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High all-cause mortality and increasing proportion of older adults with tuberculosis in Texas, 2008—2020

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Abstract

Pulmonary tuberculosis (PTB) elimination efforts must consider the global growth of the aging population. Here we used TB surveillance data from Texas, United States (US; 2008 – 2020; total n=10,656) to identify unique characteristics and outcomes in older adults (OA, ≥65 y) with PTB, compared to young (YA, 18 to 39 y.) or middle-aged adults (MAA, 40 to 64 y). We found that the proportion of OA with PTB increased from 15% in 2008 to 24% in 2020 (trend $p < 0.05$). Diabetes was highly prevalent in OA (32%) but not associated with adverse outcomes. Death was 13-fold higher in OA compared to YA and was 7% at the time of diagnosis which suggests diagnostic delays. However, once TB was suspected, we found no differences in culture, smear, or nucleic acid detection of mycobacteria (although less lung cavitations) in OA. During treatment, OA had less drug resistant TB, few adverse reactions and adhered with TB treatment. We recommend training of healthcare workers to 'think TB' in older adults, for prompt treatment initiation to diminish deaths. Furthermore, older adults should be added as a priority group to the latent TB treatment guidelines by the World Health Organization, to prevent TB disease in this highly vulnerable group.

Keywords: tuberculosis, older adults, delays, cavitation, foreign, diabetes

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Introduction

Mycobacterium tuberculosis (*Mtb*) can cause latent tuberculosis infection (LTBI) in those infected but not sick, or active tuberculosis (TB) disease [1]. After two decades of a 2% annual decline in TB cases, in 2021 we still had an estimated 10.6 million cases and 1.6 million deaths [2]. The World Health Organization's (WHO) 'End TB Strategy' is aiming at reducing TB incidence by 80% and TB deaths by 90% by 2030, compared with 2015, but its goals will not be reached at the current pace [3]. TB elimination efforts must be reaccelerated by focusing on populations at higher risk of TB.

Older adults, i.e., those 65 years and older, is one such group that represents an increasing burden of TB and worse TB treatment outcomes [4; 5]. This age group has the highest prevalence of latent TB in the United States [6] and is prone to immune-suppressive conditions that predispose them to reactivation of latent TB or new TB infection [7]. Delayed diagnosis occurs more frequently in older adults due to fewer typical TB symptoms, TB diagnostic challenges, and existing conditions that mask TB disease [7-9]. We have also shown that the epidemiological profile of older adults is different from that of younger patients, with fewer social risk factors for TB that complicates their identification [10]. Older adults are also more likely to live in congregate settings, such as nursing homes, that increase their risk of TB transmission [4].

The global population aged 65 years and over is growing faster than other age groups [11], and for the first time in the United States, older adults are expected to outnumber children under the age of 18 by 2034 [12]. With the incidence of TB already shifting towards older people in many parts of the world [13; 14], more attention needs to be directed to TB in older adults. However, there are relatively few studies of TB in older adult populations and none, that we

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found, compared older adults to two younger adult age categories in a large study [15; 16]. To address this gap, we have begun to conduct prospective studies in older versus younger adults with TB in a Hispanic-predominant community on the US-Mexico border [10; 17-19]. We recently reported on a retrospective study with thousands of patients using TB surveillance data from Tamaulipas, Mexico where we found that older people diagnosed with TB had features of a less complicated TB, less drug resistance and better treatment adherence, and yet, were more likely to die of any cause during TB (AOR 3.9; 95%CI: 2.5, 5.3) [19]. Here, we conducted a similar retrospective study on the other side of the US-Mexico border to identify unique features of older adults with pulmonary TB (PTB) under a different health system. Namely, we sought to identify unique sociodemographics and clinical features of older PTB patients in a developed country like the United States, when compared to younger adults, and identify risk factors that predict adverse PTB outcomes in this age group. Our findings reveal an increasing proportion of older adults with PTB over the 13-year period of this study, and highlights the case for diagnostic delays in this age groups given the important proportion of deaths at the time of diagnosis, before treatment has begun.

Methods

Study Population

Analysis was performed using surveillance data created by the TB Elimination program from the Texas Department of State and Health Services (DSHS) between 2008 and 2020. There were 14,887 adult TB patients reported in the state of Texas. Patients with extrapulmonary TB (n=3,758) and previous TB (n=473) were excluded, leaving 10,656 pulmonary TB patients for

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data analysis. TB patients were grouped into three age categories: young adults (YA; age 18 to 39 years; n=3,876), middle-aged adults (MAA; age 40 to 64 years; n=4,759), and older adults (OA; age 65 years and older; n=2,021) (**Fig 1**).

TB Case Definitions

Confirmed TB cases met laboratory or clinical TB case criteria as defined by the Texas DSHS. Namely, laboratory diagnosis of TB included the isolation of *M. tuberculosis complex* by culture methods, its species identification using DNA probes or high-pressure liquid chromatography (HPLC), direct detection of *M. tuberculosis complex* from a clinical specimen by nucleic acid amplification tests (NAAT), or demonstration of acid-fast bacilli (AFB) when culture or NAAT results were not available. In the absence of laboratory confirmation, a clinical case of TB was met when patients had signs and symptoms compatible with active pulmonary TB disease, an abnormal chest radiograph or other chest imaging study, and a positive tuberculin skin test (TST) or interferon gamma release assay (IGRA; T.Spot-TB, Oxford Immunotec or QuantiFERON versions not specified, Qiagen) for *M. tuberculosis*, plus current treatment with two or more anti-TB medications and a complete diagnostic evaluation. A clinical TB case included provider-diagnosed TB cases who improve on at least two anti-TB medications and cases identified at death based on autopsy or medical examiner reports.

TB patient characteristics and treatment outcomes

Sociodemographics included age, sex, race or ethnicity, country of birth (United States, Mexico, or other), self-reported excess alcohol use, drug use [i.e., intravenous (IV) or non-IV], or being homeless in the past year. Residency in a correctional facility or long-term care facility

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was documented at the time of diagnosis. Comorbidities included diabetes (self-reported or laboratory confirmed, but distinction not provided) and laboratory-confirmed human immunodeficiency virus (HIV) infection. TB characteristics at the time of diagnosis included the patient's vital status (alive or dead) and abnormal chest x-ray results (including presence of cavitations). Laboratory findings at diagnosis included results for AFB smears, *Mtb* cultures, NAAT, TST and/or IGRA. Drug resistance (DR) was available for first line drugs except ethambutol, i.e., isoniazid (INH), rifampin (RIF) and pyrazinamide (PZA), and 2nd line drugs when resistance was detected to first-line drugs. DR patterns included mono-resistance, multi-drug resistance (MDR; resistance to at least INH and RIF), pre-extensively drug resistance [Pre-XDR; resistance to INH, RIF and a fluoroquinolone, or resistant to INH, RIF and a second-line injectable (amikacin, capreomycin and kanamycin)]. Extensively drug resistant TB (XDR-TB) was defined as resistance to INH, RIF, a fluoroquinolone and a second-line injectable, or resistant to INH, RIF, a fluoroquinolone, and bedaquiline or linezolid [20]. Additional DR patterns not categorized above were reported as 'other drug resistance'. Patients were grouped into one of five PTB outcomes: Treatment completion, non-adherent to treatment either due to refusal to take treatment or lost to follow-up, treatment interruption due to an adverse event, moved/unknown, and death of any cause at the time of diagnosis or during TB treatment.

Statistical Analyses

Pearson's chi-square test was used to compare categorical variables. Variables in bivariable analysis with P values < 0.20 were included as predictors in multivariable logistic regression with backward selection models, while retaining age and sex as key sociodemographics in final models. Abnormal chest x-ray was excluded from the multivariable

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analysis due to collinearity with cavitary disease. The following variables had a higher % of missingness and imputed with null entries: resident of a correctional facility (55.8%), diabetes (60.9%), and HIV (11.7%), given presumption that surveillance workers did not enter these data uniformly when patients did not have these characteristics. Results from imputed variables were in line with TB surveillance reports from Texas [21]. NAAT data was available for 48% of participants, so test results were only analyzed for years 2018-2020 with data for 85% of the patients. About 59% of TST and IGRA results were missing and were deemed as non-random missing. Thus, these two results were not analyzed. Age was evaluated as an effect modifier (EM) of the associations between each predictor variable and TB outcomes (i.e., non-adherent or death of any cause) in simple logistic regression models. Significant interaction terms with P values < 0.05 were included in full multivariable models. Trends across age groups and across the study period, 2008 – 2020, were established by the score test for the trend of odds for categorical variables or the nonparametric test for trends across ordered groups, an extension of the Wilcoxon rank-sum test, for polytomous variables. Statistical significance was set at type I error (alpha) level < 0.05 for all tests. Data analysis was performed using STATA IC v.14 (Stata Corp LLC, College Station, TX).

Results

Characteristics of OA at the time of TB diagnosis

Between 2008 and 2020 a total of 14,887 TB cases were reported to the Texas DSHS. We selected those with new episodes of PTB (n=10,656; 75%) for data analysis (**Fig 1**). The final dataset consisted of 3,876 YA, 4,759 MAA and 2,021 OA. **Table 1** shows the characteristics of

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all adults, indicates significant differences between OA and the younger age groups, and shows p values for trends with increasing age. **Figure 2** illustrates characteristics with significant trends across increasing age groups. Two-thirds of the patients were males, and this sex distribution did not change with older age. For race and ethnicity, the Hispanics comprised more than 50% across all age groups, but there was a decrease in non-Hispanic blacks from 19% in YA to 9.8% in OA, and an increase in non-Hispanic whites from 7.1% in YA to 16.1% in OA (**Fig 2A**). More than 50% of all adults were born outside of the United States, with a shift as age increased towards more Mexicans (24% in YA to 36% in OA) and fewer from other countries (44% in YA to 26% in OA; P trend <.001; **Fig 2B**). The OA group had the lowest proportions, as well as significant reductions, with older age in the following TB risk factors: excess alcohol use (10%), drug use (3%), homelessness (3%), and residence in a correctional facility (2%; **Fig 2C** for selected features). Residence in a long-term care facility increased with age (P for trend <.001; **Fig 2C**). For comorbidities, diabetes increased with age (32%; P trend <.001), while HIV decreased (0.7%; P trend <.001; **Fig 2D**). For TB-related characteristics at the time of TB diagnosis (**Fig 2E**), death from any cause was the highest in OA (7%; P trend <.001). Although the proportion of abnormal chest x-rays was similar across age groups, detection of cavities decreased with age (P trend <.001). Detection of *Mtb* with AFB, cultures or NAAT was essentially similar across age groups. The use of NAAT increased over the study period (described below), with data between 2018-2020 suggested lower use in older adults (from 86.6% in YA to 81.6% in OA). For TB outcomes, treatment completion decreased with age while deaths at diagnosis or during treatment increased with older age and was the main contributor to treatment interruption with increasing age (P trend <.001; **Fig 2F**). Whereas

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treatment outcomes were more detrimental in males among YA, there were no significant differences by sex among the OA group (**Table S1**).

Resistance to TB Drugs

Susceptibility testing results were available for 81% of all patients (**Table 2**). Resistance to any TB drug decreased with age (P trend = .008). There were no trends across age groups for mono-resistance to INH, RIF, PZA, or other drugs, but there was a decreasing trend in MDR-TB (P trend <.001), pre-XDR TB (P trend = .018), and XDR TB (P trend = .048) with older age.

Age as a Predictor of Adverse Outcomes

Among TB patients who did not die, nonadherence to TB treatment (refused or lost to follow-up) was less likely in OA compared to YA, although statistical significance was not reached (aOR 0.69, 95% CI 0.45, 1.05; **Table 3**). Instead, predictors of nonadherence to treatment in all age groups included male sex (aOR 1.70, 95% CI 1.23, 2.29), consuming excess alcohol (aOR 1.36, 95% CI 1.04, 1.78), being homeless (aOR 2.84, 95% CI 1.99, 4.06), residence in a correctional facility (aOR 4.45, 95% CI 3.42, 5.78) and being HIV positive (aOR 1.58, 95% CI 1.05, 2.37). Death at the time of diagnosis or during treatment, increased with old age and was 13.4 times higher for OA (aOR 13.44, 95% CI 10.12, 17.84) when compared to YA. Additionally, among all age groups, male sex (aOR 1.22, 95% CI 1.03, 1.45), residing in a long-term care facility (aOR 2.71, 95% CI 1.75, 4.19), and testing positive for HIV (aOR 2.40, 95% CI 1.78, 3.24) were associated with increased odds of death. Predictors protective against all-cause death included birth in Mexico (aOR 0.64, 95% CI 0.53, 0.77) or another foreign country (aOR 0.44, 95% CI 0.35, 0.54), when compared to the United States, residing in a correctional

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facility (aOR 0.24, 95% CI 0.14, 0.40), and having chest x-ray cavities (aOR 0.81, 95% CI 0.69, 0.96).

Among the OA group (**Table S2**), homelessness was the only independent predictor of nonadherence to TB treatment (aOR 13.02, 95% CI 4.94, 34.33). The odds of death increased by 6% for each one-year increase in age and 131% for those with a positive *Mtb* culture (95% CI 1.55, 3.44). Birth in Mexico (aOR 0.74, 95% CI 0.56, 0.99) or another foreign country (aOR 0.48, 95% CI 0.33, 0.68) was protective for death when compared to OA born in the United States.

Age as an Effect Modifier

We evaluated if a TB patient's age would modify the association between different predictor variables and adverse TB treatment outcomes. In bivariate analysis, age was an effect modifier (EM) of the association between the adverse outcome, non-adherent, and the respective predictors: male sex (P value = .026) and born in Mexico (P value = .012), (**Table S3**). These two EM variables were included in the full regression model for non-adherent, but were not significantly associated with treatment nonadherence and subsequently removed from the final model. Age did not modify the association between any of the host characteristics and death from any cause, as an outcome.

Secular Trends Over the Study Period Among the OA group

We evaluated if there were changes in the prevalence and characteristics of OA with PTB over the study period, and how these may differ from changes in the YA or MAA groups. **Table 4** shows trends for all age groups and **Table S4** for the OA group. **Figure 3** illustrates significant

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findings for OA group: An increase in their proportion from 15% in 2008 to 24% in 2020 (**Fig 3A**); A lower proportion of non-Hispanic whites and higher individuals of other races/ethnicities (**Fig 3B**); Fewer US-born and more foreign-born from countries other than Mexico (**Fig 3C**); More non-injecting drug use and diabetes (**Fig 3D**); Less with abnormal chest x-rays and more with positive smears or cultures (**Table S4**). The use of NAAT for *Mtb* detection increased over the study period, with more than 80% coverage in 2018-2020, and hence, these results were used for data analysis (**Table 1; Fig 3E for OA**). There was increased use of IGRAs and reduction in TSTs over the study period in OA group (**Fig 3F**). There were no significant secular trends in the proportion of patients reported as dead at TB diagnosis or in treatment outcomes.

Discussion

The proportion of older adults diagnosed with PTB in the state of Texas increased significantly over the 13-year study period: from 15% in 2008 to 24% in 2020. Despite having more than 13-fold odds of death from any cause when compared to YA, older adults had fewer social risks for TB, e.g., less excess alcohol use, drug use, homelessness, HIV infection, and residence in a correctional facility. Diabetes occurred in more than one-third of older adults but was not associated with adverse TB outcomes. This result is similar to our previous findings across all ages in Mexico [19; 22; 23], but contrasts with studies in adults where diabetes is a predictor of death [24]. While death during TB is known to be more prevalent in older adults [25], a striking finding in our study was its 13-fold magnitude when compared to YA, as well as its reporting prior to TB diagnosis in nearly 7% of the cases, before TB treatment could be considered. Together, these findings indicate a smoldering challenge for TB control in Texas, and likely globally.

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The high proportion of deaths at the time of TB diagnosis suggests delays in TB suspicion in OA, as shown for more than two decades [26]. There are several possible explanations for failure to consider TB in the differential diagnosis of older adults. **First**, it has been suggested that older patients may have fewer "classical" symptoms of TB [7; 26]. Our Texas dataset did not provide information on symptoms, but our prospective study in patients from the same Texas-Mexico region revealed that older adults with TB were less likely to present with fever or chills (58% in OA vs 81% in younger patients)[10]. **Second**, diagnostic delays may be due to lack of TB suspicion given the lower prevalence of known social risk factors for TB, as listed above, and as reported earlier [10; 19]. **Third**, even though abnormal chest x-rays were reported in over 95% of the TB patients, failure to consider TB in the differential diagnosis could be explained by the lower prevalence of cavitations in the OA group, which is a feature of active TB. The lower prevalence of cavitary TB in OA had also been reported previously [7; 27; 28], and may seem advantageous to the host because cavities hold a very large number of bacteria and are associated with poor treatment outcomes, prolonged culture conversion and higher Mtb transmission [29]. Cavities arise upon central necrosis of some lung granulomas, which are tissue nodules formed by the immune system to contain *Mtb* [30]. We posit that the lower prevalence of cavitary TB in older adults reflects a declining immune response.

Age-related trends in race, ethnicity and country of birth can guide physicians to consider TB in the differential diagnosis of older adults. In Texas, OA were predominantly Hispanic with most born in the US and closely followed by birth in Mexico. The reduced proportion of non-Hispanic blacks among older adults may suggest death at a younger age in this race/ethnic group – this deserves further study. Regarding place of birth, the largest proportion of OA (39%) were

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born in the U.S., but over the study period, there was an increase in OA born in countries other than the U.S. or Mexico. A total of 124 countries of birth were represented in our study, including eight classified as high TB burden [2]. The shift from PTB patients born in the U.S. to other countries support the anticipated quadrupling of older immigrants in the U.S. by 2050 [31]. These changing demographics in Texas must be taken into consideration by TB elimination programs.

Once TB is considered among the differential diagnosis, the sensitivity of smears, cultures and NAATs was similar across age groups. The use of support methods for TB diagnosis shifted over the 12-year period, with increase in NAATs and IGRAs, and reduced TST. Between 2015 and 2020, more than half of OA patients had a NAAT test performed in Texas as part of their diagnostic workup, which is higher than the 2021 global average of 38% [32]. However, NAAT use was less prevalent in OA patients, and contrast with the WHO recommendation to promptly use rapid molecular test for quicker TB diagnosis in high-risk patients, such as older adults [32]. The TST has poor sensitivity in older adults due to immune defect in skin dendritic cells [33], while IGRAs are suitable for detection of LTBI in OA [17]. Hence, the availability and overall performance of diagnostic tools for detection of Mtb infection or disease in older adults should not be a limitation for prompt TB diagnosis in Texas.

Treatment adherence is very high in Texas across all age groups given the strict enforcement of the Directly observed therapy (DOT) as the standard of care for TB [34], a contrast with the 7% abandon treatment and 2% treatment failure reported in the adjacent Mexican border [19]. In Texas, the trend for lower treatment completion with older age was due to the high prevalence of deaths at diagnosis or during treatment, but not to lack of adherence to treatment. On the adjacent Mexican border, older adults adhered to TB treatment [19]. There

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were few adverse reactions in any age group, including OA, suggesting that TB treatment was well tolerated in this age group in our study population. However, this is not always the case. For example, in a meta-analysis the odds of hepatoxicity in OA increased by 32% for the treatment of active TB, and by 414% for latent TB infection [35]. The authors recommended gentler treatment regimens for older adults to minimize risks. We cannot rule out that the higher odds of death in OA in our study could attributed in part to anti-TB treatment toxicity.

Despite treatment adherence, the odds of death were still higher in the OA group. Interestingly, in multivariable analysis of all age groups, foreign-born patients were less likely to die of any cause, suggesting an immigrant paradox [36]. We posit that non-US born TB patients are more likely to have had a previous exposure to Mtb that confers immunity that tapers TB severity [37; 38].

Strengths of this study include the large sample size that allowed adequate power to compare older adults to young and middle-aged adults, and a span of 13 years to identify changes in the epidemiology of older adults with TB in Texas. Limitations included the collection of data for TB surveillance with some information missing. Missing entries were imputed with null entries for resident of a correctional facility, diabetes, and HIV, which may underestimate the association of these risk factors with our outcome measures. Nevertheless, after imputation, the prevalence rates of these risk factors in our study were similar to those reported by the Texas DSHS TB program [39]. In contrast, imputation was not assumed to be valid for NAAT, TST, and IGRA testing given the not-at-random testing practices and changes in the frequency of their use over the study period. Hence, results from these tests were excluded from analyses. The surveillance dataset had limited information on the presence and duration of TB symptoms, to ascertain diagnostic delays or differential clinical presentation that could

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contribute to this problem. Finally, we cannot ascertain the relative contribution of TB versus other comorbidities to death, although this is a general limitation of studies on TB or in older adults [25].

Together, our findings provide a foundation for recommendations. **First**, there is a need to educate physicians and public health workers to "think TB" for prompt detection of the disease in older adults. Once TB is considered in the differential diagnosis, *Mtb* detection is not compromised by old age, although less cavitary TB must be taken into consideration. Our s**econd** recommendation is to accelerate TB diagnosis- this could be lifesaving in older adults. Clinicians should consider the WHO recommendation for simultaneous use of rapid molecular diagnostic tests and chest x-ray, rather than ordering molecular tests only after AFB smears are negative [40]. Once a TB diagnosis is established, TB treatment can begin. We found that older adults were less likely to have DR-TB in Texas, and our results were similar across the Mexican border [19]. We also found that once treatment is initiated, older adults in Texas and in Mexico are generally compliant, and few have adverse drug side effects. While higher deaths during TB treatment may be inevitable for older adults given their higher fragility and multi-morbidities, we posit that this adverse event could be reduced by prompt diagnosis. Finally, we recommend the prioritization of older adults in TB prevention efforts. Older adults are listed in the 2018 global targets for preventive TB treatment by the WHO, but not included among the high risk groups for TB [2]. We propose their addition to the WHO's TB infection management guidelines priority group for latent TB testing and preventative treatment [41]. This is feasible given that IGRA testing (but not TST) is suitable to identify TB infection in older adult patients [17].

In summary, the growing proportion of older adults with TB in Texas is likely to have international relevance, given the global growth of older adult populations. The challenges we

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describe today for TB in older adults, e.g. delayed diagnosis, high death rates, have been noted for decades [42; 43]. Thus, the older adult population requires attention given their higher risk of TB infection, latent TB reactivation, and death during TB.

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Data availability statement. The datasets generated during and/or analyzed during the current study are available from the corresponding author in agreement with the Texas Department of State and Health Services on reasonable request and with approval from corresponding Internal Review Boards.

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Author contribution.

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Writing – Original draft: Belinda A. Medrano

Writing – review & editing: Belinda A. Medrano, Miryoung Lee, Gretchen Gemeinhardt, Blanca I. Restrepo, Lana Yamba

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363 official views of the National Institutes of Health.
364
365 **Competing Interest.** The Authors declare none.
366
367 **Ethical standard.** Patient data was deidentified and the protocol was approved by the Internal
368 Review Boards from UTHealth Houston (HSC-SPH-15-0489) and Texas Department of State
369 and Health Services (protocol 20-030).
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Figure legends

Figure 1. Flow chart of the study subject selection process. Patients with any extrapulmonary involvement (n=3,758) or previous TB (n=473), were excluded for a final sample size of 10,656. Pulmonary TB patients were divided into young adults (YA), middle-aged adults (MAA), and older adults (OA) for data analysis.

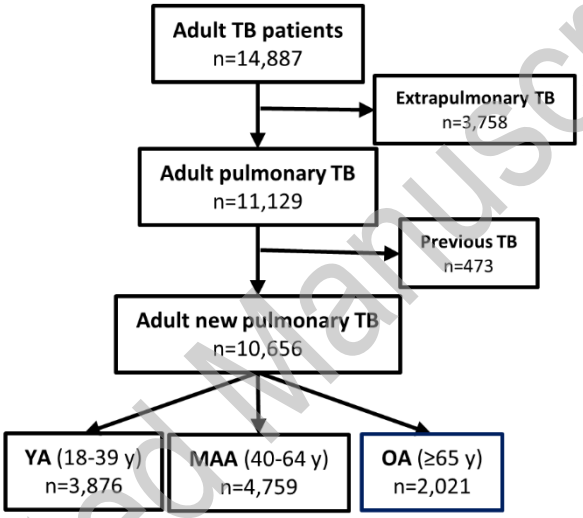

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Figure 2. Significant trends with increasing age in characteristics of PTB patients. ↑ or ↓, increasing (↑) or decreasing (↓) trends across the YA, MAA and OA age groups with trend $p < 0.05$. Correctional, resident of a correctional facility; H, Hispanic; LT care, resident of long-term care facility; MAA, middle-aged adults; OA, older adults; Rx, TB treatment; YA, young adults; US, United States.

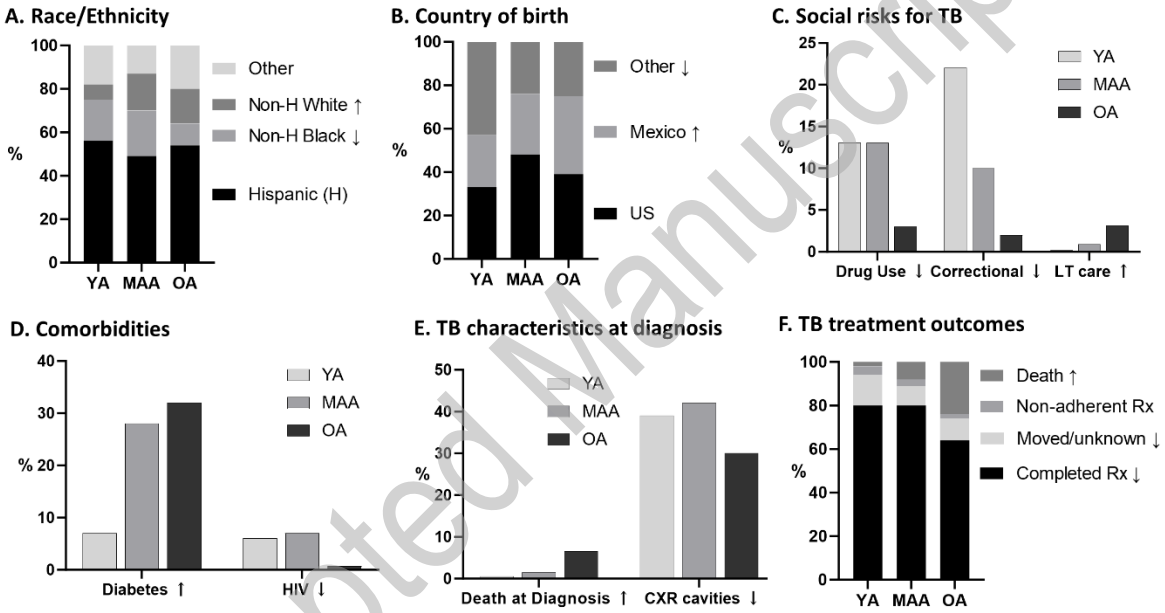

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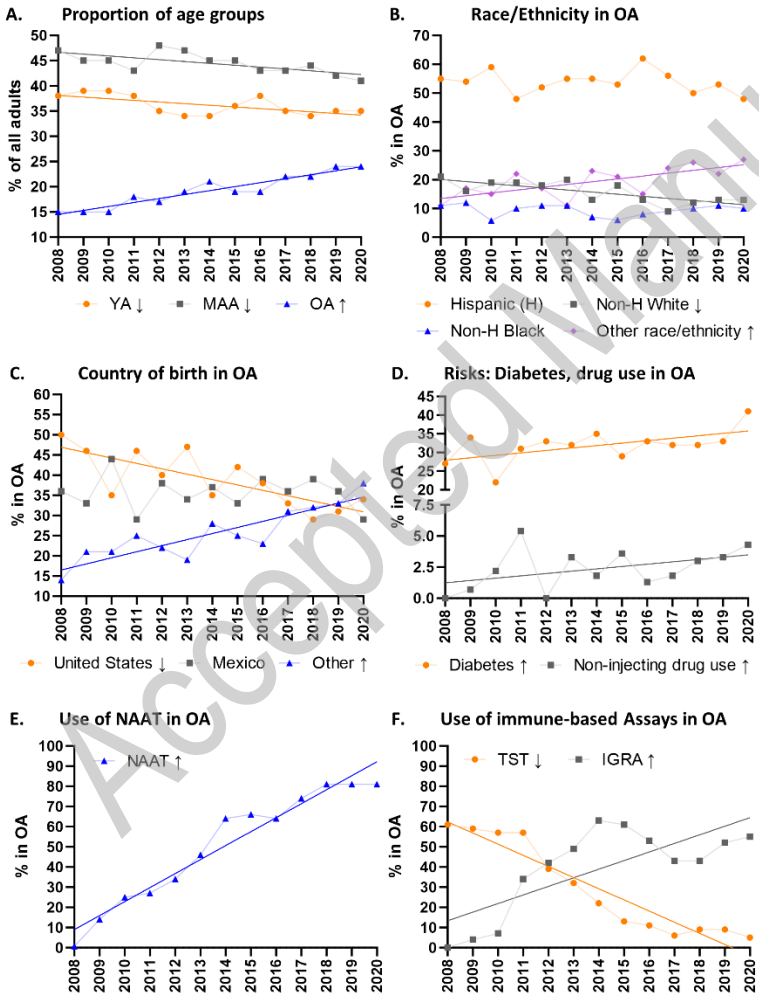
Figure 3. Significant trends between 2008 and 2020 in the proportion of age groups, the characteristics of older adults and methods used to support their TB diagnosis. Significant increasing (↑) or decreasing (↓) trends across age groups. Regression lines are shown for variables with significant trends. H, Hispanic; IGRA, IFN-gamma release assays; NAAT, nucleic acid amplification tests; MAA, middle-age adults; Older adults (OA); TST, tuberculin skin test; YA, young adults.



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536 **Table 1.** Characteristics of Pulmonary TB patients by age group, Texas 2008 – 2020

	All Adults (≥ 18 y)	YA (18 -- 39 y)	MAA (40 -- 64 y)	OA (≥65 y)	OA *vs* YA p-value[a]	OA *vs* MAA p-value[a]	Age trend p-value [b, c]
Total n (row %)	10,656	3,876 (36.4)	4,759 (44.7)	2,021 (19.0)			
Sociodemographics							
Age (mean, SD)	48 (18)	29 (6)	52 (7)	75 (7)			
Male	7,224 (67.8)	2,456 (63.4)	3,450 (72.5)	1,318 (65.2)	0.164	**<0.001**	↑ **0.001**
Race/Ethnicity							
Hispanic	5,568 (52.3)	2,162 (55.8)	2,309 (48.5)	1,097 (54.3)	**<0.001**	**<0.001**	↓ **<0.001**
Non-Hispanic Black	1,919 (18.0)	737 (19.0)	984 (20.7)	198 (9.8)			
Non-Hispanic White	1,389 (13.0)	276 (7.1)	788 (16.6)	325 (16.1)			
Other	1,780 (16.7)	701 (18.1)	678 (14.2)	401 (19.8)			
Country of Birth							
United States	4,305 (40.4)	1,262 (32.6)	2,261 (47.5)	782 (38.7)	**<0.001**	**<0.001**	↓ **<0.001**
Mexico	2,996 (28.1)	922 (23.8)	1,353 (28.4)	721 (35.7)			
Other	3,355 (31.5)	1,692 (43.7)	1,145 (24.1)	518 (25.6)			

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Risk Factors for TB							
Excess Alcohol Use	1,930 (18.1)	506 (13.1)	1,225 (25.7)	199 (9.9)	**<0.001**	**<0.001**	0.314
Drug Use	1,176 (11.0)	489 (12.6)	636 (13.4)	51 (2.5)	**<0.001**	**<0.001**	**↓ <0.001**
Homeless	568 (5.3)	111 (2.9)	406 (8.5)	51 (2.5)	0.448	**<0.001**	**↑ 0.021**
Correctional Facility	1,341 (12.6)	846 (21.8)	465 (9.8)	30 (1.5)	**<0.001**	**<0.001**	**↓<0.001**
Long-term Care Facility	114 (1.1)	8 (0.2)	44 (0.9)	62 (3.1)	**<0.001**	**<0.001**	**↑<0.001**
Comorbidities							
Diabetes	2,284 (21.4)	285 (7.4)	1,347 (28.3)	652 (32.3)	**<0.001**	**0.001**	**↑<0.001**
HIV	590 (5.5)	241 (6.2)	334 (7.0)	15 (0.7)	**<0.001**	**<0.001**	**↓ <0.001**
TB-related Characteristics							
Death at Diagnosis	227 (2.1)	22 (0.6)	72 (1.5)	133 (6.6)	**<0.001**	**<0.001**	**↑ <0.001**
Abnormal Chest X-ray (n=10,216)	9,766 (95.6)	3,607 (95.8)	4,355 (95.5)	1,804 (95.5)	0.567	0.923	0.519
Cavities on Chest X-ray (n=9,580)	3,706 (38.7)	1,373 (38.9)	1,811 (42.3)	522 (29.6)	**<0.001**	**<0.001**	**↓ <0.001**
Laboratory Diagnostic Tests							
AFB Smear + (n=9,876)	5,681 (57.5)	2,045 (55.7)	2,661 (59.5)	975 (56.4)	0.630	**0.024**	0.168
***Mtb* Culture +** (n=9,820)	7,976 (81.2)	3,038 (82.9)	3,550 (79.9)	1,388 (81.2)	0.133	0.263	**↓ 0.028**

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NAAT Test 2018-2020 (n=1,799) [d]	1799 (84.9)	634 (86.6)	765 (85.4)	400 (81.6)	0.153	0.165	↓ **0.021**
NAAT + 2018-2020 (n=1,799) [d]	472 (26.2)	185 (29.2)	187 (24.4)	100 (25.0)	0.143	0.834	0.090
PTB Outcome							
Completed Treatment	8,193 (76.9)	3,107 (80.2)	3,777 (79.4)	1,309 (64.8)	**<0.001**	**<0.001**	↓ **<0.001**
Moved/Unknown	1,158 (10.9)	524 (13.5)	432 (9.1)	202 (10.0)			
Death at diagnosis or during Rx	923 (8.7)	78 (2.0)	371 (7.8)	474 (23.5)			
Non-adherent (Refused|Lost)	366 (3.4)	164 (4.2)	171 (3.6)	31 (1.5)			
Adverse Event	16 (0.2)	3 (0.1)	8 (0.2)	5 (0.3)			

Note: Data expressed as n (column %) unless specified; n=10,656 unless n is shown.

Abbreviations: YA, young adults; MAA, middle-aged adults; OA, older adults; NHB, non-Hispanic Black; Other, other race/ethnicity; NHW, Non-Hispanic White; AFB, acid-fast bacilli; *Mtb*, *Mycobacterium tuberculosis*; NAAT, nucelic acid amplification test; TST, tuberculin skin test; IGRA, interferon-gamma release assay.

a Chi-square test.

b Score test for trend of odds for categorical variables and the nonparametric test for trend across ordered groups, an extension of the Wilcoxon rank-sum test, for polytomous variables.

c Trend direction with respect to older age is indicated by arrows preceding the trend p values.

d NAAT testing and results only evaluated between 2018-2020 when more than 80% of cases were tested.

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Table 2. TB Drug Resistance Prevalence by Age Group, Texas, United States, 2008 – 2020

	All Adults	YA (18 -- 39 y)	MAA (40 -- 64 y)	OA (≥65 y)	Age trend p-value [b, c]
Total n	10,656	3,876	4,759	2,021	
DR Testing	8,659 (81.3)	3,153 (81.4)	3,823 (80.3)	1,683 (83.3)	0.200
DR [a]	1,164 (13.4)	449 (14.2)	525 (13.7)	190 (11.3)	↓ 0.008
INH mono-R	310 (3.6)	126 (4.0)	130 (3.4)	54 (3.2)	0.124
RIF mono-R	6 (0.1)	2 (0.1)	4 (0.1)	0	0.582
PZA mono-R	99 (1.1)	35 (1.1)	38 (1.0)	26 (1.5)	0.278
MDR	87 (1.0)	43 (1.4)	40 (1.1)	4 (0.2)	↓ <0.001
Pre-XDR	12 (0.1)	8 (0.3)	4 (0.1)	0	↓ 0.018
XDR	3 (0.03)	3 (0.1)	0	0	↓ 0.048
Other DR	647 (7.5)	232 (7.4)	309 (8.1)	106 (6.3)	0.364

Abbreviations: YA, young adults; MAA, middle-aged adults; OA, older adults; DR, any TB drug resistance; INH mono-R, isoniazid monoresistance; RIF mono-R, rifampin monoresistance; PZA mono-R, pyrazinamide monoresistance; MDR, multi-drug resistant; Pre-XDR, pre-extensively resistant; XDR, extensively drug resistant; Other DR, drug resistance patterns not otherwise categorized.

a Denominator for all drug resistance results is the n shown under DR testing

b Score test for trend of odds for categorical variables

c Trend direction with respect to older age is indicated by arrows preceding the trend p values

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Table 3. Predictors of adverse TB treatment outcomes among TB patients of all age groups [a]

	Non-adherent [b]	Death [c]
Predictor Variables	**aOR (95% CI)**	**aOR (95% CI)**
Age Group		
YA (18 - 39 y)	1.00	1.00
MAA (40 - 64 y)	0.88 (0.69, 1.13)	**3.41 (2.58, 4.52)**
OA (≥65 y)	0.69 (0.45, 1.05)	**13.44 (10.12, 17.84)**
Male	**1.70 (1.23, 2.29)**	**1.22 (1.03, 1.45)**
Race		
Non-Hispanic White	1.00	
Non-Hispanic Black	**0.61 (0.42, 0.91)**	
Hispanic	0.80 (0.57, 1.10)	
Other	**0.63 (0.40, 0.99)**	
Country of Birth		
United States		1.00
Mexico		**0.64 (0.53, 0.77)**
Other		**0.44 (0.35, 0.54)**
Alcohol use	**1.36 (1.04, 1.78)**	
Homeless	**2.84 (1.99, 4.06)**	
Correctional Facility	**4.45 (3.42, 5.78)**	**0.24 (0.14, 0.40)**
Long-term Care Facility		**2.71 (1.75, 4.19)**
HIV	**1.58 (1.05, 2.37)**	**2.40 (1.78, 3.24)**
Cavities on Chest X-ray		**0.81 (0.69, 0.96)**
AFB Smear Positive	**0.71 (0.57, 0.90)**	

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Abbreviations: AFB, Acid-fast bacilli; aOR, adjusted odds ratio; CI, confidence interval; YA, young adults; MAA, middle-aged adults; OA, older adults.

a Predictor variables with p <0.20 were included in the full regression models. All reduced models (shown) include age group and sex plus predictor variables with a p <0.05.

b Non-adherent includes cases who did not die but refused treatment or were lost to follow-up when compared to those who completed. It excludes those who moved, unknown, or had an adverse event.

c Death from any cause at diagnosis or during TB treatment

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Table 4. Trends across time (2008--2020) in characteristics of pulmonary TB patients, by age groups

	All Adults (≥ 18 y) Trend p [a, b]	**YAA** (18 - 39 y) Trend p [a, b]	**MAA** (40 - 64 y) Trend p [a, b]	**OA** (≥65 y) Trend p [a, b]
Proportion of each age group	Not apply	↓ **0.003**	↓ **0.003**	↑ **<0.001**
Sociodemographics				
Male	0.881	0.588	0.654	0.395
Race/Ethnicity				
Hispanic	0.310	↓**0.007**	↑ **<0.001**	0.468
Non-Hispanic Black	↓ **0.044**	0.405	↓ **0.016**	0.824
Non-Hispanic White	↓ **<0.001**	↓ **0.008**	↓ **<0.001**	↓ **0.008**
Other	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**
Country of Birth				
United States	↓ **<0.001**	0.462	↓ **<0.001**	↓ **<0.001**
Mexico	0.138	↓ **<0.001**	↑ **<0.001**	0.693
Other	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**
Excess Alcohol Use	↓ **<0.001**	↓ **<0.001**	↓ **<0.001**	0.493
Drug Use	0.079	0.175	0.569	↑ **0.023**
IV Drug Use	↓ **0.003**	0.063	↓ **0.038**	0.344
Non-inject Drug Use	0.412	0.337	0.682	↑ **0.044**
Homeless	0.362	0.153	0.169	0.992

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Correctional Facility	↓ **0.005**	0.659	↓ **0.016**	0.164
Long-term Care Facility	0.135	0.726	↓ **0.019**	0.367
Comorbidities				
Diabetes	↑ **<0.001**	0.524	↑ **<0.001**	↑ **0.030**
HIV	↓ **<0.001**	↓ **0.002**	0.238	0.605
TB-related Characteristics				
Dead at TB Diagnosis	0.931	0.639	0.827	0.114
Abnormal Chest X-ray (n= 10,216)	↓ **<0.001**	↓ **<0.001**	↓ **<0.001**	↓ **<0.001**
Chest X-ray cavities (n= 9,580)	↓ **<0.001**	↓ **<0.001**	↓ **<0.001**	0.242
AFB Smear + (n= 9,876)	0.184	0.568	0.210	↑ **0.029**
***Mtb* Culture +** (n= 9,820)	↑ **<0.001**	0.388	↑ **<0.001**	↑ **0.011**
NAAT Test Performed	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**
TST Test Performed	↓ **<0.001**	↓ **<0.001**	↓ **<0.001**	↓ **<0.001**
IGRA Test Performed	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**	↑ **<0.001**
TB Drug susceptibility testing	0.064	↓ **0.014**	0.603	0.639
Drug-resistant TB (n= 8,659)	0.664	0.681	0.496	0.262
Adverse outcomes				
Treatment not completed (n=9,020)	0.298	0.363	0.910	0.861

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Death	0.124	0.325	0.750	0.665

Note: Total n is 10,656 unless indicated; Treatment not completed includes failure to complete treatment due to any cause except death; Death refers to mortality of any cause at the time of diagnosis or during TB treatment

Abbreviations. YA, young adults; MAA, middle-aged adults; OA, older adults; NHW, Non-Hispanic White; Other, Other Race/Ethnicity Not Specified; NHB, Non-Hispanic Black; AFB, acid-fast bacilli; MTB, Mycobacterium tuberculosis complex; NAAT, nucleic acid amplification; TST, tuberculin skin test; IGRA, interferon-gamma release assay

a Score test for trend of odds for categorical variables and the nonparametric test for trend across ordered groups, an extension of the Wilcoxon rank-sum test, for polytomous variables

b Trend direction with respect to old age is indicated by arrows preceding the trend p values

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