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ORIGINAL ARTICLE

Prevalence of Latent Tuberculosis Infection Among Persons with Chronic Hepatitis B Virus Infection: A Systematic Review and Meta-Analysis

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Abstract

Background Tuberculosis (TB) and chronic hepatitis B virus infection (HBV) can be prevented through latent tuberculosis infection (LTBI) treatment and HBV vaccination, respectively. Prevalence of LTBI and HBV are six- and ninefold higher among non-US-born compared to US-born persons, respectively. Few studies have described the prevalence of LTBI-HBV co-infection.

Aims In this study, we estimated LTBI prevalence among persons with chronic HBV.

Methods We conducted a systematic review and meta-analysis using PubMed from inception through September 1, 2019, and identified and reviewed studies that provided data regarding LTBI prevalence among adults with chronic HBV. Pooled LTBI prevalence among adults with HBV was calculated using a random-effects meta-analysis model.

Results A total of 1,205 articles were identified by systematic review of the published literature. Six studies were included in the meta-analysis; five studies were conducted in North America, and one was in China. LTBI prevalence among adults with chronic HBV was estimated to be 34.25% (95% confidence interval: 17.88–50.62%).

Conclusion LTBI prevalence among adults with chronic HBV was two times higher than the LTBI prevalence among all non-US-born persons. The high LTBI prevalence and increased risk of hepatotoxicity with TB medications among persons with chronic HBV may warrant consideration of routine screening for HBV among persons who are tested for LTBI. Reducing morbidity and mortality associated with TB and chronic HBV may require healthcare systems and public health to ensure that persons at risk of both infections are screened and treated for LTBI and chronic HBV.

Keywords Latent tuberculosis infection · Chronic hepatitis B virus infection · Systematic review

Introduction

Tuberculosis (TB) and chronic hepatitis B virus infection (HBV) are preventable infectious diseases that impact public health and clinical medicine. Worldwide, there are an estimated 10 million people with active TB disease [1], 1.7 billion people with latent TB infection (LTBI) [2, 3], and 257 million people with chronic HBV [4]. During 2019, the USA reported 8920 TB cases, which represented a TB incidence rate of 2.7 cases per 100,000 population [5]. TB disproportionately impacts non-US-born persons, and especially non-Hispanic Asians; rates of TB are 15-fold and 35-fold higher among non-US-born and non-Hispanic Asians compared to US-born and Whites, respectively [5]. Although the USA has one of the lowest TB rates in the world, elimination of TB, defined as a TB rate of < 1 per 1,000,000 population, has been difficult to achieve in the USA, in part, because of challenges in identifying, screening, and treating persons with LTBI [6, 7]. An estimated 80% of TB cases in the USA result from LTBI, and 13 million persons in the USA are estimated to have LTBI [5, 8]. Newer and shorter course LTBI regimens such as rifampin and isoniazid and rifapentine have a lower risk of hepatotoxicity, higher treatment completion rates, and similar efficacy as isoniazid for prevention of active TB disease and are now the preferred LTBI treatment regimens [9]. Despite these advances in LTBI treatment regimens, there remain

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substantial gaps in the LTBI cascade of care as a recent meta-analysis estimated that only 19% of patients complete an adequate course of LTBI treatment [10].

Chronic HBV also has significant gaps in the cascade of care and disproportionately impacts non-US-born and Asians [11]. During 2019, an estimated 1.59 million US persons were infected with chronic HBV [12]. Non-US-born persons and non-Hispanic Asians have a disproportionately higher prevalence of chronic HBV infection compared to US-born (1.28% vs. 0.15%) and non-Hispanic Whites (3.85% vs. 0.08%), respectively [11]. Among chronic HBV-infected patients in the USA, 32% of patients were aware of their HBV diagnosis, and among those who were aware of their HBV diagnosis, 28% were started on HBV antiviral treatment [13]. Although an estimated 36% of insured chronic HBV patients are eligible for antiviral treatment, only 18% were prescribed treatment [14]. Reductions in chronic HBV burden will require increased screening and linkage to care and treatment among non-US-born persons.

Although LTBI and chronic HBV are common preventable infectious diseases in the USA that disproportionately affect non-US-born persons, there are few published data regarding LTBI and chronic HBV co-infection [15, 16]. In this paper, we conducted a systematic review and meta-analysis to estimate the prevalence of LTBI among chronic HBV-infected adults.

Methods

Search Strategy and Study Selection

This study was conducted and presented according to Meta-analysis Of Observational Studies in Epidemiology (MOOSE) [17] and Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines [18]. We conducted structured searches of MEDLINE/PubMed from inception to September 1, 2019, to identify English language peer-reviewed original research articles that included adults (age > 18 years) by using different combinations of keywords for hepatitis B virus and tuberculosis. The search strategy included all of the following terms:

1. (Tuberculosis[mesh] OR Antitubercular agents [mesh] OR Interferon-gamma release tests[mesh] OR Mycobacterium tuberculosis[mesh] OR Tuberculin[mesh] OR Tuberculin test[mesh] OR tuberculosis OR antitubercul* OR “interferon gamma release test” OR “interferon gamma release tests” OR “mycobacterium tuberculosis” OR tuberculin OR mantoux OR “TB test” OR “TB tests” OR “anti-TB” OR Quantifero* OR qft-git OR t-spot.tb OR TB[ti]) AND
2. (Hepatitis B[mesh] OR Hepatitis B virus[mesh] OR Hepatitis B antigens[mesh] OR Hepatitis B antibodies[mesh] OR “hepatitis b” OR HBV[tiab] OR HBcore OR “HB core” OR “homologous serum hepatitis virus” OR “dane particle” OR HBAg OR HBeAG OR “hepatitis Be antigen” OR “hepatitis Be antigens” OR “e antigen” OR “e antigens” OR HBeAg OR “HBNE Ag-1” OR “HBe Ag-2” OR “Australia antigen” OR “Australia antigens” OR “Anti-Australia antigen” OR “Anti-Australia antigens” OR “anti-HBAg”) AND
3. (English[la])

In addition, we conducted a detailed manual review of the bibliographies of included articles and relevant systemic reviews to identify additional articles. We included both prospective and retrospective observational studies, including cohort and cross-sectional study designs. When two or more studies reported data on the same cohort over the same study period, we utilized the study that included the most comprehensive cohort and study periods. All literature searches, reviews, and selections were conducted independently by two authors (RJW and AH). The outcome of each stage of literature search was reviewed independently by a third author (ASC), who also resolved any discrepancies.

Data Extraction

Three authors independently (AH, RJW, ASC) extracted data from the included studies using a standardized data extraction form. Data extracted included year of study, country/region, study design, study period, aim of the study, study population, and diagnostic criteria for HBV and LTBI. We also extracted demographic data on patients including age, sex, and country of origin; the number of patients with chronic HBV; and the number of patients with LTBI. If available, data regarding the proportion of patients with HIV, HCV, or concurrent diabetes were also collected. For studies with missing data or incomplete data that precluded calculation of LTBI prevalence in patients with concurrent chronic HBV, corresponding authors were contacted to obtain necessary data. Any discrepancies in data extraction were resolved in consultation with a separate reviewer (RS).

Statistical Analysis

Prevalence of LTBI among patients with chronic HBV was calculated by dividing the number of patients with LTBI by the total number of patients with chronic HBV. Aggregate data on LTBI prevalence among chronic HBV-infected patients were evaluated using meta-analysis, and pooled prevalence rates were generated using random-effects models. All analyses were conducted using Review Manager

(RevMan, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration).

Results

Of the 1205 studies identified by our search strategy, 1145 (95%) studies were excluded based on title and abstract review, and 60 (5%) studies were reviewed to determine whether they included data regarding chronic HBV and LTBI (Fig. 1). Of the 60 studies, 54 (90%) were excluded based on review of the full papers. A total of 6 studies were included in the systematic review and meta-analysis of LTBI among adults with chronic HBV [15, 16, 19–22]. These 6 studies included complete data required to calculate LTBI prevalence among patients with concurrent chronic HBV, and as a result the corresponding authors of these studies were not contacted.

A summary of the demographic and clinical characteristics of the persons included in the 6 studies is provided in Table 1. Three of the studies were cross-sectional, and three were cohort studies. Three of the 6 studies were published between 1986 and 1991, and three of the 6 studies were published during 2002–2019. Five of the 6 studies were conducted in North America: two of these studies only included Southeast Asian immigrants, predominantly from Vietnam; two studies included Alaskan and Northwest Canadian Natives; and one study included homeless US veterans. One study was conducted in Zhongmu County, Central China. The proportion of males in the studies varied from 45 to 53%. Most studies included persons aged 50 years and younger; however, one study only included patients aged 50 years and older. Two studies included limited data on comorbidities. In these studies, the prevalence of hepatitis C virus infection (based on positive hepatitis C virus antibody) among patients with LTBI was 52.03% and 0.49%; HIV infection was 2.44%; and diabetes mellitus type 2 was 7.84%.

All studies defined chronic HBV as persons who had a positive hepatitis B surface antigen (HBsAg) test. Five of the 6 studies defined LTBI as persons who had a tuberculin skin test that was read as having 10 or more millimeters of induration; one study defined LTBI as having a positive QuantiFERON®-TB Gold In-Tube test. The number of persons with chronic HBV in the studies ranged from 7 to 950, and the number of persons with chronic HBV who had LTBI ranged from 1 to 259. The prevalence of LTBI among persons with chronic HBV ranged from 14.29 to 63.40%. In the meta-analysis of all 6 studies, the LTBI prevalence among persons with chronic HBV was 34.25% (95% Confidence Interval: 17.88–50.62%) (Fig. 2).

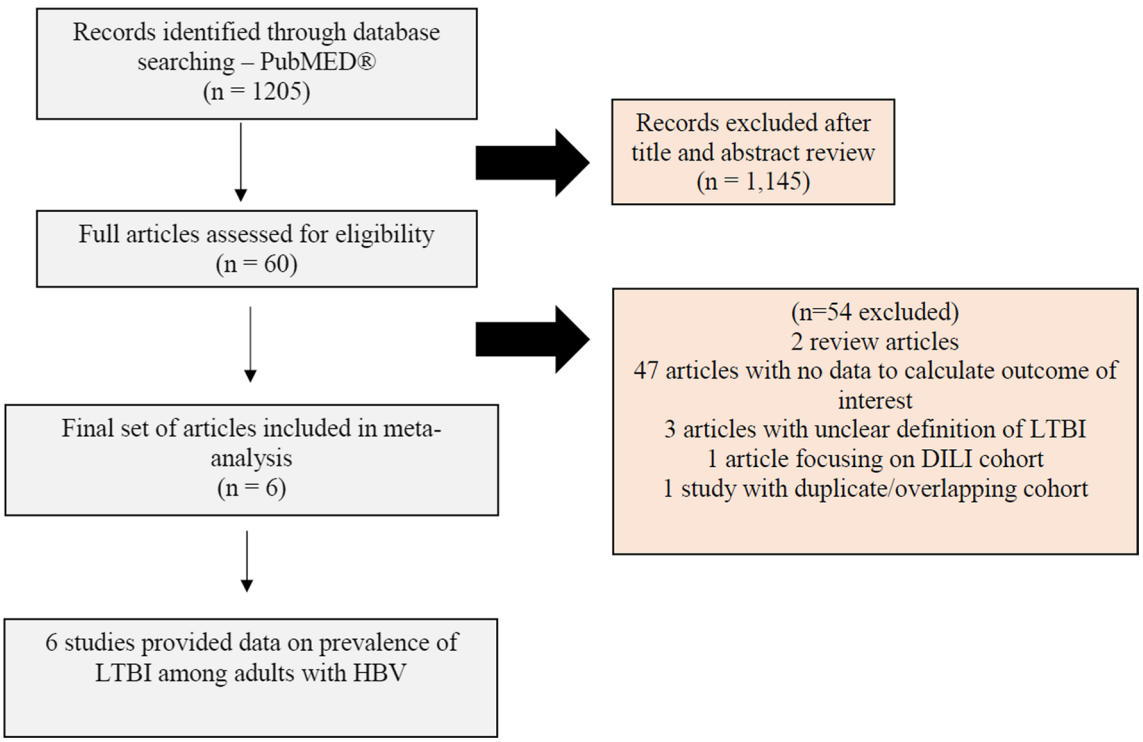

Fig. 1 PRISMA flow diagram of studies included in the meta-analysis of latent tuberculosis infection prevalence among adults with chronic hepatitis B virus infection

Table 1 Characteristics of included studies evaluating the prevalence of latent tuberculosis infection among adults with chronic hepatitis B virus infection

Author, year, country	Study design	Study population	Sex	Age	Comorbidities	LTBI and HBV treatment	HBV and LTBI Diagnostic Criteria	Prevalence of LTBI among HBV[a]
McGlynn, 1986, United States	Prospective Cohort (N = 1833)	All Southeast Asian refugees (Vietnamese, Khmer, Laos, Hmong, and ethnic Chinese) who attended 3 Philadelphia Public Health clinics	53.15% male, 46.85% female	No information provided	No information provided	148 (79%) of 187 patients with LTBI and HBV received isoniazid for LTBI treatment; 39 received no LTBI treatment No information provided regarding HBV treatment	Positive HBsAg PPD with 10 mm or greater induration	187/295 (63.40%)
McGlynn, 1987, United States	Retrospective cohort (N = 613)	Alaskan-Native HBV carriers whose HBeAg status identified using Alaska HBV registry, and PPD status obtained from Alaska State TB program and Alaska area Native Health Service	No information provided	< 20 years: 55.30%; 20–30 years: 19.58%; > 30 years: 25.12%	No information provided	No information provided regarding LTBI or HBV treatment	Positive HBsAg and HBeAg PPD with 10 mm or greater induration	38/242 (15.70%)
Larke, 1991, Canada	Retrospective cohort (N = 370)	Persons who were found to be HBsAg positive in a study of HBV in Northwest Territories of Canada	No information provided	< 20 years: 18.92%; 20–30 years: 10.81%; > 30 years: 70.27%	No information provided	No information provided regarding LTBI or HBV treatment	Positive HBsAg and HBeAg PPD with 10 mm or greater induration	11/31 (35.48%)
Cheung, 2002, United States	Cross-sectional (N = 829)	Veterans admitted to Veterans Affairs Domiciliary Care for Homeless Veterans	No information provided	Mean (SD) 43.5 years (7)	HCV antibody positive prevalence: 52.03% HIV antibody positive prevalence: 2.44%	No information provided regarding LTBI or HBV treatment	Positive HBsAg PPD with 10 mm or greater induration	1/7 (14.29%)

Table 1 (continued)

Author, year, country	Study design	Study population	Sex	Age	Comorbidities	LTBI and HBV treatment	HBV and LTBI Diagnostic Criteria	Prevalence of LTBI among HBV[a]
Patel, 2002, United States	Cross-sectional (N = 743)	Vietnamese immigrants seen at Community Center in Iowa	No information provided	Not provided	No information provided	50 (91%) of 55 patients with LTBI and HBV received isoniazid for LTBI treatment; 5 received no LTBI treatment No information provided regarding HBV treatment	Positive HBsAg PPD with 10 mm or greater induration	55/103 (53.40%)
Xin, 2019, China	Cross-sectional (N = 20,486)	Individuals aged 50–70 years old who resided in Zhongmu County, China for 6 consecutive months	44.60% male, 55.40% female	50–55 years: 32.15%; 56–60 years: 27.45%; 61–65 years: 24.31%; 66–70 years: 16.09%	Diabetes mellitus type 2 prevalence: 7.84% HCV antibody positive prevalence: 0.49%	No information provided regarding LTBI or HBV treatment	Positive HBsAg Positive QuantiFERON®-TB Gold In-Tube	259/950 (27.26%)

HBeAg: hepatitis B e antigen; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus infection; HCV: hepatitis c virus infection: HIV: human immunodeficiency virus infection; LTBI: latent tuberculosis infection; PPD: purified protein derivative; yrs: years old.

[a]Prevalence of LTBI among adults with chronic hepatitis b virus infection calculated by dividing the number of patients with LTBI by the total number of patients with chronic HBV

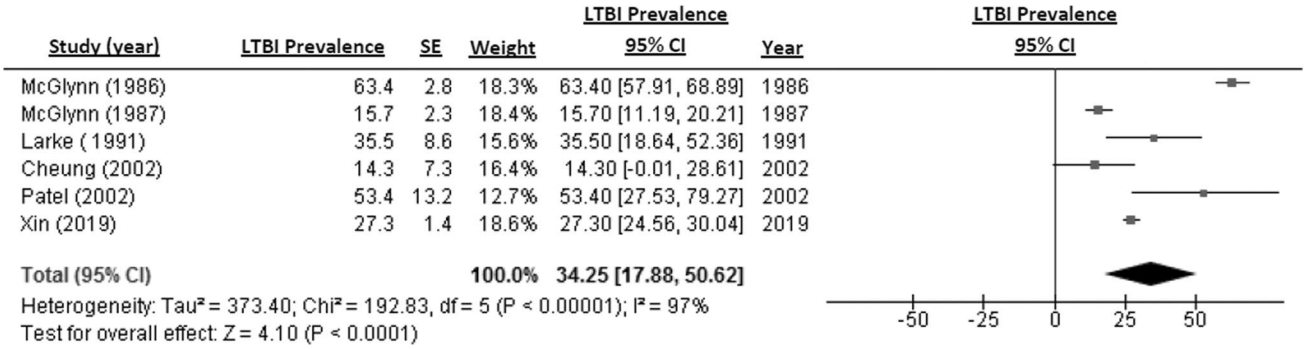

Fig. 2 Forest plot of meta-analysis evaluating the prevalence of latent tuberculosis infection among adults with chronic hepatitis B infection

Discussion

In this systematic review and meta-analysis, we detected a pooled prevalence of LTBI among adults with chronic HBV of 34.25%. This prevalence is substantially higher than published estimates of LTBI reported in the National Health and Nutrition Examination Survey (NHANES). During 2011–20,112, NHANES utilized a QuantiFERON®-TB Gold-In-Tube test to detect LTBI among participants, and noted an overall LTBI prevalence of 5.0%, a prevalence of 2.8% among US-born persons, and a prevalence of 15.8% among non-US-born persons [23]. To the best of our knowledge, our study is one of the first to estimate the prevalence of LTBI among persons with chronic HBV, and the findings from these analyses are relevant to clinical medicine and public health for several reasons.

Efforts to reduce morbidity and mortality associated with TB and chronic HBV will require healthcare systems to screen and treat persons at risk of both infections. Several studies have shown gaps in the cascade of care for both LTBI and chronic HBV [10, 14, 24, 25]. In one meta-analysis of the LTBI diagnosis and treatment cascade of care, only 72% of persons intended for TB screening received a TB screening test and 19% of persons diagnosed with LTBI completed an adequate course of LTBI treatment [10]. Primary care providers also reported suboptimal screening rates for HBV infection, and less than 20% of insured patients with chronic HBV were prescribed treatment [14, 24, 25]. Although improvements in the quality of care for LTBI and chronic HBV are needed, targeted efforts to identify individuals at risk of both infections will also be important in reducing morbidity and mortality of both infections. During 2019, there were a reported 9.2% of the US population who were uninsured, and many of these individuals are non-US-born, which is an important demographic risk factor for both TB and chronic HBV [26]. These uninsured individuals may have limited access to medical care, and targeted screening efforts may need to be conducted in community settings. TB and chronic HBV community-based screening efforts have been shown to increase diagnosis and treatment of both infections [27, 28].

Persons with LTBI and chronic HBV have a common demographic risk factor for place of nativity; however, our study also noted that they may have similar medical comorbidities. Xin et al. included data on several comorbidities [22] and detected a high prevalence of diabetes among persons with LTBI. The incidence of TB disease is higher among persons with diabetes, especially among non-US-born persons [29]. Similarly, for those with chronic HBV, an increasing proportion of patients have been noted to have diabetes [30, 31]. These findings suggest that targeted efforts for screening and treatment of LTBI and chronic HBV may be warranted among persons with diabetes who are at risk of both infections. As a result, healthcare systems may consider implementing quality improvement efforts for LTBI and chronic HBV screening and treatment among persons with diabetes. Because there are several Centers for Medicare & Medicaid Services Quality Measures regarding diabetes [32], there also may be financial incentives for healthcare systems to demonstrate that they can improve the diagnosis and treatment of other comorbidities among diabetic persons such as LTBI and chronic HBV.

Co-infection with chronic HBV may pose certain challenges for clinicians with regard to treatment of LTBI. Chronic HBV infection has been noted to increase the risk of hepatotoxicity during LTBI treatment [16, 33–36]. For example, Patel et al. evaluated 743 Vietnamese immigrants to the USA between 1991 and 1999 who underwent screening for HBV and LTBI [16]. Among this cohort, the prevalence of LTBI among patients with confirmed chronic HBV was 53%. The prevalence of drug-induced liver injury (DILI) from isoniazid prophylaxis treatment was significantly higher in HBV-TB co-infected patients than latent TB-infected patients without HBV (30.0% vs. 3.2%, $p < 0.001$). In addition, the authors observed that HBV e-antigen positivity was a strong predictor of developing DILI (RR 11.38, 955 CI 5.49–23.59, $p < 0.001$) [16]. These findings highlight the importance of screening for HBV among LTBI patients,

and monitoring liver function tests during LTBI treatment among persons with chronic HBV. Other challenges that may be encountered during LTBI treatment among chronic HBV patients are drug-drug interactions between HBV antiviral therapy and LTBI medications. For example, rifamycin medications, which are commonly used in the treatment of LTBI, may impact the clearance of certain HBV antiviral therapies such as tenofovir alafenamide, which may require changes in HBV or LTBI treatment [37–39].

This systematic review and meta-analysis are subject to certain limitations. First, several studies included in the meta-analysis were published more than 20 years ago. These studies may have a higher LTBI and HBV prevalence compared to the current prevalence of both infections because of the implementation of public health measures, such as HBV vaccination. Based on the age groups of patients included in these studies and time periods these studies were conducted, it is likely that these study populations may not have been routinely vaccinated for HBV. Second, while all the studies utilized objective laboratory criteria to identify LTBI and HBV (e.g., tuberculin skin test and QuantiFERON®-TB Gold In-Tube test for LTBI and HBsAg for HBV), for the diagnosis of HBV infection in particular, a single positive HBsAg test to define chronic HBV may have contributed to some degree of misclassification bias (e.g., patients may have had acute HBV infection). Third, the literature search was limited to PubMed® and the English language. Nevertheless, we applied comprehensive and broad search criteria, including review of the references of included studies to ensure capture of all eligible studies for inclusion. Fourth, the studies included in this meta-analysis were primarily limited to persons from the Western Pacific Region of the world. This may limit the ability to generalize our findings to other regions of the world.

In conclusion, LTBI prevalence among adults with chronic HBV was two times higher than the prevalence of LTBI among all non-US-born persons. The high LTBI prevalence and increased risk of hepatotoxicity with TB medications among persons with HBV may warrant consideration of routine screening for HBV among persons who are tested for LTBI. Reducing morbidity and mortality associated with TB and HBV may require healthcare systems and public health to ensure that persons at risk of both infections are screened and treated for LTBI and HBV.

Author's contribution AH, LB, RS, RJW, and ASC were involved in study concept and design. AH, LB, RS, RJW, and ASC were involved in acquisition of data. JC, AH, LB, RS, RJW, and ASC were involved in analysis and interpretation of data. RJW was involved in statistical analysis. JC, RJW, and ASC were involved in drafting of the manuscript. JC, AH, LB, RS, RJW, and ASC were involved in critical revision of the manuscript for important intellectual content. RJW and ASC were involved in study supervision. Drs. RJW and ASC had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

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Declarations

Conflict of interest Jennie Chen: None, Ashley Hubbard: None, Laurie Bagley: None, Rita Shiau: None, Robert J. Wong: Advisory board, consultant, and research grants – Gilead Sciences. Amit S. Chitnis: None.

References

1. World Health Organization. *Global Tuberculosis Report 2019*. Geneva: World Health Organization; 2020.
2. Cohen A, Mathiasen VD, Schon T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. *Eur Respir J.* 2019;54:1900655. https://doi.org/10.1183/13993003.00655-2019.
3. Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modeling. *PLoS Med.* 2016;13:e1002152. https://doi.org/10.1371/journal.pmed.1002152.
4. World Health Organization. *Global Hepatitis Report 2017*. Geneva: World Health Organization; 2017.
5. Centers for Disease Control and Prevention. Reported Tuberculosis in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services; 2020.
6. Reves RR, Nolan CM. Tuberculosis elimination in the United States: an achievable goal or an illusion? *Am J Respir Crit Care Med* 2012;186:1–3. https://doi.org/10.1164/rccm.201206-1039ED.
7. Cole B, Nilsen DM, Will L, Etkind SC, Burgos M, Chorba T. Essential components of a public health tuberculosis prevention, control and elimination Program: recommendations of the Advisory Council for the Elimination of Tuberculosis and the National Tuberculosis Controllers Association. *MMWR Recomm Rep.* 2020;69:1–27.
8. Shea KM, Kammerer JS, Winston CA, Navin TR, Horsburgh CR Jr. Estimated rate of reactivation of latent tuberculosis infection in the United States, overall and by population subgroup. *Am J Epidemiol.* 2014;179:216–225.
9. Sterling TR, Njie G, Zenner D et al. Guideline for the treatment of latent tuberculosis infection: recommendations from the National Tuberculosis Controllers Association and CDC, 2020. *MMWR Recomm Rep.* 2020;69:1–11.
10. Alsdurf H, Hill PC, Matteelli A, Getahun H, Menzies D. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. *Lancet Infect Dis.* 2016;16:1269–1278.
11. Le MH, Hyi Yeo Y, Cheung R, Henry L, Lok AS, Nguyen MH. Chronic hepatitis B prevalence among foreign-born and U.S.-born adults in the United States, 1999–2016. *Hepatology* 2020;71:431–443.
12. Lim JK, Nguyen MH, Kim WR, Gish R, Perumalswami P, Jacobson IM. Prevalence of chronic hepatitis B virus infection in the United States. *Am J Gastroenterol.* 2020;115:1429–1438.
13. Zhou K, Terrault NA. Gaps in viral hepatitis awareness in the United States in a population-based study. *Clin Gastroenterol Hepatol.* 2020;18:188–195. https://doi.org/10.1016/j.cgh.2019.05.047.

14. Harris AM, Osinubi A, Nelson NP, Thompson WW. The hepatitis B care cascade using administrative claims data, 2016. *Am J Manag Care* 2020;26:331–338.
15. Cheung RC, Hanson AD, Maganti K, Keeffe EB, Matsui SM. Viral hepatitis and other infectious diseases in a homeless population. *J Clin Gastroenterol.* 2002;34:476–480.
16. Patel PA, Voigt MD. Prevalence and interaction of hepatitis B and latent tuberculosis in Vietnamese immigrants to the United States. *Am J Gastroenterol.* 2002;97:1198–1203.
17. Stroup DF, Berlin JA, Morton SC et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000;283:2008–2012.
18. Moher D, Shamseer L, Clarke M et al. Preferred reporting items for systemic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4:1. https://doi.org/10.1186/2046-4053-4-1.
19. McGlynn KA, Lustbader ED, Sharrar RG, Murphy EC, London WT. Isoniazid prophylaxis in hepatitis B carriers. *Am Rev Respir Dis.* 1986;134:666–668. https://doi.org/10.1164/arrd.1986.134.4.666.
20. McGlynn KA, Lustbader ED, London WT, Heyward WL, McMahon BJ. Hepatitis B virus replication and tuberculin reactivity: studies in Alaska. *Am J Epidemiol.* 1987;126:38–43.
21. Larke RP, Harley DD, Enarson DA. Relationship between tuberculin reactivity and hepatitis B virus infection in the Northwest Territories. *Arctic Med Res*. 1991;Suppl:371–373
22. Xin H, Zhang H, Liu J et al. *Mycobacterium tuberculosis* infection among the elderly in 20 486 rural residents aged 50–70 years in Zhongmu County China. *Clin Microbiol Infect.* 2019;25:1120–1126.
23. Miramontes R, Hill AN, Yelk Woodruff RS et al. Tuberculosis infection in the United States: prevalence estimates from the National Health and Nutrition Examination Survey, 2011–2012. *PLoS ONE* 2015;10:e0140881. https://doi.org/10.1371/journal.pone.0140881.
24. Chu D, Yang JD, Lok AS et al. Hepatitis B screening and vaccination practices in asian american primary care. *Gut Liver* 2013;7:450–457.
25. Khalili M, Guy J, Yu A et al. Hepatitis B and hepatocellular carcinoma screening among asian americans: survey of safety net healthcare providers. *Dig Dis Sci.* 2011;56:1516–1523.
26. Keisler-Starkey K, Bunch, L. U.S. Census Bureau current population reports, P60-271, health insurance coverage in the United States: 2019. Washington, DC: U.S. Government Publishing Office, 2020.
27. Cegielski JP, Griffith DE, McGaha PK et al. Eliminating tuberculosis one neighborhood at a time. *Am J Public Health* 2013;103:1292–1300.
28. Harris AM, Link-Gelles R, Kim K, et al. Community-based services to improve testing and linkage to care among non-U.S.-born persons with chronic hepatitis B virus infection—three U.S. programs, October 2014–September 2017. *MMWR Morb Mortal Wkly Rep.* 2018;67:541–546.
29. Demlow SE, Oh P, Barry PM. Increased risk of tuberculosis among foreign-born persons with diabetes in California, 2010–2012. *BMC Public Health* 2015;15:263. https://doi.org/10.1186/s12889-015-1600-1.
30. Nguyen MH, Lim JK, Burak Ozbay A et al. Advancing age and comorbidity in a US insured population-based cohort of patients with chronic hepatitis B. *Hepatology* 2019;69:959–973.
31. Liu A, Le A, Zhang J et al. Increasing comorbidities in chronic hepatitis B patients: experience in primary care and referral practices during 2000–2015. *Clin Transl Gastroenterol.* 2018;9:141. https://doi.org/10.1038/s41424-018-0007-6.
32. 2018 National Impact Assessment of the Centers for Medicare & Medicaid Services (CMS) Quality Measures Report. Baltimore, MD: US Department of Health and Human Services, Centers for Medicare & Medicaid Services; February 28, 2018
33. Chen L, Bao D, Gu Y et al. Co-infection with hepatitis B virus among tuberculosis patients is associated with poor outcomes during anti-tuberculosis treatment. *BMC Infect Dis.* 2018;18:295. https://doi.org/10.1186/s12879-018-3192-8.
34. Wong WM, Wu PC, Yuen MF et al. Antituberculosis drug-related liver dysfunction in chronic hepatitis B infection. *Hepatology.* 2000;31:201–206.
35. Liu YM, Cheng YJ, Li YL, Liu CE, Hsu WH. Antituberculosis treatment and hepatotoxicity in patients with chronic viral hepatitis. *Lung* 2014;192:205–210.
36. Wang NT, Huang YS, Lin MH, Huang B, Perng CL, Lin HC. Chronic hepatitis B infection and risk of antituberculosis drug-induced liver injury: systematic review and meta-analysis. *J Chin Med Assoc.* 2016;79:368–374.
37. Cerrone M, Alfarisi O, Neary M et al. Rifampicin effect on intracellular and plasma pharmacokinetics of tenofovir alafenamide. *J Antimicrob Chemother.* 2019;74:1670–1678.
38. Maartens G, Boffito M, Flexner CW. Compatibility of next-generation first-line antiretrovirals with rifampicin-based antituberculosis therapy in resource limited settings. *Curr Opin HIV AIDS* 2017;12:355–358.
39. Custodio JM, West SK, Lutz J, et al. Twice Daily Administration of Tenofovir Alafenamide in Combination with Rifampin: Potential for Tenofovir Alafenamide Use in HIV-TB Coinfection. In: *Program and abstracts of the 16th European AIDS Conference; October 25–27, 2017*; Milan, Italy. [Abstract PS13/4 2017].

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