterminate test results were excluded from our analyses. For those with a positive QFT, we also extracted the quantitative results and defined the IFN-γ TB antigen response by subtracting TB NIL control values from TB antigen values (i.e., Ag-NIL values). To express IFN-γ TB antigen responses, instead of using the traditional manufacturer cut-off of ≥0.35, we used the 4.00 cut-off as previous studies showed that individuals with Ag-NIL values ≥4.00 are at greater risk from developing TB disease. [21 23 24] Thus, in our analyses, Ag-NIL values were categorized as "low" (<4 IU/ml) or "high" (≥4 IU/ml). For a sensitivity analysis, we performed a subgroup analysis of participants with both QFT and tuberculin skin test (TST) results. We defined "confirmed TB infection" when both TST and QFT results were positive and "no TB infection" if both TST and QFT results were negative. Participants with

discordant TST and QFT results (i.e., TST negative and QFT positive, TST positive and QFT negative) were classified as "any discordance."

Other important covariates, including age, sex, race, educational attainment, income to poverty ratio, country of birth, body mass index (BMI), diabetes mellitus status, HIV status, lipid profile, self-reported smoking behavior, alcohol consumption, statin prescription, and previous diagnosis of coronary heart disease, myocardial infarction, or stroke were also abstracted. We classified BMI as "underweight" (BMI <18.5 kg/m^2), "normal" (BMI 18.5 – 24.9 kg/m^2), "overweight" (BMI 25 – 29.9 kg/m^2), and obese (BMI ≥30kg/m^2). [26] As NHANES grouped individuals aged ≥80 years in one category, we divided age into quartile ranges and grouped as "quartile 1 (18 – 31 years)", "quartile 2 (32 – 47 years)", "quartile 3 (48 – 62 years)", and "quartile 4 (≥63 years)" to account for the non-linearity of age in sensitivity analyses.

Statistical Analysis

We estimated weighted prevalence and 95% confidence intervals (CI) to determine the burden of TBI and hypertension in the US adult population. Rao-Scott Chi-square tests were used to assess the bivariate association between participants' demographic and clinical characteristics, TBI, Ag-NIL values, and hypertension. Multivariable robust Poisson regression with quasi-likelihood was used to estimate the association between TBI and hypertension, expressed in prevalence ratios (PRs) and 95% CI. The same regression approach was used to estimate the association between Ag-NIL responses and hypertension. In addition to prevalence ratios, we also estimated prevalence differences (PDs) and their 95%CI. Covariates included in the multivariable models were based on bivariate associations (Table S1 and S2), directed acyclic graphs [27], and established risk factors reported in previously published studies. We also assessed interaction between TBI and hypertension by participant characteristics (i.e., age, BMI, glycemic status, smoking status) on the additive (prevalence difference) and multiplicative

(prevalence ratio) scales. All analyses were performed using *survey* package in R and accounted for the weighted stratified probability sample design of NHANES with a two-sided p-value less than 0.05 considered statistically significant.

Subgroup and Sensitivity Analyses

Subgroup analyses were performed among those with previously diagnosed hypertension to determine the association between TBI (including Ag-NIL values) and controlled hypertension. Sensitivity analyses were performed to quantify systematic errors due to a) TBI misclassification, b) covariate misspecification in multivariable models, and c) the classification of age as a confounder. To address error resulting from TBI misclassification, we ran additional models with confirmed TB infection as the exposure. To quantify errors due to covariate misspecification, we ran multiple robust Poisson models with different sets of covariates and observed changes in prevalence ratios estimates across models. To account for the confounding effect of age, we ran multiple iterations of robust Poisson models with different forms of age measures (i.e., continuous and age quartiles).

RESULTS

Study population

In NHANES 2011 – 2012, 9,338 participants were surveyed and examined, 60.1% (5,615/9,338) of whom were ≥18 years old (Figure 1). Among included adults, 259 did not have valid blood pressure measurements. Of those with valid blood pressure measurements, 32 had a previous diagnosis of TB disease and 335 had a missing QFT, with 4,989 participants meeting eligiblity for this analytic cohort. The weighted prevalence of TBI in the cohort was 5.7% (95% confidence interval [CI] 4.7– 6.7) and any hypertension was present for 48.9% (95%CI 45.2 – 52.7) of participants (Table 1).

Associations between tuberculosis infection and hypertension

The prevalence of any hypertension was higher among those with TBI (58.5%, 95% CI 52.4 – 64.5) than those without TBI (48.3%, 95%CI 44.5 – 52.1) (prevalence difference [PD] 10.2%, 95%CI 5.0 – 15.4) (Table 1). After adjusting for potential confounders including age (continuous), sex, race, educational attainment level (as a proxy of socioeconomic status), country of birth, diabetes mellitus status, BMI, and smoking status, the prevalence of any hypertension was similar among those with and without TBI (adjusted prevalence ratio [aPR] 1.0, 95%CI 1.0 – 1.1). The association between TBI and hypertension was similar when examining the two components used to define our primary outcome (i.e., measured hypertension and self-reported hypertension/use of antihypertensive medications) both in the crude and adjusted models (Table 1).

Association between Ag-NIL values and hypertension

The prevalence of any hypertension was highest among those with TBI and high Ag-NIL values (60.4%, 95%CI 53.0 – 67.7) compared to those with TBI and low Ag-NIL values (57.6%, 95%CI 48.7 – 66.6) or those without TBI (48.3%, 95%CI 44.5 – 52.1) (Table S3). After adjusting for age and gender, however, the prevalence of any hypertension was similar among the three QFT groups being compared (Table S4). Similar trends were also observed for the associations between Ag-NIL values and both measured hypertension and self-reported previous diagnosis of hypertension (Figure 2).

Interaction analyses: established hypertension risk factors and HIV

We observed relationships between TBI and hypertension among participants without established hypertension risk factors who would be considered at lower risk for CVD. For example, comparing individuals with with and without TBI, the prevalence of any hypertension was substantially higher among those with normal BMI (prevalence difference [PD] 17.7, 95%CI

6.3 – 29.2), euglycemia (PD 11.3, 95%CI 3.0 – 18.9), and non-smoking (PD 14.4, 95%CI 4.2 – 24.5) groups (Table 2). Product terms for BMI, glycemic level, and smoking status were non-significant on the prevalence ratio scale ($p<0.05$).

We also found that the association between TBI and hypertension was significantly different across HIV status. For instance, the prevalence difference of any hypertension comparing those with TBI to those without TBI was 4.1 percentage points (95%CI -4.3 – 12.5) among those without HIV infection and 81.6 percentage points (95%CI 61.0 – 100.0) among those with HIV infection. After adjusting for age and gender, the adjusted prevalence ratio was 0.9 (95%CI 0.8 – 1.1) among those without HIV infection and 6.2 (95%CI 1.8 – 21.7) among those with HIV infection (statistical interaction $p<0.01$) (Table S5).

Subgroup and sensitivity analyses

From subgroup analyses conducted among those with known hypertension, the prevalence of controlled hypertension without medications was significantly lower among those with positive QFT (5.2%, 95%CI 2.0 – 8.3) compared to those with negative QFT (11.8%, 95%CI 9.5 – 14.0), although the association was no longer significant after adjusting for key confounders (aPR 0.6, 95%CI 0.4 – 1.1) (Table 3). Conversely, the prevalence of uncontrolled hypertension with medications, the more severe form of hypertension, although non-significant, were slightly higher among those with positive QFT compared to those with negative QFT (Figure 2).

In models with confirmed TB infection (i.e., positive QFT and positive TST) as the study exposure, the prevalence of any hypertension was highest among those with confirmed TB infection (60.8%, 95%CI 51.4 – 70.3) compared to those with no TB infection (49.6%, 95%CI 45.7 – 53.5) or those with discordant TST and QFT results (52.7%, 95%CI 43.9 – 61.6) ($p=0.12$) (Table S6). We observed similar trends in the crude and adjusted associations between TBI and hypertension when we used both QFT and TST (Table S7) vs. QFT alone to define TBI. Results

from sensitivity analyses to quantify bias due to covariate misspecification in the multivariable models indicated that prevalence ratios of any hypertension comparing those with positive QFT to those with negative QFT were similar when age was treated continuously or grouped in quartiles (ranged from 1.0 – 1.1) (Table S8).

DISCUSSION

Using data representative of US adult population, we found a high prevalence of hypertension (i.e., nearly 1 out of 2) in the 2011 – 2012 NHANES cycle. We reported similar adjusted prevalence of hypertension among individuals with or without TBI. In our study, individuals with positive QFT and high Ag-NIL values were more likely to have any hypertension, but less likely to have the more severe form of hypertension (i.e., uncontrolled hypertension without medications). We also observed that the association between TBI and hypertension was more common among individuals without established hypertension risk factors. Collectively, our results provide preliminary epidemiologic evidence suggesting that hypertension, a well-established intermediate for CVD, was more common among individuals with TBI than those without TBI in the US populations.

Our finding suggesting that hypertension is more common among individuals with TBI than those without TBI is consistent with previous studies. For example, a retrospective cohort study conducted among 5,185 individuals with TBI and healthy controls using data from a large metropolitan healthcare system in the US reported a higher hazard rates of hypertension incidence (defined by ICD-9 codes) among those with TBI (defined by ICD-9 codes and tuberculin skin test/IFN-γ release assay) compared to healthy controls without TBI (HR 2.0, 95%CI 1.6 – 2.5). [5] In addition, a cross-sectional study conducted among 2,351 TST-positive individuals in South India reported a slightly higher prevalence of hypertension (defined as systolic >130 mmHg) among those with confirmed TBI (defined as TST and QFT positive) (15%) compared to those latent TB negative (12%) (aOR 1.18, 95%CI 1.0 – 1.56). [28] Unlike the two

studies mentioned above, we used a more comprehensive definition of hypertension by combining objectively measured blood pressure levels (systolic and diastolic) and known hypertension indications (i.e., previous hypertension diagnosis or self-reported use of antihypertensive medications) to avoid potential misclassification.

Furthermore, we also reported that the prevalence of hypertension was highest among individuals with positive QFT and high Ag-NIL values, but we observed no dose-response relationship nor statistical significance after adjusting for key risk factors. TB infection has been associated with enhanced levels of systemic inflammation and immune activation, including increased expression of tumor necrosis factor (TNF)-α, interferons, and interlukin-6 (IL-6) [4-7]. These chemokines and dysfunctional immune responses play an important role in the pathogenesis of hypertension and CVD [29 30]. Individuals with positive QFT and higher Ag-NIL values are more likely to develop to active TB [23 31] as they may have higher mycobacterial burden, [21] and thus, could potentially have higher degree of inflammation or immune responses to the bacterial infection.

Our cross-sectional study design may not be the appropriate design to observe the expected associations or dose-response relationship between TBI, IFN-γ TB antigen responses, and hypertension. Furthermore, the time of TBI in the life-course may have different implications on TBI and hypertension association. In this NHANES cohort, the majority (>90%) of foreign born with positive QFT have stayed in the US for $\geq$5 years, and thus, we postulated that TBI happened before arriving in the US. It is plausible that these individuals are either in the latent or incipient stage where there is no to minimum bacteria replication, and thus, minimum pro-inflammatory responses. [32] Prospective studies to follow individuals with recent TBI diagnosis are still warranted to determine the hypertension and CVD risk trajectories.

Interestingly, we observed associations between TBI and hypertension among those with normal BMI, euglycemic, and non-smokers. These groups may be considered at lower risk

of CVD. This finding further reinforces the premise that there is likely to be differing effects of TBI on hypertension risk within subgroups. Further investigations and modeling studies are needed to determine whether targeted TB preventive treatment is effective to reduce the global burden of CVD among these groups.

Last, we reported that HIV infection may modify the association between TBI and hypertension. However, this finding needs to be interpreted with caution considering the low prevalence of HIV infection in the 2011-2012 NHANES cycle. Previous studies demonstrated that hypertension is more common among individuals with HIV infection on antiretroviral therapy compared to those without HIV infection, [33 34] and that there are several plausible pathways regarding how HIV infection could lead to hypertension. [33] For example, the chronic inflammation among people living with HIV (PLWH), even among those with undetectable viral loads on stable antiretroviral therapy, would trigger host immune activation (e.g., upregulation of IL-6) and could lead to stiff blood vessels and impact hypertension risk. [35 36] Further clinical studies are warranted to fully assess the joint effect between HIV (including HIV clinical characteristics) and TBI, and its association with hypertension.

Our study is subject to limitations. First, our TBI definition (i.e., according to QFT positivity) may include a broad spectrum of individuals who may have cleared the infection, have latent TB, incipient TB, or even subclinical TB since no further clinical assessment was made (e.g., chest X-ray). [37] Second, we could not determine the temporal relationship between TBI and hypertension with the cross-sectional study design used in the present paper. Third, hypertension is known to be multifactorial, and we did not account for other key variables that could potentially affect blood pressure level including stress, family history, diet (e.g., sodium intake), lifestyle (e.g., physical activity), geographical delineation (i.e., rural vs. urban), or illicit drug use. If some of these variables are associated with TBI, it is plausible that our reported estimates are slightly distorted due to residual confounding effects. Additionally, we did not account for any record of hypertension prescription, or other commonly prescribed medications

that could potentially affect blood pressure levels. Fourth, we defined some of our key variables (including hypertension status and hypertension medication intake) with self-reported information that may be prone to recall bias and likely included some misclassification. However, if misclassification of hypertension was non-differential with respect to TBI, we expect any misclassification in our results would likely biased towards the null [38]. Fourth, we did not take into consideration the CD4 count for the HIV-stratified analyses due to the small, unweighted frequency of individuals with HIV infection. Last, this study was conducted using survey data representative of US adult population but may not be generalizable to other regions with higher TB burdens.

In conclusion, we reported a higher prevalence of hypertension among individuals with positive QFT, although the association was non-significant after adjusting for key confounders, particularly age. To determine the direction of the association between TBI and hypertension, a prospective study following hypertension-free individuals at TBI diagnosis is warranted and would help establish the biological pathways regarding how TBI might increase the risk of CVD. Importantly, our results underscore the need to screen for hypertension and other metabolic disorders among those with TBI, especially among those without traditional CVD risk factors; doing so may help prevent premature deaths attributed to TB and CVD.

DECLARATIONS AND ACKNOWLEDGMENTS

Competing interest

We have no conflict of interest to declare.

Funding

This work was supported in part by the National Center for Advancing Translational Sciences (grant numbers R03TR004097 to MAH), the National Institute of Allergy and Infectious Diseases (grant number UM1AI069501; grant numbers R01AI153152 and R21AI156161 to MJM; grant number K23AI134182 to SCA), and the National Heart, Lung, and Blood Institute (grant number R01HL156779 to MAH) at the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions

MAH, MJM, and ADS conceived the study design. ADS performed the analyses. ADS, MAH, and MJM wrote the first draft of the manuscript. SCA, UPG, EMU, and JRA assisted with further drafting and revisions of manuscripts. All authors reviewed and approved the final version of the manuscript.

REFERENCES

1. Behr MA, Kaufmann E, Duffin J, et al. Latent Tuberculosis: Two Centuries of Confusion. *Am J Respir Crit Care Med* 2021;204(2):142-48. doi: 10.1164/rccm.202011-4239PP [published Online First: 2021/03/25]
2. Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. *PLoS Med* 2016;13(10):e1002152. doi: 10.1371/journal.pmed.1002152
3. World Health Organization. Tuberculosis Fact Sheet 2016 [Available from: http://www.who.int/mediacentre/factsheets/fs104/en/ accessed 06/11/2017 2016.
4. Feria MG, Chang C, Ticona E, et al. Pro-Inflammatory Alterations of Circulating Monocytes in Latent Tuberculosis Infection. *Open Forum Infectious Diseases* 2022;9(12) doi: 10.1093/ofid/ofac629
5. Mandieka E, Saleh D, Chokshi AK, et al. Latent Tuberculosis Infection and Elevated Incidence of Hypertension. *Journal of the American Heart Association* 2020;9(24):e019144. doi: doi:10.1161/JAHA.120.019144
6. Dixon DL, Wohlford GF, Abbate A. Inflammation and Hypertension. *Hypertension* 2020;75(2):297-98. doi: doi:10.1161/HYPERTENSIONAHA.119.14195
7. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. *Can Commun Dis Rep* 2017;43(3-4):62-66. doi: 10.14745/ccdr.v43i34a01 [published Online First: 2017/03/02]
8. Chung WS, Lin CL, Hung CT, et al. Tuberculosis increases the subsequent risk of acute coronary syndrome: a nationwide population-based cohort study. *Int J Tuberc Lung Dis* 2014;18(1):79-83. doi: 10.5588/ijtld.13.0288 [published Online First: 2013/12/25]
9. Huaman MA, Ticona E, Miranda G, et al. The Relationship between Latent Tuberculosis Infection and Acute Myocardial Infarction. *Clin Infect Dis* 2017 doi: 10.1093/cid/cix910
10. Huaman MA, Kryscio RJ, Fichtenbaum CJ, et al. Tuberculosis and risk of acute myocardial infarction: a propensity score-matched analysis. *Epidemiol Infect* 2017;145(7):1363-67. doi: 10.1017/s0950268817000279 [published Online First: 2017/02/17]
11. Sheu JJ, Chiou HY, Kang JH, et al. Tuberculosis and the risk of ischemic stroke: a 3-year follow-up study. *Stroke* 2010;41(2):244-9. doi: 10.1161/strokeaha.109.567735 [published Online First: 2009/12/26]
12. Salindri AD, Wang JY, Lin HH, et al. Post-tuberculosis incidence of diabetes, myocardial infarction, and stroke: Retrospective cohort analysis of patients formerly treated for tuberculosis in Taiwan, 2002 - 2013. *Int J Infect Dis* 2019 doi: 10.1016/j.ijid.2019.05.015
13. Magee MJ, Salindri AD, Gujral UP, et al. Convergence of non-communicable diseases and tuberculosis: a two-way street? *Int J Tuberc Lung Dis* 2018;22(11):1258-68. doi: 10.5588/ijtld.18.0045 [published Online First: 2018/10/26]
14. Seegert AB, Rudolf F, Wejse C, et al. Tuberculosis and hypertension-a systematic review of the literature. *Int J Infect Dis* 2017;56:54-61. doi: 10.1016/j.ijid.2016.12.016 [published Online First: 2016/12/29]
15. Seegert AB, Rudolf F, Wejse C, et al. Tuberculosis and hypertension—a systematic review of the literature. *International Journal of Infectious Diseases* 2017;56:54-61. doi: 10.1016/j.ijid.2016.12.016
16. Shen TC, Huang KY, Chao CH, et al. The risk of chronic kidney disease in tuberculosis: a population-based cohort study. *QJM* 2015;108(5):397-403. doi: 10.1093/qjmed/hcu220 [published Online First: 2014/10/30]
17. Marak B, Kaur P, Rao SR, et al. Non-communicable disease comorbidities and risk factors among tuberculosis patients, Meghalaya, India. *Indian J Tuberc* 2016;63(2):123-5. doi: 10.1016/j.ijtb.2015.07.018 [published Online First: 2016/07/28]

18. Romanowski K, Baumann B, Basham CA, et al. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2019 doi: 10.1016/S1473-3099(19)30309-3
19. Khoufi EAA. Association between latent tuberculosis and ischemic heart disease: a hospital-based cross-sectional study from Saudi Arabia. *Pan Afr Med J* 2021;38:362. doi: 10.11604/pamj.2021.38.362.28110 [published Online First: 2021/08/10]
20. Alsayed Hasanain AF, El-Maghraby KM, AA HZ, et al. Latent tuberculosis infection among patients with coronary artery stenosis: A case-Control study. *International journal of mycobacteriology* 2018;7(2):143-47. doi: 10.4103/ijmy.ijmy_34_18 [published Online First: 2018/06/15]
21. Gupta RK, Lipman M, Jackson C, et al. Quantitative IFN-γ Release Assay and Tuberculin Skin Test Results to Predict Incident Tuberculosis. A Prospective Cohort Study. *Am J Respir Crit Care Med* 2020;201(8):984-91. doi: 10.1164/rccm.201905-0969OC [published Online First: 2019/12/12]
22. Zellweger JP, Sotgiu G, Block M, et al. Risk Assessment of Tuberculosis in Contacts by IFN-γ Release Assays. A Tuberculosis Network European Trials Group Study. *Am J Respir Crit Care Med* 2015;191(10):1176-84. doi: 10.1164/rccm.201502-0232OC [published Online First: 2015/03/13]
23. Andrews JR, Nemes E, Tameris M, et al. Serial QuantiFERON testing and tuberculosis disease risk among young children: an observational cohort study. *Lancet Respir Med* 2017;5(4):282-90. doi: 10.1016/s2213-2600(17)30060-7 [published Online First: 2017/02/22]
24. Winje BA, White R, Syre H, et al. Stratification by interferon-γ release assay level predicts risk of incident TB. *Thorax* 2018 doi: 10.1136/thoraxjnl-2017-211147 [published Online First: 2018/04/07]
25. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065 [published Online First: 2017/11/15]
26. Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. StatPearls. Treasure Island (FL)2022.
27. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999;10(1):37-48.
28. Munisankar S, Rajamanickam A, Balasubramanian S, et al. Prevalence of proximate risk factors of active tuberculosis in latent tuberculosis infection: A cross-sectional study from South India. *Front Public Health* 2022;10:1011388. doi: 10.3389/fpubh.2022.1011388 [published Online First: 2022/10/25]
29. De Miguel C, Rudemiller NP, Abais JM, et al. Inflammation and hypertension: new understandings and potential therapeutic targets. *Curr Hypertens Rep* 2015;17(1):507. doi: 10.1007/s11906-014-0507-z [published Online First: 2014/11/30]
30. Tanase DM, Gosav EM, Radu S, et al. Arterial Hypertension and Interleukins: Potential Therapeutic Target or Future Diagnostic Marker? *Int J Hypertens* 2019;2019:3159283. doi: 10.1155/2019/3159283 [published Online First: 2019/06/13]
31. Ledesma JR, Ma J, Zheng P, et al. Interferon-gamma release assay levels and risk of progression to active tuberculosis: a systematic review and dose-response meta-regression analysis. *BMC Infect Dis* 2021;21(1):467. doi: 10.1186/s12879-021-06141-4 [published Online First: 2021/05/24]
32. Migliori GB, Ong CWM, Petrone L, et al. The definition of tuberculosis infection based on the spectrum of tuberculosis disease. *Breathe (Sheff)* 2021;17(3):210079. doi: 10.1183/20734735.0079-2021 [published Online First: 2022/01/18]

33. Fahme SA, Bloomfield GS, Peck R. Hypertension in HIV-Infected Adults: Novel Pathophysiologic Mechanisms. *Hypertension* 2018;72(1):44-55. doi: 10.1161/hypertensionaha.118.10893 [published Online First: 2018/05/20]
34. Davis K, Perez-Guzman P, Hoyer A, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. *BMC Med* 2021;19(1):105. doi: 10.1186/s12916-021-01978-7 [published Online First: 2021/05/14]
35. Huaman MA, Juchnowski SM, Zidar DA, et al. Monocyte activation in persons living with HIV and tuberculosis coinfection. *Aids* 2021;35(3):447-52. doi: 10.1097/qad.0000000000002766 [published Online First: 2020/12/01]
36. Temu TM, Polyak SJ, Wanjalla CN, et al. Latent tuberculosis is associated with heightened levels of pro-and anti-inflammatory cytokines among Kenyan men and women living with HIV on long-term antiretroviral therapy. *AIDS (London, England)* 2023 doi: 10.1097/qad.0000000000003523 [published Online First: 2023/03/18]
37. Dowdy DW, Behr MA. Are we underestimating the annual risk of infection with Mycobacterium tuberculosis in high-burden settings? *Lancet Infect Dis* 2022;22(9):e271-e78. doi: 10.1016/s1473-3099(22)00153-0 [published Online First: 2022/05/09]
38. Lash TL, Fox MP, Fink AK. Applying Quantitative Bias Analysis to Epidemiologic Data: Statistics for Biology and Health. New York: Springer Science and Business Media 2011.

TABLE LEGENDS

FIGURE LEGENDS

MAIN RESULTS

Figure 1. Flow chart depicting unweighted frequencies and percentages of participants included in the final analyses based on the eligibility criteria, NHANES 2011 – 2012

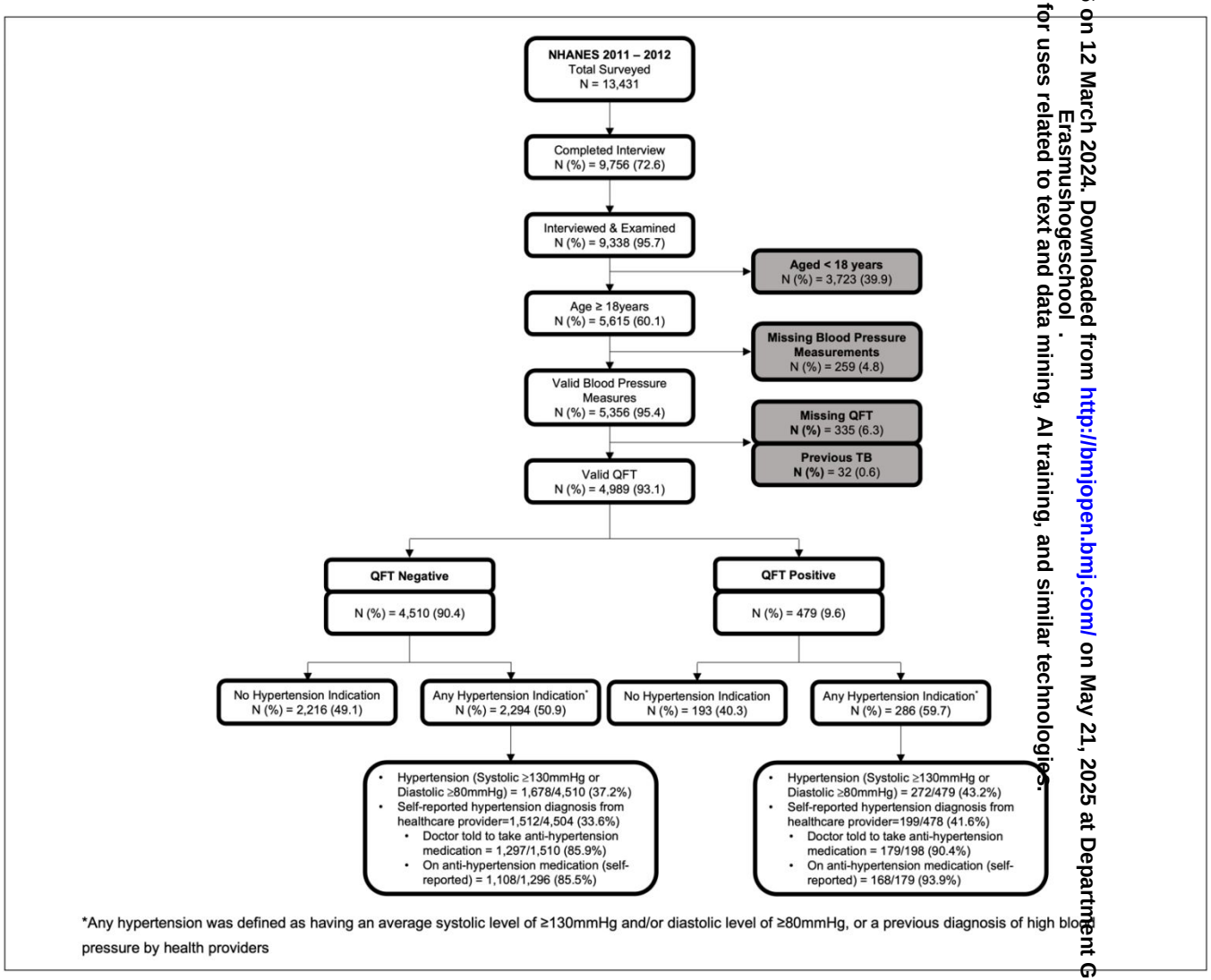


Table 1. Weighted prevalence and adjusted prevalence ratios of hypertension measures by QuantiFERON-TB Gold In-Tube status among US adults, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence of Hypertension, % (95%CI)				
	Total N=4,989	**among QFT (-) 94.3 (93.3, 95.3)**	**among QFT (+) 5.7 (4.7, 6.7)**	**Prevalence Difference* Percentage point (95%CI)**	**aPR† (95% CI)**
Primary study outcome					
Any hypertension indication[a] (n=2,580/4,989)	48.9 (45.2, 52.7)	48.3 (44.5, 52.1)	58.5 (52.4, 64.5)	**10.2 (5.1, 15.4)**	1.01 (0.97 – 1.06)
Measured blood pressure					
Hypertension[b] (n=1,885/4,989)	35.0 (32.3, 37.6)	34.5 (31.8, 37.2)	43.2 (36.4, 49.9)	**8.7 (1.9, 15.5)**	1.04 (0.97 – 1.12)
Stage 1 hypertension[c] (n=1273)	24.5 (22.4, 26.7)	24.2 (21.9, 26.5)	30.1 (22.4, 37.9)	5.9 (-2.3, 14.2)	1.13 (0.99 – 1.29)
Stage 2 hypertension[d] (n=612)	10.4 (9.1, 11.8)	10.3 (8.9, 11.7)	13.0 (9.1, 17.0)	2.8 (-1.2, 6.8)	0.88 (0.75 – 1.02)
Hypertension Diagnosis					
Previously diagnosed hypertension[e] (n=1,711)	30.8 (27.7, 33.9)	30.3 (27.1, 33.6)	38.3 (33.6, 43.1)	**8.0 (2.3, 13.6)**	0.97 (0.90 – 1.04)
Current use of anti-hypertension medication[f] (n=1,276)	86.9 (83.7, 90.1)	86.3 (82.7, 89.9)	94.7 (90.9, 98.4)	**8.4 (3.3, 14.4)**	**1.13 (1.02 – 1.09)**
Undiagnosed hypertension[g] (n=869)	18.1 (16.1, 20.2)	18.0 (15.8, 20.2)	20.2 (14.0, 26.4)	2.2 (-4.1, 8.9)	1.08 (0.91 – 1.28)

Abbreviations: CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group

†Model was adjusted for age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, body mass index, and smoking

[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or self-reported previous diagnosis of high blood pressure by health providers or use of antihypertensive medications

[b]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)

[c]Systolic 130-139 mmHg or diastolic 80-89 mmHg

[d]Systolic ≥140 mmHg or diastolic ≥90 mmHg

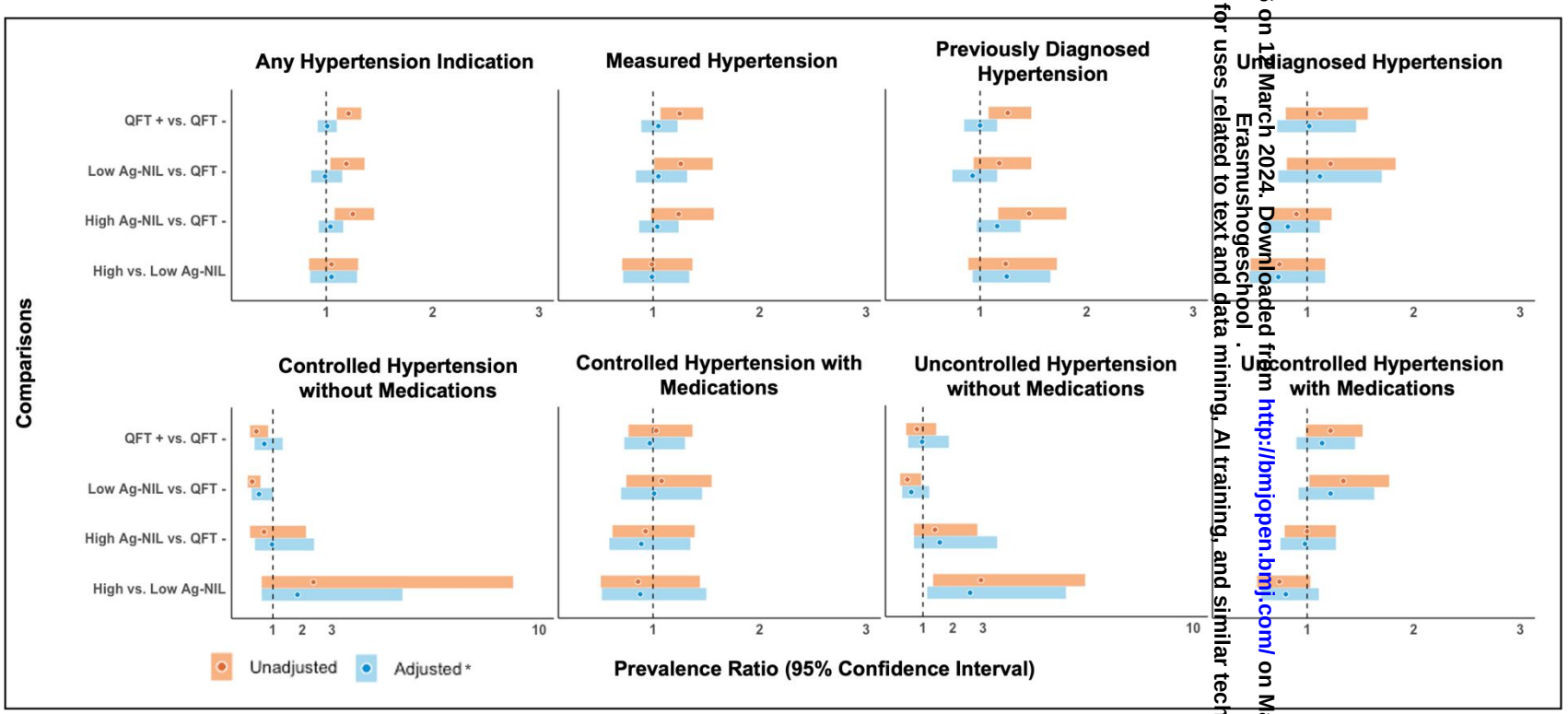
[e]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"

[f]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"

[g]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers

Bold indicates that the finding is significant at α=0.05

Figure 2. Crude and adjusted associations between QuantiFERON-TB Gold In-Tube results and select hypertension measures among US adults, NHANES 2011 – 2012



*Models were adjusted for age and gender

Table 2. Relationship between positive QuantiFERON-TB result and hypertension: Stratified by demographic and clinical characteristics among US adults, NHANES 2011 – 2012

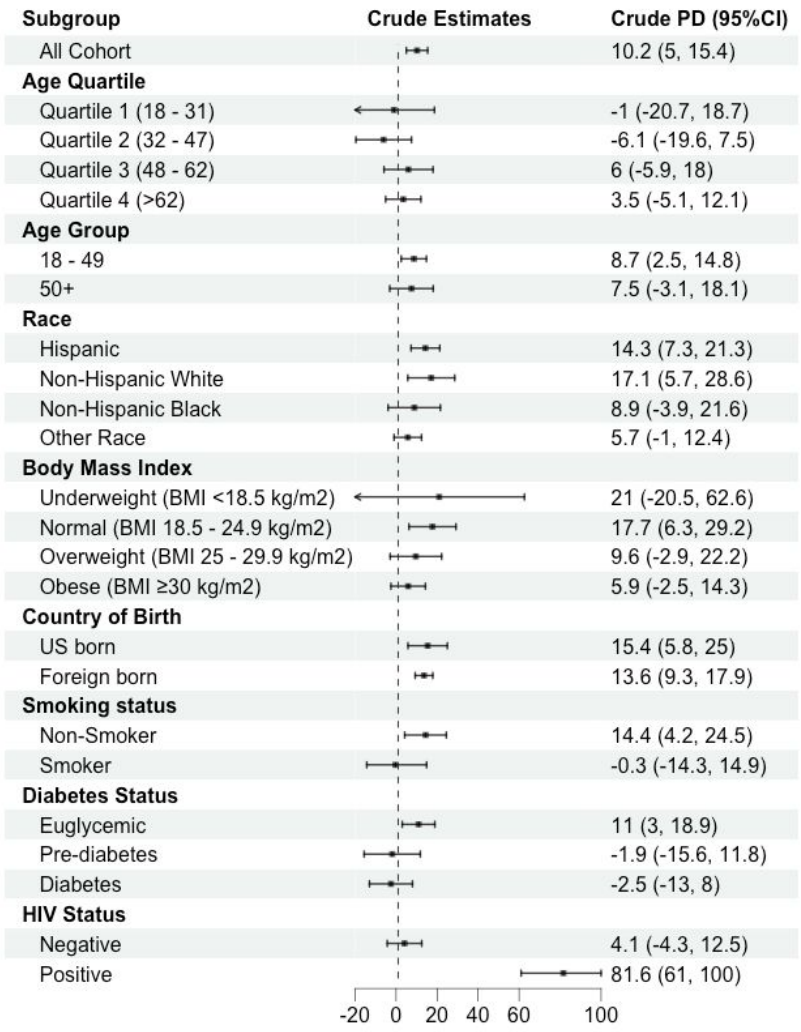


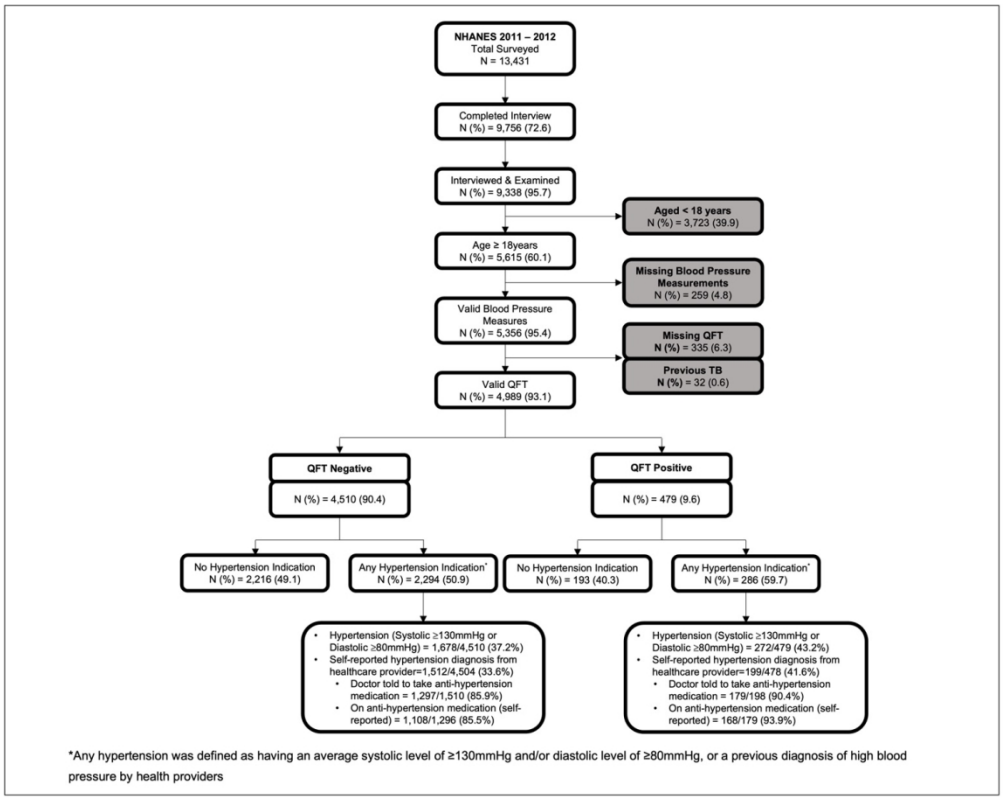
Table 3. Weighted prevalence and adjusted prevalence ratios of controlled and uncontrolled hypertension by QuantiFERON-TB Gold In-Tube status among US adults with known hypertension, NHANES 2011-2012

Hypertension Controls	Weighted Prevalence of Hypertension, % (95%CI)				
	Total N=1,711	**among QFT (-) 94.3 (93.3, 95.3)**	**among QFT (+) 5.7 (4.7, 6.7)**	**Mean/Prevalence Difference[*] Percentage point (95%CI)**	**aPR[†] (95% CI)**
Controlled without medications[a] (n=308)	11.3 (9.2, 13.3)	11.8 (9.5, 14.0)	5.2 (2.0, 8.3)	**-6.6 (-10.5, -2.7)**	0.62 (0.36 – 1.09)
Controlled with medications[b] (n=838)	33.9 (29.1, 38.8)	33.9 (28.8, 40.0)	34.8 (25.5, 44.1)	0.9 (-9.0, 10.8)	1.10 (0.84 – 1.45)
Uncontrolled without medications[c] (n=127)	15.0 (12.0, 18.1)	15.2 (12.0, 18.5)	12.2 (5.5, 18.9)	-3.1 (-10.1, 3.9)	0.80 (0.41 – 1.59)
Uncontrolled with medications[d] (n=438)	39.8 (36.7, 42.8)	39.1 (35.7, 42.6)	47.8 (40.1, 55.6)	8.7 (-1.0, 18.4)	1.16 (0.94 – 1.43)

Abbreviations: CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

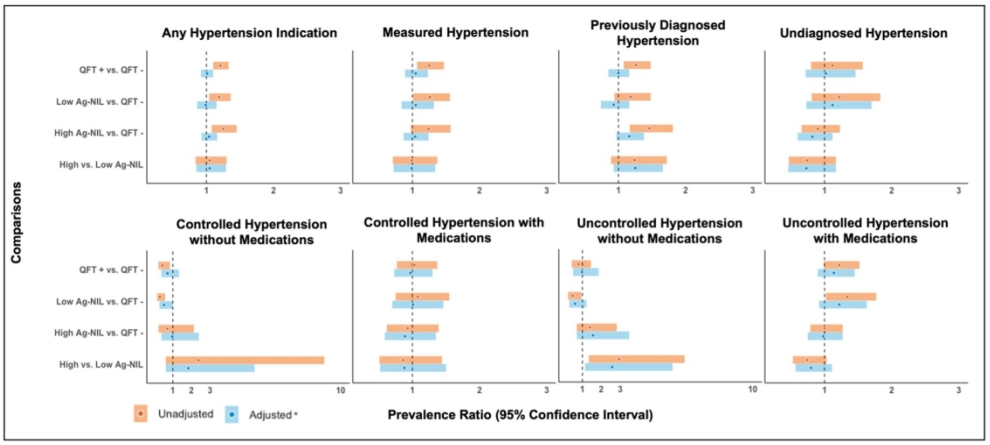
[*]Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group
[†]Model was adjusted for age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, body mass index, and smoking
[a]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[b]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[c]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[d]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05



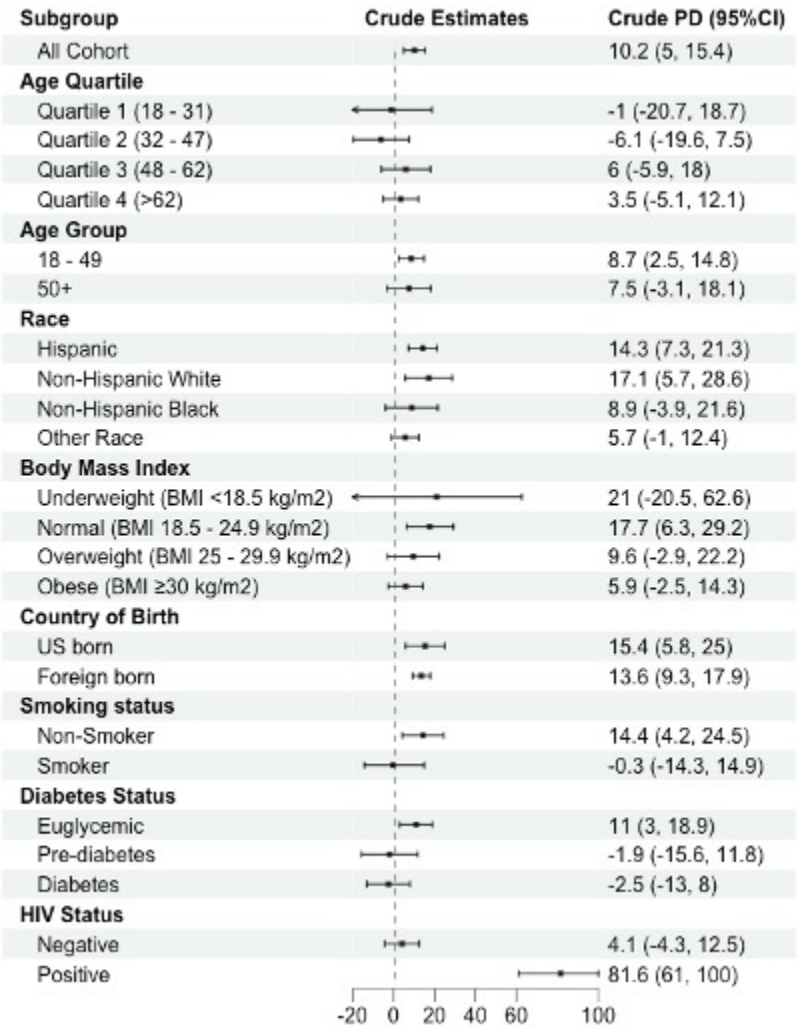
Flow chart depicting unweighted frequencies and percentages of participants included in the final analyses based on the eligibility criteria, NHANES 2011 – 2012

178x141mm (220 x 220 DPI)



Crude and adjusted associations between QuantiFERON-TB Gold In-Tube results and select hypertension measures among US adults, NHANES 2011 – 2012

227x106mm (220 x 220 DPI)



Relationship between positive QuantiFERON-TB result and hypertension: Stratified by demographic and clinical characteristics among US adults, NHANES 2011 – 2012

129x139mm (96 x 96 DPI)

SUPPEMENTAL MATERIALS

Supplemental Materials

Table S1. Weighted prevalence of and characteristics associated with tuberculosis infection among according to QuantiFERON-TB Gold In-Tube results among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference*	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	Percentage point (95%CI)	
Any hypertension indication[a]				
No	95.4 (94.4 – 96.4)	4.6 (3.6 – 5.6)	Reference	**<0.001**
Yes	93.2 (91.8 – 94.5)	6.8 (5.5 – 8.2)	2.2 (1.0, 3.4)	
Age, years				
Mean (95%CI)	46.0 (44.1 – 48.0)	53.2 (51.2 – 55.1)	7.1 (5.1, 9.2)	**<0.001**‡
Age groups				
Quartile 1 (18 – 31)	97.2 (96.2 – 98.3)	2.8 (1.7 – 3.8)	Reference	**<0.001**
Quartile 2 (32 – 47)	95.5 (94.4 – 96.6)	4.5 (3.4 – 5.6)	1.7 (0.1, 3.3)	
Quartile 3 (48 – 62)	92.0 (89.2 – 94.7)	8.0 (5.3 – 10.8)	5.3 (2.1, 8.4)	
Quartile 4 (>62)	91.9 (89.8 – 94.1)	8.1 (5.9 – 10.2)	5.3 (3.4, 7.2)	
18 – 49	94.9 (94.1 – 95.7)	5.1 (4.3 – 5.9)	Reference	**0.004**
≥50	92.5 (90.4 – 94.7)	7.5 (5.3 – 9.6)	2.4 (0.5, 4.2)	
Sex				
Male	93.4 (92.1 – 94.6)	6.6 (5.4 – 7.9)	Reference	**0.004**
Female	95.2 (94.1 – 96.2)	4.8 (3.8 – 5.9)	-1.8 (-3.2, -0.4)	
Race				
Hispanic	87.6 (85.4 – 89.9)	12.4 (10.1 – 14.6)	Reference	**<0.001**
Non-Hispanic white	96.8 (95.8 – 97.8)	3.2 (2.2 – 4.2)	-9.2 (-12.0, -6.4)	
Non-Hispanic black	92.8 (90.9 – 94.7)	7.2 (5.3 – 9.1)	-5.1 (-7.7, -2.6)	
Other race	86.7 (84.0 – 89.5)	13.3 (10.5 – 16.0)	0.9 (-2.4, 4.2)	
Education (n=4,757)				
Less than 9th grade	82.4 (77.8 – 86.9)	17.6 (13.1 – 22.2)	Reference	**<0.001**
9-11th grade	92.4 (90.1 – 94.7)	7.6 (5.3 – 9.9)	-10.4 (-15.5, -4.6)	
High school graduate	92.9 (90.5 – 95.3)	7.1 (4.7 – 9.5)	-10.6 (-15.8, -5.3)	
Some college	96.7 (95.4 – 98.0)	3.3 (2.0 – 4.6)	-14.3 (-19.2, -9.5)	
College graduate or above	95.0 (93.4 – 96.7)	5.0 (3.2 – 6.6)	-12.7 (-17.1, -8.3)	
Missing (n=264)	98.0 (95.6 – 100.0)	2.0 (0 – 4.4)		
Ratio of family income to poverty (n=4,623)				
Mean (95%CI)	2.9 (2.7 – 3.1)	2.4 (2.1 – 2.7)	-0.5 (-0.9, -0.2)	**0.005**
0 – 0.99	92.0 (89.8 – 94.2)	8.0 (5.8 -10.2)	Reference	**0.004**
1 – 1.99	92.5 (91.0 – 94.1)	7.5 (5.9 – 9.0)	-0.5 (-3.1, 2.1)	
2 – 2.99	94.9 (91.7 – 98.1)	5.1 (1.9 – 8.3)	-2.9 (-7.0, 1.2)	
3 – 3.99	95.8 (94.0 – 97.6)	4.2 (2.4 – 6.0)	-3.8 (-6.4, -1.3)	
4 – 4.99	96.7 (94.5 – 98.8)	3.3 (1.2 – 5.5)	-4.7 (-8.3, -1.1)	
≥5	95.9 (94.1 – 97.7)	4.1 (2.3 – 5.9)	-3.9 (-6.9, -0.9)	
Missing (n=396)	91.9 (88.4 – 95.5)	8.1 (4.5 – 11.6)		
Foreign born (n=4,987)				
No	96.5 (95.5 – 97.6)	3.5 (2.4 – 4.5)	Reference	**<0.001**
Yes	83.6 (80.8 – 86.3)	16.4 (14.0 – 19.2)	13.0 (9.6, 16.3)	
Missing (n=2)	100.0 (100.0 – 100.0)	0 (0 – 0)		
BMI, kg/m^2 (n=4,930)				
Mean (95%CI)	28.7 (28.2 – 29.1)	28.9 (27.8 – 30.1)	0.2 (-0.7, 1.2)	0.603‡
BMI categories				
Underweight (<18.5 kg/m^2)	93.1 (87.8 – 98.4)		0.9 (-3.7, 5.4)	0.868

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)[†]
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference[*] Percentage point (95%CI)	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)		
Normal (18.5 – 24.9 kg/m^2)	93.9 (92.0 – 95.8)	6.9 (1.6 – 12.2)	Reference	
Overweight (25 – 29.9 kg/m^2)	94.5 (93.2 – 95.9)	6.1 (4.2 – 8.0)	-0.6 (-2.6, 1.4)	
Obese (≥30 kg/m^2)	94.4 (93.2 – 95.5)	5.5 (4.1 – 6.8)	-0.4 (-2.6, 1.7)	
		5.6 (4.5 – 6.8)		
Missing (n=59)	95.8 (90.2 – 100.0)			
		4.2 (0 – 9.8)		
Smoking status (n=4,722)				
Never smokers[b]	94.9 (94.0 – 95.8)	5.1 (4.2 – 6.0)	Reference	0.144
Past smokers[c]	93.1 (90.7 – 95.4)	6.9 (4.6 – 9.3)	1.8 (-0.7, 4.3)	
Current smokers[d]	93.3 (90.7 – 95.8)	6.7 (4.2 – 9.3)	1.6 (-1.0, 4.2)	
Missing (n=267)	98.1 (95.7 – 100.0)	1.9 (0 – 4.3)		
Heavy alcohol drinking (n=3,867)				
No	95.0 (93.5 – 96.4)	5.0 (3.6 – 6.5)	Reference	0.688
Yes[e]	94.7 (93.7 – 95.8)	5.3 (4.2 – 6.3)	0.3 (-1.1, 1.6)	
Missing (n=1,122)	92.0 (90.5 – 93.6)	8.0 (6.4 – 9.5)		
HbA1c, %				
Mean (95%CI)	5.6 (5.6 – 5.7)	5.9 (5.7 – 6.0)	0.3 (0.1, 0.4)	**0.001**
Diabetes categories[f]				
Normal	95.5 (94.6 – 96.4)	4.5 (3.6 – 5.4)	Reference	**<0.001**
Prediabetes	93.4 (91.7 – 95.0)	6.6 (5.0 – 8.3)	2.1 (0.8, 3.5)	
Diabetes	88.9 (85.2 – 92.5)	11.1 (7.5 – 14.8)	6.6 (2.9, 10.4)	
HIV co-infection status (n=3,408)				
Negative	95.4 (94.4 – 96.4)	4.6 (3.6 – 5.6)	Reference	0.861
Positive	96.1 (88.3 – 100.0)	3.9 (0 – 11.7)	0.7 (-7.0, 8.3)	
Missing (n=1,600)	91.3 (89.3 – 93.3)	8.7 (6.7 – 10.7)		
Dyslipidemia Measures				
HDL (mg/dL) (n=4,889)				
Mean (95%CI)	52.8 (51.8 – 53.9)	51.7 (48.9 – 54.5)	-1.1 (-3.5, 1.2)	0.330
HDL levels[g]				
Normal	94.6 (93.5 – 95.7)	5.4 (4.3 – 6.5)	Reference	0.112
Lower	93.6 (92.4 – 94.9)	6.4 (5.1 – 7.6)	1.0 (-0.3, 2.2)	
Missing (n=100)	91.8 (82.9 – 100.0)	8.2 (0 – 17.1)		
LDL[h] (mg/dL) (n=2,236)				
Mean (95%CI)	114.8 (112.5 – 117.0)	113.1 (107.1 – 119.2)	-1.6 (-8.4, 5.1)	0.614
LDL levels	94.3 (92.8 – 95.8)	5.7 (4.2 – 7.2)	Reference	0.395
Normal (<130 mg/dL)	95.8 (94.6 – 97.2)	4.2 (2.8 – 5.6)	-1.5 (-3.3, 0.4)	
Elevated (130 – 159 mg/dL)	94.5 (90.7 – 98.4)	5.4 (1.6 – 9.3)	-0.2 (-3.9, 3.4)	
High (≥160 mg/dL)				
	99.5 (98.3 – 100.0)	0.5 (0 – 1.7)		
Missing (n=67)				
Total Cholesterol (mg/dL) (n=4,889)				
Mean (95%CI)	194.2 (191.9 – 196.4)	196.8 (192.5 – 201.0)	2.6 (-1.3, 6.5)	0.183
Total cholesterol levels				
Low (≤130 mg/dL)	93.3 (89.8 – 96.8)	6.7 (3.2 – 10.2)	Reference	0.728
Normal (131 – 199 mg/dL)	94.5 (93.3 – 95.7)	5.5 (4.2 – 6.7)	-1.3 (-5.6, 3.0)	
Elevated (≥200 mg/dL)	94.2 (82.9 – 100.0)	5.8 (4.4 – 7.2)	-0.9 (-4.9, 3.1)	
Missing (n=100)	91.8 (82.9 – 100.0)	8.2 (0 – 17.1)		
Triglyceride[h] (mg/dL) (n=2,276)				

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference*	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	Percentage point (95%CI)	
Mean (95%CI)	129.6 (118.9 – 140.2)	123.4 (111.8 – 135.0)	-6.2 (-20.5, 8.1)	0.374‡
Triglyceride levels				
Optimal (<150 mg/dL)	94.6 (93.0 – 96.2)	5.4 (3.8 -7.0)	Reference	0.796
Elevated (150 – 199 mg/dL)	94.9 (92.5 – 97.2)	5.1 (2.8 – 7.5)	-0.3 (-3.1, 2.6)	
High (≥200 mg/dL)	95.4 (93.6 – 97.2)	4.6 (2.8 – 6.4)	-0.9 (-3.2, 1.5)	
Missing (n=27)	100.00 (100.0 – 100.0)	0 (0 – 0)		
Any dyslipidemia[i&h] (n=2,277)				
No	94.4 (92.1 – 96.7)	5.6 (3.3 – 7.9)	Reference	0.63
Yes	94.9 (93.6 – 96.2)	5.1 (3.8 – 6.4)	-0.5 (-3.0, 2.0)	
Missing (n=26)	100.0 (100.0 – 100.0)	0 (0 – 0)		
Statin prescription[j] (n=2,770)				
No	94.2 (92.7 – 95.6)	5.8 (4.4 – 7.3)	Reference	0.49
Yes	93.5 (91.8 – 95.2)	6.5 (4.7 – 8.2)	0.6 (-1.3, 2.6)	
Missing (n=2,238)	94.7 (93.6 – 95.8)	5.3 (4.2 – 6.4)		
CHD[k] (n=4,712)				
No	94.1 (93.0 – 95.1)	5.9 (4.9 – 7.0)	Reference	**0.04**
Yes	96.5 (94.7 – 98.3)	3.5 (1.7 – 5.3)	-2.4 (-4.6, - 0.2)	
Missing (n=277)	97.8 (95.5 – 100.0)	2.2 (0 – 4.5)		
Heart attack[l] (n=4,723)				
No	94.1 (93.1 – 95.1)	5.9 (4.9 – 6.9)	Reference	**0.00**
Yes	96.3 (94.5 – 98.1)	3.7 (1.9 – 5.5)	-2.2 (-3.6, -0.8)	
Missing (n=266)	98.1 (95.7 – 100.0)	1.9 (0 – 4.3)		
Stroke[m] (n=4,725)				
No	94.3 (93.2 – 95.3)	5.7 (4.7 – 6.8)	Reference	**0.04**
Yes	90.7 (86.4 – 94.9)	9.3 (5.1 – 13.6)	3.6 (-0.9, 8.0)	
Missing (n=264)	98.1 (95.7 – 100.0)	1.9 (0 – 4.3)		

Abbreviations:
BMI – body mass index; CHD – coronary heart disease; CI – confidence interval; HbA1c – glycated hemoglobin; HDL – high-density lipoprotein; HIV – human immunodeficiency virus; LDL – low-density lipoprotein; NHANES – National Health and Nutrition Examination Survey; QFT - QuantiFERON Gold-In-Tube;

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group, unless indicated otherwise (with "reference" statement)
†P-values from Rao-Scott Chi-square tests, unless indicated otherwise
‡P-values from t-tests
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Survey participants answered "No" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[c]Survey participants answered "Not at all" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[d]Survey participants answered "Every day" or "Some days" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[e]Survey participants answered "Yes" to the question "Was there ever time or times in (your/SP's) life when (you/he/she) drank 4 (for female) or 5 (for male) or more drinks of any kind of alcoholic beverage almost every day?"
[f]Diabetes was categorized according to HbA1c levels and self-reported previous type-2 diabetes mellitus diagnosis by health care providers
[g]HDL level was using gender-specific cut-offs: "normal" HDL was defined if HDL level was ≥40 mg/dL for male or ≥50 mg/dL for female; and "lower" HDL was defined if HDL level was <40 mg/dL for male or <50 mg/dL for female
[h]LDL and triglyceride measurements were done among a subset of survey participants who were fasting and appropriate weight variable (for those who were fasting) was applied accordingly
[i]Any dyslipidemia was defined as having either elevated LDL, total cholesterol, triglyceride, or lower HDL levels
[j]Taken statin in the past 30 days prior to survey date, survey participants were also asked to show medicine container to surveyor/enumerator

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)[†]
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference[*]	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	Percentage point (95%CI)	

[k]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had coronary heart disease?"

[l]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a heart attack (also called myocardial infarction)?"

[m]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a stroke?"

Bold indicates that the finding is statistically significant at α=0.05

Table S2. Weighted prevalence of and characteristics associated with hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	
QFT result				
Negative	51.7 (47.9 – 55.5)	48.3 (44.5 – 52.1)	Reference	**<0.001**
Positive	41.5 (35.5 – 47.6)	58.5 (52.4 – 64.5)	10.2 (5.0, 15.4)	
Age, years				
Mean (95%CI)	38.9 (37.3 – 40.6)	54.3 (52.8 – 55.7)	15.3 (14.0, 16.6)	**<0.001**
Age group				
Quartile 1 (18 – 31)	80.8 (78.6 – 83.1)	19.2 (16.9 – 21.4)	Reference	**<0.001**
Quartile 2 (32 – 47)	57.5 (52.3 – 62.7)	42.5 (37.3 – 47.7)	23.4 (18.6, 28.1)	
Quartile 3 (48 – 62)	38.0 (34.4 – 41.7)	62.0 (58.3 – 65.6)	42.8 (37.9, 47.7)	
Quartile 4 (>62)	23.0 (18.9 – 27.1)	77.0 (72.9 – 81.1)	57.8 (53.1, 62.5)	
18 – 49	57.1 (53.1 – 61.1)	42.9 (38.9 – 46.9)	Reference	**<0.001**
≥50	34.2 (30.2 – 38.3)	65.8 (61.7 – 69.8)	22.9 (17.6, 28.2)	
Sex				
Male	47.7 (43.2 – 52.2)	52.3 (47.8 – 56.8)	Reference	**0.001**
Female	54.4 (50.4 – 58.4)	45.6 (41.6 – 49.6)	-6.7 (-10.9, -2.5)	
Race				
Hispanic	61.3 (55.8 – 66.8)	38.7 (33.2 – 44.2)	Reference	**<0.001**
Non-Hispanic white	49.6 (44.7 – 54.4)	50.4 (45.6 – 55.3)	11.7 (5.3, 18.2)	
Non-Hispanic black	43.6 (39.9 – 47.4)	56.4 (52.6 – 60.1)	17.7 (11.8, 23.5)	
Other race	56.5 (51.5 – 61.5)	43.5 (38.5 – 48.5)	4.8 (-2.2, 11.7)	
Education (n=4,725)				
Less than 9th grade	39.0 (31.3 – 46.9)	61.0 (53.3 – 68.7)	Reference	**<0.001**
9-11th grade	42.3 (36.9 – 47.6)	57.7 (52.3 – 63.1)	-3.2 (-13.4, 6.9)	
High school graduate	45.5 (40.9 – 50.1)	54.5 (49.9 – 59.1)	-6.5 (-14.9, 2.0)	
Some college	51.7 (46.3 – 57.0)	48.3 (42.9 – 53.7)	-12.7 (-20.9, -4.5)	
College graduate or above	55.3 (48.9 – 61.5)	44.7 (38.4 – 51.1)	-16.2 (-25.5, -7.0)	
Missing (n=264)	86.7 (81.8 – 91.5)	13.3 (8.5 – 18.2)		
Ratio of family income to poverty (n=4,593)				
Mean (95%CI)	2.8 (2.6 – 3.1)	2.9 (2.7 – 3.1)	0.1 (-0.1, 0.3)	0.439
0 – 0.99	55.8 (49.1 – 62.5)	44.2 (37.5 – 50.9)	Reference	0.439
1 – 1.99	49.6 (43.3 – 55.9)	50.4 (44.1 – 56.7)	6.2 (-0.5, 12.9)	
2 – 2.99	49.4 (43.7 – 55.0)	50.6 (45.0 – 56.3)	6.4 (-2.4, 15.3)	
3 – 3.99	53.5 (48.6 – 58.4)	46.5 (41.6 – 51.4)	2.3 (-4.9, 9.5)	
4 – 4.99	47.6 (39.8 – 55.0)	52.4 (44.6 – 60.2)	8.2 (-2.7, 19.0)	
≥5	50.9 (43.0 – 58.7)	49.1 (41.3 – 57.0)	4.9 (-3.5, 13.4)	
Missing (n=396)	49.4 (39.9 – 58.8)	50.6 (41.2 – 60.1)		
Foreign born (n=5,019)				
No	49.2 (45.9 – 52.6)	50.8 (47.4 – 54.1)	Reference	**<0.001**
Yes	60.1 (54.7 – 65.5)	39.9 (34.5 – 45.3)	-10.8 (-14.5, -7.2)	
Missing (n=2)	70.6 (8.7 – 100.0)	29.4 (0 – 91.3)		
BMI, kg/m^2 (n=4,930)				
Mean (95%CI)	27.2 (26.7 – 27.8)	30.2 (29.7 – 30.8)	3.0 (2.4, 3.7)	**<0.001**
BMI categories				
Underweight (<18.5 kg/m^2)	68.6 (61.2 – 76.0)	31.4 (24.0 – 38.8)	-1.2 (-9.3, 6.9)	**<0.001**
Normal (18.5 – 24.9 kg/m^2)	67.4 (62.8 – 72.0)	32.6 (28.0 – 37.2)	Reference	
Overweight (25 – 29.9 kg/m^2)	49.8 (46.2 – 53.4)	50.2 (46.6 – 53.8)	17.6 (14.4, 20.9)	
Obese (≥30 kg/m^2)	38.0 (33.6 – 42.5)	62.0 (57.5 – 66.4)	29.4 (23.3, 35.5)	

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)[†]
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference[*] Percentage point (95%CI)	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)		
Missing (n=59)	26.1 (7.3 – 45.0)	73.9 (55.0 – 92.7)		
Smoking status (n=4,722)				
Never smokers[b]	54.4 (50.5 – 58.4)	45.6 (41.6 – 49.5)	Reference	**<0.001**
Past smokers[c]	37.2 (31.6 – 42.8)	62.8 (57.2 – 68.4)	17.3 (12.6, 21.9)	
Current smokers[d]	52.7 (48.4 – 57.1)	47.3 (42.9 – 51.6)	1.7 (-3.8, 7.1)	
Missing (n=267)	86.2 (81.0 – 91.4)	13.8 (8.6 – 19.0)		
Heavy alcohol drinking (n=3,891)				
No	41.1 (36.5 – 45.7)	58.9 (54.3 – 63.5)	Reference	**<0.001**
Yes[e]	52.4 (48.3 – 56.5)	47.6 (43.9 – 51.7)	-11.3 (-14.9, -7.7)	
Missing (n=1,122)	52.9 (47.6 – 58.2)	47.1 (41.8 – 52.4)		
HbA1c, %				
Mean (95%CI)	5.4 (5.4 – 5.5)	5.9 (5.8 – 5.9)	0.4 (0.4, 0.5)	**<0.001**
Diabetes categories[f]				
Normal	59.9 (55.8 – 64.0)	40.1 (36.0 – 44.2)	Reference	**<0.001**
Prediabetes	40.3 (37.1 – 43.5)	59.7 (56.5 – 62.9)	19.6 (15.8 – 23.4)	
Diabetes	19.1 (16.5 – 21.8)	80.9 (78.2 – 83.5)	40.8 (37.3 – 44.3)	
HIV co-infection status (n=3,389)				
Negative	60.7 (57.3 – 64.2)	39.3 (35.8 – 42.7)	Reference	0.225
Positive	78.4 (54.8 – 100.0)	21.6 (0 – 45.2)	-17.7 (-43.6, 8.3)	
Missing (n=1,600)	25.3 (21.7 – 28.9)	74.7 (71.1 – 78.3)		
Dyslipidemia Measures				
HDL (mg/dL) (n=4,889)				
Mean (95%CI)	53.2 (52.1 – 54.3)	52.3 (51.0 – 53.6)	-0.9 (-2.0, 0.1)	0.083
HDL levels[g]				
Normal	53.1 (48.9 – 57.3)	46.9 (42.7 – 51.1)	Reference	**<0.001**
Lower	47.1 (43.5 – 50.7)	52.9 (49.3 – 56.5)	6.0 (2.4, 9.6)	
Missing (n=100)	37.0 (25.2 – 48.7)	63.0 (51.3 – 74.8)		
LDL[h] (mg/dL) (n=2,236)				
Mean (95%CI)	113.2 (110.5 – 115.8)	116.4 (113.0 – 119.8)	3.2 (-1.1, 7.6)	0.133
LDL levels				
Normal (<130 mg/dL)	53.7 (48.5 – 58.8)	46.3 (41.2 – 51.5)	Reference	**0.014**
Elevated (130 – 159 mg/dL)	55.8 (48.7 – 62.9)	44.2 (37.1 – 51.3)	-2.1 (-11.3, 7.1)	
High (≥160 mg/dL)	38.7 (28.1 – 49.3)	61.3 (50.7 – 71.9)	15.0 (4.7, 25.3)	
Missing (n=67)	31.7 (19.9 – 43.5)	68.3 (56.5 – 80.1)		
Total Cholesterol (mg/dL) (n=4,889)				
Mean (95%CI)	190.3 (187.7 – 192.8)	198.6 (194.7 – 202.4)	8.3 (3.4, 13.2)	**0.001**
Total cholesterol levels				
Low (≤130 mg/dL)	50.7 (44.3 – 57.0)	49.3 (43.0 – 55.7)	Reference	**<0.001**
Normal (131 – 199 mg/dL)	55.3 (50.9 – 59.8)	44.7 (40.2 – 49.1)	-4.7 (-10.6, 1.3)	
Elevated (≥200 mg/dL)	46.4 (41.1 – 51.8)	53.6 (48.2 – 58.9)	4.2 (-3.3, 11.7)	
Missing (n=100)	37.0 (25.2 – 48.7)	63.0 (51.3 – 74.8)		
Triglyceride[h] (mg/dL) (n=2,276)				
Mean (95%CI)	111.5 (105.4 – 117.6)	148.8 (134.6 – 162.9)	37.3 (26.3, 48.2)	**<0.001**
Triglyceride levels				
Optimal (<150 mg/dL)	57.9 (54.2 – 61.6)	42.1 (38.4 – 45.8)	Reference	**<0.001**

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)[†]
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference[*] Percentage point (95%CI)	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)		
Elevated (150 – 199 mg/dL)	41.8 (34.1 – 49.5)	58.2 (50.5 – 65.9)	16.1 (9.8, 22.5)	
High (≥200 mg/dL)	28.7 (21.8 – 35.6)	71.3 (64.4 – 78.2)	29.2 (22.4, 36.1)	
Missing (n=27)	25.7 (6.7 – 44.8)	74.3 (55.2 – 93.3)		
Any dyslipidemia[i&h] (n=2,277)				
No	61.0 (56.7 – 65.4)	39.0 (34.6 – 43.3)	Reference	**<0.001**
Yes	47.4 (41.9 – 52.8)	52.6 (47.2 – 58.1)	13.7 (7.7, 19.6)	
Missing (n=26)	24.6 (6.0 – 43.2)	75.4 (56.8 – 94.0)		
Statin prescription[j] (n=2,770)				
No	44.8 (40.0 – 49.6)	55.2 (50.4 – 60.0)	Reference	
Yes	20.6 (16.0 – 25.2)	79.4 (74.8 – 84.0)	24.2 (17.6, 30.9)	**<0.001**
Missing (n=2,238)	69.8 (66.6 – 73.0)	30.2 (27.0 – 33.4)		
CHD[k] (n=4,712)				
No	50.9 (47.2 – 54.6)	49.1 (45.4 – 52.8)	Reference	**<0.001**
Yes	15.3 (5.9 – 24.8)	84.7 (75.2 – 94.1)	35.6 (25.0, 46.1)	
Missing (n=277)	85.6 (80.4 – 90.8)	14.4 (9.2 – 19.6)		
Heart attack[l] (n=4,723)				
No	50.8 (47.1 – 54.5)	49.2 (45.5 – 52.9)	Reference	**<0.001**
Yes	20.9 (11.6 – 30.2)	79.1 (69.8 – 88.4)	29.9 (18.5, 41.4)	
Missing (n=266)	86.1 (80.7 – 91.5)	13.9 (8.5 – 19.3)		
Stroke[m] (n=4,725)				
No	50.9 (47.3 – 54.4)	49.1 (45.6 – 52.7)	Reference	**<0.001**
Yes	15.6 (8.8 – 22.4)	84.4 (77.6 – 91.2)	35.3 (28.1, 42.5)	
Missing (n=264)	86.9 (82.1 – 91.6)	13.1 (8.4 – 17.9)		

Abbreviations:
BMI – body mass index; CI – confidence interval; HDL – high-density lipoprotein; LDL – low-density lipoprotein; NHANES – National Health and Nutrition Examination Survey; QFT - QuantiFERON Gold-In-Tube; TST – tuberculin skin test

[*]Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group, unless indicated otherwise (with "reference" statement)
[†]P-values from Rao-Scott Chi-square tests, unless indicated otherwise
[‡]P-values from t-tests
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Survey participants answered "No" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[c]Survey participants answered "Not at all" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[d]Survey participants answered "Every day" or "Some days" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[e]Survey participants answered "Yes" to the question "Was there ever time or times in (your/SP's) life when (you/he/she) drank 4 (for female) or 5 (for male) or more drinks of any kind of alcoholic beverage almost every day?"
[f]Diabetes was categorized according to HbA1c levels and self-reported previous type-2 diabetes mellitus diagnosis by health care providers
[g]HDL level was using gender-specific cut-offs: "normal" HDL was defined if HDL level was ≥40 mg/dL for male or ≥50 mg/dL for female; and "lower" HDL was defined if HDL level was <40 mg/dL for male or <50 mg/dL for female
[h]LDL and triglyceride measurements were done among a subset of survey participants who were fasting and appropriate weight variable (for those who were fasting) was applied accordingly
[i]Any dyslipidemia was defined as having either elevated LDL, total cholesterol, triglyceride, or lower HDL levels
[j]Taken statin in the past 30 days prior to survey date, survey participants were also asked to show medicine container to surveyor/enumerator
[k]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had coronary heart disease?"
[l]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a heart attack (also called myocardial infarction)?"

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)[†]
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference[*]	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	

[m]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a stroke?"

Bold indicates that the finding is statistically significant at α=0.05

Table S3. Weighted prevalence of various hypertension classifications by interferon gamma tuberculosis antigen responses among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence (95%CI)			Prevalence Difference (95%CI)		
		QFT Positive				
		Ag-NIL Values*				
	QFT Negative N=4510 94.3% (93.3 – 95.2)	Low (<4 IU/ml) N=299 4.0% (3.2 – 4.7)	High (≥4 IU/ml) N=140 1.7% (1.1 – 2.3)	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL
Primary study outcome						
Any hypertension indication[a]	48.3 (44.5, 52.1)	57.6 (48.7, 66.6)	60.4 (53.1, 67.7)	9.4 (1.6, 17.1)	12.1 (3.6, 20.5)	2.7 (-10.1, 15.5)
Measured blood pressure categories						
Normal blood pressure[b]	47.9 (44.6, 51.2)	35.6 (25.1, 46.1)	39.5 (31.2, 49.7)	-12.3 (-22.7, -1.9)	-8.4 (-18.1, 1.2)	3.8 (-9.7, 17.4)
Borderline hypertension[c]	17.6 (15.9, 19.3)	21.1 (14.2, 27.9)	17.7 (11.1, 25.1)	3.4 (-3.0, 9.9)	0.1 (-7.5, 7.6)	-3.4 (-13.9, 7.2
Hypertension[d]	34.5 (31.8, 37.2)	43.3 (34.0, 52.7)	42.8 (33.6, 52.1)	8.8 (-0.4, 18.1)	8.4 (-1.4, 18.2)	-0.5 (-14.6, 13.7)
Stage 1 hypertension[e]	24.2 (21.9, 26.5)	28.8 (18.9, 38.8)	33.2 (23.3, 414.1)	4.6 (-5.7, 14.9)	9.0(-2.7, 20.7)	4.4 (-10.2, 19.0)
Stage 2 hypertension[f]	10.3 (8.9, 11.7)	14.5 (10.3, 18.7)	9.6 (5.1, 14.2)	4.2 (-0.3, 8.7)	-0.6 (-5.2, 3.9)	-4.9 (-9.0, -0.7)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	30.3 (27.1, 33.6)	35.8 (28.3, 43.3)	44.2 (36.1, 52.2)	5.4 (-2.5, 13.4)	13.9 (5.0, 22.7)	8.4 (-4.7, 21.6)
Self-reported current use of anti-hypertension medication[h]	86.3 (82.7, 90.0)	95.0 (90.7, 98.9)	94.4 (87.7, 100.0)	8.5 (2.3, 14.6)	8.1 (-0.6, 16.8)	-0.6 (-7.8, 6.9)
Undiagnosed hypertension[i]	18.0 (15.8, 20.2)	21.9 (13.6, 30.3)	16.2 (12.1, 20.3)	3.9 (-4.8, 12.7)	-1.8 (-7.1, 3.4)	-5.8 (-12.7, 4.8)
Hypertension Control†						
Controlled hypertension without medications[j]	11.8 (9.5, 14.0)	3.5 (1.2, 5.7)	8.3 (0.0, 17.0)	-8.3 (-11.4, -5.2)	-3.5 (-12.8, 5.8)	4.8 (-4.7, 14.3)
Controlled hypertension with medications[k]	33.9 (28.8, 39.0)	36.6 (25.1, 48.2)	31.4 (17.9, 44.9)	2.9 (-10.4, 15.9)	-2.5 (-15.1, 10.2)	-5.2 (-22.5, 12.1)
Uncontrolled hypertension without medications[l]	15.2 (12.0, 18.5)	7.3 (2.6, 12.0)	21.3 (7.9, 34.7)	-8.0 (-13.6, -2.3)	6.1 (-8.3, 20.4)	14.0 (-0.9, 27.2)
Uncontrolled hypertension with medications[m]	39.1 (35.7, 42.6)	52.6 (40.8, 64.4)	39.0 (30.7, 47.3)	13.5 (-0.2, 27.1)	-0.1 (-9.5, 9.2)	-13.6 (-28.9, 1.7)

Abbreviations:
CI – confidence interval; IFN-γ - interferon gamma; QFT – QuantiFERON-TB Gold In-Tube

*Estimated by subtracting TB antigen value by TB Nil control value (LBXTBA - TBXTBN)
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,711)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S4. Crude and adjusted associations between interferon gamma tuberculosis antigen responses and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Stratification Variables	Prevalence Ratio (95%CI)					
	Unadjusted Estimates			Adjusted Estimates*		
	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL
Primary study outcome						
Any hypertension indication[a]	**1.19 (1.04 – 1.36)**	**1.25 (1.08 – 1.45)**	1.05 (0.84 – 1.30)	0.99 (0.86 – 1.15)	1.04 (0.93 – 1.16)	1.05 (0.85 – 1.29)
Measured blood pressure categories						
Normal blood pressure[b]	**0.74 (0.56 – 0.99)**	0.82 (0.64 – 1.05)	1.11 (0.78 – 1.59)	0.89 (0.66 – 1.21)	0.99 (0.80 – 1.24)	1.12 (0.76 – 1.63)
Borderline hypertension[c]	1.20 (0.88 – 1.62)	1.00 (0.66 – 1.54)	0.84 (0.47 – 1.46)	1.12 (0.82 – 1.54)	0.94 (0.61 – 1.45)	0.84 (0.47 – 1.50)
Hypertension[d]	**1.26 (1.01 – 1.56)**	1.24 (0.98 – 1.57)	0.99 (0.71 – 1.37)	1.05 (0.84 – 1.32)	1.04 (0.87 – 1.24)	0.99 (0.72 – 1.34)
Stage 1 hypertension[e]	1.19 (0.83 – 1.77)	1.37 (0.96 – 1.97)	1.15 (0.73 – 1.85)	1.06 (0.73 – 1.55)	1.22 (0.89 – 1.66)	1.15 (0.72 – 1.82)
Stage 2 hypertension[f]	**1.41 (1.02 – 1.95)**	0.94 (0.59 – 1.50)	**0.67 (0.44 – 0.99)**	1.03 (0.74 – 1.44)	0.70 (0.40 – 1.23)	0.67 (0.43 – 1.05)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	1.18 (0.94 – 1.48)	**1.46 (1.17 – 1.81)**	1.24 (0.93 – 1.72)	0.93 (0.74 – 1.16)	1.16 (0.97 – 1.38)	1.25 (0.93 – 1.66)
Self-reported current use of anti-hypertension medication[h]	**1.10 (1.03 – 1.18)**	1.09 (0.99 – 1.20)	1.00 (0.93 – 1.08)	**1.07 (1.00 – 1.14)**	1.07 (0.98 – 1.17)	1.00 (0.92 – 1.09)
Undiagnosed hypertension[i]	1.22 (0.81 – 1.83)	0.90 (0.66 – 1.23)	0.74 (0.47 – 1.17)	1.12 (0.73 – 1.70)	0.82 (0.60 – 1.12)	0.73 (0.46 – 1.17)
Hypertension Control†						
Controlled hypertension without medications[j]	**0.30 (0.15 – 0.58)**	0.70 (0.23 – 2.12)	2.37 (0.82 – 6.84)	**0.53 (0.28 – 1.00)**	0.97 (0.39 – 2.39)	1.83 (0.62 – 5.38)
Controlled hypertension with medications[k]	1.08 (0.75 – 1.55)	0.93 (0.62 – 1.39)	0.86 (0.51 – 1.44)	1.01 (0.70 – 1.46)	0.89 (0.59 – 1.35)	0.88 (0.52 – 1.50)
Uncontrolled hypertension without medications[l]	**0.48 (0.24 – 0.94)**	1.40 (0.70 – 2.81)	**2.93 (1.34 – 6.40)**	0.61 (0.31 – 1.21)	1.56 (0.70 – 3.47)	**2.57 (1.14 – 5.76)**
Uncontrolled hypertension with medications[m]	**1.34 (1.02 – 1.77)**	1.00 (0.79 – 1.27)	0.74 (0.53 – 1.03)	1.22 (0.92 – 1.63)	0.98 (0.75 – 1.27)	0.80 (0.57 – 1.11)

Abbreviations:
CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

*Models adjusted for age (continuous) and gender
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,711)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S5. The crude and adjusted prevalence odds ratios of any hypertension stratified by race, body mass index category, and foreign-born status, among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Stratification Variables	QFT Status	Unweighted frequency Hypertension*/Total	Weighted Prevalence of Hypertension* (95%CI)	Prevalence Difference (95%CI)	Prevalence Ratios	
					Crude	Adjusted†
					cPR (95%CI)	aPR (95%CI)
All cohort	Negative	2294/4510	48.3 (44.5 – 52.1)	Reference	Reference	Reference
	Positive	286/479	58.5 (52.4 – 64.5)	10.2 (5.0, 15.4)	**1.21 (1.10 – 1.33)**	1.01 (0.92 – 1.10)
Stratified by age quartiles‡						
Quartile 1 (18 – 31)	Negative	253/1256	19.2 (16.9 – 21.5)	Reference	Reference	Reference
	Positive	6/40	18.2 (0 – 37.5)	-1.0 (-20.7, 18.7)	0.95 (0.32 – 2.81)	0.81 (0.25 – 2.64)
Quartile 2 (32 – 47)	Negative	512/1186	42.8 (37.8 – 47.8)	Reference	Reference	Reference
	Positive	32/94	36.7 (20.0 – 52.4)	-6.1 (-19.6, 7.5)	0.86 (0.59 – 1.25)	0.87 (0.59 – 1.26)
Quartile 3 (48 – 62)	Negative	678/1033	61.5 (58.0 – 65.0)	Reference	Reference	Reference
	Positive	105/166	67.5 (55.0 – 80.1)	6.0 (-5.9, 18.0)	1.10 (0.92 – 1.31)	1.03 (0.88 – 1.21)
Quartile 4 (>62)	Negative	851/1035	76.7 (72.3 – 81.1)	Reference	Reference	Reference
	Positive	143/179	80.2 (72.9 – 87.5)	3.5 (-5.1, 12.1)	1.05 (0.94 – 1.17)	1.03 (0.91 – 1.17)
Stratified by age group						
18 – 49	Negative	1568/3454	42.5 (38.5 – 46.4)	Reference	Reference	Reference
	Positive	175/307	51.1 (43.4 – 58.9)	8.7 (2.5, 14.8)	**1.20 (1.07 – 1.36)**	0.95 (0.84 – 1.08)
50+	Negative	726/1056	65.2 (61.2 – 69.2)	Reference	Reference	Reference
	Positive	111/172	72.7 (61.4 – 84.0)	7.5 (-3.1, 18.1)	1.11 (0.96 – 1.29)	1.07 (0.93 – 1.24)
Stratified by race						
Hispanic	Negative	374/864	36.9 (31.4 – 42.5)	Reference	Reference	Reference
	Positive	67/158	51.2 (42.0 – 60.4)	14.3 (7.3, 21.3)	**1.39 (1.20 – 1.60)**	0.98 (0.86 – 1.11)
Non-Hispanic White	Negative	947/1769	49.9 (45.0 – 54.8)	Reference	Reference	Reference
	Positive	47/71	67.0 (55.3 – 78.7)	17.1 (5.7, 28.6)	**1.34 (1.12 – 1.60)**	1.08 (0.91 – 1.27)
Non-Hispanic Black	Negative	711/1196	55.7 (51.8 – 59.7)	Reference	Reference	Reference
	Positive	80/115	64.6 (52.0 – 77.2)	8.9 (-3.9, 21.6)	1.16 (0.95 – 1.42)	0.86 (0.71 – 1.05)
Other Race/Ethnicity	Negative	262/681	42.7 (37.5 – 47.9)	Reference	Reference	Reference
	Positive	68/135	48.4 (41.3 – 55.6)	5.7 (-1.0, 12.4)	1.13 (0.98 – 1.31)	0.88 (0.71 – 1.09)
Stratified by body mass index category						
Underweight (BMI <18.5 kg/m^2)	Negative	28/96	29.9 (22.4 – 37.5)	Reference	Reference	Reference
	Positive	7/11	50.9 (10.6 – 91.2)	21.0 (-20.5, 62.6)	1.70 (0.71 – 4.05)	0.71 (0.34 – 1.51)
Normal (BMI 18.5 – 24.9 kg/m^2)	Negative	478/1367	31.5 (26.9 – 36.1)	Reference	Reference	Reference
	Positive	75/149	49.2 (36.8 – 61.7)	17.7 (6.3, 29.2)	1.56 (1.23 – 1.98)	**1.24 (1.00 – 1.52)**
Overweight (BMI 25 – 29.9 kg/m^2)	Negative	709/1400	49.7 (46.2 – 53.2)	Reference	Reference	Reference
	Positive	96/160	59.3 (46.0 – 72.6)	9.6 (-2.9, 22.2)	1.19 (0.97 – 1.48)	0.98 (0.81 – 1.20)
Obese (BMI ≥30 kg/m^2)	Negative	1040/1592	61.6 (57.2 – 66.1)	Reference	Reference	Reference
	Positive	107/155	67.5 (57.9 – 77.1)	5.9 (-2.5, 14.3)	1.10 (0.97 – 1.24)	0.98 (0.89 – 1.08)
Stratified by foreign born status						
US Born	Negative	1793/3341	50.2 (46.8 – 53.7)	Reference	Reference	Reference
	Positive	120/172	65.6 (56.1 – 75.1)	15.4 (5.8, 25.0)	**1.31 (1.12 – 1.52)**	1.05 (0.92 – 1.21)

Stratification Variables	QFT Status	Unweighted frequency Hypertension*/Total	Weighted Prevalence of Hypertension* (95%CI)	Prevalence Difference (95%CI)	Prevalence Ratios	
					Crude	Adjusted†
					cPR (95%CI)	aPR (95%CI)
Foreign Born	Negative	500/1167	37.7 (31.9 – 43.4)	Reference	Reference	Reference
	Positive	166/307	51.3 (45.4 – 57.1)	13.6 (9.3, 17.9)	**1.36 (1.22 – 1.51)**	1.05 (0.92 – 1.21)
Stratified by current smoking status						
No	Negative	627/954	61.8 (56.0 – 67.7)	Reference	Reference	Reference
	Positive	95/130	76.2 (66.8 – 85.6)	14.4 (4.2, 24.5)	**1.23 (1.07 – 1.42)**	1.09 (0.93 – 1.27)
Yes	Negative	439/851	47.2 (42.5 – 52.0)	Reference	Reference	Reference
	Positive	56/101	47.5 (34.4 – 60.7)	0.3 (-14.3, 14.9)	1.01 (0.74 – 1.37)	0.89 (0.69 – 1.14)
Stratified by diabetes status						
Euglycemic	Negative	1083/2764	39.6 (35.4 – 43.8)	Reference	Reference	Reference
	Positive	114/223	50.6 (42.6 – 58.5)	11.0 (3.0, 18.9)	**1.28 (1.08 – 1.51)**	1.01 (0.86 – 1.18)
Pre-diabetes	Negative	689/1102	59.8 (56.6 – 63.0)	Reference	Reference	Reference
	Positive	83/141	57.9 (44.2 – 71.6)	-1.9 (-15.6, 11.8)	0.97 (0.76 – 1.23)	0.95 (0.76 – 1.18)
Diabetes	Negative	522/644	81.1 (78.3 – 83.9)	Reference	Reference	Reference
	Positive	89/115	78.6 (68.7 – 88.5)	-2.5 (-13.0, 8.0)	0.97 (0.85 – 1.11)	0.94 (0.82 – 1.07)
Stratified by HIV Status						
HIV negative	Negative	1226/3130	39.1 (35.5 – 42.6)	Reference	Reference	Reference
	Positive	102/243	43.2 (34.8 – 51.6)	4.1 (-4.3, 12.5)	1.11 (0.91 – 1.35)	0.93 (0.81 – 1.07)
HIV positive	Negative	4/15	18.4 (0 – 39.0)	Reference	Reference	Reference
	Positive	1/1	100.0 (100.0 – 100.0)	81.6 (61.0 – 100.0)	**5.43 (1.92 – 15.36)**	6.24 (1.79 – 21.72)

aPR – adjusted prevalence ratio; CI – Confidence interval; PR – prevalence ratio; QFT – QuantiFERON-TB Gold In-Tube; US – United States

*Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
†Adjusted for age (continuous) and gender
‡Adjusted for gender

Table S6. Weighted prevalence of various hypertension classifications by confirmed tuberculosis infection status among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence (95%CI) Confirmed TB Infection Status N=4,266				
	Confirmed		Discordant TST and QFT		
	Negative N=3706 92.2% (90.5 – 93.9)	Positive N=190 2.1% (1.4 – 2.8)	TST* – and QFT + N=177 2.5 (1.4 – 3.5)	TST + and QFT – N=193 3.2 (2.5 – 4.00)	Any Discordance N=370 5.7% (4.6 – 6.8)
Primary study outcome					
Any hypertension indication[a] (n=2,250/4,266)	49.6 (45.7 – 53.5)	60.8 (51.4 – 70.3)	50.5 (38.9 – 62.2)	54.4 (43.5 – 65.4)	52.7 (43.9 – 61.6)
Measured blood pressure categories					
Normal blood pressure[b] (n=1,914)	47.0 (42.9 – 51.1)	36.6 (27.6 – 45.5)	49.8 (40.9 – 58.7)	39.6 (26.1 – 53.0)	44.0 (35.2 – 52.9)
Borderline hypertension[c] (n=714)	17.8 (15.5 – 20.0)	15.3 (8.3 – 22.3)	16.3 (8.2 – 24.4)	25.1 (14.7 – 35.5)	21.3 (13.4 – 29.1)
Hypertensiond (n=1,638/4,266)	35.2 (32.3 – 38.1)	48.1 (38.7 – 57.6)	33.9 (25.4 – 42.4)	35.3 (26.9 – 43.7)	34.7 (28.3 – 41.1)
Stage 1 hypertension[e] (n=1121)	24.9 (22.5 – 27.3)	37.0 (28.6 – 45.4)	25.4 (16.7 – 34.1)	24.0 (12.6 – 35.4)	24.6 (16.3 – 32.9)
Stage 2 hypertension[f] (n=517)	10.3 (8.9 – 11.7)	11.1 (6.2 – 16.1)	8.5 (3.3 – 13.7)	11.3 (4.0 – 18.5)	10.1 (5.5 – 14.6)
Hypertension Diagnosis					
Previously diagnosed hypertension[g] (n=1,496/4,266)	30.9 (27.5 – 34.3)	35.8 (27.6 – 44.0)	29.4 (17.9 – 40.8)	37.1 (25.9 – 48.4)	33.8 (27.0 – 40.6)
Self-reported current use of anti-hypertension medication[h] (n=1,292/1,496)	86.0 (82.2 – 89.9)	90.2 (79.7 – 100.0)	81.5 (65.8 – 97.1)	98.6 (96.0 – 100.0)	92.5 (87.4 – 97.5)
Undiagnosed hypertension[i] (n=754/4,266)	18.7 (16.4 – 21.0)	25.2 (18.1 – 32.3)	21.4 (12.2 – 30.6)	17.3 (6.1 – 28.5)	19.1 (12.2 – 25.9)
Hypertension Control (n=1,496)					
Controlled hypertension without medications[j] (n=1,286)	11.8 (9.6, 13.9)	6.9 (0.1, 13.0)	13.5 (1.6, 25.4)	5.4 (1.0, 9.8)	8.4 (3.5, 13.3)
Controlled hypertension with medications[k] (n=79)	34.8 (29.2, 40.4)	28.9 (16.2, 41.6)	43.6 (20.8, 66.4)	46.1 (34.0, 58.2)	45.2 (35.4, 55.0)
Uncontrolled hypertension without medications[l] (n=51)	15.0 (11.5, 18.4)	17.2 (5.7, 28.7)	18.9 (6.1, 29.7)	5.4 (0.3, 10.5)	10.1 (5.5, 14.7)
Uncontrolled hypertension with medications[m] (n=80)	38.5 (34.7, 42.2)	47.0 (36.2, 57.8)	25.0 (12.3, 37.7)	43.1 (28.9, 57.3)	36.3 (26.4, 46.2)

Abbreviations:
CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube; TST – tuberculin skin test

*TST positive was defined as skin induration ≥5mm among HIV-positive individuals or >10mm among HIV negative (following NHANES analytical notes). Induration <5mm (for HIV-positive individuals) or ≤10mm (for HIV-negative individuals) was considered negative

[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"

[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S7. Crude and adjusted associations between confirmed tuberculosis infection status and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Hypertension Measures	Measures of Association					
	Prevalence Difference (95%CI)		Prevalence Ratios (PR)			
			Crude PR (95%CI)		Adjusted* PR (95%CI)	
	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI
Primary study outcome						
Any hypertension indication[a]	11.3 (1.0, 21.5)	3.2 (-5.1 – 11.5)	**1.23 (1.03 – 1.46)**	1.06 (0.91 – 1.25)	1.08 (0.90 – 1.30)	0.98 (0.84 – 1.14)
Measured blood pressure categories						
Normal blood pressure[b]	-10.5 (-19.4, -1.6)	3.0 (-12.5, 6.4)	**0.78 (0.63 – 0.99)**	0.94 (0.76 – 1.16)	0.89 (0.69 – 1.15)	1.03 (0.84 – 1.26)
Borderline hypertension[c]	-2.4 (-9.5, 4.6)	3.5 (-4.1, 11.1)	0.86 (0.55 – 1.36)	1.20 (0.84 – 1.71)	0.82 (0.51 – 1.32)	1.15 (0.81 – 1.63)
Hypertension[d]	12.9 (2.8, 23.0)	-0.5 (-7.1, 6.1)	**1.37 (1.10 – 1.70)**	0.99 (0.82 – 1.19)	1.21 (0.98 – 1.49)	0.91 (0.75 – 1.10)
Stage 1 hypertension[e]	12.1 (2.8, 21.5)	-0.2 (-8.5, 8.0)	**1.49 (1.24 – 1.94)**	0.99 (0.71 – 1.38)	**1.37 (1.06 – 1.77)**	0.93 (0.66 – 1.32)
Stage 2 hypertension[f]	0.8 (-4.1, 5.7)	-0.3 (-5.2, 4.7)	1.08 (0.68 – 1.68)	0.98 (0.60 – 1.59)	0.88 (0.53 – 1.48)	0.86 (0.52 – 1.42)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	4.9 (-3.0, 12.7)	2.9 (-5.0, 10.7)	1.16 (0.93 – 1.44)	1.09 (0.86 – 1.38)	0.99 (0.77 – 1.28)	1.00 (0.81 – 1.23)
Self-reported current use of anti-hypertension medication[h]	4.2 (-8.1, 16.5)	6.4 (0.6, 12.3)	1.05 (0.84 – 1.30)	**1.07 (1.01 – 1.15)**	1.03 (0.91 – 1.18)	**1.08 (1.01 – 1.16)**
Undiagnosed hypertension[i]	6.5 (-0.3, 13.3)	0.4 (-6.9, 7.7)	**1.35 (1.03 – 1.77)**	1.02 (0.70 – 1.50)	1.26 (0.97 – 1.64)	0.96 (0.65 – 1.41)
Hypertension Control†						
Controlled hypertension without medications[j]	-4.9 (-14.2, 4.4)	-3.3 (-8.6, 2.0)	0.59 (0.39 – 1.10)	0.72 (0.39 – 1.32)	0.85 (0.27 – 2.70)	0.85 (0.48 – 1.53)
Controlled hypertension with medications[k]	-5.9 (-18.6, 6.8)	10.4 (-0.6, 21.4)	0.83 (0.54 – 1.28)	1.30 (1.00 – 1.69)	0.81 (0.53 – 1.22)	1.26 (0.97 – 1.65)
Uncontrolled hypertension without medications[l]	2.3 (-9.7, 14.2)	-4.9 (-10.3, 5.4)	1.15 (0.57 – 2.33)	0.68 (0.42 – 1.10)	1.32 (0.68 – 2.58)	0.70 (0.41 – 1.18)
Uncontrolled hypertension with medications[m]	8.5 (-3.4, 20.4)	-2.2 (-12.4, 8.1)	1.22 (0.94 – 1.58)	0.94 (0.71 – 1.25)	1.20 (0.91 – 1.58)	**1.27 (1.05 – 1.54)**

Abbreviations:
CI – confidence interval; PR – prevalence ratio; TBI – tuberculosis infection

*Models adjusted for age and gender
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,496)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S8. Sensitivity analysis to account for misclassification of covariates and different ways to handle age (confounder) included in the multivariable survey-weighted robus Poisson models to estimate the association between tuberculosis infection and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Models	Covariate(s) included in the model	QFT Result	Adjusted Prevalence Ratios	
			A (Age, continuous)	B (Age Group - Quartiles)
			aPR (95%CI)	aPR (95%CI)
Model 1	Age	Negative Positive	Reference 1.02 (0.93 – 1.13)	Reference 1.03 (0.93 – 1.14)
Model 2	Age, sex	Negative Positive	Reference 1.01 (0.92 – 1.10)	Reference 1.01 (0.91 – 1.13)
Model 3	Age, sex, BMI	Negative Positive	Reference 1.02 (0.92 – 1.13)	Reference 1.03 (0.93 – 1.15)
Model 4	Age, sex, income to poverty ratio	Negative Positive	Reference 1.00 (0.91 – 1.09)	Reference 1.01 (0.91 – 1.12)
Model 5	Age, sex, country of birth	Negative Positive	Reference 1.05 (0.96 – 1.14)	Reference 1.07 (0.97 – 1.19)
Model 6	Age, sex, income to poverty ratio, country of birth, BMI	Negative Positive	Reference 1.05 (0.95 – 1.17)	Reference 1.08 (0.97 – 1.21)
Model 7	Age, sex, income to poverty ratio, country of birth, BMI, current smoking status	Negative Positive	Reference 1.05 (0.93 – 1.17)	Reference 1.07 (0.93- 1.24)
Model 8	Age, sex, income to poverty ratio, country of birth, BMI, current smoking status, type-2 diabetes mellitus status, HIV status	Negative Positive	Reference 1.03 (0.99 – 1.08)	Reference 1.04 (0.99 – 1.08)
Model 9	Age, sex, income to poverty ratio, country of birth, BMI, type-2 diabetes mellitus status, HIV status	Negative Positive	Reference 1.04 (0.90 – 1.20)	Reference 1.05 (1.00 – 1.09)
Model 10*	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, BMI, smoking	Negative Positive	Reference 1.01 (0.97 – 1.06)	Reference 1.04 (0.99 – 1.09)
Model 11	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, and stroke	Negative Positive	Reference 1.00 (0.96 – 1.05)	Reference 1.03 (0.98 – 1.08)
Model 12	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, and stroke, BMI, smoking	Negative Positive	Reference 1.01 (0.96 – 1.05)	Reference 1.04 (0.99 – 1.08)
Model 13	Age, sex, race education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, stroke, BMI, current smoking	Negative Positive	Reference 1.07 (0.97 – 1.18)	Reference 1.09 (1.00 – 1.18)

	status, heavy alcohol consumption, any dyslipidemia, statin prescription, HIV status			

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	Figure1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	22
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10

		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Tuberculosis infection and hypertension: Prevalence estimates from the US National Health and Nutrition Examination Survey

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-075176.R1
Article Type:	Original research
Date Submitted by the Author:	12-Sep-2023
Complete List of Authors:	Salindri, Argita; Stanford University School of Medicine, Department of Medicine Auld, Sara; Emory University School of Medicine, Division of Pulmonary and Critical Care Medicine; Emory University School of Public Health, Department of Epidemiology Gujral, Unjali; Emory University School of Public Health, Hubert Department of Global Health Urbina, Elaine; University of Cincinnati College of Medicine, Department of Pediatrics Andrews, Jason R; Stanford University School of Medicine, Division of Infectious Diseases and Geographic Medicine, Department of Medicine Huaman, Moises; University of Cincinnati College of Medicine, Department of Internal Medicine Magee, Matthew J.; Emory University School of Public Health, Hubert Department of Global Health; Emory University School of Public Health, Department of Epidemiology
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Public health, Epidemiology
Keywords:	Hypertension < CARDIOLOGY, Tuberculosis < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title Page

Prepared according to manuscript instructions for *BMJ Open* (original research)

Version: R1.Sep 10, 2023

Title: Tuberculosis infection and hypertension: Prevalence estimates from the US National Health and Nutrition Examination Survey

Authors:

Argita D. Salindri[1], Sara C. Auld[2,3], Unjali P. Gujral[4], Elaine M. Urbina[5], Jason R. Andrews[1], Moises A. Huaman[6*], Matthew J. Magee[3,4*]

Affiliations:

1. Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, CA, USA
2. Division of Pulmonary and Critical Care Medicine, Emory University School of Medicine, Atlanta, GA, USA
3. Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
4. Hubert Department of Global Health, Emory University Rollins School of Public Health, Atlanta, GA, USA
5. Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH, USA
6. Department of Internal Medicine, College of Medicine, University of Cincinnati, Cincinnati, OH, USA

*Equal contribution

Main Article word count: 3737/4000

Abstract count: 276/300

Key points: 37/40

Tables & Figures: 5/5

References: 44/40

Keywords: latent tuberculosis infection, interferon-γ response, hypertension

Summary:

The prevalence of hypertension was high (59%) among adults with tuberculosis infection in the U.S. In addition, we found that the prevalence of hypertension was significantly higher among adults with positive QFT without established hypertension risk factors.

Corresponding Author:

Argita Salindri, PhD, MPH

Division of Infectious Diseases and Geographic Medicine

Department of Medicine

Stanford University School of Medicine

Biomedical Innovations Building, Stanford, CA 94304

Email: adsalind@stanford.edu

Phone: +1 404 490 5906

ABSTRACT

Objectives: Latent Tuberculosis infection (LTBI) is marked by dynamic host-pathogen interactions with persistent low-grade inflammation and is associated with increased risk of cardiovascular diseases (CVD) including acute coronary syndrome, myocardial infarction, and stroke. However, few studies assess the relationship between LTBI and hypertension, an intermediate of CVD. We sought to determine the association between LTBI and hypertension using data representative of the adult US population.

Methods: We performed cross-sectional analyses using data from the 2011–2012 US National Health and Nutrition Examination Survey (NHANES). Eligible participants included adults with valid QuantiFERON-TB Gold In-Tube (QFT-GIT) test results who also had blood pressure measures and no history of TB disease. LTBI was defined by a positive QFT-GIT. We defined hypertension by either elevated measured blood pressure levels (i.e., systolic ≥130mmHg or diastolic ≥80mmHg) or known hypertension indications (i.e., self-reported previous diagnosis or use of antihypertensive medications). Analyses were performed using robust quasi-Poisson regressions and accounted for the stratified probability sampling design of NHANES.

Results: The overall prevalence of LTBI was 5.7% (95%CI 4.7–6.7) and hypertension was present among 48.9% (95%CI 45.2–52.7) of participants. The prevalence of hypertension was higher among those with LTBI (58.5%, 95%CI 52.4–64.5) than those without LTBI (48.3%, 95%CI 44.5–52.1) (prevalence ratio [PR]=1.2, 95%CI 1.1–1.3). However, after adjusting for confounders, the prevalence of hypertension was similar for those with and without LTBI (adjusted PR=1.0, 95%CI 0.9 –1.1). The unadjusted prevalence of hypertension was higher among those with LTBI vs. no LTBI, especially among individuals without CVD risk factors including those with normal BMI (PR=1.6, 95%CI 1.2–2.0), euglycemia (PR=1.3, 95%CI 1.1–1.5), or non-smokers (PR =1.2, 95%CI 1.1–1.4).

Conclusions: More than half of adults with LTBI in the US had hypertension. Importantly, we observed a relationship between LTBI and hypertension among those without established CVD risk factors.

Strengths and limitations

Strengths:

- These analyses were conducted using data representative of civilian, non-institutionalized US adults, and thus, provide a robust population estimate of the prevalence of latent tuberculosis infection and hypertension in the US
- Comprehensive definitions and different cut-offs of hypertension were used (i.e., measured blood pressure level, previous diagnosis hypertension by healthcare providers) to model the association between latent tuberculosis infection and hypertension

Limitations:

Our findings may not be representative to other regions with higher burdens of tuberculosis

- The cross-sectional study design of NHANES prevented us from assessing the temporal relationship between latent tuberculosis infection and hypertension

INTRODUCTION

About one-quarter of the world's population (~2 billion) has been infected to *Mycobacterium tuberculosis* (*Mtb*). [1] Among individuals infected with the bacteria, 5-10% are at risk of developing TB disease at some point in their life. [2 3] Tuberculosis infection (TBI), or most commonly known as latent tuberculosis infection or LTBI, is increasingly recognized as a heterogenous clinical state in which some individuals have dynamic host-pathogen interactions with persistent low-grade inflammation. This immune dysregulation has been associated with an increased risk of cardiovascular diseases (CVD) including acute coronary syndromes, myocardial infarction, and stroke. [1 4-12] This convergence of TBI and CVD risk poses a particular challenge for low- and middle-income countries where TBI is most prevalent and incidence of chronic non-communicable diseases, including CVD, is increasing rapidly. [13 14] Improved understanding of the impact of TBI on CVD risk is vital in settings where TBI and CVD are highly co-prevalent in order to design public health intervention programs aiming to reduce the burden of two diseases.

Epidemiologic data from observational cohort studies support an increased risk of CVD among people with TB disease. [8-12] Several studies also indicated that hypertension, an established intermediate of CVD, may be more common among patients with TB disease compared to non-TB controls. [8 11 14-16] Furthermore, CVD was the leading contributor to post-TB mortality, accounting for 15 – 26% of deaths among TB survivors in a recent systematic review and meta-analysis. [17] In addition to these associations between TB disease and CVD, recent observational studies have found an association between TBI and various CVDs including acute myocardial infarction and coronary artery disease. [9 18 19] However, studies assessing the association between TBI and hypertension remain limited.

To date, few studies have evaluated the relationship between TBI and hypertension. One cohort study from a large metropolitan healthcare system in the U.S. reported that

individuals with TBI had greater incidence of hypertension compared to those without TBI and that rates were highest among those untreated for TBI. [5] Furthermore, it is unknown whether the quantitative measures of IGRA, which may indicate the underlying mycobaterial burden and has been associated with increased risks of progression to TB disease, [20-23] is associated with hypertension. Improved understanding of the association between TBI, quantitative measures of IGRA, and and hypertension may clarify the role that TB prevention efforts in reducing the burden of CVD, both in the U.S. and globally.

Given existing knowledge gaps, we aimed to estimate the association between TBI and hypertension prevalence. We also investigated whether the magnitude of host immune responses to *Mtb* was associated with hypertension among those with positive IGRA test results.

METHODS

Study Design and Eligible Participants

We performed an analysis of cross-sectional data from the 2011 – 2012 US National Health and Nutrition Examination Survey (NHANES), [24] the most recent NHANES cycle released that includes measures of TBI. NHANES is a study led by the US Centers for Disease Control and Prevention (CDC) which aims to assess the health and nutritional status of non-institutionalized civilians representative of the US population using a complex, stratified, multistage probability cluster sampling design. NHANES collects demographic and health information using questionnaires administered by trained interviewers and standardized physical examinations performed in mobile examination centers. Eligible NHANES participants for our analyses were adults (≥18 years) with valid TBI test results and blood pressure measurements, and no history of TB disease (Figure 1).

Study Measures and Definitions

Our primary study outcome, any hypertension, was defined as having either (1) "measured hypertension," defined as an average systolic blood pressure level of ≥130 mmHg or diastolic blood pressure level of ≥80 mmHg across three consecutive measurements, or (2) a self-reported previous hypertension diagnosis by a health care provider or current use of antihypertensive medications (i.e., known hypertension). We categorized measured blood pressure levels into "normal" (i.e., systolic <120mmHg and diastolic <80mmHg), "borderline hypertension" (i.e., systolic 120-129mmHg and diastolic <80mmHg), "stage 1 hypertension" (i.e., systolic 130 – 139mmHg or diastolic 80-89mmHg), and "stage 2 hypertension" (i.e., systolic ≥140mmHg or diastolic ≥90mmHg) according to American College of Cardiology/American Heart Association guidelines. [25] Among participants with a prior diagnosis of hypertension, we classified blood pressure as "controlled" (systolic <130 mmHg and diastolic <80 mmHg) or "uncontrolled" (systolic ≥130mmHg or diastolic ≥80mmHg) with or without a self-reported use of antihypertensive medications.

Our primary study exposure, TBI, was defined by a positive QuantiFERON-TB Gold In Tube or QFT test, an in-vitro laboratory test to detect TB infection by measuring cell-mediated immune responses to TB-specific antigens. [26 27] Individuals with indeterminate test results were excluded from our analyses. For those with a positive QFT, we also extracted the quantitative results and defined the IFN-γ TB antigen response by subtracting TB NIL control values from TB antigen values (i.e., Ag-NIL values). To express IFN-γ TB antigen responses, instead of using the traditional manufacturer cut-off of ≥0.35, we used the 4.00 cut-off as previous studies showed that individuals with Ag-NIL values ≥4.00 are at greater risk from developing TB disease. [20 22 23] Thus, in our analyses, Ag-NIL values were categorized as "low" (<4 IU/ml) or "high" (≥4 IU/ml). For a sensitivity analysis, we performed a subgroup analysis of participants with both QFT and tuberculin skin test (TST) results. We defined "confirmed TB infection" when both TST and QFT results were positive and "no TB infection" if

both TST and QFT results were negative. Participants with discordant TST and QFT results (i.e., TST negative and QFT positive, TST positive and QFT negative) were classified as "any discordance."

Other important covariates, including age, sex, race, educational attainment, income to poverty ratio, country of birth, body mass index (BMI), diabetes mellitus status, HIV status, lipid profile, self-reported smoking behavior, alcohol consumption, statin prescription, and previous diagnosis of coronary heart disease, myocardial infarction, or stroke were also abstracted. We classified BMI as "underweight" (BMI <18.5 kg/m^2), "normal" (BMI 18.5 – 24.9 kg/m^2), "overweight" (BMI 25 – 29.9 kg/m^2), and obese (BMI ≥30kg/m^2). [28] As NHANES grouped individuals aged ≥80 years in one category, we divided age into quartile ranges and grouped as "quartile 1 (18 – 31 years)", "quartile 2 (32 – 47 years)", "quartile 3 (48 – 62 years)", and "quartile 4 (≥63 years)" to account for the non-linearity of age in sensitivity analyses.

Patient and Public Involvement

None

Statistical Analysis

We estimated weighted prevalence and 95% confidence intervals (CI) to determine the burden of TBI and hypertension in the US adult population. Rao-Scott Chi-square tests were used to assess the bivariate association between participants' demographic and clinical characteristics, TBI, Ag-NIL values, and hypertension. Multivariable robust Poisson regression with quasi-likelihood was used to estimate the association between TBI and hypertension, expressed in prevalence ratios (PRs) and 95% CI. The same regression approach was used to estimate the association between Ag-NIL responses and hypertension. In addition to prevalence ratios, we also estimated prevalence differences (PDs) and their 95%CI. Covariates included in

the multivariable models were based on bivariate associations (Table S1 and S2), established risk factors reported in previously published studies, and directed acyclic graphs (DAG). [29] Briefly, we identified potential confounders using bivariate associations and previously published literature, which then mapped into a DAG to determine inclusion in the final model. To account for the missingness of key covariates in the final adjusted model, we assigned aberrant values to any missing information to avoid deletion. We also assessed interaction between TBI and hypertension by participant characteristics (i.e., age, BMI, glycemic status, smoking status) on the additive (prevalence difference) and multiplicative (prevalence ratio) scales by including the cross-product terms within multivariable models. All analyses were performed using *survey* package in R and accounted for the weighted stratified probability sample design of NHANES by applying weight (*WTMEC2YR*), cluster (*SDMVPSU*), and strata (*SDMVSTRA*) variables. Taylor Series Linearization was used to produce design-adjusted standard errors and a two-sided p-value less than 0.05 considered statistically significant in all analyses.

Subgroup and Sensitivity Analyses

Sub-group analyses were conducted using an analytic approach with “domain” variables created to indicate sub-populations of interest. [30 31] Subgroup analyses were performed among those with previously diagnosed hypertension to determine the association between TBI (including Ag-NIL values) and controlled hypertension. Sensitivity analyses were performed to quantify systematic errors due to a) TBI misclassification, b) hypertension misclassification, c) covariate misspecification in multivariable models, and d) the classification of age as a confounder. To account for errors resulting from TBI misclassification, we ran additional models with confirmed TB infection as the exposure. To address potential biases due to hypertension misclassification, we ran an additional analysis using the prior hypertension clinical cut off. [25] In this additional model, we defined any hypertension as having (1) an average systolic blood pressure level of ≥140 mmHg or diastolic blood pressure level of ≥90 mmHg across three

consecutive measurements, or (2) a self-reported previous hypertension diagnosis by a health care provider or current use of antihypertensive medications. To quantify errors due to covariate misspecification, we ran multiple robust Poisson models with different sets of covariates and observed changes in prevalence ratios estimates across models. To account for the confounding effect of age, we ran multiple iterations of robust Poisson models with different forms of age measures (i.e., continuous and age quartiles).

RESULTS

Study population

In NHANES 2011 – 2012, 9,338 participants were surveyed and examined (response rate of 69.5%), 60.1% (5,615/9,338) of whom were ≥18 years old (Figure 1). Among included adults, 259 did not have valid blood pressure measurements. Of those with valid blood pressure measurements, 32 had a previous diagnosis of TB disease and 335 had a missing QFT, with 4,989 participants meeting eligiblity for this analytic cohort. The weighted prevalence of TBI in the cohort was 5.7% (95% confidence interval [CI] 4.7– 6.7) and any hypertension was present for 48.9% (95%CI 45.2 – 52.7) of participants (Table 1).

Associations between tuberculosis infection and hypertension

The prevalence of any hypertension was higher among those with TBI (58.5%, 95% CI 52.4 – 64.5) than those without TBI (48.3%, 95%CI 44.5 – 52.1) (prevalence difference [PD] 10.2%, 95%CI 5.0 – 15.4) (Table 1). After adjusting for potential confounders including age (continuous), sex, race, educational attainment level (as a proxy of socioeconomic status), country of birth, diabetes mellitus status, BMI, and smoking status, the prevalence of any hypertension was similar among those with and without TBI (adjusted prevalence ratio [aPR] 1.0, 95%CI 1.0 – 1.1). The association between TBI and hypertension was similar when examining the two components used to define our primary outcome (i.e., measured

hypertension and self-reported hypertension/use of antihypertensive medications) both in the crude and adjusted models (Table 1).

Association between Ag-NIL values and hypertension

The prevalence of any hypertension was highest among those with TBI and high Ag-NIL values (60.4%, 95%CI 53.0 – 67.7) compared to those with TBI and low Ag-NIL values (57.6%, 95%CI 48.7 – 66.6) or those without TBI (48.3%, 95%CI 44.5 – 52.1) (Table S3). After adjusting for age and gender, however, the prevalence of any hypertension was similar among the three QFT groups being compared (Table S4). Similar trends were also observed for the associations between Ag-NIL values and both measured hypertension and self-reported previous diagnosis of hypertension (Figure 2).

Interaction analyses: established hypertension risk factors and HIV

We observed relationships between TBI and hypertension among participants without established hypertension risk factors who would be considered at lower risk for CVD. For example, comparing individuals with and without TBI, the prevalence difference of any hypertension was substantially higher among those with normal BMI (prevalence difference [PD] 17.7, 95%CI 6.3 – 29.2), euglycemia (PD 11.3, 95%CI 3.0 – 18.9), and non-smoking (PD 14.4, 95%CI 4.2 – 24.5) groups (Figure 3) compared to those with BMI <18.5 kg/m^2 or BMI ≥25 kg/m^2, pre-diabetes/diabetes or smokers. Product terms for BMI, glycemic level, and smoking status were non-significant on the prevalence ratio scale ($p<0.05$).

We also found that the association between TBI and hypertension was significantly different across HIV status. For instance, the prevalence difference of any hypertension comparing those with TBI to those without TBI was 4.1 percentage points (95%CI -4.3 – 12.5) among those without HIV infection and 81.6 percentage points (95%CI 61.0 – 100.0) among those with HIV infection. After adjusting for age and gender, the adjusted prevalence ratio was

0.9 (95%CI 0.8 – 1.1) among those without HIV infection and 6.2 (95%CI 1.8 – 21.7) among those with HIV infection (statistical interaction p<0.01) (Table S5).

Subgroup and sensitivity analyses

From subgroup analyses conducted among those with known hypertension, the prevalence of controlled hypertension without medications was significantly lower among those with positive QFT (5.2%, 95%CI 2.0 – 8.3) compared to those with negative QFT (11.8%, 95%CI 9.5 – 14.0), although the association was no longer significant after adjusting for key confounders (aPR 0.6, 95%CI 0.4 – 1.1) (Table 2). Conversely, the prevalence of uncontrolled hypertension with medications, the more severe form of hypertension, although non-significant, were slightly higher among those with positive QFT compared to those with negative QFT (Figure 2).

In models with confirmed TB infection (i.e., positive QFT and positive TST) as the study exposure, the prevalence of any hypertension was highest among those with confirmed TB infection (60.8%, 95%CI 51.4 – 70.3) compared to those with no TB infection (49.6%, 95%CI 45.7 – 53.5) or those with discordant TST and QFT results (52.7%, 95%CI 43.9 – 61.6) (p=0.12) (Table S6). We observed similar trends in the crude and adjusted associations between TBI and hypertension when we used both QFT and TST (Table S7) vs. QFT alone to define TBI. Results from models that used prior clinical cut-offs to define hypertension (systolic blood pressure level of ≥140 mmHg or diastolic blood pressure level of ≥90 mmHg) were similar to results from models with current hypertension definitions (aPR_{prior}=1.01, 95%CI 0.97 – 1.06 vs. $aPR_{current}$=0.94, 95%CI 0.89 – 1.00) (data not shown). Results from sensitivity analyses to quantify bias due to covariate misspecification in the multivariable models indicated that prevalence ratios of any hypertension comparing those with positive QFT to those with negative QFT were similar when age was treated continuously or grouped in quartiles (ranged from 1.0 – 1.1) (Table S8).

DISCUSSION

Using data representative of US adult population, we found a high prevalence of hypertension (i.e., nearly 1 out of 2) in the 2011 – 2012 NHANES cycle. We reported similar adjusted prevalence of hypertension among individuals with or without TBI. In our study, individuals with positive QFT and high Ag-NIL values were more likely to have any hypertension, but less likely to have the more severe form of hypertension (i.e., uncontrolled hypertension without medications). We also observed that the association between TBI and hypertension was more common among individuals without established hypertension risk factors. Collectively, our results provide preliminary epidemiologic evidence suggesting that hypertension, a well-established intermediate for CVD, was more common among individuals with TBI than those without TBI in the US populations.

Our finding suggesting that hypertension is more common among individuals with TBI than those without TBI is consistent with previous studies. For example, a retrospective cohort study conducted among 5,185 individuals with TBI and healthy controls using data from a large metropolitan healthcare system in the US reported a higher hazard rates of hypertension incidence (defined by ICD-9 codes) among those with TBI (defined by ICD-9 codes and tuberculin skin test/IFN-γ release assay) compared to healthy controls without TBI (HR 2.0, 95%CI 1.6 – 2.5). [5] In addition, a cross-sectional study conducted among 2,351 TST-positive individuals in South India reported a slightly higher prevalence of hypertension (defined as systolic >130 mmHg) among those with confirmed TBI (defined as TST and QFT positive) (15%) compared to those latent TB negative (12%) (aOR 1.18, 95%CI 1.0 – 1.56). [32] Unlike the two studies mentioned above, we used a more comprehensive definition of hypertension by combining objectively measured blood pressure levels (systolic and diastolic) and known hypertension indications (i.e., previous hypertension diagnosis or self-reported use of antihypertensive medications) to avoid potential misclassification.

There are several plausible mechanisms that explain how TBI may be associated with hypertension. First, underlying pathophysiology related to chronic inflammation, even at relatively low levels, is linked to hypertension and therefore the proinflammatory state that accompanies TBI may increase blood pressure. [33 34] Second, TBI may be a proxy of other key factors related to social position which in turn impact hypertension risk. Hypertension is known to be multifactorial spanning from the group or community to the individual. Several physical, social, political, and environments risk factors that may influence hypertension were not fully accounted for in our analyses (e.g., stress, family history, diet, lifestyle, physical activity, geographical delineation, illicit drug use, access to healthcare, or insurance coverage). If some of these variables are associated with TBI, it is plausible that our reported estimates are distorted due to residual confounding effects. Further studies utilizing social ecological models and longitudinal designs are warranted to better understand the true effect of TBI on hypertension.

Furthermore, we also reported that the prevalence of hypertension was highest among individuals with positive QFT and high Ag-NIL values, but we observed no dose-response relationship nor statistical significance after adjusting for key risk factors. TB infection has been associated with enhanced levels of systemic inflammation and immune activation, including increased expression of tumor necrosis factor (TNF)-α, interferons, and interlukin-6 (IL-6). [4-7] These chemokines and dysfunctional immune responses play an important role in the pathogenesis of hypertension and CVD. [35 36] Individuals with positive QFT and higher Ag-NIL values are more likely to develop to active TB [22 37] as they may have higher mycobacterial burden, [20] and thus, could potentially have higher degree of inflammation or immune responses to the bacterial infection. Interestingly, among those with previously diagnosed hypertension, we found that individuals with TBI may have higher levels of hypertension compared to those without TBI. This was indicated by the higher prevalence of uncontrolled

hypertension without medications among those with TBI. However, the available data do not allow us to discern if these differences are due to clinical differences or access to care.

Our cross-sectional study design may not be the appropriate design to observe the expected associations or dose-response relationship between TBI, IFN-γ TB antigen responses, and hypertension. Furthermore, the time of TBI in the life-course may have different implications on TBI and hypertension association. In this NHANES cohort, the majority (>90%) of foreign born with positive QFT have stayed in the US for ≥5 years, and thus, we postulated that TBI happened before arriving in the US. It is plausible that these individuals are either in the latent or incipient stage where there is no to minimum bacteria replication, and thus, minimum pro-inflammatory responses. [38] Newly arrived immigrants may face higher level of stress with acculturation and other social-environmental pressures which could impact systemic inflammation, immune responses, and/or increased risks of hypertension. Prospective studies to follow individuals with recent TBI diagnosis are still warranted to determine the hypertension and CVD risk trajectories.

Interestingly, we observed associations between TBI and hypertension among those with normal BMI, euglycemic, and non-smokers. These groups may be considered at lower risk of CVD. This finding further reinforces the premise that there is likely to be differing effects of TBI on hypertension risk within subgroups. While the significant TBI-hypertension associations observed among those with lower risk of CVD may be due to the larger sample sizes in NHANES, these preliminary results suggest the need for mechanistic studies. Further clinical investigations and modeling studies are needed to determine whether targeted TB preventive treatment is effective to reduce the global burden of CVD among these groups.

Last, we reported that HIV infection may modify the association between TBI and hypertension. However, this finding needs to be interpreted with caution considering the low prevalence of HIV infection in the 2011-2012 NHANES cycle. Previous studies demonstrated

that hypertension is more common among individuals with HIV infection on antiretroviral therapy compared to those without HIV infection, [39 40] and that there are several plausible pathways regarding how HIV infection could lead to hypertension. [39] For example, the chronic inflammation among people living with HIV (PLWH), even among those with undetectable viral loads on stable antiretroviral therapy, would trigger host immune activation (e.g., upregulation of IL-6) and could lead to stiff blood vessels and impact hypertension risk. [41 42] Further clinical studies with larger sample size are still warranted to fully assess the joint effect between HIV (including HIV clinical characteristics) and TBI, and its association with hypertension.

Our study is subject to limitations. First, our TBI definition (i.e., according to QFT positivity) may include a broad spectrum of individuals who may have cleared the infection, have latent TB, incipient TB, or subclinical TB since no further clinical assessment was made (e.g., symptom screening, chest X-ray, culture test). [43 44] Second, we could not determine the temporal relationship between TBI and hypertension with the cross-sectional study design used in the present paper. Third, we did not account for any record of hypertension prescription, or other commonly prescribed medications that could potentially affect blood pressure levels. Fourth, we defined some of our key variables (including hypertension status and hypertension medication intake) with self-reported information that may be prone to recall bias and likely included some misclassification. However, if misclassification of hypertension was non-differential with respect to TBI, we expect any misclassification in our results would likely biased towards the null. [45] Fourth, we did not take into consideration the CD4 count for the HIV-stratified analyses due to the small, unweighted frequency of individuals with HIV infection. Last, this study was conducted using survey data representative of US adult population but may not be generalizable to other regions with higher TB burdens. Furthermore, we used data from NHANES 2011 – 2012 and were not able to determine whether the prevalence of TB infection and hypertension reported in this study cycle is reflective of the current US population. An

updated analysis to assess trends in the association across multiple NHANES cycles is warranted.

In conclusion, we reported a higher prevalence of hypertension among individuals with positive QFT, although the association was non-significant after adjusting for key confounders, particularly age. To determine the direction of the association between TBI and hypertension, a prospective study following hypertension-free individuals at TBI diagnosis is warranted and would help establish the biological pathways regarding how TBI might increase the risk of CVD. Future prospective work should address the question whether individuals treated for LTBI have lower risk of hypertension. Importantly, our results underscore the need to screen for hypertension and other metabolic disorders among those with TBI, especially among those without traditional CVD risk factors; doing so may help prevent premature deaths attributed to TB and CVD.

DECLARATIONS AND ACKNOWLEDGMENTS

Competing interest

We have no conflict of interest to declare.

Funding

This work was supported in part by the National Center for Advancing Translational Sciences (grant numbers R03TR004097 to MAH), the National Institute of Allergy and Infectious Diseases (grant number UM1AI069501; grant numbers R01AI153152 and R21AI156161 to MJM; grant number K23AI134182 to SCA), and the National Heart, Lung, and Blood Institute (grant number R01HL156779 to MAH) at the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions

MAH, MJM, and ADS conceived the study design. ADS performed the analyses. ADS, MAH, and MJM wrote the first draft of the manuscript. SCA, UPG, EMU, and JRA assisted with further drafting and revisions of manuscripts. All authors reviewed and approved the final version of the manuscript.

Data Availability Statement

This work used publicly available data of the US National Health and Nutrition Examination Survey (NHANES) 2011 – 2012 that can be downloaded directly from CDC's webpage.

TABLE LEGENDS

Table 1 (p.24) Weighted prevalence and adjusted prevalence ratios of hypertension measures by QuantiFERON-TB Gold In-Tube status among US adults, NHANES 2011-2012

This table shows the prevalence of select hypertension measures in the overall adult cohort of NHANES 2011 – 2012 as well as stratified by their tuberculosis infection status. The crude measure of association was expressed as prevalence difference (PD), while the adjusted measure of association was expressed as prevalence ratio (PR).

Table 2 (p.25) Weighted prevalence and adjusted prevalence ratios of controlled and uncontrolled hypertension by QuantiFERON-TB Gold In-Tube status among US adults with known hypertension, NHANES 2011-2012

This table summarizes findings on whether latent tuberculosis infection is associated with severe clinical manifestation of hypertension, indicated by elevated measured blood pressure levels with the use of antihypertensive medications among individuals with known hypertension indications (n=1,711)

FIGURE LEGENDS

Figure 1 Flow chart depicting unweighted frequencies and percentages of participants included in the final analyses based on the eligibility criteria, NHANES 2011 – 2012

This study flow chart provides description of the stepwise exclusion of ineligible participants. From 9,338 individuals who completed NHANES interview and medical examination, we included 4,989 (53.4%) individuals in our primary analyses after excluding those who are <18 years old or those with a record of previous TB disease, or missing blood pressure data and QuantiFERON results

Figure 2 Crude and adjusted associations between QuantiFERON-TB Gold In-Tube results and select hypertension measures among US adults, NHANES 2011 – 2012

Circles in this panel of figures indicate point estimates from the robust Poisson models, expressed as prevalence ratios with the colored bands indicating the accompanying 95% confidence intervals. The vertical dashed line on the x axis value of 1 marks the study null value (i.e., β estimates=0 or prevalence ratio=1.00), suggesting no association. The top panel figures were produced from analyses performed among eligible participants (n=4,989). The lower panel figures were produced from analyses performed among a subset of participants with known hypertension indication(n=1,711)

Figure 3 Relationship between positive QuantiFERON-TB result and hypertension: Stratified by demographic and clinical characteristics among US adults, NHANES 2011 – 2012

This figure shows results from the analyses with statistical interaction term included in the robust Poisson models to evaluate the joint effect between tuberculosis infection and other key risk factors on hypertension. We selected these "moderator" variables by identifying common risk factors for cardiovascular diseases from published studies (e.g., age, race, body mass index, country of birth, smoking status, diabetes status, and HIV status.

REFERENCES

1. Behr MA, Kaufmann E, Duffin J, et al. Latent Tuberculosis: Two Centuries of Confusion. *Am J Respir Crit Care Med* 2021;204(2):142-48. doi: 10.1164/rccm.202011-4239PP [published Online First: 2021/03/25]
2. Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. *PLoS Med* 2016;13(10):e1002152. doi: 10.1371/journal.pmed.1002152
3. WorldHealthOrganization. Tuberculosis Fact Sheet 2016 [Available from: http://www.who.int/mediacentre/factsheets/fs104/en/ accessed 06/11/2017 2016.
4. Feria MG, Chang C, Ticona E, et al. Pro-Inflammatory Alterations of Circulating Monocytes in Latent Tuberculosis Infection. *Open Forum Infectious Diseases* 2022;9(12) doi: 10.1093/ofid/ofac629
5. Mandieka E, Saleh D, Chokshi AK, et al. Latent Tuberculosis Infection and Elevated Incidence of Hypertension. *Journal of the American Heart Association* 2020;9(24):e019144. doi: doi:10.1161/JAHA.120.019144
6. Dixon DL, Wohlford GF, Abbate A. Inflammation and Hypertension. *Hypertension* 2020;75(2):297-98. doi: doi:10.1161/HYPERTENSIONAHA.119.14195
7. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. *Can Commun Dis Rep* 2017;43(3-4):62-66. doi: 10.14745/ccdr.v43i34a01 [published Online First: 2017/03/02]
8. Chung WS, Lin CL, Hung CT, et al. Tuberculosis increases the subsequent risk of acute coronary syndrome: a nationwide population-based cohort study. *Int J Tuberc Lung Dis* 2014;18(1):79-83. doi: 10.5588/ijtld.13.0288 [published Online First: 2013/12/25]
9. Huaman MA, Ticona E, Miranda G, et al. The Relationship between Latent Tuberculosis Infection and Acute Myocardial Infarction. *Clin Infect Dis* 2017 doi: 10.1093/cid/cix910
10. Huaman MA, Kryscio RJ, Fichtenbaum CJ, et al. Tuberculosis and risk of acute myocardial infarction: a propensity score-matched analysis. *Epidemiol Infect* 2017;145(7):1363-67. doi: 10.1017/s0950268817000279 [published Online First: 2017/02/17]
11. Sheu JJ, Chiou HY, Kang JH, et al. Tuberculosis and the risk of ischemic stroke: a 3-year follow-up study. *Stroke* 2010;41(2):244-9. doi: 10.1161/strokeaha.109.567735 [published Online First: 2009/12/26]
12. Salindri AD, Wang JY, Lin HH, et al. Post-tuberculosis incidence of diabetes, myocardial infarction, and stroke: Retrospective cohort analysis of patients formerly treated for tuberculosis in Taiwan, 2002 - 2013. *Int J Infect Dis* 2019 doi: 10.1016/j.ijid.2019.05.015
13. Magee MJ, Salindri AD, Gujral UP, et al. Convergence of non-communicable diseases and tuberculosis: a two-way street? *Int J Tuberc Lung Dis* 2018;22(11):1258-68. doi: 10.5588/ijtld.18.0045 [published Online First: 2018/10/26]
14. Seegert AB, Rudolf F, Wejse C, et al. Tuberculosis and hypertension—a systematic review of the literature. *International Journal of Infectious Diseases* 2017;56:54-61. doi: 10.1016/j.ijid.2016.12.016
15. Shen TC, Huang KY, Chao CH, et al. The risk of chronic kidney disease in tuberculosis: a population-based cohort study. *QJM* 2015;108(5):397-403. doi: 10.1093/qjmed/hcu220 [published Online First: 2014/10/30]
16. Marak B, Kaur P, Rao SR, et al. Non-communicable disease comorbidities and risk factors among tuberculosis patients, Meghalaya, India. *Indian J Tuberc* 2016;63(2):123-5. doi: 10.1016/j.ijtb.2015.07.018 [published Online First: 2016/07/28]
17. Romanowski K, Baumann B, Basham CA, et al. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2019 doi: 10.1016/S1473-3099(19)30309-3

18. Khoufi EAA. Association between latent tuberculosis and ischemic heart disease: a hospital-based cross-sectional study from Saudi Arabia. *Pan Afr Med J* 2021;38:362. doi: 10.11604/pamj.2021.38.362.28110 [published Online First: 2021/08/10]
19. Alsayed Hasanain AF, El-Maghraby KM, AA HZ, et al. Latent tuberculosis infection among patients with coronary artery stenosis: A case-Control study. *International journal of mycobacteriology* 2018;7(2):143-47. doi: 10.4103/ijmy.ijmy_34_18 [published Online First: 2018/06/15]
20. Gupta RK, Lipman M, Jackson C, et al. Quantitative IFN-γ Release Assay and Tuberculin Skin Test Results to Predict Incident Tuberculosis. A Prospective Cohort Study. *Am J Respir Crit Care Med* 2020;201(8):984-91. doi: 10.1164/rccm.201905-0969OC [published Online First: 2019/12/12]
21. Zellweger JP, Sotgiu G, Block M, et al. Risk Assessment of Tuberculosis in Contacts by IFN-γ Release Assays. A Tuberculosis Network European Trials Group Study. *Am J Respir Crit Care Med* 2015;191(10):1176-84. doi: 10.1164/rccm.201502-0232OC [published Online First: 2015/03/13]
22. Andrews JR, Nemes E, Tameris M, et al. Serial QuantiFERON testing and tuberculosis disease risk among young children: an observational cohort study. *Lancet Respir Med* 2017;5(4):282-90. doi: 10.1016/s2213-2600(17)30060-7 [published Online First: 2017/02/22]
23. Winje BA, White R, Syre H, et al. Stratification by interferon-γ release assay level predicts risk of incident TB. *Thorax* 2018 doi: 10.1136/thoraxjnl-2017-211147 [published Online First: 2018/04/07]
24. [dataset] CDC. National Health and Nutrition Examination Survey 2011 - 2012. In: CDC, ed. NHANES 2011 - 2012. USA, 2011 - 2012. [Available from: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=2011.
25. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065 [published Online First: 2017/11/15]
26. Mazurek GH, Jereb J, Lobue P, et al. Guidelines for using the QuantiFERON-TB Gold test for detecting Mycobacterium tuberculosis infection, United States. *MMWR Recomm Rep* 2005;54(Rr-15):49-55. [published Online First: 2005/12/17]
27. Banaei N, Gaur RL, Pai M. Interferon Gamma Release Assays for Latent Tuberculosis: What Are the Sources of Variability? *J Clin Microbiol* 2016;54(4):845-50. doi: 10.1128/jcm.02803-15 [published Online First: 2016/01/15]
28. Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. StatPearls. Treasure Island (FL)2022.
29. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999;10(1):37-48.
30. CDC. NHANES Survey Methods and Analytic Guidelines [Available from: https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx#analytic-guidelines.
31. CDC. NHANES Sample Code [Available from: https://wwwn.cdc.gov/nchs/nhanes/tutorials/samplecode.aspx.
32. Munisankar S, Rajamanickam A, Balasubramanian S, et al. Prevalence of proximate risk factors of active tuberculosis in latent tuberculosis infection: A cross-sectional study from South India. *Front Public Health* 2022;10:1011388. doi: 10.3389/fpubh.2022.1011388 [published Online First: 2022/10/25]
33. Huaman MA, Henson D, Ticona E, et al. Tuberculosis and Cardiovascular Disease: Linking the Epidemics. *Tropical diseases, travel medicine and vaccines* 2015;1 doi: 10.1186/s40794-015-0014-5 [published Online First: 2016/02/03]

34. Huaman MA, De Cecco CN, Bittencourt MS, et al. Latent Tuberculosis Infection and Subclinical Coronary Atherosclerosis in Peru and Uganda. *Clin Infect Dis* 2021;73(9):e3384-e90. doi: 10.1093/cid/ciaa1934 [published Online First: 2021/01/04]
35. De Miguel C, Rudemiller NP, Abais JM, et al. Inflammation and hypertension: new understandings and potential therapeutic targets. *Curr Hypertens Rep* 2015;17(1):507. doi: 10.1007/s11906-014-0507-z [published Online First: 2014/11/30]
36. Tanase DM, Gosav EM, Radu S, et al. Arterial Hypertension and Interleukins: Potential Therapeutic Target or Future Diagnostic Marker? *Int J Hypertens* 2019;2019:3159283. doi: 10.1155/2019/3159283 [published Online First: 2019/06/13]
37. Ledesma JR, Ma J, Zheng P, et al. Interferon-gamma release assay levels and risk of progression to active tuberculosis: a systematic review and dose-response meta-regression analysis. *BMC Infect Dis* 2021;21(1):467. doi: 10.1186/s12879-021-06141-4 [published Online First: 2021/05/24]
38. Migliori GB, Ong CWM, Petrone L, et al. The definition of tuberculosis infection based on the spectrum of tuberculosis disease. *Breathe (Sheff)* 2021;17(3):210079. doi: 10.1183/20734735.0079-2021 [published Online First: 2022/01/18]
39. Fahme SA, Bloomfield GS, Peck R. Hypertension in HIV-Infected Adults: Novel Pathophysiologic Mechanisms. *Hypertension* 2018;72(1):44-55. doi: 10.1161/hypertensionaha.118.10893 [published Online First: 2018/05/20]
40. Davis K, Perez-Guzman P, Hoyer A, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. *BMC Med* 2021;19(1):105. doi: 10.1186/s12916-021-01978-7 [published Online First: 2021/05/14]
41. Huaman MA, Juchnowski SM, Zidar DA, et al. Monocyte activation in persons living with HIV and tuberculosis coinfection. *Aids* 2021;35(3):447-52. doi: 10.1097/qad.0000000000002766 [published Online First: 2020/12/01]
42. Temu TM, Polyak SJ, Wanjalla CN, et al. Latent tuberculosis is associated with heightened levels of pro-and anti-inflammatory cytokines among Kenyan men and women living with HIV on long-term antiretroviral therapy. *AIDS (London, England)* 2023 doi: 10.1097/qad.0000000000003523 [published Online First: 2023/03/18]
43. Dowdy DW, Behr MA. Are we underestimating the annual risk of infection with Mycobacterium tuberculosis in high-burden settings? *Lancet Infect Dis* 2022;22(9):e271-e78. doi: 10.1016/s1473-3099(22)00153-0 [published Online First: 2022/05/09]
44. Anwar A, Hamdan AJ, Salim B, et al. Diagnostic Utility of QuantiFERON-TB Gold (QFT-G) in Active Pulmonary Tuberculosis. *J Glob Infect Dis* 2015;7(3):108-12. doi: 10.4103/0974-777x.162231 [published Online First: 2015/09/24]
45. Lash TL, Fox MP, Fink AK. Applying Quantitative Bias Analysis to Epidemiologic Data: Statistics for Biology and Health. New York: Springer Science and Business Media 2011.

MAIN RESULTS

Table 1. Weighted prevalence and adjusted prevalence ratios of hypertension measures by QuantiFERON-TB Gold In-Tube status among US adults, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence of Hypertension, % (95%CI)				
	Total N=4,989	among QFT (-) 94.3 (93.3, 95.3)	among QFT (+) 5.7 (4.7, 6.7)	Prevalence Difference* Percentage point (95%CI)	aPR† (95% CI)
Primary study outcome					
Any hypertension indication[a] (n=2,580/4,989)	48.9 (45.2, 52.7)	48.3 (44.5, 52.1)	58.5 (52.4, 64.5)	**10.2 (5.1, 15.4)**	1.01 (0.97 – 1.06)
Measured blood pressure					
Hypertension[b] (n=1,885/4,989)	35.0 (32.3, 37.6)	34.5 (31.8, 37.2)	43.2 (36.4, 49.9)	**8.7 (1.9, 15.5)**	1.04 (0.97 – 1.12)
Stage 1 hypertension[c] (n=1273)	24.5 (22.4, 26.7)	24.2 (21.9, 26.5)	30.1 (22.4, 37.9)	5.9 (-2.3, 14.2)	1.13 (0.99 – 1.29)
Stage 2 hypertension[d] (n=612)	10.4 (9.1, 11.8)	10.3 (8.9, 11.7)	13.0 (9.1, 17.0)	2.8 (-1.3, 6.8)	0.88 (0.75 – 1.02)
Hypertension Diagnosis					
Previously diagnosed hypertension[e] (n=1,711)	30.8 (27.7, 33.9)	30.3 (27.1, 33.6)	38.3 (33.6, 43.1)	**8.0 (2.4, 13.6)**	0.97 (0.90 – 1.04)
Current use of anti-hypertension medication[f] (n=1,276)	86.9 (83.7, 90.1)	86.3 (82.7, 89.9)	94.7 (90.9, 98.4)	**8.4 (2.4, 14.4)**	**1.13 (1.02 – 1.09)**
Undiagnosed hypertension[g] (n=869)	18.1 (16.1, 20.2)	18.0 (15.8, 20.2)	20.2 (14.0, 26.4)	2.2 (-4.4, 8.9)	1.08 (0.91 – 1.28)

Abbreviations: CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group

†Model was adjusted for age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, body mass index, and smoking

[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or self-reported previous diagnosis of high blood pressure by health providers or use of antihypertensive medications

[b]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)

[c]Systolic 130-139 mmHg or diastolic 80-89 mmHg

[d]Systolic ≥140 mmHg or diastolic ≥90 mmHg

[e]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you's/he) had hypertension, also called high blood pressure?"

[f]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"

[g]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers

Bold indicates that the finding is significant at α=0.05

Table 2. Weighted prevalence and adjusted prevalence ratios of controlled and uncontrolled hypertension by QuantiFERON-TB Gold In-Tube status among US adults with known hypertension, NHANES 2011-2012

Hypertension Controls	Weighted Prevalence of Hypertension, % (95%CI)				
	Total N=1,711	**among QFT (-) 94.3 (93.3, 95.3)**	**among QFT (+) 5.7 (4.7, 6.7)**	**Mean/Prevalence Difference[*] Percentage point (95%CI)**	**aPR[†] (95% CI)**
Controlled without medications[a] (n=308)	11.3 (9.2, 13.3)	11.8 (9.5, 14.0)	5.2 (2.0, 8.3)	**-6.6 (-10.5, -2.7)**	0.62 (0.36 – 1.09)
Controlled with medications[b] (n=838)	33.9 (29.1, 38.8)	33.9 (28.8, 40.0)	34.8 (25.5, 44.1)	0.9 (-9.0, 10.8)	1.10 (0.84 – 1.45)
Uncontrolled without medications[c] (n=127)	15.0 (12.0, 18.1)	15.2 (12.0, 18.5)	12.2 (5.5, 18.9)	-3.1 (-10.1, 3.9)	0.80 (0.41 – 1.59)
Uncontrolled with medications[d] (n=438)	39.8 (36.7, 42.8)	39.1 (35.7, 42.6)	47.8 (40.1, 55.6)	8.7 (-1.0, 18.4)	1.16 (0.94 – 1.43)

Abbreviations: CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

[*]Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group

[†]Model was adjusted for age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, body mass index, and smoking

[a]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels

[b]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[c]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels

[d]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

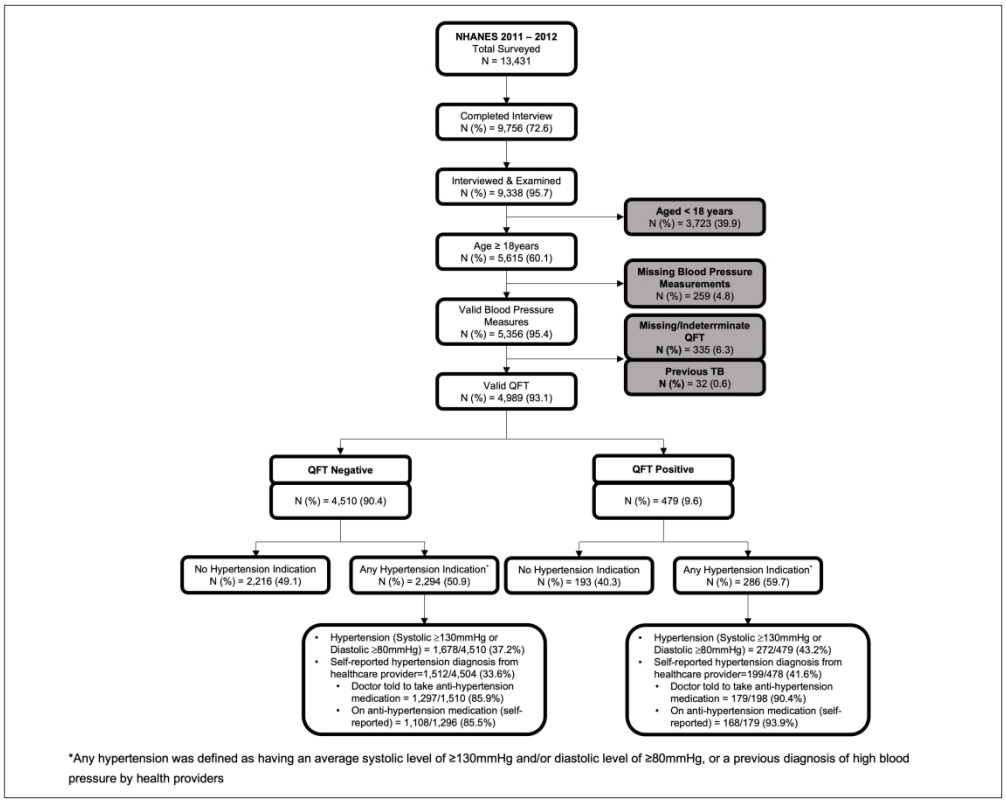


Figure 1. Flow chart depicting unweighted frequencies and percentages of participants included in the final analyses based on the eligibility criteria, NHANES 2011 – 2012

772x613mm (130 x 130 DPI)

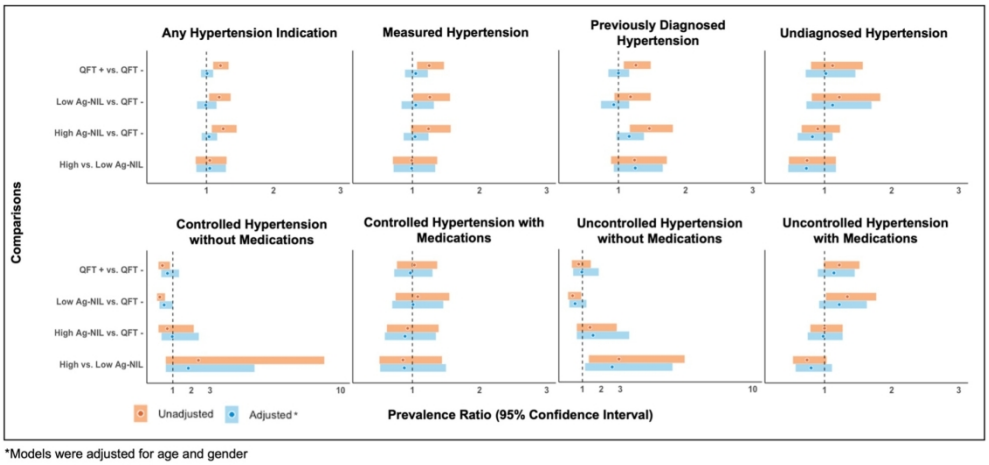


Figure 2. Crude and adjusted associations between QuantiFERON-TB Gold In-Tube results and select hypertension measures among US adults, NHANES 2011 – 2012

227x106mm (220 x 220 DPI)

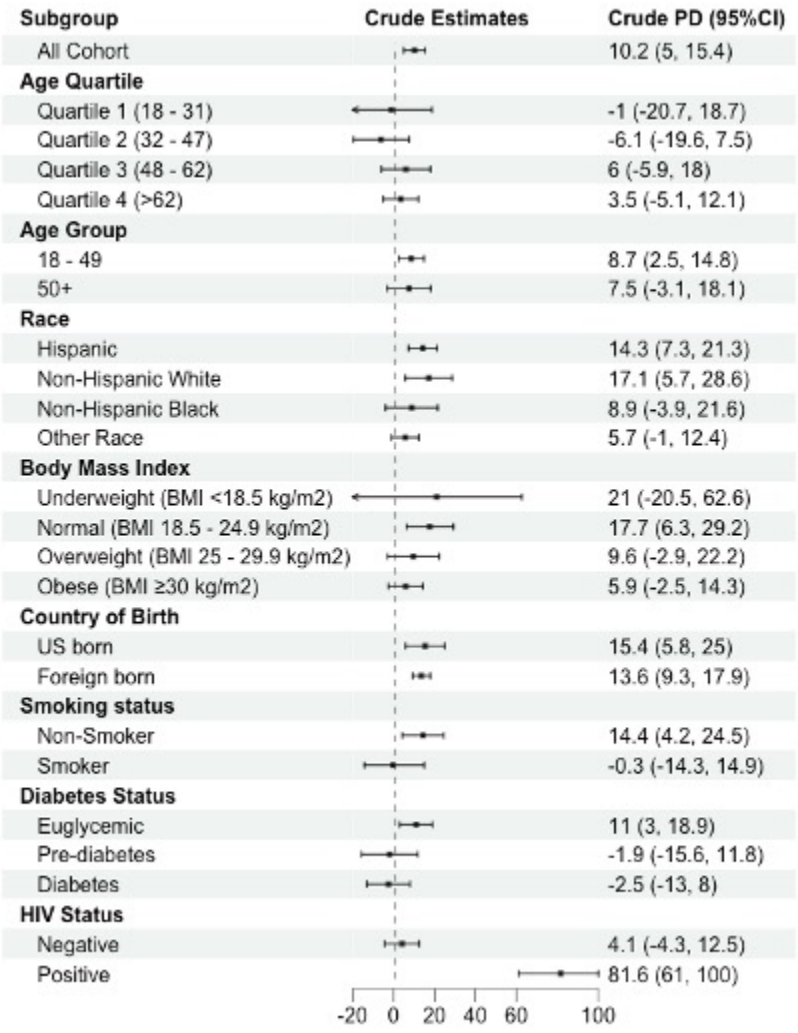


Figure 3. Relationship between positive QuantiFERON-TB result and hypertension: Stratified by demographic and clinical characteristics among US adults, NHANES 2011 – 2012

129x139mm (96 x 96 DPI)

SUPPEMENTAL MATERIALS

Supplemental Materials

Table S1. Weighted prevalence of and characteristics associated with tuberculosis infection among according to QuantiFERON-TB Gold In-Tube results among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference* Percentage point (95%CI)	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)		
Any hypertension indication[a]				
No	95.4 (94.4 – 96.4)	4.6 (3.6 – 5.6)	Reference	**<0.001**
Yes	93.2 (91.8 – 94.5)	6.8 (5.5 – 8.2)	2.2 (1.0, 3.4)	
Age, years				
Mean (95%CI)	46.0 (44.1 – 48.0)	53.2 (51.2 – 55.1)	7.1 (5.1, 9.2)	**<0.001**‡
Age groups				
Quartile 1 (18 – 31)	97.2 (96.2 – 98.3)	2.8 (1.7 – 3.8)	Reference	**<0.001**
Quartile 2 (32 – 47)	95.5 (94.4 – 96.6)	4.5 (3.4 – 5.6)	1.7 (0.1, 3.3)	
Quartile 3 (48 – 62)	92.0 (89.2 – 94.7)	8.0 (5.3 – 10.8)	5.3 (2.1, 8.4)	
Quartile 4 (>62)	91.9 (89.8 – 94.1)	8.1 (5.9 – 10.2)	5.3 (3.4, 7.2)	
18 – 49	94.9 (94.1 – 95.7)	5.1 (4.3 – 5.9)	Reference	**0.004**
≥50	92.5 (90.4 – 94.7)	7.5 (5.3 – 9.6)	2.4 (0.5, 4.2)	
Sex				
Male	93.4 (92.1 – 94.6)	6.6 (5.4 – 7.9)	Reference	**0.004**
Female	95.2 (94.1 – 96.2)	4.8 (3.8 – 5.9)	-1.8 (-3.2, -0.4)	
Race				
Hispanic	87.6 (85.4 – 89.9)	12.4 (10.1 – 14.6)	Reference	**<0.001**
Non-Hispanic white	96.8 (95.8 – 97.8)	3.2 (2.2 – 4.2)	-9.2 (-12.0, -6.4)	
Non-Hispanic black	92.8 (90.9 – 94.7)	7.2 (5.3 – 9.1)	-5.1 (-7.7, -2.6)	
Other race	86.7 (84.0 – 89.5)	13.3 (10.5 – 16.0)	0.9 (-2.4, 4.2)	
Education (n=4,757)				
Less than 9th grade	82.4 (77.8 – 86.9)	17.6 (13.1 – 22.2)	Reference	**<0.001**
9-11th grade	92.4 (90.1 – 94.7)	7.6 (5.3 – 9.9)	-10.4 (-15.5, -4.6)	
High school graduate	92.9 (90.5 – 95.3)	7.1 (4.7 – 9.5)	-10.6 (-15.8, -5.3)	
Some college	96.7 (95.4 – 98.0)	3.3 (2.0 – 4.6)	-14.3 (-19.2, -9.5)	
College graduate or above	95.0 (93.4 – 96.7)	5.0 (3.2 – 6.6)	-12.7 (-17.1, -8.3)	
Missing (n=264)	98.0 (95.6 – 100.0)	2.0 (0 – 4.4)		
Ratio of family income to poverty (n=4,623)				
Mean (95%CI)	2.9 (2.7 – 3.1)	2.4 (2.1 – 2.7)	-0.5 (-0.9, -0.2)	**0.005**
0 – 0.99	92.0 (89.8 – 94.2)	8.0 (5.8 -10.2)	Reference	**0.004**
1 – 1.99	92.5 (91.0 – 94.1)	7.5 (5.9 – 9.0)	-0.5 (-3.1, 2.1)	
2 – 2.99	94.9 (91.7 – 98.1)	5.1 (1.9 – 8.3)	-2.9 (-7.0, 1.2)	
3 – 3.99	95.8 (94.0 – 97.6)	4.2 (2.4 – 6.0)	-3.8 (-6.4, -1.3)	
4 – 4.99	96.7 (94.5 – 98.8)	3.3 (1.2 – 5.5)	-4.7 (-8.3, -1.1)	
≥5	95.9 (94.1 – 97.7)	4.1 (2.3 – 5.9)	-3.9 (-6.9, -0.9)	
Missing (n=396)	91.9 (88.4 – 95.5)	8.1 (4.5 – 11.6)		
Foreign born (n=4,987)				
No	96.5 (95.5 – 97.6)	3.5 (2.4 – 4.5)	Reference	**<0.001**
Yes	83.6 (80.8 – 86.3)	16.4 (14.0 – 19.2)	13.0 (9.6, 16.3)	
Missing (n=2)	100.0 (100.0 – 100.0)	0 (0 – 0)		
BMI, kg/m^2 (n=4,930)				
Mean (95%CI)	28.7 (28.2 – 29.1)	28.9 (27.8 – 30.1)	0.2 (-0.7, 1.2)	0.603‡
BMI categories				
Underweight (<18.5 kg/m^2)	93.1 (87.8 – 98.4)		0.9 (-3.7, 5.4)	0.868

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference* Percentage point (95%CI)	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)		
Normal (18.5 – 24.9 kg/m^2)	93.9 (92.0 – 95.8)	6.9 (1.6 – 12.2)	Reference	
Overweight (25 – 29.9 kg/m^2)	94.5 (93.2 – 95.9)	6.1 (4.2 – 8.0)	-0.6 (-2.6, 1.4)	
Obese (≥30 kg/m^2)	94.4 (93.2 – 95.5)	5.5 (4.1 – 6.8)	-0.4 (-2.6, 1.7)	
		5.6 (4.5 – 6.8)		
Missing (n=59)	95.8 (90.2 – 100.0)			
		4.2 (0 – 9.8)		
Smoking status (n=4,722)				
Never smokers[b]	94.9 (94.0 – 95.8)	5.1 (4.2 – 6.0)	Reference	0.144
Past smokers[c]	93.1 (90.7 – 95.4)	6.9 (4.6 – 9.3)	1.8 (-0.7, 4.3)	
Current smokers[d]	93.3 (90.7 – 95.8)	6.7 (4.2 – 9.3)	1.6 (-1.0, 4.2)	
Missing (n=267)	98.1 (95.7 – 100.0)	1.9 (0 – 4.3)		
Heavy alcohol drinking (n=3,867)				
No	95.0 (93.5 – 96.4)	5.0 (3.6 – 6.5)	Reference	0.688
Yes[e]	94.7 (93.7 – 95.8)	5.3 (4.2 – 6.3)	0.3 (-1.1, 1.6)	
Missing (n=1,122)	92.0 (90.5 – 93.6)	8.0 (6.4 – 9.5)		
HbA1c, %				
Mean (95%CI)	5.6 (5.6 – 5.7)	5.9 (5.7 – 6.0)	0.3 (0.1, 0.4)	**0.001**
Diabetes categories[f]				
Normal	95.5 (94.6 – 96.4)	4.5 (3.6 – 5.4)	Reference	**<0.001**
Prediabetes	93.4 (91.7 – 95.0)	6.6 (5.0 – 8.3)	2.1 (0.8, 3.5)	
Diabetes	88.9 (85.2 – 92.5)	11.1 (7.5 – 14.8)	6.6 (2.9, 10.4)	
HIV co-infection status (n=3,408)				
Negative	95.4 (94.4 – 96.4)	4.6 (3.6 – 5.6)	Reference	0.861
Positive	96.1 (88.3 – 100.0)	3.9 (0 – 11.7)	0.7 (-7.0, 8.3)	
Missing (n=1,600)	91.3 (89.3 – 93.3)	8.7 (6.7 – 10.7)		
Dyslipidemia Measures				
HDL (mg/dL) (n=4,889)				
Mean (95%CI)	52.8 (51.8 – 53.9)	51.7 (48.9 – 54.5)	-1.1 (-3.5, 1.2)	0.330
HDL levels[g]				
Normal	94.6 (93.5 – 95.7)	5.4 (4.3 – 6.5)	Reference	0.117
Lower	93.6 (92.4 – 94.9)	6.4 (5.1 – 7.6)	1.0 (-0.3, 2.2)	
Missing (n=100)	91.8 (82.9 – 100.0)	8.2 (0 – 17.1)		
LDL[h] (mg/dL) (n=2,236)				
Mean (95%CI)	114.8 (112.5 – 117.0)	113.1 (107.1 – 119.2)	-1.6 (-8.4, 5.1)	0.614
LDL levels	94.3 (92.8 – 95.8)	5.7 (4.2 – 7.2)	Reference	0.395
Normal (<130 mg/dL)	95.8 (94.6 – 97.2)	4.2 (2.8 – 5.6)	-1.5 (-3.3, 0.4)	
Elevated (130 – 159 mg/dL)	94.5 (90.7 – 98.4)	5.4 (1.6 – 9.3)	-0.2 (-3.9, 3.4)	
High (≥160 mg/dL)				
	99.5 (98.3 – 100.0)	0.5 (0 – 1.7)		
Missing (n=67)				
Total Cholesterol (mg/dL) (n=4,889)				
Mean (95%CI)	194.2 (191.9 – 196.4)	196.8 (192.5 – 201.0)	2.6 (-1.3, 6.5)	0.183
Total cholesterol levels				
Low (≤130 mg/dL)	93.3 (89.8 – 96.8)	6.7 (3.2 – 10.2)	Reference	0.728
Normal (131 – 199 mg/dL)	94.5 (93.3 – 95.7)	5.5 (4.2 – 6.7)	-1.3 (-5.6, 3.0)	
Elevated (≥200 mg/dL)	94.2 (82.9 – 100.0)	5.8 (4.4 – 7.2)	-0.9 (-4.9, 3.1)	
Missing (n=100)	91.8 (82.9 – 100.0)	8.2 (0 – 17.1)		
Triglyceride[h] (mg/dL) (n=2,276)				

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference* Percentage point (95%CI)	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)		
Mean (95%CI)	129.6 (118.9 – 140.2)	123.4 (111.8 – 135.0)	-6.2 (-20.5, 8.1)	0.374‡
Triglyceride levels				
Optimal (<150 mg/dL)	94.6 (93.0 – 96.2)	5.4 (3.8 -7.0)	Reference	0.796
Elevated (150 – 199 mg/dL)	94.9 (92.5 – 97.2)	5.1 (2.8 – 7.5)	-0.3 (-3.1, 2.6)	
High (≥200 mg/dL)	95.4 (93.6 – 97.2)	4.6 (2.8 – 6.4)	-0.9 (-3.2, 1.5)	
Missing (n=27)	100.00 (100.0 – 100.0)	0 (0 – 0)		
Any dyslipidemia[i&h] (n=2,277)				
No	94.4 (92.1 – 96.7)	5.6 (3.3 – 7.9)	Reference	0.63
Yes	94.9 (93.6 – 96.2)	5.1 (3.8 – 6.4)	-0.5 (-3.0, 2.0)	
Missing (n=26)	100.0 (100.0 – 100.0)	0 (0 – 0)		
Statin prescription[j] (n=2,770)				
No	94.2 (92.7 – 95.6)	5.8 (4.4 – 7.3)	Reference	0.49
Yes	93.5 (91.8 – 95.2)	6.5 (4.7 – 8.2)	0.6 (-1.3, 2.6)	
Missing (n=2,238)	94.7 (93.6 – 95.8)	5.3 (4.2 – 6.4)		
CHD[k] (n=4,712)				
No	94.1 (93.0 – 95.1)	5.9 (4.9 – 7.0)	Reference	**0.04**
Yes	96.5 (94.7 – 98.3)	3.5 (1.7 – 5.3)	-2.4 (-4.6, - 0.2)	
Missing (n=277)	97.8 (95.5 – 100.0)	2.2 (0 – 4.5)		
Heart attack[l] (n=4,723)				
No	94.1 (93.1 – 95.1)	5.9 (4.9 – 6.9)	Reference	**0.005**
Yes	96.3 (94.5 – 98.1)	3.7 (1.9 – 5.5)	-2.2 (-3.6, -0.8)	
Missing (n=266)	98.1 (95.7 – 100.0)	1.9 (0 – 4.3)		
Stroke[m] (n=4,725)				
No	94.3 (93.2 – 95.3)	5.7 (4.7 – 6.8)	Reference	**0.04**
Yes	90.7 (86.4 – 94.9)	9.3 (5.1 – 13.6)	3.6 (-0.9, 8.0)	
Missing (n=264)	98.1 (95.7 – 100.0)	1.9 (0 – 4.3)		

Abbreviations:
BMI – body mass index; CHD – coronary heart disease; CI – confidence interval; HbA1c – glycated hemoglobin; HDL – high-density lipoprotein; HIV – human immunodeficiency virus; LDL – low-density lipoprotein; NHANES – National Health and Nutrition Examination Survey; QFT - QuantiFERON Gold-In-Tube;

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group, unless indicated otherwise (with "reference" statement)
†P-values from Rao-Scott Chi-square tests, unless indicated otherwise
‡P-values from t-tests
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Survey participants answered "No" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[c]Survey participants answered "Not at all" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[d]Survey participants answered "Every day" or "Some days" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[e]Survey participants answered "Yes" to the question "Was there ever time or times in (your/SP's) life when (you/he/she) drank 4 (for female) or 5 (for male) or more drinks of any kind of alcoholic beverage almost every day?"
[f]Diabetes was categorized according to HbA1c levels and self-reported previous type-2 diabetes mellitus diagnosis by health care providers
[g]HDL level was using gender-specific cut-offs: "normal" HDL was defined if HDL level was ≥40 mg/dL for male or ≥50 mg/dL for female; and "lower" HDL was defined if HDL level was <40 mg/dL for male or <50 mg/dL for female
[h]LDL and triglyceride measurements were done among a subset of survey participants who were fasting and appropriate weight variable (for those who were fasting) was applied accordingly
[i]Any dyslipidemia was defined as having either elevated LDL, total cholesterol, triglyceride, or lower HDL levels
[j]Taken statin in the past 30 days prior to survey date, survey participants were also asked to show medicine container to surveyor/enumerator

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Mean/Prevalence Difference* Percentage point (95%CI)	
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)		

[k]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had coronary heart disease?"

[l]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a heart attack (also called myocardial infarction)?"

[m]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a stroke?"

Bold indicates that the finding is statistically significant at α=0.05

Table S2. Weighted prevalence of and characteristics associated with hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	
QFT result				
Negative	51.7 (47.9 – 55.5)	48.3 (44.5 – 52.1)	Reference	**<0.001**
Positive	41.5 (35.5 – 47.6)	58.5 (52.4 – 64.5)	10.2 (5.0, 15.4)	
Age, years				
Mean (95%CI)	38.9 (37.3 – 40.6)	54.3 (52.8 – 55.7)	15.3 (14.0, 16.6)	**<0.001**
Age group				
Quartile 1 (18 – 31)	80.8 (78.6 – 83.1)	19.2 (16.9 – 21.4)	Reference	**<0.001**
Quartile 2 (32 – 47)	57.5 (52.3 – 62.7)	42.5 (37.3 – 47.7)	23.4 (18.6, 28.1)	
Quartile 3 (48 – 62)	38.0 (34.4 – 41.7)	62.0 (58.3 – 65.6)	42.8 (37.9, 47.7)	
Quartile 4 (>62)	23.0 (18.9 – 27.1)	77.0 (72.9 – 81.1)	57.8 (53.1, 62.5)	
18 – 49	57.1 (53.1 – 61.1)	42.9 (38.9 – 46.9)	Reference	**<0.001**
≥50	34.2 (30.2 – 38.3)	65.8 (61.7 – 69.8)	22.9 (17.6, 28.2)	
Sex				
Male	47.7 (43.2 – 52.2)	52.3 (47.8 – 56.8)	Reference	**0.004**
Female	54.4 (50.4 – 58.4)	45.6 (41.6 – 49.6)	-6.7 (-10.9, -2.5)	
Race				
Hispanic	61.3 (55.8 – 66.8)	38.7 (33.2 – 44.2)	Reference	**<0.001**
Non-Hispanic white	49.6 (44.7 – 54.4)	50.4 (45.6 – 55.3)	11.7 (5.3, 18.2)	
Non-Hispanic black	43.6 (39.9 – 47.4)	56.4 (52.6 – 60.1)	17.7 (11.8, 23.5)	
Other race	56.5 (51.5 – 61.5)	43.5 (38.5 – 48.5)	4.8 (-2.2, 11.7)	
Education (n=4,725)				
Less than 9th grade	39.0 (31.3 – 46.9)	61.0 (53.3 – 68.7)	Reference	**<0.001**
9-11th grade	42.3 (36.9 – 47.6)	57.7 (52.3 – 63.1)	-3.2 (-13.4, 6.9)	
High school graduate	45.5 (40.9 – 50.1)	54.5 (49.9 – 59.1)	-6.5 (-14.9, 2.0)	
Some college	51.7 (46.3 – 57.0)	48.3 (42.9 – 53.7)	-12.7 (-20.9, -4.5)	
College graduate or above	55.3 (48.9 – 61.5)	44.7 (38.4 – 51.1)	-16.2 (-25.5, -7.0)	
Missing (n=264)	86.7 (81.8 – 91.5)	13.3 (8.5 – 18.2)		
Ratio of family income to poverty (n=4,593)				
Mean (95%CI)	2.8 (2.6 – 3.1)	2.9 (2.7 – 3.1)	0.1 (-0.1, 0.3)	0.439
0 – 0.99	55.8 (49.1 – 62.5)	44.2 (37.5 – 50.9)	Reference	0.431
1 – 1.99	49.6 (43.3 – 55.9)	50.4 (44.1 – 56.7)	6.2 (-0.5, 12.9)	
2 – 2.99	49.4 (43.7 – 55.0)	50.6 (45.0 – 56.3)	6.4 (-2.4, 15.3)	
3 – 3.99	53.5 (48.6 – 58.4)	46.5 (41.6 – 51.4)	2.3 (-4.9, 9.5)	
4 – 4.99	47.6 (39.8 – 55.0)	52.4 (44.6 – 60.2)	8.2 (-2.7, 19.0)	
≥5	50.9 (43.0 – 58.7)	49.1 (41.3 – 57.0)	4.9 (-3.5, 13.4)	
Missing (n=396)	49.4 (39.9 – 58.8)	50.6 (41.2 – 60.1)		
Foreign born (n=5,019)				
No	49.2 (45.9 – 52.6)	50.8 (47.4 – 54.1)	Reference	**<0.001**
Yes	60.1 (54.7 – 65.5)	39.9 (34.5 – 45.3)	-10.8 (-14.5, -7.2)	
Missing (n=2)	70.6 (8.7 – 100.0)	29.4 (0 – 91.3)		
BMI, kg/m^2 (n=4,930)				
Mean (95%CI)	27.2 (26.7 – 27.8)	30.2 (29.7 – 30.8)	3.0 (2.4, 3.7)	**<0.001**
BMI categories				
Underweight (<18.5 kg/m^2)	68.6 (61.2 – 76.0)	31.4 (24.0 – 38.8)	-1.2 (-9.3, 6.9)	**<0.001**
Normal (18.5 – 24.9 kg/m^2)	67.4 (62.8 – 72.0)	32.6 (28.0 – 37.2)	Reference	
Overweight (25 – 29.9 kg/m^2)	49.8 (46.2 – 53.4)	50.2 (46.6 – 53.8)	17.6 (14.4, 20.9)	
Obese (≥30 kg/m^2)	38.0 (33.6 – 42.5)	62.0 (57.5 – 66.4)	29.4 (23.3, 35.5)	

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	
Missing (n=59)	26.1 (7.3 – 45.0)	73.9 (55.0 – 92.7)		
Smoking status (n=4,722)				
Never smokers[b]	54.4 (50.5 – 58.4)	45.6 (41.6 – 49.5)	Reference	**<0.001**
Past smokers[c]	37.2 (31.6 – 42.8)	62.8 (57.2 – 68.4)	17.3 (12.6, 21.9)	
Current smokers[d]	52.7 (48.4 – 57.1)	47.3 (42.9 – 51.6)	1.7 (-3.8, 7.1)	
Missing (n=267)	86.2 (81.0 – 91.4)	13.8 (8.6 – 19.0)		
Heavy alcohol drinking (n=3,891)				
No	41.1 (36.5 – 45.7)	58.9 (54.3 – 63.5)	Reference	**<0.001**
Yes[e]	52.4 (48.3 – 56.5)	47.6 (43.9 – 51.7)	-11.3 (-14.9, -7.7)	
Missing (n=1,122)	52.9 (47.6 – 58.2)	47.1 (41.8 – 52.4)		
HbA1c, %				
Mean (95%CI)	5.4 (5.4 – 5.5)	5.9 (5.8 – 5.9)	0.4 (0.4, 0.5)	**<0.001**
Diabetes categories[f]				
Normal	59.9 (55.8 – 64.0)	40.1 (36.0 – 44.2)	Reference	**<0.001**
Prediabetes	40.3 (37.1 – 43.5)	59.7 (56.5 – 62.9)	19.6 (15.8 – 23.4)	
Diabetes	19.1 (16.5 – 21.8)	80.9 (78.2 – 83.5)	40.8 (37.3 – 44.3)	
HIV co-infection status (n=3,389)				
Negative	60.7 (57.3 – 64.2)	39.3 (35.8 – 42.7)	Reference	0.22
Positive	78.4 (54.8 – 100.0)	21.6 (0 – 45.2)	-17.7 (-43.6, 8.3)	
Missing (n=1,600)	25.3 (21.7 – 28.9)	74.7 (71.1 – 78.3)		
Dyslipidemia Measures				
HDL (mg/dL) (n=4,889)				
Mean (95%CI)	53.2 (52.1 – 54.3)	52.3 (51.0 – 53.6)	-0.9 (-2.0, 0.1)	0.08
HDL levels[g]				
Normal	53.1 (48.9 – 57.3)	46.9 (42.7 – 51.1)	Reference	**<0.001**
Lower	47.1 (43.5 – 50.7)	52.9 (49.3 – 56.5)	6.0 (2.4, 9.6)	
Missing (n=100)	37.0 (25.2 – 48.7)	63.0 (51.3 – 74.8)		
LDL[h] (mg/dL) (n=2,236)				
Mean (95%CI)	113.2 (110.5 – 115.8)	116.4 (113.0 – 119.8)	3.2 (-1.1, 7.6)	0.13
LDL levels				
Normal (<130 mg/dL)	53.7 (48.5 – 58.8)	46.3 (41.2 – 51.5)	Reference	**0.014**
Elevated (130 – 159 mg/dL)	55.8 (48.7 – 62.9)	44.2 (37.1 – 51.3)	-2.1 (-11.3, 7.1)	
High (≥160 mg/dL)	38.7 (28.1 – 49.3)	61.3 (50.7 – 71.9)	15.0 (4.7, 25.3)	
Missing (n=67)	31.7 (19.9 – 43.5)	68.3 (56.5 – 80.1)		
Total Cholesterol (mg/dL) (n=4,889)				
Mean (95%CI)	190.3 (187.7 – 192.8)	198.6 (194.7 – 202.4)	8.3 (3.4, 13.2)	**0.001**
Total cholesterol levels				
Low (≤130 mg/dL)	50.7 (44.3 – 57.0)	49.3 (43.0 – 55.7)	Reference	**<0.001**
Normal (131 – 199 mg/dL)	55.3 (50.9 – 59.8)	44.7 (40.2 – 49.1)	-4.7 (-10.6, 1.3)	
Elevated (≥200 mg/dL)	46.4 (41.1 – 51.8)	53.6 (48.2 – 58.9)	4.2 (-3.3, 11.7)	
Missing (n=100)	37.0 (25.2 – 48.7)	63.0 (51.3 – 74.8)		
Triglyceride[h] (mg/dL) (n=2,276)				
Mean (95%CI)	111.5 (105.4 – 117.6)	148.8 (134.6 – 162.9)	37.3 (26.3, 48.2)	**<0.001**
Triglyceride levels				
Optimal (<150 mg/dL)	57.9 (54.2 – 61.6)	42.1 (38.4 – 45.8)	Reference	**<0.001**

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference* Percentage point (95%CI)	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)		
Elevated (150 – 199 mg/dL)	41.8 (34.1 – 49.5)	58.2 (50.5 – 65.9)	16.1 (9.8, 22.5)	
High (≥200 mg/dL)	28.7 (21.8 – 35.6)	71.3 (64.4 – 78.2)	29.2 (22.4, 36.1)	
Missing (n=27)	25.7 (6.7 – 44.8)	74.3 (55.2 – 93.3)		
Any dyslipidemia[i&h] (n=2,277)				
No	61.0 (56.7 – 65.4)	39.0 (34.6 – 43.3)	Reference	**<0.001**
Yes	47.4 (41.9 – 52.8)	52.6 (47.2 – 58.1)	13.7 (7.7, 19.6)	
Missing (n=26)	24.6 (6.0 – 43.2)	75.4 (56.8 – 94.0)		
Statin prescription[j] (n=2,770)				
No	44.8 (40.0 – 49.6)	55.2 (50.4 – 60.0)	Reference	
Yes	20.6 (16.0 – 25.2)	79.4 (74.8 – 84.0)	24.2 (17.6, 30.9)	**<0.001**
Missing (n=2,238)	69.8 (66.6 – 73.0)	30.2 (27.0 – 33.4)		
CHD[k] (n=4,712)				
No	50.9 (47.2 – 54.6)	49.1 (45.4 – 52.8)	Reference	**<0.001**
Yes	15.3 (5.9 – 24.8)	84.7 (75.2 – 94.1)	35.6 (25.0, 46.1)	
Missing (n=277)	85.6 (80.4 – 90.8)	14.4 (9.2 – 19.6)		
Heart attack[l] (n=4,723)				
No	50.8 (47.1 – 54.5)	49.2 (45.5 – 52.9)	Reference	**<0.001**
Yes	20.9 (11.6 – 30.2)	79.1 (69.8 – 88.4)	29.9 (18.5, 41.4)	
Missing (n=266)	86.1 (80.7 – 91.5)	13.9 (8.5 – 19.3)		
Stroke[m] (n=4,725)				
No	50.9 (47.3 – 54.4)	49.1 (45.6 – 52.7)	Reference	**<0.001**
Yes	15.6 (8.8 – 22.4)	84.4 (77.6 – 91.2)	35.3 (28.1, 42.5)	
Missing (n=264)	86.9 (82.1 – 91.6)	13.1 (8.4 – 17.9)		

Abbreviations:
BMI – body mass index; CI – confidence interval; HDL – high-density lipoprotein; LDL – low-density lipoprotein; NHANES – National Health and Nutrition Examination Survey; QFT - QuantiFERON Gold-In-Tube; TST – tuberculin skin test

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group, unless indicated otherwise (with "reference" statement)
†P-values from Rao-Scott Chi-square tests, unless indicated otherwise
‡P-values from t-tests
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Survey participants answered "No" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[c]Survey participants answered "Not at all" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[d]Survey participants answered "Every day" or "Some days" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[e]Survey participants answered "Yes" to the question "Was there ever time or times in (your/SP's) life when (you/he/she) drank 4 (for female) or 5 (for male) or more drinks of any kind of alcoholic beverage almost every day?"
[f]Diabetes was categorized according to HbA1c levels and self-reported previous type-2 diabetes mellitus diagnosis by health care providers
[g]HDL level was using gender-specific cut-offs: "normal" HDL was defined if HDL level was ≥40 mg/dL for male or ≥50 mg/dL for female; and "lower" HDL was defined if HDL level was <40 mg/dL for male or <50 mg/dL for female
[h]LDL and triglyceride measurements were done among a subset of survey participants who were fasting and appropriate weight variable (for those who were fasting) was applied accordingly
[i]Any dyslipidemia was defined as having either elevated LDL, total cholesterol, triglyceride, or lower HDL levels
[j]Taken statin in the past 30 days prior to survey date, survey participants were also asked to show medicine container to surveyor/enumerator
[k]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had coronary heart disease?"
[l]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a heart attack (also called myocardial infarction)?"

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	

[m]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a stroke?"

Bold indicates that the finding is statistically significant at α=0.05

Table S3. Weighted prevalence of various hypertension classifications by interferon gamma tuberculosis antigen responses among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence (95%CI)			Prevalence Difference (95%CI)		
	QFT Negative N=4510 94.3% (93.3 – 95.2)	QFT Positive Ag-NIL Values* Low (<4 IU/ml) N=299 4.0% (3.2 – 4.7)	QFT Positive Ag-NIL Values* High (≥4 IU/ml) N=190 1.7% (1.2 – 2.3)	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL
Primary study outcome						
Any hypertension indication[a]	48.3 (44.5, 52.1)	57.6 (48.7, 66.6)	60.4 (53.2, 67.7)	9.4 (1.6, 17.1)	12.1 (3.6, 20.5)	2.7 (-10.1, 15.5)
Measured blood pressure categories						
Normal blood pressure[b]	47.9 (44.6, 51.2)	35.6 (25.1, 46.1)	39.5 (29.3, 49.7)	-12.3 (-22.7, -1.9)	-8.4 (-18.1, 1.2)	3.8 (-9.7, 17.4)
Borderline hypertension[c]	17.6 (15.9, 19.3)	21.1 (14.2, 27.9)	17.7 (10.2, 25.1)	3.4 (-3.0, 9.9)	0.1 (-7.5, 7.6)	-3.4 (-13.9, 7.2
Hypertension[d]	34.5 (31.8, 37.2)	43.3 (34.0, 52.7)	42.8 (33.5, 52.1)	8.8 (-0.4, 18.1)	8.4 (-1.4, 18.2)	-0.5 (-14.6, 13.7)
Stage 1 hypertension[e]	24.2 (21.9, 26.5)	28.8 (18.9, 38.8)	33.2 (23.3, 414.1)	4.6 (-5.7, 14.9)	9.0(-2.7, 20.7)	4.4 (-10.2, 19.0)
Stage 2 hypertension[f]	10.3 (8.9, 11.7)	14.5 (10.3, 18.7)	9.6 (5.1, 14.2)	4.2 (-0.3, 8.7)	-0.6 (-5.2, 3.9)	-4.9 (-9.0, -0.7)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	30.3 (27.1, 33.6)	35.8 (28.3, 43.3)	44.2 (36.2, 52.2)	5.4 (-2.5, 13.4)	13.9 (5.0, 22.7)	8.4 (-4.7, 21.6)
Self-reported current use of anti-hypertension medication[h]	86.3 (82.7, 90.0)	95.0 (90.7, 98.9)	94.4 (87.7, 100.0)	8.5 (2.3, 14.6)	8.1 (-0.6, 16.8)	-0.6 (-7.8, 6.9)
Undiagnosed hypertension[i]	18.0 (15.8, 20.2)	21.9 (13.6, 30.3)	16.2 (12.1, 20.3)	3.9 (-4.8, 12.7)	-1.8 (-7.1, 3.4)	-5.8 (-12.7, 4.8)
Hypertension Control†						
Controlled hypertension without medications[j]	11.8 (9.5, 14.0)	3.5 (1.2, 5.7)	8.3 (0.0, 17.0)	-8.3 (-11.4, -5.2)	-3.5 (-12.8, 5.8)	4.8 (-4.7, 14.3)
Controlled hypertension with medications[k]	33.9 (28.8, 39.0)	36.6 (25.1, 48.2)	31.4 (17.8, 44.9)	2.9 (-10.4, 15.9)	-2.5 (-15.1, 10.2)	-5.2 (-22.5, 12.1)
Uncontrolled hypertension without medications[l]	15.2 (12.0, 18.5)	7.3 (2.6, 12.0)	21.2 (7.8, 34.7)	-8.0 (-13.6, -2.3)	6.1 (-8.3, 20.4)	14.0 (-0.9, 27.2)
Uncontrolled hypertension with medications[m]	39.1 (35.7, 42.6)	52.6 (40.8, 64.4)	39.0 (30.7, 47.3)	13.5 (-0.2, 27.1)	-0.1 (-9.5, 9.2)	-13.6 (-28.9, 1.7)

Abbreviations:
CI – confidence interval; IFN-γ - interferon gamma; QFT – QuantiFERON-TB Gold In-Tube

*Estimated by subtracting TB antigen value by TB Nil control value (LBXTBA - TBXTBN)
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,711)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S4. Crude and adjusted associations between interferon gamma tuberculosis antigen responses and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Stratification Variables	Prevalence Ratio (95%CI)					
	Unadjusted Estimates			Adjusted Estimates*		
	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL
Primary study outcome						
Any hypertension indication[a]	**1.19 (1.04 – 1.36)**	**1.25 (1.08 – 1.45)**	1.05 (0.84 – 1.30)	0.99 (0.86 – 1.15)	1.04 (0.93 – 1.16)	1.05 (0.85 – 1.29)
Measured blood pressure categories						
Normal blood pressure[b]	**0.74 (0.56 – 0.99)**	0.82 (0.64 – 1.05)	1.11 (0.80 – 1.59)	0.89 (0.66 – 1.21)	0.99 (0.80 – 1.24)	1.12 (0.76 – 1.63)
Borderline hypertension[c]	1.20 (0.88 – 1.62)	1.00 (0.66 – 1.54)	0.84 (0.47 – 1.46)	1.12 (0.82 – 1.54)	0.94 (0.61 – 1.45)	0.84 (0.47 – 1.50)
Hypertension[d]	**1.26 (1.01 – 1.56)**	1.24 (0.98 – 1.57)	0.99 (0.71 – 1.37)	1.05 (0.84 – 1.32)	1.04 (0.87 – 1.24)	0.99 (0.72 – 1.34)
Stage 1 hypertension[e]	1.19 (0.83 – 1.77)	1.37 (0.96 – 1.97)	1.15 (0.73 – 1.85)	1.06 (0.73 – 1.55)	1.22 (0.89 – 1.66)	1.15 (0.72 – 1.82)
Stage 2 hypertension[f]	**1.41 (1.02 – 1.95)**	0.94 (0.59 – 1.50)	**0.67 (0.44 – 0.99)**	1.03 (0.74 – 1.44)	0.70 (0.40 – 1.23)	0.67 (0.43 – 1.05)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	1.18 (0.94 – 1.48)	**1.46 (1.17 – 1.81)**	1.24 (0.93 – 1.72)	0.93 (0.74 – 1.16)	1.16 (0.97 – 1.38)	1.25 (0.93 – 1.66)
Self-reported current use of anti-hypertension medication[h]	**1.10 (1.03 – 1.18)**	1.09 (0.99 – 1.20)	1.00 (0.93 – 1.08)	**1.07 (1.00 – 1.14)**	1.07 (0.98 – 1.17)	1.00 (0.92 – 1.09)
Undiagnosed hypertension[i]	1.22 (0.81 – 1.83)	0.90 (0.66 – 1.23)	0.74 (0.47 – 1.17)	1.12 (0.73 – 1.70)	0.82 (0.60 – 1.12)	0.73 (0.46 – 1.17)
Hypertension Control†						
Controlled hypertension without medications[j]	**0.30 (0.15 – 0.58)**	0.70 (0.23 – 2.12)	2.37 (0.82 – 9.12)	**0.53 (0.28 – 1.00)**	0.97 (0.39 – 2.39)	1.83 (0.62 – 5.38)
Controlled hypertension with medications[k]	1.08 (0.75 – 1.55)	0.93 (0.62 – 1.39)	0.86 (0.51 – 1.44)	1.01 (0.70 – 1.46)	0.89 (0.59 – 1.35)	0.88 (0.52 – 1.50)
Uncontrolled hypertension without medications[l]	**0.48 (0.24 – 0.94)**	1.40 (0.70 – 2.81)	**2.93 (1.34 – 6.40)**	0.61 (0.31 – 1.21)	1.56 (0.70 – 3.47)	**2.57 (1.14 – 5.76)**
Uncontrolled hypertension with medications[m]	**1.34 (1.02 – 1.77)**	1.00 (0.79 – 1.27)	0.74 (0.53 – 1.03)	1.22 (0.92 – 1.63)	0.98 (0.75 – 1.27)	0.80 (0.57 – 1.11)

Abbreviations:
CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

*Models adjusted for age (continuous) and gender
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,711)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/she) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S5. The crude and adjusted prevalence odds ratios of any hypertension stratified by race, body mass index category, and foreign-born status, among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Stratification Variables	QFT Status	Unweighted frequency Hypertension*/Total	Weighted Prevalence of Hypertension* (95%CI)	Prevalence Difference (95%CI)	Statistical interaction p-values	Prevalence Ratios: Crude cPR (95%CI)	Prevalence Ratios: Adjusted† aPR (95%CI)
All cohort	Negative	2294/4510	48.3 (44.5 – 52.1)	Reference	NA	Reference	Reference
	Positive	286/479	58.5 (52.4 – 64.5)	10.2 (5.0, 15.4)		**1.21 (1.10 – 1.33)**	1.01 (0.92 – 1.10)
Stratified by age quartiles‡							
Quartile 1 (18 – 31)	Negative	253/1256	19.2 (16.9 – 21.5)	Reference	0.6374	Reference	Reference
	Positive	6/40	18.2 (0 – 37.5)	-1.0 (-20.7, 18.7)		0.95 (0.32 – 2.81)	0.81 (0.25 – 2.64)
Quartile 2 (32 – 47)	Negative	512/1186	42.8 (37.8 – 47.8)	Reference		Reference	Reference
	Positive	32/94	36.7 (20.0 – 52.4)	-6.1 (-19.6, 7.5)		0.86 (0.59 – 1.25)	0.87 (0.59 – 1.26)
Quartile 3 (48 – 62)	Negative	678/1033	61.5 (58.0 – 65.0)	Reference		Reference	Reference
	Positive	105/166	67.5 (55.0 – 80.1)	6.0 (-5.7, 18.0)		1.10 (0.92 – 1.31)	1.03 (0.88 – 1.21)
Quartile 4 (>62)	Negative	851/1035	76.7 (72.3 – 81.1)	Reference		Reference	Reference
	Positive	143/179	80.2 (72.9 – 87.5)	3.5 (-5.1, 12.1)		1.05 (0.94 – 1.17)	1.03 (0.91 – 1.17)
Stratified by age group							
18 – 49	Negative	1568/3454	42.5 (38.5 – 46.4)	Reference	0.9998	Reference	Reference
	Positive	175/307	51.1 (43.4 – 58.9)	8.7 (2.5, 14.8)		**1.20 (1.07 – 1.36)**	0.95 (0.84 – 1.08)
50+	Negative	726/1056	65.2 (61.2 – 69.2)	Reference		Reference	Reference
	Positive	111/172	72.7 (61.4 – 84.0)	7.5 (-3.1, 18.1)		1.11 (0.96 – 1.29)	1.07 (0.93 – 1.24)
Stratified by race							
Hispanic	Negative	374/864	36.9 (31.4 – 42.5)	Reference	0.1584	Reference	Reference
	Positive	67/158	51.2 (42.0 – 60.4)	14.3 (7.3, 21.3)		**1.39 (1.20 – 1.60)**	0.98 (0.86 – 1.11)
Non-Hispanic White	Negative	947/1769	49.9 (45.0 – 54.8)	Reference		Reference	Reference
	Positive	47/71	67.0 (55.3 – 78.7)	17.1 (5.7, 28.6)		**1.34 (1.12 – 1.60)**	1.08 (0.91 – 1.27)
Non-Hispanic Black	Negative	711/1196	55.7 (51.8 – 59.7)	Reference		Reference	Reference
	Positive	80/115	64.6 (52.0 – 77.2)	8.9 (-3.9, 21.6)		1.16 (0.95 – 1.42)	0.86 (0.71 – 1.05)
Other Race/Ethnicity	Negative	262/681	42.7 (37.5 – 47.9)	Reference		Reference	Reference
	Positive	68/135	48.4 (41.3 – 55.6)	5.7 (-1.0, 12.4)		1.13 (0.98 – 1.31)	0.88 (0.71 – 1.09)
Stratified by body mass index category							
Underweight (BMI <18.5 kg/m^2)	Negative	28/96	29.9 (22.4 – 37.5)	Reference	0.1194	Reference	Reference
	Positive	7/11	50.9 (10.6 – 91.2)	21.0 (-20.5, 62.6)		1.70 (0.71 – 4.05)	0.71 (0.34 – 1.51)
Normal (BMI 18.5 – 24.9 kg/m^2)	Negative	478/1367	31.5 (26.9 – 36.1)	Reference		Reference	Reference
	Positive	75/149	49.2 (36.8 – 61.7)	17.7 (6.3, 29.2)		1.56 (1.23 – 1.98)	**1.24 (1.00 – 1.52)**
Overweight (BMI 25 – 29.9 kg/m^2)	Negative	709/1400	49.7 (46.2 – 53.2)	Reference		Reference	Reference
	Positive	96/160	59.3 (46.0 – 72.6)	9.6 (-2.9, 22.2)		1.19 (0.97 – 1.48)	0.98 (0.81 – 1.20)
Obese (BMI ≥30 kg/m^2)	Negative	1040/1592	61.6 (57.2 – 66.1)	Reference		Reference	Reference
	Positive	107/155	67.5 (57.9 – 77.1)	5.9 (-2.5, 14.3)		1.10 (0.97 – 1.24)	0.98 (0.89 – 1.08)
Stratified by foreign born status							
US Born	Negative	1793/3341	50.2 (46.8 – 53.7)	Reference	0.1385	Reference	Reference

Stratification Variables	QFT Status	Unweighted frequency Hypertension*/Total	Weighted Prevalence of Hypertension* (95%CI)	Prevalence Difference (95%CI)	Statistical interaction p-values	Prevalence Ratios	
						Crude	Adjusted†
						cPR (95%CI)	aPR (95%CI)
	Positive	120/172	65.6 (56.1 – 75.1)	15.4 (5.8, 25.0)		**1.31 (1.12 – 1.52)**	1.05 (0.92 – 1.21)
Foreign Born	Negative	500/1167	37.7 (31.9 – 43.4)	Reference		Reference	Reference
	Positive	166/307	51.3 (45.4 – 57.1)	13.6 (9.3, 17.9)		**1.36 (1.22 – 1.51)**	1.05 (0.92 – 1.21)
Stratified by current smoking status							
No	Negative	627/954	61.8 (56.0 – 67.7)	Reference	0.0886	Reference	Reference
	Positive	95/130	76.2 (66.8 – 85.6)	14.4 (4.2, 24.5)		**1.23 (1.07 – 1.42)**	1.09 (0.93 – 1.27)
Yes	Negative	439/851	47.2 (42.5 – 52.0)	Reference		Reference	Reference
	Positive	56/101	47.5 (34.4 – 60.7)	-0.3 (-14.3, 14.9)		1.01 (0.74 – 1.37)	0.89 (0.69 – 1.14)
Stratified by diabetes status							
Euglycemic	Negative	1083/2764	39.6 (35.4 – 43.8)	Reference	0.1235	Reference	Reference
	Positive	114/223	50.6 (42.6 – 58.5)	11.0 (3.0, 18.9)		**1.28 (1.08 – 1.51)**	1.01 (0.86 – 1.18)
Pre-diabetes	Negative	689/1102	59.8 (56.6 – 63.0)	Reference		Reference	Reference
	Positive	83/141	57.9 (44.2 – 71.6)	-1.9 (-16.6, 11.8)		0.97 (0.76 – 1.23)	0.95 (0.76 – 1.18)
Diabetes	Negative	522/644	81.1 (78.3 – 83.9)	Reference		Reference	Reference
	Positive	89/115	78.6 (68.7 – 88.5)	-2.5 (-13.0, 8.0)		0.97 (0.85 – 1.11)	0.94 (0.82 – 1.07)
Stratified by HIV Status							
HIV negative	Negative	1226/3130	39.1 (35.5 – 42.6)	Reference	**<0.001**	Reference	Reference
	Positive	102/243	43.2 (34.8 – 51.6)	4.1 (-4.3, 12.5)		1.11 (0.91 – 1.35)	0.93 (0.81 – 1.07)
HIV positive	Negative	4/15	18.4 (0 – 39.0)	Reference		Reference	Reference
	Positive	1/1	100.0 (100.0 – 100.0)	81.6 (62.0, 100.0)		**5.43 (1.92 – 15.36)**	6.24 (1.79 – 21.72)

aPR – adjusted prevalence ratio; CI – Confidence interval; PR – prevalence ratio; QFT – QuantiFERON-TB Gold Tube; US – United States

*Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
†Adjusted for age (continuous) and gender
‡Adjusted for gender

Table S6. Weighted prevalence of various hypertension classifications by confirmed tuberculosis infection status among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence (95%CI) Confirmed TB Infection Status N=4,266				
	Confirmed		Discordant TST and QFT		
	Negative N=3706 92.2% (90.5 – 93.9)	Positive N=190 2.1% (1.4 – 3.8)	TST* – and QFT + N=177 2.5 (1.4 – 3.5)	TST + and QFT – N=193 3.2 (2.5 – 4.00)	Any Discordance N=370 5.7% (4.6 – 6.8)
Primary study outcome					
Any hypertension indication[a] (n=2,250/4,266)	49.6 (45.7 – 53.5)	60.8 (51.4 – 70.3)	50.5 (38.9 – 62.2)	54.4 (43.5 – 65.4)	52.7 (43.9 – 61.6)
Measured blood pressure categories					
Normal blood pressure[b] (n=1,914)	47.0 (42.9 – 51.1)	36.6 (27.6 – 45.5)	49.8 (40.9 – 58.7)	39.6 (26.1 – 53.0)	44.0 (35.2 – 52.9)
Borderline hypertension[c] (n=714)	17.8 (15.5 – 20.0)	15.3 (8.3 – 22.3)	16.3 (8.2 – 24.4)	25.1 (14.7 – 35.5)	21.3 (13.4 – 29.1)
Hypertensiond (n=1,638/4,266)	35.2 (32.3 – 38.1)	48.1 (38.7 – 57.6)	33.9 (25.4 – 42.4)	35.3 (26.9 – 43.7)	34.7 (28.3 – 41.1)
Stage 1 hypertension[e] (n=1121)	24.9 (22.5 – 27.3)	37.0 (28.6 – 45.4)	25.4 (16.7 – 34.1)	24.0 (12.6 – 35.4)	24.6 (16.3 – 32.9)
Stage 2 hypertension[f] (n=517)	10.3 (8.9 – 11.7)	11.1 (6.1 – 16.1)	8.5 (3.3 – 13.7)	11.3 (4.0 – 18.5)	10.1 (5.5 – 14.6)
Hypertension Diagnosis					
Previously diagnosed hypertension[g] (n=1,496/4,266)	30.9 (27.5 – 34.3)	35.8 (27.6 – 44.0)	29.4 (17.9 – 40.8)	37.1 (25.9 – 48.4)	33.8 (27.0 – 40.6)
Self-reported current use of anti-hypertension medication[h] (n=1,292/1,496)	86.0 (82.2 – 89.9)	90.2 (79.7 – 100.0)	81.5 (65.8 – 97.1)	98.6 (96.0 – 100.0)	92.5 (87.4 – 97.5)
Undiagnosed hypertension[i] (n=754/4,266)	18.7 (16.4 – 21.0)	25.2 (18.1 – 32.3)	21.4 (12.2 – 30.6)	17.3 (6.1 – 28.5)	19.1 (12.2 – 25.9)
Hypertension Control (n=1,496)					
Controlled hypertension without medications[j] (n=1,286)	11.8 (9.6, 13.9)	6.9 (0.0, 13.0)	13.5 (1.6, 25.4)	5.4 (1.0, 9.8)	8.4 (3.5, 13.3)
Controlled hypertension with medications[k] (n=79)	34.8 (29.2, 40.4)	28.9 (13.2, 44.6)	43.6 (20.8, 66.4)	46.1 (34.0, 58.2)	45.2 (35.4, 55.0)
Uncontrolled hypertension without medications[l] (n=51)	15.0 (11.5, 18.4)	17.2 (5.7, 28.7)	18.9 (6.1, 29.7)	5.4 (0.3, 10.5)	10.1 (5.5, 14.7)
Uncontrolled hypertension with medications[m] (n=80)	38.5 (34.7, 42.2)	47.0 (36.2, 57.8)	25.0 (12.3, 37.7)	43.1 (28.9, 57.3)	36.3 (26.4, 46.2)

Abbreviations:
CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube; TST – tuberculin skin test

*TST positive was defined as skin induration ≥5mm among HIV-positive individuals or >10mm among HIV negative (following NHANES analytical notes). Induration <5mm (for HIV-positive individuals) or ≤10mm (for HIV-negative individuals) was considered negative

[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"

[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S7. Crude and adjusted associations between confirmed tuberculosis infection status and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Hypertension Measures	Measures of Association					
	Prevalence Difference (95%CI)		Prevalence Ratios (PR)			
			Crude PR (95%CI)		Adjusted* PR (95%CI)	
	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI
Primary study outcome						
Any hypertension indication[a]	11.3 (1.0, 21.5)	3.2 (-5.1 – 11.5)	**1.23 (1.03 – 1.46)**	1.06 (0.91 – 1.25)	1.08 (0.90 – 1.30)	0.98 (0.84 – 1.14)
Measured blood pressure categories						
Normal blood pressure[b]	-10.5 (-19.4, -1.6)	3.0 (-12.5, 6.4)	**0.78 (0.61 – 0.99)**	0.94 (0.76 – 1.16)	0.89 (0.69 – 1.15)	1.03 (0.84 – 1.26)
Borderline hypertension[c]	-2.4 (-9.5, 4.6)	3.5 (-4.1, 11.1)	0.86 (0.65 – 1.13)	1.20 (0.84 – 1.71)	0.82 (0.51 – 1.32)	1.15 (0.81 – 1.63)
Hypertension[d]	12.9 (2.8, 23.0)	-0.5 (-7.1, 6.1)	**1.37 (1.10 – 1.70)**	0.99 (0.82 – 1.19)	1.21 (0.98 – 1.49)	0.91 (0.75 – 1.10)
Stage 1 hypertension[e]	12.1 (2.8, 21.5)	-0.2 (-8.5, 8.0)	**1.49 (1.14 – 1.94)**	0.99 (0.71 – 1.38)	**1.37 (1.06 – 1.77)**	0.93 (0.66 – 1.32)
Stage 2 hypertension[f]	0.8 (-4.1, 5.7)	-0.3 (-5.2, 4.7)	1.08 (0.89 – 1.31)	0.98 (0.60 – 1.59)	0.88 (0.53 – 1.48)	0.86 (0.52 – 1.42)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	4.9 (-3.0, 12.7)	2.9 (-5.0, 10.7)	1.16 (0.93 – 1.44)	1.09 (0.86 – 1.38)	0.99 (0.77 – 1.28)	1.00 (0.81 – 1.23)
Self-reported current use of anti-hypertension medication[h]	4.2 (-8.1, 16.5)	6.4 (0.6, 12.3)	1.05 (0.81 – 1.36)	**1.07 (1.01 – 1.15)**	1.03 (0.91 – 1.18)	**1.08 (1.01 – 1.16)**
Undiagnosed hypertension[i]	6.5 (-0.3, 13.3)	0.4 (-6.9, 7.7)	**1.35 (1.03 – 1.77)**	1.02 (0.70 – 1.50)	1.26 (0.97 – 1.64)	0.96 (0.65 – 1.41)
Hypertension Control†						
Controlled hypertension without medications[j]	-4.9 (-14.2, 4.4)	-3.3 (-8.6, 2.0)	0.59 (0.19 – 1.80)	0.72 (0.39 – 1.32)	0.85 (0.27 – 2.70)	0.85 (0.48 – 1.53)
Controlled hypertension with medications[k]	-5.9 (-18.6, 6.8)	10.4 (-0.6, 21.4)	0.83 (0.54 – 1.28)	1.30 (1.00 – 1.69)	0.81 (0.53 – 1.22)	1.26 (0.97 – 1.65)
Uncontrolled hypertension without medications[l]	2.3 (-9.7, 14.2)	-4.9 (-10.3, 5.4)	1.15 (0.57 – 2.33)	0.68 (0.42 – 1.10)	1.32 (0.68 – 2.58)	0.70 (0.41 – 1.18)
Uncontrolled hypertension with medications[m]	8.5 (-3.4, 20.4)	-2.2 (-12.4, 8.1)	1.22 (0.94 – 1.58)	0.94 (0.71 – 1.25)	1.20 (0.91 – 1.58)	**1.27 (1.05 – 1.54)**

Abbreviations:
CI – confidence interval; PR – prevalence ratio; TBI – tuberculosis infection

*Models adjusted for age and gender
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,496)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S8. Sensitivity analysis to account for misclassification of covariates and different ways to handle age (confounder) included in the multivariable survey-weighted robust Poisson models to estimate the association between tuberculosis infection and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Models	Covariate(s) included in the model	QFT Result	Adjusted Prevalence Ratios	
			A (Age, continuous)	B (Age Group - Quartiles)
			aPR (95%CI)	aPR (95%CI)
Model 1	Age	Negative Positive	Reference 1.02 (0.93 – 1.13)	Reference 1.03 (0.93 – 1.14)
Model 2	Age, sex	Negative Positive	Reference 1.01 (0.92 – 1.10)	Reference 1.01 (0.91 – 1.13)
Model 3	Age, sex, BMI	Negative Positive	Reference 1.02 (0.92 – 1.13)	Reference 1.03 (0.93 – 1.15)
Model 4	Age, sex, income to poverty ratio	Negative Positive	Reference 1.00 (0.91 – 1.09)	Reference 1.01 (0.91 – 1.12)
Model 5	Age, sex, country of birth	Negative Positive	Reference 1.05 (0.96 – 1.14)	Reference 1.07 (0.97 – 1.19)
Model 6	Age, sex, income to poverty ratio, country of birth, BMI	Negative Positive	Reference 1.05 (0.95 – 1.17)	Reference 1.08 (0.97 – 1.21)
Model 7	Age, sex, income to poverty ratio, country of birth, BMI, current smoking status	Negative Positive	Reference 1.05 (0.93 – 1.17)	Reference 1.07 (0.93- 1.24)
Model 8	Age, sex, income to poverty ratio, country of birth, BMI, current smoking status, type-2 diabetes mellitus status, HIV status	Negative Positive	Reference 1.03 (0.99 – 1.08)	Reference 1.04 (0.99 – 1.08)
Model 9	Age, sex, income to poverty ratio, country of birth, BMI, type-2 diabetes mellitus status, HIV status	Negative Positive	Reference 1.04 (0.90 – 1.20)	Reference 1.05 (1.00 – 1.09)
Model 10*	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, BMI, smoking	Negative Positive	Reference 1.01 (0.97 – 1.06)	Reference 1.04 (0.99 – 1.09)
Model 11	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, and stroke	Negative Positive	Reference 1.00 (0.96 – 1.05)	Reference 1.03 (0.98 – 1.08)
Model 12	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, and stroke, BMI, smoking	Negative Positive	Reference 1.01 (0.96 – 1.05)	Reference 1.04 (0.99 – 1.08)
Model 13	Age, sex, race education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, stroke, BMI, current smoking	Negative Positive	Reference 1.07 (0.97 – 1.18)	Reference 1.09 (1.00 – 1.18)

	status, heavy alcohol consumption, any dyslipidemia, statin prescription, HIV status			

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	Figure1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	22
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10

		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Tuberculosis infection and hypertension: Prevalence estimates from the US National Health and Nutrition Examination Survey

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-075176.R2
Article Type:	Original research
Date Submitted by the Author:	13-Nov-2023
Complete List of Authors:	Salindri, Argita; Stanford University School of Medicine, Department of Medicine Auld, Sara; Emory University School of Medicine, Division of Pulmonary and Critical Care Medicine; Emory University School of Public Health, Department of Epidemiology Gujral, Unjali; Emory University School of Public Health, Hubert Department of Global Health Urbina, Elaine; University of Cincinnati College of Medicine, Department of Pediatrics Andrews, Jason R; Stanford University School of Medicine, Division of Infectious Diseases and Geographic Medicine, Department of Medicine Huaman, Moises; University of Cincinnati College of Medicine, Department of Internal Medicine Magee, Matthew J.; Emory University School of Public Health, Hubert Department of Global Health; Emory University School of Public Health, Department of Epidemiology
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Public health, Epidemiology
Keywords:	Hypertension < CARDIOLOGY, Tuberculosis < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, EPIDEMIOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Title Page

Prepared according to manuscript instructions for *BMJ Open* (original research)

Version: R2.Nov 9, 2023

Title: Tuberculosis infection and hypertension: Prevalence estimates from the US National Health and Nutrition Examination Survey

Authors:

Argita D. Salindri[1], Sara C. Auld[2,3], Unjali P. Gujral[4], Elaine M. Urbina[5], Jason R. Andrews[1], Moises A. Huaman[6*], Matthew J. Magee[3,4*]

Affiliations:

1. Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, CA, USA
2. Division of Pulmonary and Critical Care Medicine, Emory University School of Medicine, Atlanta, GA, USA
3. Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA
4. Hubert Department of Global Health, Emory University Rollins School of Public Health, Atlanta, GA, USA
5. Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH, USA
6. Department of Internal Medicine, College of Medicine, University of Cincinnati, Cincinnati, OH, USA

*Equal contribution

Main Article word count: 3740/4000

Abstract count: 303/300

Key points: 37/40

Tables & Figures: 5/5

References: 45/40

Keywords: latent tuberculosis infection, interferon-γ response, hypertension

Summary:

The prevalence of hypertension was high (59%) among adults with tuberculosis infection in the U.S. In addition, we found that the prevalence of hypertension was significantly higher among adults with positive QFT without established hypertension risk factors.

Corresponding Author:

Argita Salindri, PhD, MPH

Division of Infectious Diseases and Geographic Medicine

Department of Medicine

Stanford University School of Medicine

Biomedical Innovations Building, Stanford, CA 94304

Email: adsalind@stanford.edu

Phone: +1 404 490 5906

ABSTRACT

Objectives: Tuberculosis infection (TBI) is marked by dynamic host-pathogen interactions with persistent low-grade inflammation and is associated with increased risk of cardiovascular diseases (CVD) including acute coronary syndrome, myocardial infarction, and stroke. However, few studies assess the relationship between TBI and hypertension, an intermediate of CVD. We sought to determine the association between TBI and hypertension using data representative of the adult US population.

Methods: We performed cross-sectional analyses using data from the 2011–2012 US National Health and Nutrition Examination Survey (NHANES). Eligible participants included adults with valid QuantiFERON-TB Gold In-Tube (QFT-GIT) test results who also had blood pressure measures and no history of TB disease. TBI was defined by a positive QFT-GIT. We defined hypertension by either elevated measured blood pressure levels (i.e., systolic ≥130mmHg or diastolic ≥80mmHg) or known hypertension indications (i.e., self-reported previous diagnosis or use of antihypertensive medications). Analyses were performed using robust quasi-Poisson regressions and accounted for the stratified probability sampling design of NHANES.

Results: The overall prevalence of TBI was 5.7% (95%CI 4.7–6.7) and hypertension was present among 48.9% (95%CI 45.2–52.7) of participants. The prevalence of hypertension was higher among those with TBI (58.5%, 95%CI 52.4–64.5) than those without TBI (48.3%, 95%CI 44.5–52.1) (prevalence ratio [PR]=1.2, 95%CI 1.1–1.3). However, after adjusting for confounders, the prevalence of hypertension was similar for those with and without TBI (adjusted PR=1.0, 95%CI 0.9 –1.1). The unadjusted prevalence of hypertension was higher among those with TBI vs. no TBI, especially among individuals without CVD risk factors including those with normal BMI (PR=1.6, 95%CI 1.2–2.0), euglycemia (PR=1.3, 95%CI 1.1–1.5), or non-smokers (PR =1.2, 95%CI 1.1–1.4).

Conclusions: More than half of adults with TBI in the US had hypertension. Importantly, we observed a relationship between TBI and hypertension among those without established CVD risk factors.

Strengths and limitations

Strengths:

- These analyses were conducted using data representative of civilian, non-institutionalized US adults, and thus, provide a robust population estimate of the prevalence of latent tuberculosis infection and hypertension in the US
- Comprehensive definitions and different cut-offs of hypertension were used (i.e., measured blood pressure level, previous diagnosis hypertension by healthcare providers) to model the association between latent tuberculosis infection and hypertension

Limitations:

Our findings may not be representative to other regions with higher burdens of tuberculosis

- The cross-sectional study design of NHANES prevented us from assessing the temporal relationship between latent tuberculosis infection and hypertension

INTRODUCTION

About one-quarter of the world's population (~2 billion) has been infected to *Mycobacterium tuberculosis* (*Mtb*). [1] Among individuals infected with the bacteria, 5-10% are at risk of developing TB disease at some point in their life. [2 3] Tuberculosis infection (TBI), or most commonly known as latent tuberculosis infection or LTBI, is increasingly recognized as a heterogenous clinical state in which some individuals have dynamic host-pathogen interactions with persistent low-grade inflammation. This immune dysregulation has been associated with an increased risk of cardiovascular diseases (CVD) including acute coronary syndromes, myocardial infarction, and stroke. [1 4-12] This convergence of TBI and CVD risk poses a particular challenge for low- and middle-income countries where TBI is most prevalent and incidence of chronic non-communicable diseases, including CVD, is increasing rapidly. [13 14] Improved understanding of the impact of TBI on CVD risk is vital in settings where TBI and CVD are highly co-prevalent in order to design public health intervention programs aiming to reduce the burden of two diseases.

Epidemiologic data from observational cohort studies support an increased risk of CVD among people with TB disease. [8-12] Several studies also indicated that hypertension, an established intermediate of CVD, may be more common among patients with TB disease compared to non-TB controls. [8 11 14-16] Furthermore, CVD was the leading contributor to post-TB mortality, accounting for 15 – 26% of deaths among TB survivors in a recent systematic review and meta-analysis. [17] In addition to these associations between TB disease and CVD, recent observational studies have found an association between TBI and various CVDs including acute myocardial infarction and coronary artery disease. [9 18 19] However, studies assessing the association between TBI and hypertension remain limited.

To date, few studies have evaluated the relationship between TBI and hypertension. One cohort study from a large metropolitan healthcare system in the U.S. reported that

individuals with TBI had greater incidence of hypertension compared to those without TBI and that rates were highest among those untreated for TBI. [5] Furthermore, it is unknown whether the quantitative measures of IGRA, which may indicate the underlying mycobaterial burden and has been associated with increased risks of progression to TB disease, [20-23] is associated with hypertension. Improved understanding of the association between TBI, quantitative measures of IGRA, and and hypertension may clarify the role that TB prevention efforts in reducing the burden of CVD, both in the U.S. and globally.

Given existing knowledge gaps, we aimed to estimate the association between TBI and hypertension prevalence. We also investigated whether the magnitude of host immune responses to *Mtb* was associated with hypertension among those with positive IGRA test results.

METHODS

Study Design and Eligible Participants

We performed an analysis of cross-sectional data from the 2011 – 2012 US National Health and Nutrition Examination Survey (NHANES), [24] the most recent NHANES cycle released that includes measures of TBI. NHANES is a study led by the US Centers for Disease Control and Prevention (CDC) which aims to assess the health and nutritional status of non-institutionalized civilians representative of the US population using a complex, stratified, multistage probability cluster sampling design. NHANES collects demographic and health information using questionnaires administered by trained interviewers and standardized physical examinations performed in mobile examination centers. Eligible NHANES participants for our analyses were adults (≥18 years) with valid TBI test results and blood pressure measurements, and no history of TB disease (Figure 1).

Study Measures and Definitions

Our primary study outcome, any hypertension, was defined as having either (1) "measured hypertension," defined as an average systolic blood pressure level of ≥130 mmHg or diastolic blood pressure level of ≥80 mmHg across three consecutive measurements, or (2) a self-reported previous hypertension diagnosis by a health care provider or current use of antihypertensive medications (i.e., known hypertension). We categorized measured blood pressure levels into "normal" (i.e., systolic <120mmHg and diastolic <80mmHg), "borderline hypertension" (i.e., systolic 120-129mmHg and diastolic <80mmHg), "stage 1 hypertension" (i.e., systolic 130 – 139mmHg or diastolic 80-89mmHg), and "stage 2 hypertension" (i.e., systolic ≥140mmHg or diastolic ≥90mmHg) according to American College of Cardiology/American Heart Association guidelines. [25] Among participants with a prior diagnosis of hypertension, we classified blood pressure as "controlled" (systolic <130 mmHg and diastolic <80 mmHg) or "uncontrolled" (systolic ≥130mmHg or diastolic ≥80mmHg) with or without a self-reported use of antihypertensive medications.

Our primary study exposure, TBI, was defined by a positive QuantiFERON-TB Gold In Tube or QFT test, an in-vitro laboratory test to detect TB infection by measuring cell-mediated immune responses to TB-specific antigens. [26 27] Individuals with indeterminate test results were excluded from our analyses. For those with a positive QFT, we also extracted the quantitative results and defined the IFN-γ TB antigen response by subtracting TB NIL control values from TB antigen values (i.e., Ag-NIL values). To express IFN-γ TB antigen responses, instead of using the traditional manufacturer cut-off of ≥0.35, we used the 4.00 cut-off as previous studies showed that individuals with Ag-NIL values ≥4.00 are at greater risk from developing TB disease. [20 22 23] Thus, in our analyses, Ag-NIL values were categorized as "low" (<4 IU/ml) or "high" (≥4 IU/ml). For a sensitivity analysis, we performed a subgroup analysis of participants with both QFT and tuberculin skin test (TST) results. We defined "confirmed TB infection" when both TST and QFT results were positive and "no TB infection" if

both TST and QFT results were negative. Participants with discordant TST and QFT results (i.e., TST negative and QFT positive, TST positive and QFT negative) were classified as "any discordance."

Other important covariates, including age, sex, race, educational attainment, income to poverty ratio, country of birth, body mass index (BMI), diabetes mellitus status, HIV status, lipid profile, self-reported smoking behavior, alcohol consumption, statin prescription, and previous diagnosis of coronary heart disease, myocardial infarction, or stroke were also abstracted. We classified BMI as "underweight" (BMI <18.5 kg/m^2), "normal" (BMI 18.5 – 24.9 kg/m^2), "overweight" (BMI 25 – 29.9 kg/m^2), and obese (BMI ≥30kg/m^2). [28] As NHANES grouped individuals aged ≥80 years in one category, we divided age into quartile ranges and grouped as "quartile 1 (18 – 31 years)", "quartile 2 (32 – 47 years)", "quartile 3 (48 – 62 years)", and "quartile 4 (≥63 years)" to account for the non-linearity of age in sensitivity analyses.

Patient and Public Involvement

None

Statistical Analysis

We estimated weighted prevalence and 95% confidence intervals (CI) to determine the burden of TBI and hypertension in the US adult population. Rao-Scott Chi-square tests were used to assess the bivariate association between participants' demographic and clinical characteristics, TBI, Ag-NIL values, and hypertension. Multivariable robust Poisson regression with quasi-likelihood was used to estimate the association between TBI and hypertension, expressed in prevalence ratios (PRs) and 95% CI. The same regression approach was used to estimate the association between Ag-NIL responses and hypertension. In addition to prevalence ratios, we also estimated prevalence differences (PDs) and their 95%CI. Covariates included in

the multivariable models were based on bivariate associations (Table S1 and S2), established risk factors reported in previously published studies, and directed acyclic graphs (DAG). [29] Briefly, we identified potential confounders using bivariate associations and previously published literature, which then mapped into a DAG to determine inclusion in the final model. To account for the missingness of key covariates in the final adjusted model, we assigned aberrant values to any missing information to avoid deletion. We also assessed interaction between TBI and hypertension by participant characteristics (i.e., age, BMI, glycemic status, smoking status) on the additive (prevalence difference) and multiplicative (prevalence ratio) scales by including the cross-product terms within multivariable models. All analyses were performed using SAS *Survey Analysis PROCs (SAS version 9.4; Cary, North Carolina)* and *survey* package in R and accounted for the weighted stratified probability sample design of NHANES by applying weight (*WTMEC2YR*), cluster (*SDMVPSU*), and strata (*SDMVSTRA*) variables (samples of analytic codes are provided in Table S3). Taylor Series Linearization was used to produce design-adjusted standard errors and a two-sided p-value less than 0.05 considered statistically significant in all analyses.

Subgroup and Sensitivity Analyses

Sub-group analyses were conducted using an analytic approach with “domain” variables created to indicate sub-populations of interest. [30 31] Subgroup analyses were performed among those with previously diagnosed hypertension to determine the association between TBI (including Ag-NIL values) and controlled hypertension. Sensitivity analyses were performed to quantify systematic errors due to a) TBI misclassification, b) hypertension misclassification, c) covariate misspecification in multivariable models, and d) the classification of age as a confounder. To account for errors resulting from TBI misclassification, we ran additional models with confirmed TB infection as the exposure. To address potential biases due to hypertension misclassification, we ran an additional analysis using the prior hypertension clinical cut off. [25]

In this additional model, we defined any hypertension as having (1) an average systolic blood pressure level of ≥140 mmHg or diastolic blood pressure level of ≥90 mmHg across three consecutive measurements, or (2) a self-reported previous hypertension diagnosis by a health care provider or current use of antihypertensive medications. To quantify errors due to covariate misspecification, we ran multiple robust Poisson models with different sets of covariates and observed changes in prevalence ratios estimates across models. To account for the confounding effect of age, we ran multiple iterations of robust Poisson models with different forms of age measures (i.e., continuous and age quartiles).

RESULTS

Study population

In NHANES 2011 – 2012, 9,338 participants were surveyed and examined (response rate of 69.5%), 60.1% (5,615/9,338) of whom were ≥18 years old (Figure 1). Among included adults, 259 did not have valid blood pressure measurements. Of those with valid blood pressure measurements, 32 had a previous diagnosis of TB disease and 335 had a missing QFT, with 4,989 participants meeting eligiblity for this analytic cohort. The weighted prevalence of TBI in the cohort was 5.7% (95% confidence interval [CI] 4.7– 6.7) and any hypertension was present for 48.9% (95%CI 45.2 – 52.7) of participants (Table 1).

Associations between tuberculosis infection and hypertension

The prevalence of any hypertension was higher among those with TBI (58.5%, 95% CI 52.4 – 64.5) than those without TBI (48.3%, 95%CI 44.5 – 52.1) (prevalence difference [PD] 10.2%, 95%CI 5.0 – 15.4) (Table 1). After adjusting for potential confounders including age (continuous), sex, race, educational attainment level (as a proxy of socioeconomic status), country of birth, diabetes mellitus status, BMI, and smoking status, the prevalence of any hypertension was similar among those with and without TBI (adjusted prevalence ratio [aPR]

1.0, 95%CI 1.0 – 1.1). The association between TBI and hypertension was similar when examining the two components used to define our primary outcome (i.e., measured hypertension and self-reported hypertension/use of antihypertensive medications) both in the crude and adjusted models (Table 1).

Association between Ag-NIL values and hypertension

The prevalence of any hypertension was highest among those with TBI and high Ag-NIL values (60.4%, 95%CI 53.0 – 67.7) compared to those with TBI and low Ag-NIL values (57.6%, 95%CI 48.7 – 66.6) or those without TBI (48.3%, 95%CI 44.5 – 52.1) (Table S4). After adjusting for age and gender, however, the prevalence of any hypertension was similar among the three QFT groups being compared (Table S5). Similar trends were also observed for the associations between Ag-NIL values and both measured hypertension and self-reported previous diagnosis of hypertension (Figure 2).

Interaction analyses: established hypertension risk factors and HIV

We observed relationships between TBI and hypertension among participants without established hypertension risk factors who would be considered at lower risk for CVD. For example, comparing individuals with and without TBI, the crude prevalence ratios of any hypertension was substantially higher among those with normal BMI (crude prevalence ratio [cPR] 1.6, 95%CI 1.2 – 2.0), euglycemia (cPR 1.3, 95%CI 1.1 – 1.5), and non-smoking (cPR 1.2, 95%CI 1.1 – 1.5) groups (Figure 3) compared to those with or BMI ≥25 kg/m^2, pre-diabetes/diabetes or smokers. However, after adjusting for age and gender, the association between TBI and hypertension among these groups were attenuated. Additionally, product terms for BMI, glycemic level, and smoking status were non-significant on the adjusted prevalence ratio scale (p>0.05) (Table S6).

We also found that the association between TBI and hypertension may be different across HIV status. For instance, the crude prevalence difference of any hypertension comparing those with TBI to those without TBI was 4.1 percentage points (95%CI -4.3 – 12.5) among those without HIV infection and 81.6 percentage points (95%CI 61.0 – 100.0) among those with HIV infection.

Subgroup and sensitivity analyses

From subgroup analyses conducted among those with known hypertension, the prevalence of controlled hypertension without medications was significantly lower among those with positive QFT (5.2%, 95%CI 2.0 – 8.3) compared to those with negative QFT (11.8%, 95%CI 9.5 – 14.0), although the association was no longer significant after adjusting for key confounders (aPR 0.6, 95%CI 0.4 – 1.1) (Table 2). Conversely, the prevalence of uncontrolled hypertension with medications, the more severe form of hypertension, although non-significant, were slightly higher among those with positive QFT compared to those with negative QFT (Figure 2).

In models with confirmed TB infection (i.e., positive QFT and positive TST) as the study exposure, the prevalence of any hypertension was highest among those with confirmed TB infection (60.8%, 95%CI 51.4 – 70.3) compared to those with no TB infection (49.6%, 95%CI 45.7 – 53.5) or those with discordant TST and QFT results (52.7%, 95%CI 43.9 – 61.6) (p=0.12) (Table S7). We observed similar trends in the crude and adjusted associations between TBI and hypertension when we used both QFT and TST (Table S8) vs. QFT alone to define TBI. Results from models that used prior clinical cut-offs to define hypertension (systolic blood pressure level of ≥140 mmHg or diastolic blood pressure level of ≥90 mmHg) were similar to results from models with current hypertension definitions (aPR_{prior}=1.01, 95%CI 0.97 – 1.06 vs. $aPR_{current}$=0.94, 95%CI 0.89 – 1.00) (data not shown). Results from sensitivity analyses to quantify bias due to covariate misspecification in the multivariable models indicated that

prevalence ratios of any hypertension comparing those with positive QFT to those with negative QFT were similar when age was treated continuously or grouped in quartiles (ranged from 1.0 – 1.1) (Table S9).

DISCUSSION

Using data representative of US adult population, we found a high prevalence of hypertension (i.e., nearly 1 out of 2) in the 2011 – 2012 NHANES cycle. We reported similar adjusted prevalence of hypertension among individuals with or without TBI. In our study, individuals with positive QFT and high Ag-NIL values were more likely to have any hypertension, but less likely to have the more severe form of hypertension (i.e., uncontrolled hypertension without medications). We also observed that the association between TBI and hypertension was more common among individuals without established hypertension risk factors. Collectively, our results provide preliminary epidemiologic evidence suggesting that hypertension, a well-established intermediate for CVD, was more common among individuals with TBI than those without TBI in the US populations.

Our finding suggesting that hypertension is more common among individuals with TBI than those without TBI is consistent with previous studies, although the prevalence were similar after adjusting for key confounders. Our null adjusted findings may indicate that the association between TBI and hypertension among NHANES cohort were confounded by demographic characteristics (e.g., age, sex). In contrast, a retrospective cohort study conducted among 5,185 individuals with TBI and healthy controls using data from a large metropolitan healthcare system in the US reported a higher hazard rates of hypertension incidence (defined by ICD-9 codes) among those with TBI (defined by ICD-9 codes and tuberculin skin test/IFN-γ release assay) compared to healthy controls without TBI (HR 2.0, 95%CI 1.6 – 2.5). [5] In addition, a cross-sectional study conducted among 2,351 TST-positive individuals in South India reported a slightly higher prevalence of hypertension (defined as systolic >130 mmHg) among those with

confirmed TBI (defined as TST and QFT positive) (15%) compared to those latent TB negative (12%) (aOR 1.18, 95%CI 1.0 – 1.56). [32] Unlike the two studies mentioned above, we used a more comprehensive definition of hypertension by combining objectively measured blood pressure levels (systolic and diastolic) and known hypertension indications (i.e., previous hypertension diagnosis or self-reported use of antihypertensive medications) to avoid potential misclassification.

Despite our null findings, we identified several plausible mechanisms that may explain how TBI may be associated with hypertension. First, underlying pathophysiology related to chronic inflammation, even at relatively low levels, is linked to hypertension and therefore the proinflammatory state that accompanies TBI may increase blood pressure. [33 34] Second, TBI may be a proxy of other key factors related to social position which in turn impact hypertension risk. Hypertension is known to be multifactorial spanning from the group or community to the individual. Several physical, social, political, and environments risk factors that may influence hypertension were not fully accounted for in our analyses (e.g., stress, family history, diet, lifestyle, physical activity, geographical delineation, illicit drug use, access to healthcare, or insurance coverage). If some of these variables are associated with TBI, it is plausible that our reported estimates are distorted due to residual confounding effects. Further studies utilizing social ecological models and longitudinal designs are warranted to better understand the true effect of TBI on hypertension.

Furthermore, we also reported that the prevalence of hypertension was highest among individuals with positive QFT and high Ag-NIL values, but we observed no dose-response relationship nor statistical significance after adjusting for key risk factors. TB infection has been associated with enhanced levels of systemic inflammation and immune activation, including increased expression of tumor necrosis factor (TNF)-α, interferons, and interlukin-6 (IL-6). [4-7] These chemokines and dysfunctional immune responses play an important role in the pathogenesis of hypertension and CVD. [35 36] Individuals with positive QFT and higher Ag-NIL

values are more likely to develop to active TB [22 37] as they may have higher mycobacterial burden, [20] and thus, could potentially have higher degree of inflammation or immune responses to the bacterial infection. Interestingly, among those with previously diagnosed hypertension, we found that individuals with TBI may have more severe hypertension manifestation compared to those without TBI. This was indicated by the higher prevalence of uncontrolled hypertension without medications among those with TBI. However, the available data do not allow us to discern if these differences are due to clinical differences or access to care.

Our cross-sectional study design may not be the appropriate design to observe the expected associations or dose-response relationship between TBI, IFN-γ TB antigen responses, and hypertension. Furthermore, the time of TBI in the life-course may have different implications on TBI and hypertension association. In this NHANES cohort, the majority (>90%) of foreign born with positive QFT have stayed in the US for ≥5 years, and thus, we postulated that TBI happened before arriving in the US. It is plausible that these individuals are either in the latent or incipient stage where there is no to minimum bacteria replication, and thus, minimum pro-inflammatory responses. [38] Newly arrived immigrants may face higher level of stress with acculturation and other social-environmental pressures which could impact systemic inflammation, immune responses, and/or increased risks of hypertension. Prospective studies to follow individuals with recent TBI diagnosis are still warranted to determine the hypertension and CVD risk trajectories.

Interestingly, we observed associations between TBI and hypertension among those with normal BMI, euglycemic, and non-smokers without adjusting for potential confounders. These groups may be considered at lower risk of CVD. Although the associations were attenuated and non-significant after controlling for potential confounders, the prevalence of hypertension remained higher when comparing those with TBI than those without TBI among

these groups. This further reinforces the premise that there is likely to be differing effects of TBI on hypertension risk within subgroups. While the significant TBI-hypertension associations observed among those with lower risk of CVD may be due to the larger sample sizes in NHANES, these preliminary results suggest the need for mechanistic studies. Further clinical investigations and modeling studies are needed to determine whether targeted TB preventive treatment is effective to reduce the global burden of CVD among these groups.

Our study is subject to limitations. First, our TBI definition (i.e., according to QFT positivity) may include a broad spectrum of individuals who may have cleared the infection, have latent TB, incipient TB, or subclinical TB since no further clinical assessment was made (e.g., symptom screening, chest X-ray, culture test). [39 40] Second, we could not determine the temporal relationship between TBI and hypertension with the cross-sectional study design used in the present paper. Third, we did not account for any record of hypertension prescription, or other commonly prescribed medications that could potentially affect blood pressure levels. Fourth, we defined some of our key variables (including hypertension status and hypertension medication intake) with self-reported information that may be prone to recall bias and likely included some misclassification. However, if misclassification of hypertension was non-differential with respect to TBI, we expect any misclassification in our results would likely biased towards the null. [41] Fourth, we did not estimate a) stratum specific prevalence ratios for HIV and b) effects of HIV clinical information (e.g., CD4 counts) in our stratified models due to the small, unweighted frequency of individuals with HIV infection. The wide confidence intervals reported around our prevalence differences among HIV and non-HIV group also needs to be interpreted with caution considering the low prevalence of HIV infection in the 2011-2012 NHANES cycle. Further clinical studies with larger sample size are still warranted to fully assess the joint effect between HIV (including HIV clinical characteristics) and TBI, and its association with hypertension. Last, this study was conducted using survey data representative of US adult population but may not be generalizable to other regions with higher TB burdens. Furthermore,

we used data from NHANES 2011 – 2012 and were not able to determine whether the prevalence of TB infection and hypertension reported in this study cycle is reflective of the current US population. An updated analysis to assess trends in the association across multiple NHANES cycles is warranted.

In conclusion, we reported a higher prevalence of hypertension among individuals with positive QFT, although the association was non-significant after adjusting for key confounders, particularly age. To determine the direction of the association between TBI and hypertension, a prospective study following hypertension-free individuals at TBI diagnosis is warranted and would help establish the biological pathways regarding how TBI might increase the risk of CVD. Future prospective work should address the question whether individuals treated for LTBI have lower risk of hypertension. Importantly, our results underscore the need to screen for hypertension and other metabolic disorders among those with TBI, especially among those without traditional CVD risk factors; doing so may help prevent premature deaths attributed to TB and CVD.

DECLARATIONS AND ACKNOWLEDGMENTS

Competing interest

We have no conflict of interest to declare.

Ethical review statement

Following federal regulations, this work was determined as “non-human subject research” by the Institutional Review Boards (IRB) at Emory University, and thus, does not require IRB review.

Funding

This work was supported in part by the National Center for Advancing Translational Sciences (grant numbers R03TR004097 to MAH), the National Institute of Allergy and Infectious Diseases (grant number UM1AI069501; grant numbers R01AI153152 and R21AI156161 to MJM; grant number K23AI134182 to SCA), and the National Heart, Lung, and Blood Institute (grant number R01HL156779 to MAH) at the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions

MAH, MJM, and ADS conceived the study design. ADS performed the analyses. ADS, MAH, and MJM wrote the first draft of the manuscript. SCA, UPG, EMU, and JRA assisted with further drafting and revisions of manuscripts. All authors reviewed and approved the final version of the manuscript.

Data Availability Statement

This work used publicly available data of the US National Health and Nutrition Examination Survey (NHANES) 2011 – 2012 that can be downloaded directly from CDC’s webpage.

TABLE LEGENDS

Table 1 (p.24) Weighted prevalence and adjusted prevalence ratios of hypertension measures by QuantiFERON-TB Gold In-Tube status among US adults, NHANES 2011-2012

This table shows the prevalence of select hypertension measures in the overall adult cohort of NHANES 2011 – 2012 as well as stratified by their tuberculosis infection status. The crude measure of association was expressed as prevalence difference (PD), while the adjusted measure of association was expressed as prevalence ratio (PR).

Table 2 (p.25) Weighted prevalence and adjusted prevalence ratios of controlled and uncontrolled hypertension by QuantiFERON-TB Gold In-Tube status among US adults with known hypertension, NHANES 2011-2012

This table summarizes findings on whether latent tuberculosis infection is associated with severe clinical manifestation of hypertension, indicated by elevated measured blood pressure levels with the use of antihypertensive medications among individuals with known hypertension indications (n=1,711)

FIGURE LEGENDS

Figure 1 Flow chart depicting unweighted frequencies and percentages of participants included in the final analyses based on the eligibility criteria, NHANES 2011 – 2012

This study flow chart provides description of the stepwise exclusion of ineligible participants. From 9,338 individuals who completed NHANES interview and medical examination, we included 4,989 (53.4%) individuals in our primary analyses after excluding those who are <18 years old or those with a record of previous TB disease, or missing blood pressure data and QuantiFERON results

Figure 2 Crude and adjusted associations between QuantiFERON-TB Gold In-Tube results and select hypertension measures among US adults, NHANES 2011 – 2012

Circles in this panel of figures indicate point estimates from the robust Poisson models, expressed as prevalence ratios with the colored bands indicating the accompanying 95% confidence intervals. The vertical dashed line on the x axis value of 1 marks the study null value (i.e., β estimates=0 or prevalence ratio=1.00), suggesting no association. The top panel figures were produced from analyses performed among eligible participants (n=4,989). The lower panel figures were produced from analyses performed among a subset of participants with known hypertension indication(n=1,711)

Figure 3 Relationship between positive QuantiFERON-TB result and hypertension: Stratified by demographic and clinical characteristics among US adults, NHANES 2011 – 2012

This figure shows results from the analyses with statistical interaction term included in the robust Poisson models to evaluate the joint effect between tuberculosis infection and other key risk factors on hypertension. We selected these "moderator" variables by identifying common risk factors for cardiovascular diseases from published studies (e.g., age, race, body mass index, country of birth, smoking status, and diabetes status).

REFERENCES

1. Behr MA, Kaufmann E, Duffin J, et al. Latent Tuberculosis: Two Centuries of Confusion. *Am J Respir Crit Care Med* 2021;204(2):142-48. doi: 10.1164/rccm.202011-4239PP [published Online First: 2021/03/25]
2. Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. *PLoS Med* 2016;13(10):e1002152. doi: 10.1371/journal.pmed.1002152
3. WorldHealthOrganization. Tuberculosis Fact Sheet 2016 [Available from: http://www.who.int/mediacentre/factsheets/fs104/en/ accessed 06/11/2017 2016.
4. Feria MG, Chang C, Ticona E, et al. Pro-Inflammatory Alterations of Circulating Monocytes in Latent Tuberculosis Infection. *Open Forum Infectious Diseases* 2022;9(12) doi: 10.1093/ofid/ofac629
5. Mandieka E, Saleh D, Chokshi AK, et al. Latent Tuberculosis Infection and Elevated Incidence of Hypertension. *Journal of the American Heart Association* 2020;9(24):e019144. doi: doi:10.1161/JAHA.120.019144
6. Dixon DL, Wohlford GF, Abbate A. Inflammation and Hypertension. *Hypertension* 2020;75(2):297-98. doi: doi:10.1161/HYPERTENSIONAHA.119.14195
7. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. *Can Commun Dis Rep* 2017;43(3-4):62-66. doi: 10.14745/ccdr.v43i34a01 [published Online First: 2017/03/02]
8. Chung WS, Lin CL, Hung CT, et al. Tuberculosis increases the subsequent risk of acute coronary syndrome: a nationwide population-based cohort study. *Int J Tuberc Lung Dis* 2014;18(1):79-83. doi: 10.5588/ijtld.13.0288 [published Online First: 2013/12/25]
9. Huaman MA, Ticona E, Miranda G, et al. The Relationship between Latent Tuberculosis Infection and Acute Myocardial Infarction. *Clin Infect Dis* 2017 doi: 10.1093/cid/cix910
10. Huaman MA, Kryscio RJ, Fichtenbaum CJ, et al. Tuberculosis and risk of acute myocardial infarction: a propensity score-matched analysis. *Epidemiol Infect* 2017;145(7):1363-67. doi: 10.1017/s0950268817000279 [published Online First: 2017/02/17]
11. Sheu JJ, Chiou HY, Kang JH, et al. Tuberculosis and the risk of ischemic stroke: a 3-year follow-up study. *Stroke* 2010;41(2):244-9. doi: 10.1161/strokeaha.109.567735 [published Online First: 2009/12/26]
12. Salindri AD, Wang JY, Lin HH, et al. Post-tuberculosis incidence of diabetes, myocardial infarction, and stroke: Retrospective cohort analysis of patients formerly treated for tuberculosis in Taiwan, 2002 - 2013. *Int J Infect Dis* 2019 doi: 10.1016/j.ijid.2019.05.015
13. Magee MJ, Salindri AD, Gujral UP, et al. Convergence of non-communicable diseases and tuberculosis: a two-way street? *Int J Tuberc Lung Dis* 2018;22(11):1258-68. doi: 10.5588/ijtld.18.0045 [published Online First: 2018/10/26]
14. Seegert AB, Rudolf F, Wejse C, et al. Tuberculosis and hypertension—a systematic review of the literature. *International Journal of Infectious Diseases* 2017;56:54-61. doi: 10.1016/j.ijid.2016.12.016
15. Shen TC, Huang KY, Chao CH, et al. The risk of chronic kidney disease in tuberculosis: a population-based cohort study. *QJM* 2015;108(5):397-403. doi: 10.1093/qjmed/hcu220 [published Online First: 2014/10/30]
16. Marak B, Kaur P, Rao SR, et al. Non-communicable disease comorbidities and risk factors among tuberculosis patients, Meghalaya, India. *Indian J Tuberc* 2016;63(2):123-5. doi: 10.1016/j.ijtb.2015.07.018 [published Online First: 2016/07/28]
17. Romanowski K, Baumann B, Basham CA, et al. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2019 doi: 10.1016/S1473-3099(19)30309-3

18. Khoufi EAA. Association between latent tuberculosis and ischemic heart disease: a hospital-based cross-sectional study from Saudi Arabia. *Pan Afr Med J* 2021;38:362. doi: 10.11604/pamj.2021.38.362.28110 [published Online First: 2021/08/10]
19. Alsayed Hasanain AF, El-Maghraby KM, AA HZ, et al. Latent tuberculosis infection among patients with coronary artery stenosis: A case-Control study. *International journal of mycobacteriology* 2018;7(2):143-47. doi: 10.4103/ijmy.ijmy_34_18 [published Online First: 2018/06/15]
20. Gupta RK, Lipman M, Jackson C, et al. Quantitative IFN-γ Release Assay and Tuberculin Skin Test Results to Predict Incident Tuberculosis. A Prospective Cohort Study. *Am J Respir Crit Care Med* 2020;201(8):984-91. doi: 10.1164/rccm.201905-0969OC [published Online First: 2019/12/12]
21. Zellweger JP, Sotgiu G, Block M, et al. Risk Assessment of Tuberculosis in Contacts by IFN-γ Release Assays. A Tuberculosis Network European Trials Group Study. *Am J Respir Crit Care Med* 2015;191(10):1176-84. doi: 10.1164/rccm.201502-0232OC [published Online First: 2015/03/13]
22. Andrews JR, Nemes E, Tameris M, et al. Serial QuantiFERON testing and tuberculosis disease risk among young children: an observational cohort study. *Lancet Respir Med* 2017;5(4):282-90. doi: 10.1016/s2213-2600(17)30060-7 [published Online First: 2017/02/22]
23. Winje BA, White R, Syre H, et al. Stratification by interferon-γ release assay level predicts risk of incident TB. *Thorax* 2018 doi: 10.1136/thoraxjnl-2017-211147 [published Online First: 2018/04/07]
24. CDC. National Health and Nutrition Examination Survey 2011 - 2012. In: CDC, ed. NHANES 2011 - 2012. USA, 2011 - 2012.
25. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):e13-e115. doi: 10.1161/HYP.0000000000000065 [published Online First: 2017/11/15]
26. Mazurek GH, Jereb J, Lobue P, et al. Guidelines for using the QuantiFERON-TB Gold test for detecting Mycobacterium tuberculosis infection, United States. *MMWR Recomm Rep* 2005;54(Rr-15):49-55. [published Online First: 2005/12/17]
27. Banaei N, Gaur RL, Pai M. Interferon Gamma Release Assays for Latent Tuberculosis: What Are the Sources of Variability? *J Clin Microbiol* 2016;54(4):845-50. doi: 10.1128/jcm.02803-15 [published Online First: 2016/01/15]
28. Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. StatPearls. Treasure Island (FL)2022.
29. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology* 1999;10(1):37-48.
30. CDC. NHANES Survey Methods and Analytic Guidelines [Available from: https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx#analytic-guidelines.
31. CDC. NHANES Sample Code [Available from: https://wwwn.cdc.gov/nchs/nhanes/tutorials/samplecode.aspx.
32. Munisankar S, Rajamanickam A, Balasubramanian S, et al. Prevalence of proximate risk factors of active tuberculosis in latent tuberculosis infection: A cross-sectional study from South India. *Front Public Health* 2022;10:1011388. doi: 10.3389/fpubh.2022.1011388 [published Online First: 2022/10/25]
33. Huaman MA, Henson D, Ticona E, et al. Tuberculosis and Cardiovascular Disease: Linking the Epidemics. *Tropical diseases, travel medicine and vaccines* 2015;1 doi: 10.1186/s40794-015-0014-5 [published Online First: 2016/02/03]

34. Huaman MA, De Cecco CN, Bittencourt MS, et al. Latent Tuberculosis Infection and Subclinical Coronary Atherosclerosis in Peru and Uganda. *Clin Infect Dis* 2021;73(9):e3384-e90. doi: 10.1093/cid/ciaa1934 [published Online First: 2021/01/04]
35. De Miguel C, Rudemiller NP, Abais JM, et al. Inflammation and hypertension: new understandings and potential therapeutic targets. *Curr Hypertens Rep* 2015;17(1):507. doi: 10.1007/s11906-014-0507-z [published Online First: 2014/11/30]
36. Tanase DM, Gosav EM, Radu S, et al. Arterial Hypertension and Interleukins: Potential Therapeutic Target or Future Diagnostic Marker? *Int J Hypertens* 2019;2019:3159283. doi: 10.1155/2019/3159283 [published Online First: 2019/06/13]
37. Ledesma JR, Ma J, Zheng P, et al. Interferon-gamma release assay levels and risk of progression to active tuberculosis: a systematic review and dose-response meta-regression analysis. *BMC Infect Dis* 2021;21(1):467. doi: 10.1186/s12879-021-06141-4 [published Online First: 2021/05/24]
38. Migliori GB, Ong CWM, Petrone L, et al. The definition of tuberculosis infection based on the spectrum of tuberculosis disease. *Breathe (Sheff)* 2021;17(3):210079. doi: 10.1183/20734735.0079-2021 [published Online First: 2022/01/18]
39. Dowdy DW, Behr MA. Are we underestimating the annual risk of infection with Mycobacterium tuberculosis in high-burden settings? *Lancet Infect Dis* 2022;22(9):e271-e78. doi: 10.1016/s1473-3099(22)00153-0 [published Online First: 2022/05/09]
40. Anwar A, Hamdan AJ, Salim B, et al. Diagnostic Utility of QuantiFERON-TB Gold (QFT-G) in Active Pulmonary Tuberculosis. *J Glob Infect Dis* 2015;7(3):108-12. doi: 10.4103/0974-777x.162231 [published Online First: 2015/09/24]
41. Lash TL, Fox MP, Fink AK. Applying Quantitative Bias Analysis to Epidemiologic Data: Statistics for Biology and Health. New York: Springer Science and Business Media 2011.

MAIN RESULTS

Table 1. Weighted prevalence and adjusted prevalence ratios of hypertension measures by QuantiFERON-TB Gold In-Tube status among US adults, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence of Hypertension, % (95%CI)				
	Total N=4,989	among QFT (-) 94.3 (93.3, 95.3)	among QFT (+) 5.7 (4.7, 6.7)	Prevalence Difference* Percentage point (95%CI)	aPR† (95% CI)
Primary study outcome					
Any hypertension indication[a] (n=2,580/4,989)	48.9 (45.2, 52.7)	48.3 (44.5, 52.1)	58.5 (52.4, 64.5)	**10.2 (5.1, 15.4)**	1.01 (0.97 – 1.06)
Measured blood pressure					
Hypertension[b] (n=1,885/4,989)	35.0 (32.3, 37.6)	34.5 (31.8, 37.2)	43.2 (36.4, 49.9)	**8.7 (1.9, 15.5)**	1.04 (0.97 – 1.12)
Stage 1 hypertension[c] (n=1273)	24.5 (22.4, 26.7)	24.2 (21.9, 26.5)	30.1 (22.4, 37.9)	5.9 (-2.3, 14.2)	1.13 (0.99 – 1.29)
Stage 2 hypertension[d] (n=612)	10.4 (9.1, 11.8)	10.3 (8.9, 11.7)	13.0 (9.1, 17.0)	2.8 (-1.3, 6.8)	0.88 (0.75 – 1.02)
Hypertension Diagnosis					
Previously diagnosed hypertension[e] (n=1,711)	30.8 (27.7, 33.9)	30.3 (27.1, 33.6)	38.3 (33.6, 43.1)	**8.0 (2.4, 13.6)**	0.97 (0.90 – 1.04)
Current use of anti-hypertension medication[f] (n=1,276)	86.9 (83.7, 90.1)	86.3 (82.7, 89.9)	94.7 (90.9, 98.4)	**8.4 (2.4, 14.4)**	**1.13 (1.02 – 1.09)**
Undiagnosed hypertension[g] (n=869)	18.1 (16.1, 20.2)	18.0 (15.8, 20.2)	20.2 (14.0, 26.4)	2.2 (-4.4, 8.9)	1.08 (0.91 – 1.28)

Abbreviations: CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group

†Model was adjusted for age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, body mass index, and smoking

[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or self-reported previous diagnosis of high blood pressure by health providers or use of antihypertensive medications

[b]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)

[c]Systolic 130-139 mmHg or diastolic 80-89 mmHg

[d]Systolic ≥140 mmHg or diastolic ≥90 mmHg

[e]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"

[f]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"

[g]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers

Bold indicates that the finding is significant at α=0.05

Table 2. Weighted prevalence and adjusted prevalence ratios of controlled and uncontrolled hypertension by QuantiFERON-TB Gold In-Tube status among US adults with known hypertension, NHANES 2011-2012

Hypertension Controls	Weighted Prevalence of Hypertension, % (95%CI)				
	Total N=1,711	**among QFT (-) 94.3 (93.3, 95.3)**	**among QFT (+) 5.7 (4.7, 6.7)**	**Mean/Prevalence Difference[*] Percentage point (95%CI)**	**aPR[†] (95% CI)**
Controlled without medications[a] (n=308)	11.3 (9.2, 13.3)	11.8 (9.5, 14.0)	5.2 (2.0, 8.3)	**-6.6 (-10.5, -2.7)**	0.62 (0.36 – 1.09)
Controlled with medications[b] (n=838)	33.9 (29.1, 38.8)	33.9 (28.8, 40.0)	34.8 (25.5, 44.1)	0.9 (-9.0, 10.8)	1.10 (0.84 – 1.45)
Uncontrolled without medications[c] (n=127)	15.0 (12.0, 18.1)	15.2 (12.0, 18.5)	12.2 (5.5, 18.9)	-3.1 (-10.1, 3.9)	0.80 (0.41 – 1.59)
Uncontrolled with medications[d] (n=438)	39.8 (36.7, 42.8)	39.1 (35.7, 42.6)	47.8 (40.1, 55.6)	8.7 (-1.0, 18.4)	1.16 (0.94 – 1.43)

Abbreviations: CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

[*]Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group

[†]Model was adjusted for age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, body mass index, and smoking

[a]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels

[b]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[c]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels

[d]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

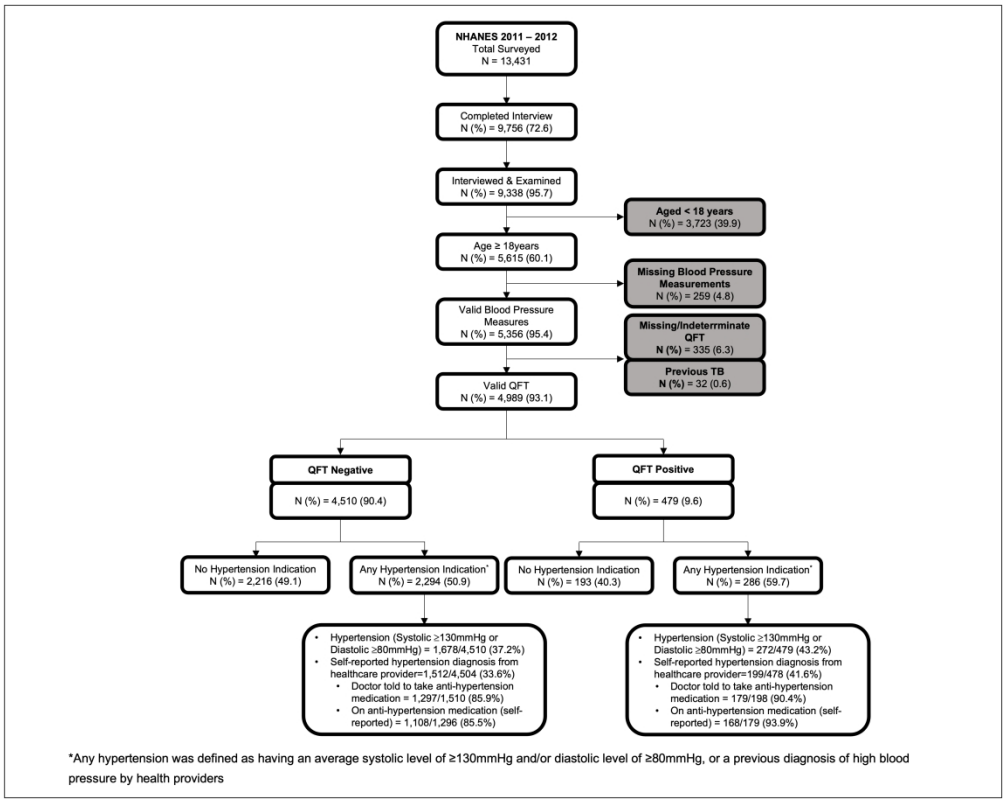


Figure 1. Flow chart depicting unweighted frequencies and percentages of participants included in the final analyses based on the eligibility criteria, NHANES 2011 – 2012

772x613mm (130 x 130 DPI)

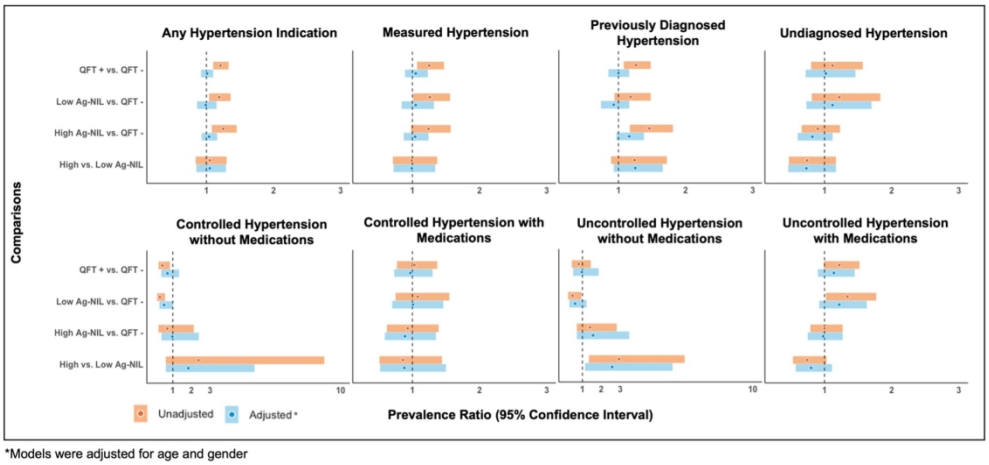


Figure 2. Crude and adjusted associations between QuantiFERON-TB Gold In-Tube results and select hypertension measures among US adults, NHANES 2011 – 2012

227x106mm (220 x 220 DPI)

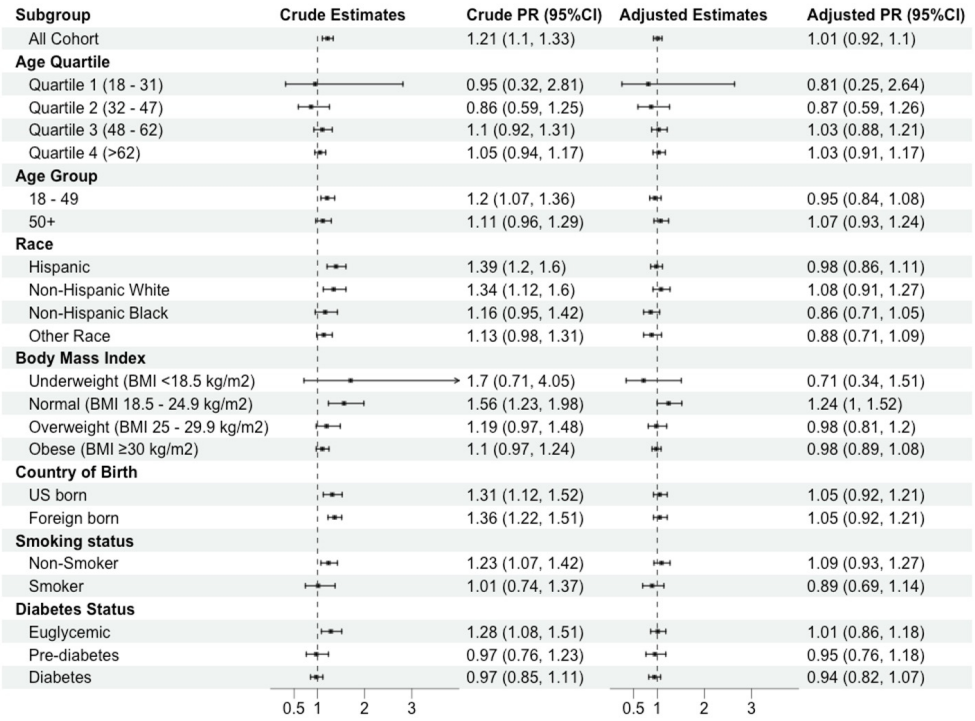


Figure 3. Relationship between positive QuantiFERON-TB result and hypertension: Stratified by demographic and clinical characteristics among US adults, NHANES 2011 – 2012

254x186mm (144 x 144 DPI)

SUPPEMENTAL MATERIALS

Supplemental Materials

Table S1. Weighted prevalence of and characteristics associated with tuberculosis infection among according to QuantiFERON-TB Gold In-Tube results among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012 (COLUMN PERCENTAGE)

Characteristics	Weighted Prevalence, % (95%CI)		
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Odds Ratios* (95%CI)
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	
Any hypertension indication[a]			
No	51.7 (47.9 – 55.5)	41.5 (35.5 – 47.6)	Reference
Yes	48.3 (44.5 – 52.1)	58.5 (52.5 – 64.5)	**1.5 (1.2 – 1.9)**
Age, years			
Mean (95%CI)	46.0 (44.1 – 48.0)	53.2 (51.2 – 55.1)	7.1 (5.1, 9.2)
Age groups			
Quartile 1 (18 – 31)	25.9 (20.9 – 30.9)	12.1 (8.1 – 16.2)	Reference
Quartile 2 (32 – 47)	28.6 (25.6 – 31.5)	22.1 (16.5 – 27.6)	**1.6 (1.0 – 2.7)**
Quartile 3 (48 – 62)	25.1 (22.2 – 27.9)	36.2 (28.0 – 44.5)	**3.1 (1.7 – 5.6)**
Quartile 4 (>62)	20.4 (17.7 – 23.2)	29.5 (23.1 – 36.0)	**3.1 (2.1 – 4.5)**
18 – 49	74.3 (71.4 – 77.3)	65.9 (60.1 – 71.6)	Reference
≥50	25.7 (22.7 – 28.6)	34.1 (28.4 – 39.9)	**1.5 (1.2 – 2.0)**
Sex			
Male	48.2 (46.6 – 49.8)	56.6 (50.5 – 60.7)	Reference
Female	51.8 (50.2 – 53.4)	43.4 (37.3 – 49.5)	**0.7 (0.6 – 0.9)**
Race			
Hispanic	13.4 (8.2 – 18.5)	31.1 (20.6 – 41.6)	Reference
Non-Hispanic white	68.6 (60.3 – 76.9)	37.0 (27.4 – 46.7)	**0.2 (0.2 – 0.4)**
Non-Hispanic black	11.1 (6.1 – 16.1)	14.3 (8.8 – 19.8)	**0.6 (0.4 – 0.7)**
Other race	7.0 (4.8 – 9.1)	17.6 (11.9 – 23.3)	1.1 (0.8 – 1.5)
Education (n=4,757)			
Less than 9th grade	4.8 (3.7 – 5.9)	16.7 (11.4 – 22.0)	Reference
9-11th grade	10.5 (7.3 – 13.6)	13.7 (10.2 – 17.5)	**0.4 (0.2 – 0.6)**
High school graduate	19.7 (16.5 – 22.9)	24.2 (18.1 – 30.3)	**0.4 (0.2 – 0.6)**
Some college	33.2 (29.8 – 36.5)	18.4 (12.8 – 23.9)	**0.2 (0.1 – 0.3)**
College graduate or above	31.8 (26.3 – 37.3)	26.8 (18.7 – 34.8)	**0.2 (0.2 – 0.4)**
Missing (n=264)	259	5	**0.1 (0.0 – 0.3)**
Ratio of family income to poverty (n=4,623)			
Mean (95%CI)	2.9 (2.7 – 3.1)	2.4 (2.1 – 2.7)	-0.5 (-0.9, -0.2)
0 – 0.99	17.0 (13.3 – 20.8)	25.1 (19.4 – 30.9)	Reference
1 – 1.99	20.7 (17.6 – 23.8)	28.4 (22.2 – 34.6)	0.9 (0.6 – 1.3)
2 – 2.99	14.3 (11.8 – 16.7)	13.1 (6.6 – 19.6)	0.6 (0.3 – 1.3)
3 – 3.99	12.6 (9.6 – 15.5)	9.3 (4.2 – 14.4)	**0.5 (0.3 – 0.8)**
4 – 4.99	10.7 (6.2 – 13.2)	6.2 (.1 – 9.4)	**0.4 (0.2 – 0.9)**
≥5	24.7 (19.8 – 29.6)	17.9 (10.5 – 25.6)	**0.5 (0.3 – 0.9)**
Missing (n=396)	344	52	1.0 (0.6 – 1.8)
Foreign born (n=4,987)			
No	84.7 (80.7 – 88.6)	50.2 (39.0 – 61.5)	Reference
Yes	15.3 (11.4 – 19.3)	49.8 (38.5 – 61.0)	**5.5 (3.5 – 8.5)**
Missing (n=2)	2	0	NA
BMI, kg/m^2 (n=4,930)			
Mean (95%CI)	28.7 (28.2 – 29.1)	28.9 (27.8 – 30.1)	0.2 (-0.7, 1.2)
BMI categories			
Underweight (<18.5 kg/m^2)	1.8 (1.6 – 2.4)	2.2 (0.4 – 4.1)	1.2 (0.6 – 2.3)

Characteristics	Weighted Prevalence, % (95%CI)		
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Odds Ratios* (95%CI)
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	
Normal (18.5 – 24.9 kg/m^2)	29.8 (26.6 – 32.9)	31.6 (23.6 – 39.7)	Reference
Overweight (25 – 29.9 kg/m^2)	33.6 (30.9 – 36.4)	32.0 (25.3 – 38.7)	0.9 (0.6 – 1.3)
Obese (≥30 kg/m^2)	34.8 (31.7 – 37.8)	34.1 (25.8 – 42.4)	0.9 (0.6 – 1.4)
Missing (n=59)	55	4	0.7 (0.2 – 2.8)
Smoking status (n=4,722)			
Never smokers[b]	56.5 (53.2 – 59.8)	48.7 (41.7 – 55.6)	Reference
Past smokers[c]	24.2 (21.3 – 27.2)	29.0 (22.5 – 35.5)	1.4 (0.9 – 2.1)
Current smokers[d]	19.3 (16.9 – 21.6)	22.3 (16.4 – 28.3)	1.3 (0.9 – 2.1)
Missing (n=267)	262	5	0.4 (0.1 – 1.3)
Heavy alcohol drinking (n=3,867)			
No	14.7 (12.0 – 17.3)	14.0 (10.6 – 17.5)	Reference
Yes[e]	85.3 (82.7 – 88.0)	86.0 (82.5 – 89.4)	1.1 (0.8 – 1.4)
Missing (n=1,122)	986	136	**1.6 (1.2 – 2.3)**
HbA1c, %			
Mean (95%CI)	5.6 (5.6 – 5.7)	5.9 (5.7 – 6.0)	0.3 (0.1, 0.4)
Diabetes categories[f]			
Normal	68.0 (65.7 – 70.3)	53.1 (46.9 – 59.4)	Reference
Prediabetes	21.5 (19.8 – 23.2)	25.3 (21.4 – 29.1)	**1.5 (1.2 – 1.9)**
Diabetes	10.4 (8.8 – 12.1)	21.6 (15.9 – 27.3)	**2.6 (1.7 – 4.0)**
HIV co-infection status (n=3,408)			
Negative	99.6 (99.3 – 99.9)	99.7 (99.1 – 100.0)	Reference
Positive	0.4 (0.1 – 0.7)	0.3 (0.0 – 0.9)	0.8 (0.1 – 6.5)
Missing (n=1,600)	1365	235	
Dyslipidemia Measures			
HDL (mg/dL) (n=4,889)			
Mean (95%CI)	52.8 (51.8 – 53.9)	51.7 (48.9 – 54.5)	-1.1 (-3.5, 1.2)
HDL levels[g]			
Normal	71.5 (68.0 – 75.0)	67.7 (61.1 – 74.4)	Reference
Lower	28.5 (25.0 – 32.0)	32.3 (25.6 – 38.9)	1.2 (1.0 – 1.5)
Missing (n=100)	90	10	1.6 (0.5 – 4.9)
LDL[h] (mg/dL) (n=2,236)			
Mean (95%CI)	114.8 (112.5 – 117.0)	113.1 (107.1 – 119.2)	-1.6 (-8.4, 5.1)
LDL levels			
Normal (<130 mg/dL)	68.5 (66.4 – 70.5)	73.1 (65.6 – 80.5)	Reference
Elevated (130 – 159 mg/dL)	21.9 (19.9 – 24.0)	17.1 (10.9 – 23.4)	0.7 (0.5 – 1.1)
High (≥160 mg/dL)	9.6 (7.6 – 11.7)	9.8 (4.4 – 15.2)	1.0 (0.5 – 1.9)
Missing (n=67)	66	1	0.1 (0.0 – 0.8)
Total Cholesterol (mg/dL) (n=4,889)			
Mean (95%CI)	194.2 (191.9 – 196.4)	196.8 (192.5 – 201.0)	2.6 (-1.3, 6.5)
Total cholesterol levels			
Low (≤130 mg/dL)	4.2 (3.4 – 5.1)	5.1 (2.1 – 8.1)	Reference
Normal (131 – 199 mg/dL)	53.8 (51.8 – 55.7)	51.7 (45.2 – 58.2)	0.8 (0.4 – 1.6)
Elevated (≥200 mg/dL)	42.0 (39.9 – 44.1)	43.2 (37.2 – 49.2)	0.9 (0.4 – 1.7)
Missing (n=100)	90	10	1.2 (0.4 – 3.9)
Triglyceride[h] (mg/dL) (n=2,276)			
Mean (95%CI)	129.6 (118.9 – 140.2)	123.4 (111.8 – 135.0)	-6.2 (-20.5, 8.1)

Characteristics	Weighted Prevalence, % (95%CI)		
	QFT Negative % (95% CI)	QFT Positive % (95% CI)	Odds Ratios* (95%CI)
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	
Triglyceride levels			
Optimal (<150 mg/dL)	74.9 (70.6- 79.1)	76.9 (68.7 (85.1)	Reference
Elevated (150 – 199 mg/dL)	13.5 (11.1 – 15.9)	13.1 (6.5 – 19.7)	0.9 (0.5 – 1.7)
High (≥200 mg/dL)	11.6 (8.0 – 15.3)	10.0 (5.8 – 14.1)	0.8 (0.5 – 1.4)
Missing (n=27)	27	0	NA
Any dyslipidemia[i&h] (n=2,277)			
No	36.5 (33.8 – 39.2)	39.0 (25.9 – 52.1)	Reference
Yes	63.5 (60.8 – 66.2)	71.0 (47.9 – 74.1)	0.9 (0.6 – 1.5)
Missing (n=26)	26	0	NA
Statin prescription[j] (n=2,770)			
No	70.8 (67.6 – 74.0)	68.5 (60.7 – 76.2)	Reference
Yes	29.2 (26.0 – 31.4)	31.5 (23.8 – 39.3)	1.1 (0.8 – 1.6)
Missing (n=2,238)	2058	180	0.9 (0.6 – 1.2)
CHD[k] (n=4,712)			
No	96.9 (95.9 – 97.9)	98.2 (97.0 – 99.3)	Reference
Yes	3.1 (2.1 – 4.1)	1.8 (0.7 – 3.0)	0.6 (0.3 – 1.1)
Missing (n=277)	270	7	0.4 (0.1 – 1.1)
Heart attack[l] (n=4,723)			
No	96.8 (96.1 – 97.5)	98.0 (97.0 – 98.9)	Reference
Yes	3.2 (2.5 – 3.9)	2.0 (1.1 – 3.0)	**0.6 (0.4 – 0.9)**
Missing (n=266)	261	5	0.3 (0.1 – 1.1)
Stroke[m] (n=4,725)			
No	97.3 (96.5 – 98.0)	95.5 (96.5 – 98.0)	Reference
Yes	2.7 (2.0 – 3.5)	4.5 (2.6 – 6.5)	**1.7 (1.0 – 2.9)**
Missing (n=264)	259	5	

Abbreviations:
BMI – body mass index; CHD – coronary heart disease; CI – confidence interval; HbA1c – glycated hemoglobin; HDL – high-density lipoprotein; HIV – human immunodeficiency virus; LDL – low-density lipoprotein; NHANES – National Health and Nutrition Examination Survey; QFT - QuantiFERON Gold-In-Tube;

*Crude odds ratio
†P-values from Rao-Scott Chi-square tests, unless indicated otherwise
‡P-values from t-tests
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Survey participants answered "No" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[c]Survey participants answered "Not at all" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[d]Survey participants answered "Every day" or "Some days" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[e]Survey participants answered "Yes" to the question "Was there ever time or times in (your/SP's) life when (you/he/she) drank 4 (for female) or 5 (for male) or more drinks of any kind of alcoholic beverage almost every day?"
[f]Diabetes was categorized according to HbA1c levels and self-reported previous type-2 diabetes mellitus diagnosis by health care providers
[g]HDL level was using gender-specific cut-offs: "normal" HDL was defined if HDL level was ≥40 mg/dL for male or ≥50 mg/dL for female; and "lower" HDL was defined if HDL level was <40 mg/dL for male or <50 mg/dL for female
[h]LDL and triglyceride measurements were done among a subset of survey participants who were fasting and appropriate weight variable (for those who were fasting) was applied accordingly
[i]Any dyslipidemia was defined as having either elevated LDL, total cholesterol, triglyceride, or lower HDL levels
[j]Taken statin in the past 30 days prior to survey date, survey participants were also asked to show medicine container to surveyor/enumerator

Characteristics	Weighted Prevalence, % (95%CI)		
	QFT Negative % (95% CI)	**QFT Positive % (95% CI)**	**Odds Ratios* (95%CI)**
	94.3 (93.3 – 95.3)	5.7 (4.7 – 6.7)	

[k]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had coronary heart disease?"
[l]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a heart attack (also called myocardial infarction)?"
[m]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a stroke?"

Bold indicates that the finding is statistically significant at α=0.05

Table S2. Weighted prevalence of and characteristics associated with hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	
QFT result				
Negative	51.7 (47.9 – 55.5)	48.3 (44.5 – 52.1)	Reference	**<0.001**
Positive	41.5 (35.5 – 47.6)	58.5 (52.4 – 64.5)	10.2 (5.0, 15.4)	
Age, years				
Mean (95%CI)	38.9 (37.3 – 40.6)	54.3 (52.8 – 55.7)	15.3 (14.0, 16.6)	**<0.001**
Age group				
Quartile 1 (18 – 31)	80.8 (78.6 – 83.1)	19.2 (16.9 – 21.4)	Reference	**<0.001**
Quartile 2 (32 – 47)	57.5 (52.3 – 62.7)	42.5 (37.3 – 47.7)	23.4 (18.6, 28.1)	
Quartile 3 (48 – 62)	38.0 (34.4 – 41.7)	62.0 (58.3 – 65.6)	42.8 (37.9, 47.7)	
Quartile 4 (>62)	23.0 (18.9 – 27.1)	77.0 (72.9 – 81.1)	57.8 (53.1, 62.5)	
18 – 49	57.1 (53.1 – 61.1)	42.9 (38.9 – 46.9)	Reference	**<0.001**
≥50	34.2 (30.2 – 38.3)	65.8 (61.7 – 69.8)	22.9 (17.6, 28.2)	
Sex				
Male	47.7 (43.2 – 52.2)	52.3 (47.8 – 56.8)	Reference	**0.001**
Female	54.4 (50.4 – 58.4)	45.6 (41.6 – 49.6)	-6.7 (-10.9, -2.5)	
Race				
Hispanic	61.3 (55.8 – 66.8)	38.7 (33.2 – 44.2)	Reference	**<0.001**
Non-Hispanic white	49.6 (44.7 – 54.4)	50.4 (45.6 – 55.3)	11.7 (5.3, 18.2)	
Non-Hispanic black	43.6 (39.9 – 47.4)	56.4 (52.6 – 60.1)	17.7 (11.8, 23.5)	
Other race	56.5 (51.5 – 61.5)	43.5 (38.5 – 48.5)	4.8 (-2.2, 11.7)	
Education (n=4,725)				
Less than 9th grade	39.0 (31.3 – 46.9)	61.0 (53.3 – 68.7)	Reference	**<0.001**
9-11th grade	42.3 (36.9 – 47.6)	57.7 (52.3 – 63.1)	-3.2 (-13.4, 6.9)	
High school graduate	45.5 (40.9 – 50.1)	54.5 (49.9 – 59.1)	-6.5 (-14.9, 2.0)	
Some college	51.7 (46.3 – 57.0)	48.3 (42.9 – 53.7)	-12.7 (-20.9, -4.5)	
College graduate or above	55.3 (48.9 – 61.5)	44.7 (38.4 – 51.1)	-16.2 (-25.5, -7.0)	
Missing (n=264)	86.7 (81.8 – 91.5)	13.3 (8.5 – 18.2)		
Ratio of family income to poverty (n=4,593)				
Mean (95%CI)	2.8 (2.6 – 3.1)	2.9 (2.7 – 3.1)	0.1 (-0.1, 0.3)	0.43
0 – 0.99	55.8 (49.1 – 62.5)	44.2 (37.5 – 50.9)	Reference	0.43
1 – 1.99	49.6 (43.3 – 55.9)	50.4 (44.1 – 56.7)	6.2 (-0.5, 12.9)	
2 – 2.99	49.4 (43.7 – 55.0)	50.6 (45.0 – 56.3)	6.4 (-2.4, 15.3)	
3 – 3.99	53.5 (48.6 – 58.4)	46.5 (41.6 – 51.4)	2.3 (-4.9, 9.5)	
4 – 4.99	47.6 (39.8 – 55.0)	52.4 (44.6 – 60.2)	8.2 (-2.7, 19.0)	
≥5	50.9 (43.0 – 58.7)	49.1 (41.3 – 57.0)	4.9 (-3.5, 13.4)	
Missing (n=396)	49.4 (39.9 – 58.8)	50.6 (41.2 – 60.1)		
Foreign born (n=5,019)				
No	49.2 (45.9 – 52.6)	50.8 (47.4 – 54.1)	Reference	**<0.001**
Yes	60.1 (54.7 – 65.5)	39.9 (34.5 – 45.3)	-10.8 (-14.5, -7.2)	
Missing (n=2)	70.6 (8.7 – 100.0)	29.4 (0 – 91.3)		
BMI, kg/m^2 (n=4,930)				
Mean (95%CI)	27.2 (26.7 – 27.8)	30.2 (29.7 – 30.8)	3.0 (2.4, 3.7)	**<0.001**
BMI categories				
Underweight (<18.5 kg/m^2)	68.6 (61.2 – 76.0)	31.4 (24.0 – 38.8)	-1.2 (-9.3, 6.9)	**<0.001**
Normal (18.5 – 24.9 kg/m^2)	67.4 (62.8 – 72.0)	32.6 (28.0 – 37.2)	Reference	
Overweight (25 – 29.9 kg/m^2)	49.8 (46.2 – 53.4)	50.2 (46.6 – 53.8)	17.6 (14.4, 20.9)	
Obese (≥30 kg/m^2)	38.0 (33.6 – 42.5)	62.0 (57.5 – 66.4)	29.4 (23.3, 35.5)	

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	
Missing (n=59)	26.1 (7.3 – 45.0)	73.9 (55.0 – 92.7)		
Smoking status (n=4,722)				
Never smokers[b]	54.4 (50.5 – 58.4)	45.6 (41.6 – 49.5)	Reference	**<0.001**
Past smokers[c]	37.2 (31.6 – 42.8)	62.8 (57.2 – 68.4)	17.3 (12.6, 21.9)	
Current smokers[d]	52.7 (48.4 – 57.1)	47.3 (42.9 – 51.6)	1.7 (-3.8, 7.1)	
Missing (n=267)	86.2 (81.0 – 91.4)	13.8 (8.6 – 19.0)		
Heavy alcohol drinking (n=3,891)				
No	41.1 (36.5 – 45.7)	58.9 (54.3 – 63.5)	Reference	**<0.001**
Yes[e]	52.4 (48.3 – 56.5)	47.6 (43.9 – 51.7)	-11.3 (-14.9, -7.7)	
Missing (n=1,122)	52.9 (47.6 – 58.2)	47.1 (41.8 – 52.4)		
HbA1c, %				
Mean (95%CI)	5.4 (5.4 – 5.5)	5.9 (5.8 – 5.9)	0.4 (0.4, 0.5)	**<0.001**
Diabetes categories[f]				
Normal	59.9 (55.8 – 64.0)	40.1 (36.0 – 44.2)	Reference	**<0.001**
Prediabetes	40.3 (37.1 – 43.5)	59.7 (56.5 – 62.9)	19.6 (15.8 – 23.4)	
Diabetes	19.1 (16.5 – 21.8)	80.9 (78.2 – 83.5)	40.8 (37.3 – 44.3)	
HIV co-infection status (n=3,389)				
Negative	60.7 (57.3 – 64.2)	39.3 (35.8 – 42.7)	Reference	0.22
Positive	78.4 (54.8 – 100.0)	21.6 (0 – 45.2)	-17.7 (-43.6, 8.3)	
Missing (n=1,600)	25.3 (21.7 – 28.9)	74.7 (71.1 – 78.3)		
Dyslipidemia Measures				
HDL (mg/dL) (n=4,889)				
Mean (95%CI)	53.2 (52.1 – 54.3)	52.3 (51.0 – 53.6)	-0.9 (-2.0, 0.1)	0.08
HDL levels[g]				
Normal	53.1 (48.9 – 57.3)	46.9 (42.7 – 51.1)	Reference	**<0.001**
Lower	47.1 (43.5 – 50.7)	52.9 (49.3 – 56.5)	6.0 (2.4, 9.6)	
Missing (n=100)	37.0 (25.2 – 48.7)	63.0 (51.3 – 74.8)		
LDL[h] (mg/dL) (n=2,236)				
Mean (95%CI)	113.2 (110.5 – 115.8)	116.4 (113.0 – 119.8)	3.2 (-1.1, 7.6)	0.13
LDL levels				
Normal (<130 mg/dL)	53.7 (48.5 – 58.8)	46.3 (41.2 – 51.5)	Reference	**0.014**
Elevated (130 – 159 mg/dL)	55.8 (48.7 – 62.9)	44.2 (37.1 – 51.3)	-2.1 (-11.3, 7.1)	
High (≥160 mg/dL)	38.7 (28.1 – 49.3)	61.3 (50.7 – 71.9)	15.0 (4.7, 25.3)	
Missing (n=67)	31.7 (19.9 – 43.5)	68.3 (56.5 – 80.1)		
Total Cholesterol (mg/dL) (n=4,889)				
Mean (95%CI)	190.3 (187.7 – 192.8)	198.6 (194.7 – 202.4)	8.3 (3.4, 13.2)	**0.001**
Total cholesterol levels				
Low (≤130 mg/dL)	50.7 (44.3 – 57.0)	49.3 (43.0 – 55.7)	Reference	**<0.001**
Normal (131 – 199 mg/dL)	55.3 (50.9 – 59.8)	44.7 (40.2 – 49.1)	-4.7 (-10.6, 1.3)	
Elevated (≥200 mg/dL)	46.4 (41.1 – 51.8)	53.6 (48.2 – 58.9)	4.2 (-3.3, 11.7)	
Missing (n=100)	37.0 (25.2 – 48.7)	63.0 (51.3 – 74.8)		
Triglyceride[h] (mg/dL) (n=2,276)				
Mean (95%CI)	111.5 (105.4 – 117.6)	148.8 (134.6 – 162.9)	37.3 (26.3, 48.2)	**<0.001**
Triglyceride levels				
Optimal (<150 mg/dL)	57.9 (54.2 – 61.6)	42.1 (38.4 – 45.8)	Reference	**<0.001**

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference* Percentage point (95%CI)	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)		
Elevated (150 – 199 mg/dL)	41.8 (34.1 – 49.5)	58.2 (50.5 – 65.9)	16.1 (9.8, 22.5)	
High (≥200 mg/dL)	28.7 (21.8 – 35.6)	71.3 (64.4 – 78.2)	29.2 (22.4, 36.1)	
Missing (n=27)	25.7 (6.7 – 44.8)	74.3 (55.2 – 93.3)		
Any dyslipidemia[i&h] (n=2,277)				
No	61.0 (56.7 – 65.4)	39.0 (34.6 – 43.3)	Reference	**<0.001**
Yes	47.4 (41.9 – 52.8)	52.6 (47.2 – 58.1)	13.7 (7.7, 19.6)	
Missing (n=26)	24.6 (6.0 – 43.2)	75.4 (56.8 – 94.0)		
Statin prescription[j] (n=2,770)				
No	44.8 (40.0 – 49.6)	55.2 (50.4 – 60.0)	Reference	
Yes	20.6 (16.0 – 25.2)	79.4 (74.8 – 84.0)	24.2 (17.6, 30.9)	**<0.001**
Missing (n=2,238)	69.8 (66.6 – 73.0)	30.2 (27.0 – 33.4)		
CHD[k] (n=4,712)				
No	50.9 (47.2 – 54.6)	49.1 (45.4 – 52.8)	Reference	**<0.001**
Yes	15.3 (5.9 – 24.8)	84.7 (75.2 – 94.1)	35.6 (25.0, 46.1)	
Missing (n=277)	85.6 (80.4 – 90.8)	14.4 (9.2 – 19.6)		
Heart attack[l] (n=4,723)				
No	50.8 (47.1 – 54.5)	49.2 (45.5 – 52.9)	Reference	**<0.001**
Yes	20.9 (11.6 – 30.2)	79.1 (69.8 – 88.4)	29.9 (18.5, 41.4)	
Missing (n=266)	86.1 (80.7 – 91.5)	13.9 (8.5 – 19.3)		
Stroke[m] (n=4,725)				
No	50.9 (47.3 – 54.4)	49.1 (45.6 – 52.7)	Reference	**<0.001**
Yes	15.6 (8.8 – 22.4)	84.4 (77.6 – 91.2)	35.3 (28.1, 42.5)	
Missing (n=264)	86.9 (82.1 – 91.6)	13.1 (8.4 – 17.9)		

Abbreviations:
BMI – body mass index; CI – confidence interval; HDL – high-density lipoprotein; LDL – low-density lipoprotein; NHANES – National Health and Nutrition Examination Survey; QFT - QuantiFERON Gold-In-Tube; TST – tuberculin skin test

*Mean/prevalence difference was calculated by setting those without TBI (i.e., QFT negative) as the referent group, unless indicated otherwise (with "reference" statement)
†P-values from Rao-Scott Chi-square tests, unless indicated otherwise
‡P-values from t-tests
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Survey participants answered "No" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[c]Survey participants answered "Not at all" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[d]Survey participants answered "Every day" or "Some days" to the question "(Do you/does SP) now smoke cigarettes?" and "Yes" to the question "(Have you/has SP) smoked at least 100 cigarettes in life?
[e]Survey participants answered "Yes" to the question "Was there ever time or times in (your/SP's) life when (you/he/she) drank 4 (for female) or 5 (for male) or more drinks of any kind of alcoholic beverage almost every day?"
[f]Diabetes was categorized according to HbA1c levels and self-reported previous type-2 diabetes mellitus diagnosis by health care providers
[g]HDL level was using gender-specific cut-offs: "normal" HDL was defined if HDL level was ≥40 mg/dL for male or ≥50 mg/dL for female; and "lower" HDL was defined if HDL level was <40 mg/dL for male or <50 mg/dL for female
[h]LDL and triglyceride measurements were done among a subset of survey participants who were fasting and appropriate weight variable (for those who were fasting) was applied accordingly
[i]Any dyslipidemia was defined as having either elevated LDL, total cholesterol, triglyceride, or lower HDL levels
[j]Taken statin in the past 30 days prior to survey date, survey participants were also asked to show medicine container to surveyor/enumerator
[k]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had coronary heart disease?"
[l]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a heart attack (also called myocardial infarction)?"

Characteristics	Weighted Prevalence, % (95%CI)			P-Values (X^2)†
	No Hypertension % (95% CI)	Any Hypertension[a] % (95% CI)	Mean/Prevalence Difference*	
	51.1 (47.4 – 54.8)	48.9% (45.2 – 52.6)	Percentage point (95%CI)	

[m]Survey participants answered "Yes" to the question "Has a doctor or other health professional ever told (you/SP) that (you/s/he) had a stroke?"

Bold indicates that the finding is statistically significant at α=0.05

Table S3. Weighted prevalence of various hypertension classifications by interferon gamma tuberculosis antigen responses among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence (95%CI)			Prevalence Difference (95%CI)		
	QFT Negative N=4510 94.3% (93.3 – 95.2)	QFT Positive Ag-NIL Values* Low (<4 IU/ml) N=299 4.0% (3.2 – 4.7)	QFT Positive Ag-NIL Values* High (≥4 IU/ml) N=190 1.7% (1.2 – 2.3)	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL
Primary study outcome						
Any hypertension indication[a]	48.3 (44.5, 52.1)	57.6 (48.7, 66.6)	60.4 (53.2, 67.7)	9.4 (1.6, 17.1)	12.1 (3.6, 20.5)	2.7 (-10.1, 15.5)
Measured blood pressure categories						
Normal blood pressure[b]	47.9 (44.6, 51.2)	35.6 (25.1, 46.1)	39.5 (29.3, 49.7)	-12.3 (-22.7, -1.9)	-8.4 (-18.1, 1.2)	3.8 (-9.7, 17.4)
Borderline hypertension[c]	17.6 (15.9, 19.3)	21.1 (14.2, 27.9)	17.7 (10.2, 25.1)	3.4 (-3.0, 9.9)	0.1 (-7.5, 7.6)	-3.4 (-13.9, 7.2
Hypertension[d]	34.5 (31.8, 37.2)	43.3 (34.0, 52.7)	42.8 (33.5, 52.1)	8.8 (-0.4, 18.1)	8.4 (-1.4, 18.2)	-0.5 (-14.6, 13.7)
Stage 1 hypertension[e]	24.2 (21.9, 26.5)	28.8 (18.9, 38.8)	33.2 (23.3, 414.1)	4.6 (-5.7, 14.9)	9.0(-2.7, 20.7)	4.4 (-10.2, 19.0)
Stage 2 hypertension[f]	10.3 (8.9, 11.7)	14.5 (10.3, 18.7)	9.6 (5.0, 14.2)	4.2 (-0.3, 8.7)	-0.6 (-5.2, 3.9)	-4.9 (-9.0, -0.7)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	30.3 (27.1, 33.6)	35.8 (28.3, 43.3)	44.2 (36.2, 52.2)	5.4 (-2.5, 13.4)	13.9 (5.0, 22.7)	8.4 (-4.7, 21.6)
Self-reported current use of anti-hypertension medication[h]	86.3 (82.7, 90.0)	95.0 (90.7, 98.9)	94.4 (87.7, 100.0)	8.5 (2.3, 14.6)	8.1 (-0.6, 16.8)	-0.6 (-7.8, 6.9)
Undiagnosed hypertension[i]	18.0 (15.8, 20.2)	21.9 (13.6, 30.3)	16.2 (12.1, 20.3)	3.9 (-4.8, 12.7)	-1.8 (-7.1, 3.4)	-5.8 (-12.7, 4.8)
Hypertension Control†						
Controlled hypertension without medications[j]	11.8 (9.5, 14.0)	3.5 (1.2, 5.7)	8.3 (0.0, 17.0)	-8.3 (-11.4, -5.2)	-3.5 (-12.8, 5.8)	4.8 (-4.7, 14.3)
Controlled hypertension with medications[k]	33.9 (28.8, 39.0)	36.6 (25.1, 48.2)	31.4 (17.9, 44.9)	2.9 (-10.4, 15.9)	-2.5 (-15.1, 10.2)	-5.2 (-22.5, 12.1)
Uncontrolled hypertension without medications[l]	15.2 (12.0, 18.5)	7.3 (2.6, 12.0)	21.2 (7.8, 34.7)	-8.0 (-13.6, -2.3)	6.1 (-8.3, 20.4)	14.0 (-0.9, 27.2)
Uncontrolled hypertension with medications[m]	39.1 (35.7, 42.6)	52.6 (40.8, 64.4)	39.0 (30.7, 47.3)	13.5 (-0.2, 27.1)	-0.1 (-9.5, 9.2)	-13.6 (-28.9, 1.7)

Abbreviations:
CI – confidence interval; IFN-γ - interferon gamma; QFT – QuantiFERON-TB Gold In-Tube

*Estimated by subtracting TB antigen value by TB Nil control value (LBXTBA - TBXTBN)
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,711)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S4. Crude and adjusted associations between interferon gamma tuberculosis antigen responses and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Stratification Variables	Prevalence Ratio (95%CI)					
	Unadjusted Estimates			Adjusted Estimates*		
	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL	Low Ag-NIL vs. QFT (-)	High Ag-NIL vs. QFT (-)	High vs. Low Ag-NIL
Primary study outcome						
Any hypertension indication[a]	**1.19 (1.04 – 1.36)**	**1.25 (1.08 – 1.45)**	1.05 (0.84 – 1.30)	0.99 (0.86 – 1.15)	1.04 (0.93 – 1.16)	1.05 (0.85 – 1.29)
Measured blood pressure categories						
Normal blood pressure[b]	**0.74 (0.56 – 0.99)**	0.82 (0.64 – 1.05)	1.11 (0.79 – 1.59)	0.89 (0.66 – 1.21)	0.99 (0.80 – 1.24)	1.12 (0.76 – 1.63)
Borderline hypertension[c]	1.20 (0.88 – 1.62)	1.00 (0.66 – 1.54)	0.84 (0.47 – 1.46)	1.12 (0.82 – 1.54)	0.94 (0.61 – 1.45)	0.84 (0.47 – 1.50)
Hypertension[d]	**1.26 (1.01 – 1.56)**	1.24 (0.98 – 1.57)	0.99 (0.71 – 1.37)	1.05 (0.84 – 1.32)	1.04 (0.87 – 1.24)	0.99 (0.72 – 1.34)
Stage 1 hypertension[e]	1.19 (0.83 – 1.77)	1.37 (0.96 – 1.97)	1.15 (0.75 – 1.85)	1.06 (0.73 – 1.55)	1.22 (0.89 – 1.66)	1.15 (0.72 – 1.82)
Stage 2 hypertension[f]	**1.41 (1.02 – 1.95)**	0.94 (0.59 – 1.50)	**0.67 (0.44 – 0.99)**	1.03 (0.74 – 1.44)	0.70 (0.40 – 1.23)	0.67 (0.43 – 1.05)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	1.18 (0.94 – 1.48)	**1.46 (1.17 – 1.81)**	1.24 (0.93 – 1.72)	0.93 (0.74 – 1.16)	1.16 (0.97 – 1.38)	1.25 (0.93 – 1.66)
Self-reported current use of anti-hypertension medication[h]	**1.10 (1.03 – 1.18)**	1.09 (0.99 – 1.20)	1.00 (0.91 – 1.08)	**1.07 (1.00 – 1.14)**	1.07 (0.98 – 1.17)	1.00 (0.92 – 1.09)
Undiagnosed hypertension[i]	1.22 (0.81 – 1.83)	0.90 (0.66 – 1.23)	0.74 (0.47 – 1.17)	1.12 (0.73 – 1.70)	0.82 (0.60 – 1.12)	0.73 (0.46 – 1.17)
Hypertension Control†						
Controlled hypertension without medications[j]	**0.30 (0.15 – 0.58)**	0.70 (0.23 – 2.12)	2.37 (0.62 – 9.12)	**0.53 (0.28 – 1.00)**	0.97 (0.39 – 2.39)	1.83 (0.62 – 5.38)
Controlled hypertension with medications[k]	1.08 (0.75 – 1.55)	0.93 (0.62 – 1.39)	0.86 (0.51 – 1.44)	1.01 (0.70 – 1.46)	0.89 (0.59 – 1.35)	0.88 (0.52 – 1.50)
Uncontrolled hypertension without medications[l]	**0.48 (0.24 – 0.94)**	1.40 (0.70 – 2.81)	**2.93 (1.34 – 6.40)**	0.61 (0.31 – 1.21)	1.56 (0.70 – 3.47)	**2.57 (1.14 – 5.76)**
Uncontrolled hypertension with medications[m]	**1.34 (1.02 – 1.77)**	1.00 (0.79 – 1.27)	0.74 (0.53 – 1.03)	1.22 (0.92 – 1.63)	0.98 (0.75 – 1.27)	0.80 (0.57 – 1.11)

Abbreviations:
CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube

*Models adjusted for age (continuous) and gender
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,711)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S5. The crude and adjusted prevalence odds ratios of any hypertension stratified by race, body mass index category, and foreign-born status, among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Stratification Variables	QFT Status	Unweighted frequency Hypertension*/Total	Weighted Prevalence of Hypertension* (95%CI)	Prevalence Difference (95%CI)	Prevalence Ratios		Statistical interaction p-values¶
					Crude cPR (95%CI)	Adjusted† aPR (95%CI)	
All cohort	Negative	2294/4510	48.3 (44.5 – 52.1)	Reference	Reference	Reference	NA
	Positive	286/479	58.5 (52.4 – 64.5)	10.2 (5.1, 15.4)	**1.21 (1.10 – 1.33)**	1.01 (0.92 – 1.10)	
***Stratified by age quartiles*‡**							
Quartile 1 (18 – 31)	Negative	253/1256	19.2 (16.9 – 21.5)	Reference	Reference	Reference	0.6316
	Positive	6/40	18.2 (0 – 37.5)	-1.0 (-20.7, 18.7)	0.95 (0.32 – 2.81)	0.81 (0.25 – 2.64)	
Quartile 2 (32 – 47)	Negative	512/1186	42.8 (37.8 – 47.8)	Reference	Reference	Reference	
	Positive	32/94	36.7 (20.0 – 52.4)	-6.1 (-24.6, 7.5)	0.86 (0.59 – 1.25)	0.87 (0.59 – 1.26)	
Quartile 3 (48 – 62)	Negative	678/1033	61.5 (58.0 – 65.0)	Reference	Reference	Reference	
	Positive	105/166	67.5 (55.0 – 80.1)	6.0 (-7.1, 18.0)	1.10 (0.92 – 1.31)	1.03 (0.88 – 1.21)	
Quartile 4 (>62)	Negative	851/1035	76.7 (72.3 – 81.1)	Reference	Reference	Reference	
	Positive	143/179	80.2 (72.9 – 87.5)	3.5 (-5.1, 12.1)	1.05 (0.94 – 1.17)	1.03 (0.91 – 1.17)	
Stratified by age group							
18 – 49	Negative	1568/3454	42.5 (38.5 – 46.4)	Reference	Reference	Reference	0.9998
	Positive	175/307	51.1 (43.4 – 58.9)	8.7 (2.4, 14.8)	**1.20 (1.07 – 1.36)**	0.95 (0.84 – 1.08)	
50+	Negative	726/1056	65.2 (61.2 – 69.2)	Reference	Reference	Reference	
	Positive	111/172	72.7 (61.4 – 84.0)	7.5 (-3.1, 18.1)	1.11 (0.96 – 1.29)	1.07 (0.93 – 1.24)	
Stratified by race							
Hispanic	Negative	374/864	36.9 (31.4 – 42.5)	Reference	Reference	Reference	0.1584
	Positive	67/158	51.2 (42.0 – 60.4)	14.3 (7.3, 21.3)	**1.39 (1.20 – 1.60)**	0.98 (0.86 – 1.11)	
Non-Hispanic White	Negative	947/1769	49.9 (45.0 – 54.8)	Reference	Reference	Reference	
	Positive	47/71	67.0 (55.3 – 78.7)	17.1 (5.7, 28.6)	**1.34 (1.12 – 1.60)**	1.08 (0.91 – 1.27)	
Non-Hispanic Black	Negative	711/1196	55.7 (51.8 – 59.7)	Reference	Reference	Reference	
	Positive	80/115	64.6 (52.0 – 77.2)	8.9 (-3.3, 21.6)	1.16 (0.95 – 1.42)	0.86 (0.71 – 1.05)	
Other Race/Ethnicity	Negative	262/681	42.7 (37.5 – 47.9)	Reference	Reference	Reference	
	Positive	68/135	48.4 (41.3 – 55.6)	5.7 (-1.1, 12.4)	1.13 (0.98 – 1.31)	0.88 (0.71 – 1.09)	
Stratified by body mass index category							
Underweight (BMI <18.5 kg/m^2)	Negative	28/96	29.9 (22.4 – 37.5)	Reference	Reference	Reference	0.1194
	Positive	7/11	50.9 (10.6 – 91.2)	21.0 (-20.5, 62.6)	1.70 (0.71 – 4.05)	0.71 (0.34 – 1.51)	
Normal (BMI 18.5 – 24.9 kg/m^2)	Negative	478/1367	31.5 (26.9 – 36.1)	Reference	Reference	Reference	
	Positive	75/149	49.2 (36.8 – 61.7)	17.7 (6.1, 29.2)	**1.56 (1.23 – 1.98)**	**1.24 (1.00 – 1.52)**	
Overweight (BMI 25 – 29.9 kg/m^2)	Negative	709/1400	49.7 (46.2 – 53.2)	Reference	Reference	Reference	
	Positive	96/160	59.3 (46.0 – 72.6)	9.6 (-2.4, 22.2)	1.19 (0.97 – 1.48)	0.98 (0.81 – 1.20)	
Obese (BMI ≥30 kg/m^2)	Negative	1040/1592	61.6 (57.2 – 66.1)	Reference	Reference	Reference	
	Positive	107/155	67.5 (57.9 – 77.1)	5.9 (-2.5, 14.3)	1.10 (0.97 – 1.24)	0.98 (0.89 – 1.08)	
Stratified by foreign born status							
US Born	Negative	1793/3341	50.2 (46.8 – 53.7)	Reference	Reference	Reference	0.1385

Stratification Variables	QFT Status	Unweighted frequency Hypertension*/Total	Weighted Prevalence of Hypertension* (95%CI)	Prevalence Difference (95%CI)	Prevalence Ratios Crude cPR (95%CI)	Prevalence Ratios Adjusted† aPR (95%CI)	Statistical interaction p-values¶
	Positive	120/172	65.6 (56.1 – 75.1)	15.4 (5.8, 25.0)	**1.31 (1.12 – 1.52)**	1.05 (0.92 – 1.21)	
Foreign Born	Negative	500/1167	37.7 (31.9 – 43.4)	Reference	Reference	Reference	
	Positive	166/307	51.3 (45.4 – 57.1)	13.6 (9.3, 17.9)	**1.36 (1.22 – 1.51)**	1.05 (0.92 – 1.21)	
Stratified by current smoking status							
No	Negative	627/954	61.8 (56.0 – 67.7)	Reference	Reference	Reference	0.0886
	Positive	95/130	76.2 (66.8 – 85.6)	14.4 (4.3, 24.5)	**1.23 (1.07 – 1.42)**	1.09 (0.93 – 1.27)	
Yes	Negative	439/851	47.2 (42.5 – 52.0)	Reference	Reference	Reference	
	Positive	56/101	47.5 (34.4 – 60.7)	-0.3 (-14.3, 14.9)	1.01 (0.74 – 1.37)	0.89 (0.69 – 1.14)	
Stratified by diabetes status							
Euglycemic	Negative	1083/2764	39.6 (35.4 – 43.8)	Reference	Reference	Reference	0.1235
	Positive	114/223	50.6 (42.6 – 58.5)	11.0 (3.1, 18.9)	**1.28 (1.08 – 1.51)**	1.01 (0.86 – 1.18)	
Pre-diabetes	Negative	689/1102	59.8 (56.6 – 63.0)	Reference	Reference	Reference	
	Positive	83/141	57.9 (44.2 – 71.6)	-1.9 (-15.6, 11.8)	0.97 (0.76 – 1.23)	0.95 (0.76 – 1.18)	
Diabetes	Negative	522/644	81.1 (78.3 – 83.9)	Reference	Reference	Reference	
	Positive	89/115	78.6 (68.7 – 88.5)	-2.5 (-13.0, 8.0)	0.97 (0.85 – 1.11)	0.94 (0.82 – 1.07)	
Stratified by HIV Status							
HIV negative	Negative	1226/3130	39.1 (35.5 – 42.6)	Reference	Reference	Reference	NA§
	Positive	102/243	43.2 (34.8 – 51.6)	4.1 (-4.3, 12.5)	NA§	NA§	
HIV positive	Negative	4/15	18.4 (0 – 39.0)	Reference	Reference	Reference	
	Positive	1/1	100.0 (100.0 – 100.0)	81.6 (61.0 – 100.0)	NA§	NA§	

aPR – adjusted prevalence ratio; CI – Confidence interval; PR – prevalence ratio; QFT – QuantiFERON-TB Gold In-Tube; US – United States

*Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
†Adjusted for age (continuous) and gender
‡Adjusted for gender
¶p-values for the cross-product terms included in the adjusted models
§Crude and adjusted stratum specific prevalence ratios were not reported due to the small unweighted sample size of the HIV positive group

Table S6. Weighted prevalence of various hypertension classifications by confirmed tuberculosis infection status among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Hypertension Measures	Weighted Prevalence (95%CI)				
	Confirmed TB Infection Status N=4,266				
	Confirmed		Discordant TST and QFT		
	Negative N=3706 92.2% (90.5 – 93.9)	Positive N=190 2.1% (1.4 – 2.8)	TST* – and QFT + N=177 2.5 (1.4 – 3.5)	TST + and QFT – N=193 3.2 (2.5 – 4.00)	Any Discordance N=370 5.7% (4.6 – 6.8)
Primary study outcome					
Any hypertension indication[a] (n=2,250/4,266)	49.6 (45.7 – 53.5)	60.8 (51.4 – 70.3)	50.5 (38.9 – 62.2)	54.4 (43.5 – 65.4)	52.7 (43.9 – 61.6)
Measured blood pressure categories					
Normal blood pressure[b] (n=1,914)	47.0 (42.9 – 51.1)	36.6 (27.6 – 45.5)	49.8 (40.9 – 58.7)	39.6 (26.1 – 53.0)	44.0 (35.2 – 52.9)
Borderline hypertension[c] (n=714)	17.8 (15.5 – 20.0)	15.3 (8.3 – 22.3)	16.3 (8.2 – 24.4)	25.1 (14.7 – 35.5)	21.3 (13.4 – 29.1)
Hypertensiond (n=1,638/4,266)	35.2 (32.3 – 38.1)	48.1 (38.7 – 57.6)	33.9 (25.4 – 42.4)	35.3 (26.9 – 43.7)	34.7 (28.3 – 41.1)
Stage 1 hypertension[e] (n=1121)	24.9 (22.5 – 27.3)	37.0 (28.8 – 45.4)	25.4 (16.7 – 34.1)	24.0 (12.6 – 35.4)	24.6 (16.3 – 32.9)
Stage 2 hypertension[f] (n=517)	10.3 (8.9 – 11.7)	11.1 (6.1 – 16.1)	8.5 (3.3 – 13.7)	11.3 (4.0 – 18.5)	10.1 (5.5 – 14.6)
Hypertension Diagnosis					
Previously diagnosed hypertension[g] (n=1,496/4,266)	30.9 (27.5 – 34.3)	35.8 (27.6 – 44.0)	29.4 (17.9 – 40.8)	37.1 (25.9 – 48.4)	33.8 (27.0 – 40.6)
Self-reported current use of anti-hypertension medication[h] (n=1,292/1,496)	86.0 (82.2 – 89.9)	90.2 (79.7 – 100.0)	81.5 (65.8 – 97.1)	98.6 (96.0 – 100.0)	92.5 (87.4 – 97.5)
Undiagnosed hypertension[i] (n=754/4,266)	18.7 (16.4 – 21.0)	25.2 (18.1 – 32.3)	21.4 (12.2 – 30.6)	17.3 (6.1 – 28.5)	19.1 (12.2 – 25.9)
Hypertension Control (n=1,496)					
Controlled hypertension without medications[j] (n=1,286)	11.8 (9.6, 13.9)	6.9 (0.0, 13.0)	13.5 (1.6, 25.4)	5.4 (1.0, 9.8)	8.4 (3.5, 13.3)
Controlled hypertension with medications[k] (n=79)	34.8 (29.2, 40.4)	28.9 (13.2, 44.6)	43.6 (20.8, 66.4)	46.1 (34.0, 58.2)	45.2 (35.4, 55.0)
Uncontrolled hypertension without medications[l] (n=51)	15.0 (11.5, 18.4)	17.2 (5.7, 28.7)	18.9 (6.1, 29.7)	5.4 (0.3, 10.5)	10.1 (5.5, 14.7)
Uncontrolled hypertension with medications[m] (n=80)	38.5 (34.7, 42.2)	47.0 (36.2, 57.8)	25.0 (12.3, 37.7)	43.1 (28.9, 57.3)	36.3 (26.4, 46.2)

Abbreviations:
CI – confidence interval; QFT – QuantiFERON-TB Gold In-Tube; TST – tuberculin skin test

*TST positive was defined as skin induration ≥5mm among HIV-positive individuals or >10mm among HIV negative (following NHANES analytical notes). Induration <5mm (for HIV-positive individuals) or ≤10mm (for HIV-negative individuals) was considered negative

[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"

[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels
[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S7. Crude and adjusted associations between confirmed tuberculosis infection status and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011 – 2012

Hypertension Measures	Measures of Association					
	Prevalence Difference (95%CI)		Prevalence Ratios (PR)			
			Crude PR (95%CI)		Adjusted* PR (95%CI)	
	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI	Confirmed TBI vs. non-TBI	Any Discordance vs. non-TBI
Primary study outcome						
Any hypertension indication[a]	11.3 (1.0, 21.5)	3.2 (-5.1 – 11.5)	**1.23 (1.03 – 1.46)**	1.06 (0.91 – 1.25)	1.08 (0.90 – 1.30)	0.98 (0.84 – 1.14)
Measured blood pressure categories						
Normal blood pressure[b]	-10.5 (-19.4, -1.6)	3.0 (-12.5, 6.4)	**0.78 (0.61 – 0.99)**	0.94 (0.76 – 1.16)	0.89 (0.69 – 1.15)	1.03 (0.84 – 1.26)
Borderline hypertension[c]	-2.4 (-9.5, 4.6)	3.5 (-4.1, 11.1)	0.86 (0.65 – 1.13)	1.20 (0.84 – 1.71)	0.82 (0.51 – 1.32)	1.15 (0.81 – 1.63)
Hypertension[d]	12.9 (2.8, 23.0)	-0.5 (-7.1, 6.1)	**1.37 (1.10 – 1.70)**	0.99 (0.82 – 1.19)	1.21 (0.98 – 1.49)	0.91 (0.75 – 1.10)
Stage 1 hypertension[e]	12.1 (2.8, 21.5)	-0.2 (-8.5, 8.0)	**1.49 (1.14 – 1.94)**	0.99 (0.71 – 1.38)	**1.37 (1.06 – 1.77)**	0.93 (0.66 – 1.32)
Stage 2 hypertension[f]	0.8 (-4.1, 5.7)	-0.3 (-5.2, 4.7)	1.08 (0.89 – 1.31)	0.98 (0.60 – 1.59)	0.88 (0.53 – 1.48)	0.86 (0.52 – 1.42)
Hypertension Diagnosis						
Previously diagnosed hypertension[g]	4.9 (-3.0, 12.7)	2.9 (-5.0, 10.7)	1.16 (0.93 – 1.44)	1.09 (0.86 – 1.38)	0.99 (0.77 – 1.28)	1.00 (0.81 – 1.23)
Self-reported current use of anti-hypertension medication[h]	4.2 (-8.1, 16.5)	6.4 (0.6, 12.3)	1.05 (0.91 – 1.20)	**1.07 (1.01 – 1.15)**	1.03 (0.91 – 1.18)	**1.08 (1.01 – 1.16)**
Undiagnosed hypertension[i]	6.5 (-0.3, 13.3)	0.4 (-6.9, 7.7)	**1.35 (1.03 – 1.77)**	1.02 (0.70 – 1.50)	1.26 (0.97 – 1.64)	0.96 (0.65 – 1.41)
Hypertension Control[†]						
Controlled hypertension without medications[j]	-4.9 (-14.2, 4.4)	-3.3 (-8.6, 2.0)	0.59 (0.19 – 1.80)	0.72 (0.39 – 1.32)	0.85 (0.27 – 2.70)	0.85 (0.48 – 1.53)
Controlled hypertension with medications[k]	-5.9 (-18.6, 6.8)	10.4 (-0.6, 21.4)	0.83 (0.54 – 1.28)	1.30 (1.00 – 1.69)	0.81 (0.53 – 1.22)	1.26 (0.97 – 1.65)
Uncontrolled hypertension without medications[l]	2.3 (-9.7, 14.2)	-4.9 (-10.3, 5.4)	1.15 (0.57 – 2.33)	0.68 (0.42 – 1.10)	1.32 (0.68 – 2.58)	0.70 (0.41 – 1.18)
Uncontrolled hypertension with medications[m]	8.5 (-3.4, 20.4)	-2.2 (-12.4, 8.1)	1.22 (0.94 – 1.58)	0.94 (0.71 – 1.25)	1.20 (0.91 – 1.58)	**1.27 (1.05 – 1.54)**

Abbreviations:
CI – confidence interval; PR – prevalence ratio; TBI – tuberculosis infection

*Models adjusted for age and gender
†Calculated among those with a previous diagnosis of hypertension by healthcare providers (n=1,496)
[a]Systolic ≥130mmHg and/or diastolic ≥80mmHg or any previous diagnosis of high blood pressure by health providers
[b]Systolic <120 mmHg and diastolic <80 mmHg
[c]Systolic 120-129 mmHg and diastolic <80 mmHg
[d]Including stage 1 and 2 hypertensions (i.e., Systolic ≥130mmHg or diastolic ≥80mmHg)
[e]Systolic 130-139 mmHg or diastolic 80-89 mmHg
[f]Systolic ≥140 mmHg or diastolic ≥90 mmHg
[g]Survey participants answered "yes" to the question "(Have you/has SP) ever been told by a doctor or other health professional that (you/s/he) had hypertension, also called high blood pressure?"
[h]Among those who answered "yes" to "Because of (your/SP's) (high blood pressure/hypertension), (have you, has s/he) ever been told to take prescribed medicine?", survey participants also answered "yes" to the question "(Are you/Is SP) now taking prescribed medicine (for high blood pressure/hypertension)?"
[i]Elevated blood pressure levels (Systolic ≥130mmHg or diastolic ≥80mmHg) with no prior diagnosis of hypertension by health care providers
[j]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg without a record of taking medications to lower blood pressure levels
[k]Having systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg with a record of taking medications to lower blood pressure levels

[l]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg without a record of taking medications to lower blood pressure levels
[m]Having systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg with a record of taking medications to lower blood pressure levels

Bold indicates that the finding is significant at α=0.05

Table S8. Sensitivity analysis to account for misclassification of covariates and different ways to handle age (confounder) included in the multivariable survey-weighted robust Poisson models to estimate the association between tuberculosis infection and hypertension among representative of civilian, non-institutionalized US adult population, NHANES 2011-2012

Models	Covariate(s) included in the model	QFT Result	Adjusted Prevalence Ratios	
			A (Age, continuous)	B (Age Group - Quartiles)
			aPR (95%CI)	aPR (95%CI)
Model 1	Age	Negative Positive	Reference 1.02 (0.93 – 1.13)	Reference 1.03 (0.93 – 1.14)
Model 2	Age, sex	Negative Positive	Reference 1.01 (0.92 – 1.10)	Reference 1.01 (0.91 – 1.13)
Model 3	Age, sex, BMI	Negative Positive	Reference 1.02 (0.92 – 1.13)	Reference 1.03 (0.93 – 1.15)
Model 4	Age, sex, income to poverty ratio	Negative Positive	Reference 1.00 (0.91 – 1.09)	Reference 1.01 (0.91 – 1.12)
Model 5	Age, sex, country of birth	Negative Positive	Reference 1.05 (0.96 – 1.14)	Reference 1.07 (0.97 – 1.19)
Model 6	Age, sex, income to poverty ratio, country of birth, BMI	Negative Positive	Reference 1.05 (0.95 – 1.17)	Reference 1.08 (0.97 – 1.21)
Model 7	Age, sex, income to poverty ratio, country of birth, BMI, current smoking status	Negative Positive	Reference 1.05 (0.93 – 1.17)	Reference 1.07 (0.93- 1.24)
Model 8	Age, sex, income to poverty ratio, country of birth, BMI, current smoking status, type-2 diabetes mellitus status, HIV status	Negative Positive	Reference 1.03 (0.99 – 1.08)	Reference 1.04 (0.99 – 1.08)
Model 9	Age, sex, income to poverty ratio, country of birth, BMI, type-2 diabetes mellitus status, HIV status	Negative Positive	Reference 1.04 (0.90 – 1.20)	Reference 1.05 (1.00 – 1.09)
Model 10*	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus, BMI, smoking	Negative Positive	Reference 1.01 (0.97 – 1.06)	Reference 1.04 (0.99 – 1.09)
Model 11	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, and stroke	Negative Positive	Reference 1.00 (0.96 – 1.05)	Reference 1.03 (0.98 – 1.08)
Model 12	Age, sex, race, education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, and stroke, BMI, smoking	Negative Positive	Reference 1.01 (0.96 – 1.05)	Reference 1.04 (0.99 – 1.08)
Model 13	Age, sex, race education attainment level, country of birth, type-2 diabetes mellitus status, self-reported previous diagnosis of coronary heart disease, heart attack, stroke, BMI, current smoking status, heavy alcohol consumption, any dyslipidemia, statin prescription, HIV status	Negative Positive	Reference 1.07 (0.97 – 1.18)	Reference 1.09 (1.00 – 1.18)

Table S9. Sample analytical codes

SAS MACRO PROGRAM
********** LTBI - HYPERTENSION MACRO STATEMENTS ********** **********; *Frequency Table; %MACRO SURVEYFREQF (data=, outcome=, select=, weight=); proc surveyfreq data=&data; cluster SDMVPSU; strata SDMVSTRA; tables &select*&outcome/nostd column row cl chisq; weight &weight; run; %MEND SURVEYFREQF; *Bivariate Association; %MACRO SURVEYFREQ (data=, exp=, outcome=, select=, weight=); proc surveyfreq data=&data; cluster SDMVPSU; strata SDMVSTRA; tables &select*&exp*&outcome/nostd column row cl chisq; weight &weight; run; %MEND SURVEYFREQ; *Risk Difference; %MACRO SURVEYFREQRD (data=, exp=, outcome=, select=, weight=); proc surveyfreq data=&data; cluster SDMVPSU; strata SDMVSTRA; tables &select*&exp*&outcome/nostd column row cl chisq risk; weight &weight; run; %MEND SURVEYFREQRD;

```
*------------------------------------------------*
| PART D : PROC SURVEYLOGISTIC |
*------------------------------------------------*
;

%MACRO SURVEYLOG (data=, exp=, outcome=, select=, weight=);
proc surveylogistic data=&data;
strata SDMVSTRA;
cluster SDMVPSU;
class &exp (ref="0")/param=ref;
model &outcome (event="1")=&exp;
weight &weight;
domain &select;
run;
%MEND SURVEYLOG;

%MACRO SURVEYLOGAD (data=, exp=, outcome=, select=, weight=);
proc surveylogistic data=&data;
strata SDMVSTRA;
cluster SDMVPSU;
class &exp (ref="0") age_group (ref="1") RIAGENDR (ref="2") cob9 (ref="1") bmicat99 (ref="1")/param=ref;
model &outcome (event="1")=&exp age_group RIAGENDR INDFMPIR cob9 bmicat99;
weight &weight;
domain &select;
run;
%MEND SURVEYLOGAD;

*Adjsuted for age and gender;
%MACRO SURVEYLOGAD2 (data=, exp=, outcome=, select=, weight=);
proc surveylogistic data=&data;
strata SDMVSTRA;
cluster SDMVPSU;
class &exp (ref="0") age_group (ref="1") RIAGENDR (ref="2")/param=ref;
model &outcome (event="1")=&exp age_group RIAGENDR;
weight &weight;
domain &select;
```

```
run;
%MEND SURVEYLOGAD2;

 *STRATIFICATION;
%MACRO SURVEYLOGSTR (data=, exp=, outcome=, select=, weight=, strat=);
proc surveylogistic data=&data;
strata SDMVSTRA;
cluster SDMVPSU;
class &exp (ref="0")/param=ref;
model &outcome (event="1")=&exp;
weight &weight;
domain &select*&strat;
run;
%MEND SURVEYLOGSTR;

*ADJUSTED STRATIFICATION;
%MACRO SURVEYLOGADSTR (data=, exp=, outcome=, select=, weight=, strat=);
proc surveylogistic data=&data;
strata SDMVSTRA;
cluster SDMVPSU;
class &exp (ref="0") RIAGENDR (ref="2") POVRATIO (ref="6") cob9 (ref="1")/param=ref;
model &outcome (event="1")=&exp RIDAGEYR RIAGENDR POVRATIO cob9;
weight &weight;
domain &select*&strat;
run;
%MEND SURVEYLOGADSTR;

*ADJUSTED STRATIFICATION WITHOUT COB;
%MACRO SURVEYLOGADSTR2 (data=, exp=, outcome=, select=, weight=, strat=);
proc surveylogistic data=&data;
strata SDMVSTRA;
cluster SDMVPSU;
class &exp (ref="0") RIAGENDR (ref="2")/param=ref;
model &outcome (event="1")=&exp RIDAGEYR RIAGENDR;
weight &weight;
domain &select*&strat;
```

```
run;
%MEND SURVEYLOGADSTR2;


*****************************************************************************************************;

*****NON-WEIGHTED ANALYSES***;
%MACRO LOGISTIC (data=, exp=, outcome=);
proc logistic data=&data;
class &exp (ref="0")/param=ref;
model &outcome (event="1")=&exp;
run;
%MEND LOGISTIC;

%MACRO ADJUSTED (data=, exp=, outcome=);
proc logistic data=&data;
class &exp (ref="0") age_group (ref="1") RIAGENDR (ref="2") POVRATIO (ref="6") cob9 (ref="1")/param=ref;
model &outcome (event="1")=&exp age_group RIAGENDR POVRATIO cob9;
run;
%MEND ADJUSTED;
option mprint;
```

R – Robust Poisson with quasi distribution

```
logit21 <- (svyglm(htn~factor(qft), family=quasipoisson(log), design=NHANES))
tidy(logit21, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit21old <- (svyglm(htn2~factor(qft), family=quasipoisson(log), design=NHANES))
tidy(logit21old, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit28 <- (svyglm(mhtn2~factor(qft), family=quasipoisson(log), design=NHANES))
tidy(logit28, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit26 <- (svyglm(htn4_2~factor(qft), family=quasipoisson(log), design=NHANES))
tidy(logit26, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit27 <- (svyglm(htn4_3~factor(qft), family=quasipoisson(log), design=NHANES))
```

```
tidy(logit27, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit215 <- (svyglm(htq~factor(qft), family=quasipoisson(log), design=NHANES))
tidy(logit215, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit217 <- (svyglm(on_htmeds~factor(qft), family=quasipoisson(log), design=NHANES))
tidy(logit217, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_21a <- (svyglm(htn~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                       factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
                     family=quasipoisson(log), design=NHANES))
summary(logit_21a, df=degf(NHANES))
tidy(logit_21a, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_21a_old <- (svyglm(htn2~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                       factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
                     family=quasipoisson(log), design=NHANES))
summary(logit_21a_old, df=degf(NHANES))
tidy(logit_21a_old, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_28a <- (svyglm(mhtn2~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                       factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
                     family=quasipoisson(log), design=NHANES))
summary(logit_28a, df=degf(NHANES))
tidy(logit_28a, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_26a <- (svyglm(htn4_2~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                       factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
                     family=quasipoisson(log), design=NHANES))
summary(logit_26a, df=degf(NHANES))
tidy(logit_26a, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_27a <- (svyglm(htn4_3~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                       factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
                     family=quasipoisson(log), design=NHANES))
summary(logit_27a, df=degf(NHANES))
```

```
tidy(logit_27a, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_215a <- (svyglm(htq~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                 factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
               family=quasipoisson(log), design=NHANES))
summary(logit_215a, df=degf(NHANES))
tidy(logit_215a, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)

logit_217a <- (svyglm(on_htmeds~factor(qft)+RIDAGEYR+factor(RIAGENDR)+factor(race5)+factor(edu9)+
                 factor(cob9)+factor(dmcat)+factor(bmicat9)+factor(csmk29),
               family=quasipoisson(log), design=NHANES))
summary(logit_217a, df=degf(NHANES))
tidy(logit_217a, conf.int = TRUE, conf.level = 0.95, exponentiate = TRUE)
```

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	Figure1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	22
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10

		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Table A1. PRICSSA document for the US National Health and Nutrition Examination Survey (NHANES) 2011 - 2012

Design: multistage, stratified cluster sample
Variance estimation: Taylor Series Linearization
Weight and design variables (primarily used in our manuscript)
Weight: WTMEC2YR
Cluster: SDMVPSU
Stratum: SDMVSTRA
Unweighted **total** sample size: 9,338 Unweighted total sample included in the primary analyses: 4,989
Weighted total sample size: 306,590,681 Weighted total sample included in the primary analyses: 210,906,894
Unweighted Response rate: 72.6% (Interviewed Sample), 69.5% (Examined Sample)
Location of example code: https://wwwn.cdc.gov/nchs/nhanes/tutorials/samplecode.aspx

Table A2. Itemized list of each PRICSSA item, a detailed description of each item, and where in manuscript each item could be found

PRICSSA item	Description	Page(s)/section in the manuscript
1.1 Data collection dates	Describe the survey's data collection dates (e.g., range) to provide historical context that could affect survey responses and nonresponse.	Methods (page 6)
1.2 Data collection mode(s)	Describe the survey's data collection mode(s). Data collection mode can affect survey responses (e.g., to sensitive questions), including nonresponse, and a survey's data collection mode may change over time (e.g., during the COVID-19 pandemic).	Methods (page 6)
1.3 Target population	State the target population the survey was designed to represent and describe all weighted estimates with respect to this target population.	Methods (page 6)
1.4 Sample design	Describe the survey's sample design, including information about stratification, cluster sampling, and unequal probabilities of selection.	Methods (page 6)
1.5 Survey response rate(s)	State the survey's response rate and how it was calculated.	Results (page 10)
2.1 Missingness rates	Report rates of missingness for variables of interest and models, and describe any methods (if any) for dealing with missing data (e.g., multiple imputation).	Results (Methods, pages 8 – 9 & Figure 1, page 23)
2.2 Observation deletion	State whether any observations were deleted from the dataset. If observations were deleted, provide a justification. Note: It is best practice to avoid deleting cases and use available subpopulation analysis commands no matter what variance estimation method is used.	Methods (page 9)
2.3 Sample sizes	Include unweighted sample sizes for all weighted estimates.	Results (Tables, pages 25, 27)
2.4 Confidence intervals/ standard errors	Include confidence intervals or standard errors when reporting all estimates to inform the reliability/precision of each estimate.	Results (pages 10 – 12, tables and figures pages 24 – 28)
2.5 Weighting	State which analyses were weighted and specify which weight variables were used in analysis.	Methods (Page 9)
2.6 Variance estimation	Describe the variance estimation method used in the analysis and specify which design variables (e.g., PSU/stratum, replicate weights) were used.	Methods (page 9)

2.7 Subpopulation analysis	Describe the procedures used for conducting subpopulation analyses (e.g., Stata's "subpop" command, SAS's "domain" command).	Methods (page 9)
2.8 Suppression rules	State whether or not a suppression rule was followed (e.g., minimum sample size or relative standard error).	N/A
2.9 Software and code	Report which statistical software was used, comprehensively describe data management and analysis in the manuscript, and provide all statistical software code.	Methods (page 7)
2.10 Singleton problem (as needed)	Taylor Series Linearization requires at least two PSUs per stratum for variance estimation. Sometimes an analysis is being performed and there is only a single PSU in a stratum. There are several possible fixes to this problem, which should be detailed if the singleton problem is encountered.	N/A
2.11 Public/restricted data (as needed)	If applicable, state whether the public use or restricted version of the dataset was analyzed.	N/A (This manuscript only used publicly available data)
2.12 Embedded experiments (as needed)	If applicable, provide information about split sample embedded experiments (e.g., mode of data collection or varying participant incentives) and detail whether experimental factors were accounted for in the analyses.	N/A