Leveraging Data to Strengthen Hepatitis B and Tuberculosis Elimination Strategies Workshop

Hep B United / TB Elimination Alliance Virtual Summit
November 2, 2021

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Objectives

- Review epidemiology of tuberculosis (TB) and chronic hepatitis B virus infection (CHB) in the United States

- Discuss estimates of TB-CHB and latent TB-CHB co-infection prevalence in published literature, National Health and Nutrition Examination Survey, and a large national laboratory database

- Describe testing practices for latent TB infection (LTBI) and CHB in a large national laboratory database, and LTBI screening in clinical trials evaluating CHB treatments

- Provide an estimate of prevalence and risk of drug-induced liver injury among persons with TB-CHB co-infection compared to TB disease only

Conversations About Mutual Patients Result in Interest to Further Understand TB and CHB

- 60-year-old Burmese male s/p liver transplant 6 years ago for hepatocellular carcinoma and hepatitis B-associated cirrhosis, possible LTBI treatment in 2012 who developed mild cough and was diagnosed with smear-positive pulmonary TB

- 50-year-old Afghan male (arrived in 2015) diagnosed with smear-negative, culture-positive pulmonary TB in another State, and started TB treatment in California. Unclear if ever screened for CHB in past and at Highland clinic diagnosed with hepatitis B virus infection (HBsAg positive, HBeAg negative, HBV DNA 2000 IU/mL)

Journal of Immigrant and Minority Health
https://doi.org/10.1007/s10903-021-01231-6

REVIEW PAPER

Epidemiology and Prevention of Tuberculosis and Chronic Hepatitis B Virus Infection in the United States

Amit S. Chitnis[1] · Ramsey Cheung[2,3] · Robert G. Gish[4] · Robert J. Wong[2,3]

Accepted: 12 June 2021

Abstract
Tuberculosis (TB) and chronic hepatitis B virus (CHB) infection can be prevented with treatment and vaccination, respectively. We reviewed epidemiology and guidelines for TB and CHB to inform strategies for reducing United States (U.S.) burden of both infections. Non-U.S.-born, compared to U.S.-born, persons have a 15-, 6-, and 8-fold higher TB incidence and latent TB infection (LTBI) and CHB prevalence, respectively; all infections disproportionately impact non-U.S.-born Asians. TB and CHB each are associated with ~ 10% mortality that results in 7- and 14-years per life lost, respectively. LTBI and CHB have significant gaps in their care cascade as 40% of LTBI and 20% of CHB patients are diagnosed, and 20% of LTBI and CHB diagnosed patients receive treatment. Reducing TB and CHB burden will require healthcare provider-, system-, and policy-level interventions, and increased funding and collaboration between public health departments and healthcare systems.
Institutional Review Board Statement: Since this review article did not include primary data on patients and only focused on reviewing published data, approval by an institutional review board was not needed.

Keywords Epidemiology · Prevention · Tuberculosis · Chronic hepatitis B virus infection

Table 1 Epidemiologic, demographic, and clinical characteristics of patients with tuberculosis, latent tuberculosis infection, and chronic hepatitis B virus infection, United States

Characteristics	Tuberculosis	Latent tuberculosis infection	Chronic hepatitis B virus infection
Epidemiologic	2019 U.S. TB Incidence rate: 2.7/100,000	LTBI prevalence estimated to be 5.0%, or 14.1 million, among persons aged 6 years and older in NHANES	CHB prevalence estimated to be 0.3%, or 0.84 million, among persons aged 18 years and older in NHANES
	TB rates significantly decreased among U.S.-born, but not among non-U.S.-born		Review of published literature that included non-NHANES population estimated 1.59 million persons with CHB
	Majority of TB cases reported in four U.S. states: California, New York, Florida, and Texas		32% of patients with CHB in NHANES were aware of infection; knowledge of HBV prevention practices sub-optimal in population-based surveys of patients
	Estimated 80% of TB cases result from reactivation of LTBI; 20% from recent transmission	Cost-effective to screen non-U.S.-born persons with an IGRA, and treat with short course LTBI regimens such as isoniazid and rifapentine or rifampin	Only 19% of insured CHB patients have been diagnosed with HBV
Demographic	TB rates highest among non-U.S.-born, Asians, and persons aged 65 years and older	Non-U.S.-born persons have higher prevalence than U.S.-born; non-Hispanic Asians, Hispanics, and non-Hispanic Blacks have highest LTBI prevalence	Non-U.S.-born have higher CHB prevalence; prevalence highest for non-U.S.-born persons from Africa, Asia, Oceania, and Caribbean
			Asians and non-Hispanic Blacks have highest prevalence
	High proportion of non-U.S.-born TB cases are uninsured or undocumented	Persons aged 65 years and older and 45–64 years old have highest LTBI prevalence	Persons aged 65 years and older, 50–64 years old, and 35–49 years old have highest CHB prevalence
Clinical	Non-U.S.-born TB cases more likely to have diabetes and end-stage renal disease; less likely to have traditional TB risk factors such as HIV infection, homelessness, or substance abuse; Non-U.S.-born pulmonary TB cases more likely to have negative AFB sputum smears, and less likely to have a TB NAAT ordered	Persons who have highest-risk for LTBI include household contacts to persons with active TB disease; non-U.S.-born persons from TB countries with rate of 20/100,000 or higher; and residents or employees of congregate settings	Median age of CHB patients increased during 2000–2015
			Prevalence of liver comorbidities (i.e., fatty liver disease, cirrhosis, and hepatocellular carcinoma) and non-liver comorbidities (i.e., diabetes, hypertension, chronic kidney disease, and osteoporosis) increased
	Undocumented persons have longer symptom onset, and more likely to have positive AFB sputum smears		Hospitalization for CHB is on average 6 days; estimated cost for hospitalization is $6,200–$8,000
	Majority of TB cases hospitalized; average length of stay 9–17 days, and average cost of hospitalization is $6,000–$66,000		13% of CHB cases who were followed for 5 years died
	Nearly 10% of reported TB cases died; of whom, almost 25% died before TB diagnosis		CHB mortality associated with 14 years per life lost
	TB mortality associated with 7 years per life lost	Substantial gaps in LTBI cascade of care as 72% receive a diagnostic test, 44% diagnosed with LTBI, 31% accept LTBI treatment, and 19% complete treatment	Substantial gaps in CHB cascade of care as an estimated 20% of patients are diagnosed; less than 50% of patients receive appropriate laboratory and radiographic monitoring; and 20% of diagnosed patients started on HBV antiviral therapy

AFB acid-fast bacilli, *CHB* chronic hepatitis B virus infection, *HBV* hepatitis B virus, *HIV* human immunodeficiency virus, *IGRA* interferon gamma-release assay, *LTBI* latent tuberculosis infection, *NAAT* nucleic acid amplification test, *NHANES* National Health and Nutrition Examination Survey, *TB* tuberculosis

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Table 3 Strategies for prevention of tuberculosis, latent tuberculosis infection, and chronic hepatitis B virus infection

Stakeholder	Strategies for prevention of tuberculosis, latent tuberculosis infection, and chronic hepatitis B virus infection
Healthcare provider	• Prioritize screening and treatment of LTBI and CHB among non-U.S.-born persons given overlapping epidemiologic and demographic risk factors for both infections • Vaccinate persons who are at risk for HBV infection • Screen for LTBI with an IGRA and treat infected persons with short course LTBI regimens such as rifampin or isoniazid and rifapentine • Screen for CHB with HBsAg, anti-HBs, and total or IgG anti-HBc Certain persons[a] who test HBsAg negative and positive or negative for anti-HBs or anti-HBc may warrant additional screening with an HBV DNA to detect occult HBV infection •Ensure patients with CHB receive appropriate laboratory and radiographic monitoring, and treatment in accordance with guidelines
Healthcare system	• Require electronic medical records to have reminders and best practices for LTBI and CHB screening and treatment, HBV vaccination, and laboratory and radiographic monitoring of CHB infected persons • Implement quality improvement projects to increase LTBI and CHB screening and treatment, HBV vaccination, and monitoring of CHB infected persons • Develop, and invest in, multidisciplinary clinical teams for the management of LTBI and CHB that include patient navigators • Collaborate with public health departments to: Develop registries to link LTBI and CHB infected patients to care, and improve cascade of care for both infections Conduct community-based screening and provide LTBI and CHB education to communities and populations at increased risk
Public health	• Engage with healthcare providers and healthcare systems to identify patients at risk for LTBI and CHB, and improve cascade of care for both infections • Enhance surveillance systems so able to quantify burden of TB and CHB coinfections
Policy makers	• Reduce cost barriers to LTBI and CHB screening and treatment, CHB monitoring, and HBV vaccination • Develop CMS quality measures regarding LTBI and CHB screening and treatment

anti-HBc antibody to hepatitis B core antigen, *anti-HBs* antibody to hepatitis B surface antigen *CHB* chronic hepatitis B virus infection, *CMS* Centers for Medicare & Medicaid Services, *DNA* deoxyribonucleic acid, *HBsAg* hepatitis B surface antigen, *HBV* hepatitis B virus, *IGRA* interferon gamma-release assay, *LTBI* latent tuberculosis infection, *TB* tuberculosis

[a]Persons who are at increased risk for occult hepatitis B virus infection are immunocompromised, have HCV, end-stage renal disease and are on dialysis, inject drugs, or have chronic liver disease

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Diagnosis and Treatment of Latent Tuberculosis Infection

Amit S. Chitnis, MD, MPH[1], Devan Jaganath, MD, MPH[2,3], Robert G. Gish, MD[4] and Robert J. Wong, MD, MS[5,6]

Am J Gastroenterol 2021;00:1–4. https://doi.org/10.14309/ajg.0000000000001398; published on

- Reviewed LTBI diagnosis and treatment guidelines
- Discussed common clinical scenarios regarding LTBI encountered by gastroenterologists

Table 1. Summary of latent tuberculosis infection diagnosis and treatment guidelines

	ATS/CDC/IDSA	USPSTF	CDPH
Who should be screened for LTBI?	Risk for TB infection[a] Risk for progression to TB disease[b] Benefit of LTBI treatment[c]	Asymptomatic persons in primary care clinics who are at increased risk for LTBI[d]	Birth, travel, or residence in a country[e] with an elevated TB rate for >1 mo Current or planned immunosuppression[f] Close contact with someone with infectious TB disease during their lifetime
What LTBI diagnostic test should be used?	IGRA recommended among persons who meet all of the following criteria: • Aged ≥ 5 year old • Low or intermediate risk of TB progression[b] • History of BCG vaccination or unlikely to return for TST read • Likely to be infected with TB[a] Insufficient evidence to recommend IGRA over TST among persons who meet all of the following criteria: • Aged ≥ 5 year old • High risk for progression of TB disease[b] • Likely to be infected with TB[a] Consider conducting second LTBI test if first test is negative in persons at high risk for progression of TB disease[b]	IGRA or TST acceptable	IGRA is preferred; TST is acceptable Consider conducting second LTBI test if first test is negative in persons at high risk for progression of TB disease[b]
What are recommended LTBI treatment regimens?[g]	Preferred LTBI regimens: • Isoniazid and rifapentine both taken once a wk for 12 wks[h] • Rifampin taken daily for 4 mo[h] • Isoniazid and rifampin both taken daily for 3 mo[h] Alternative LTBI regimen: • Isoniazid taken daily for 6–9 mo[h]	Not reviewed	Preferred LTBI regimens: • Isoniazid and rifapentine both taken once a wk for 12 wks[h] • Rifampin taken daily for 4 mo[h] Alternative LTBI regimen: • Isoniazid taken daily for 6–9 months[h]

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ORIGINAL ARTICLE

Estimating Prevalence of Hepatitis B Virus Coinfection Among Adults With Tuberculosis

A Systematic Review With Meta-analysis

Robert J. Wong, MD, MS,† Ashley Hubbard, DO,‡ Laurie Bagley, MLIS,§ Rita Shiau, MPH,‖ and Amit S. Chitnis, MD, MPH¶*

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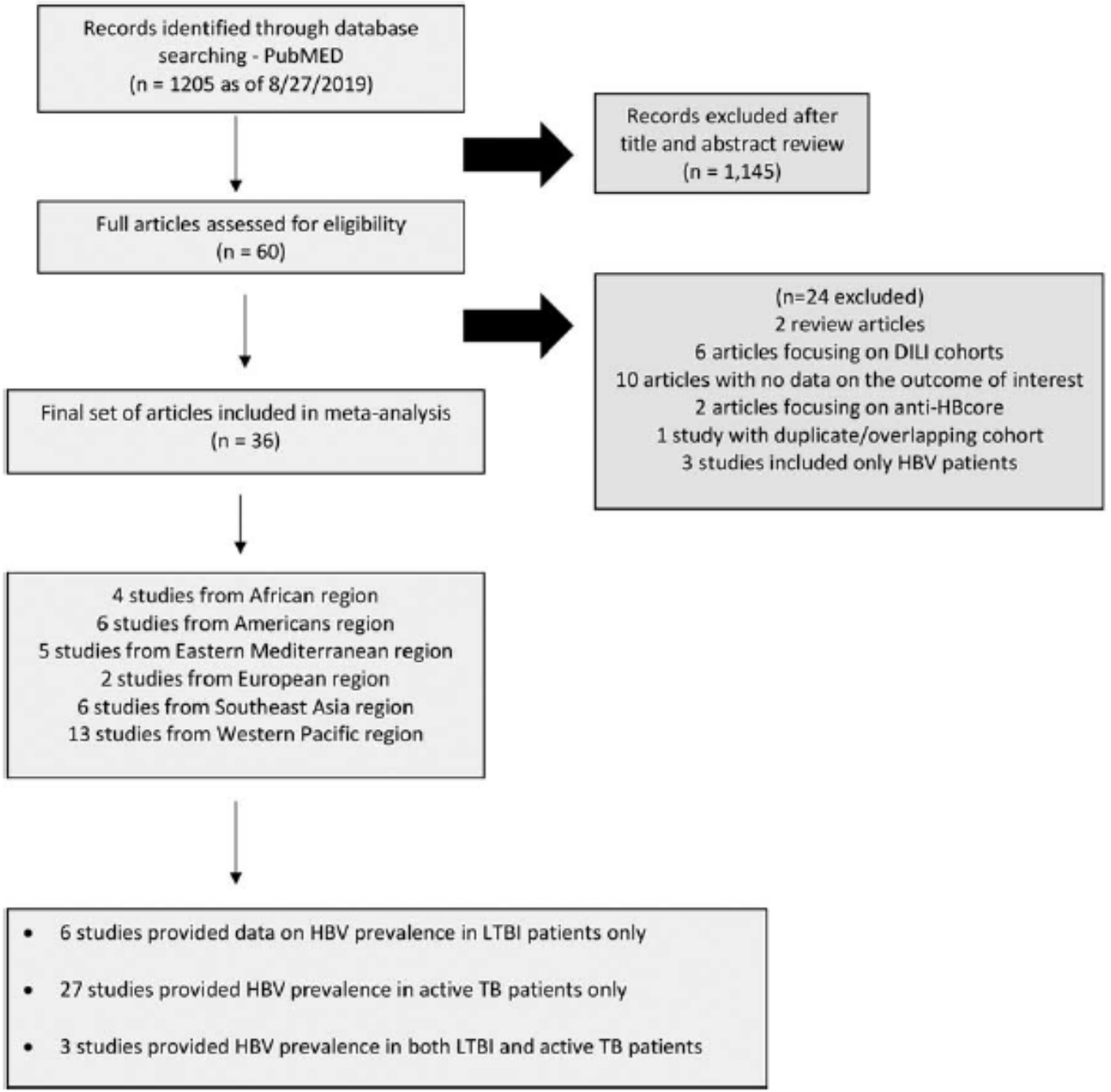

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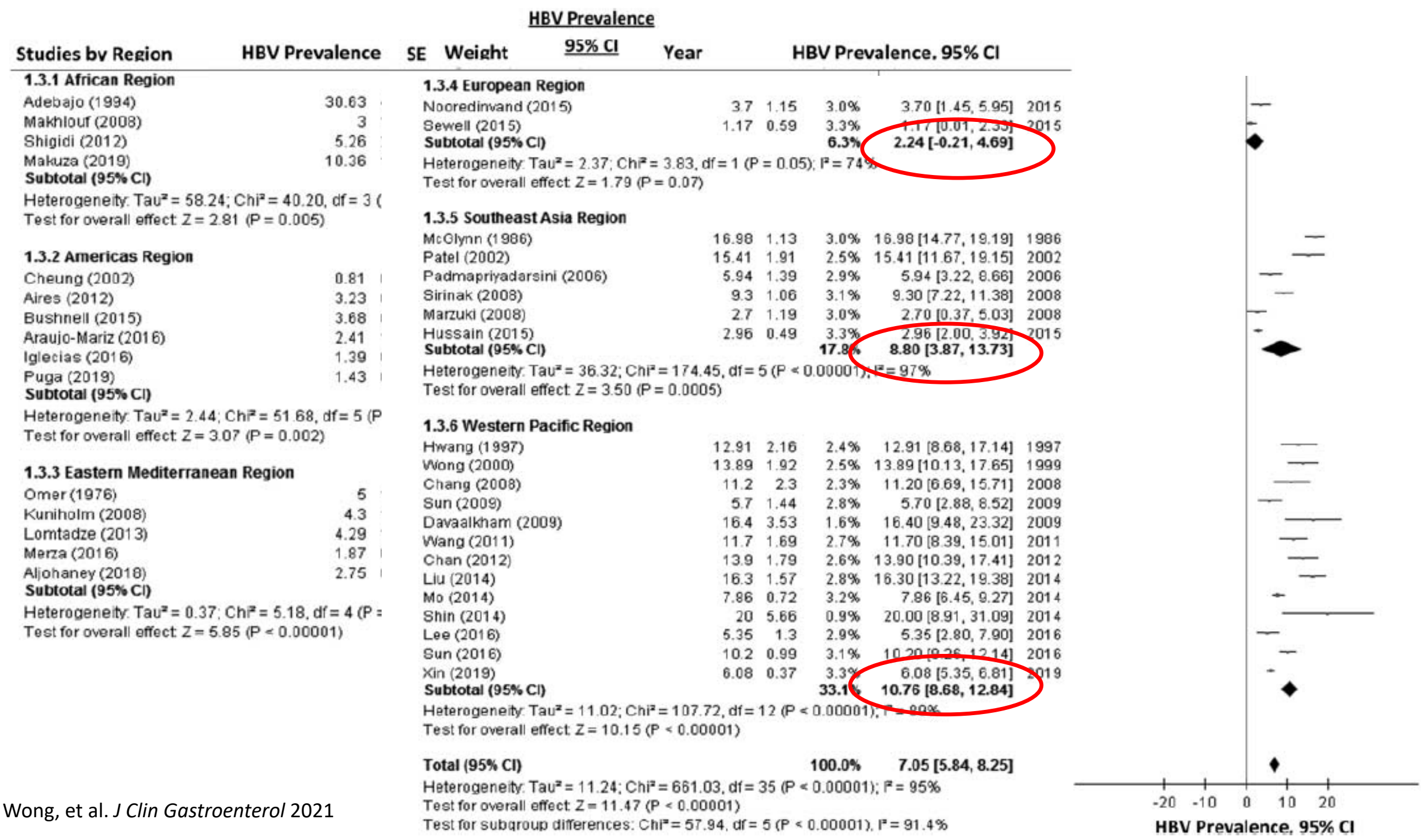


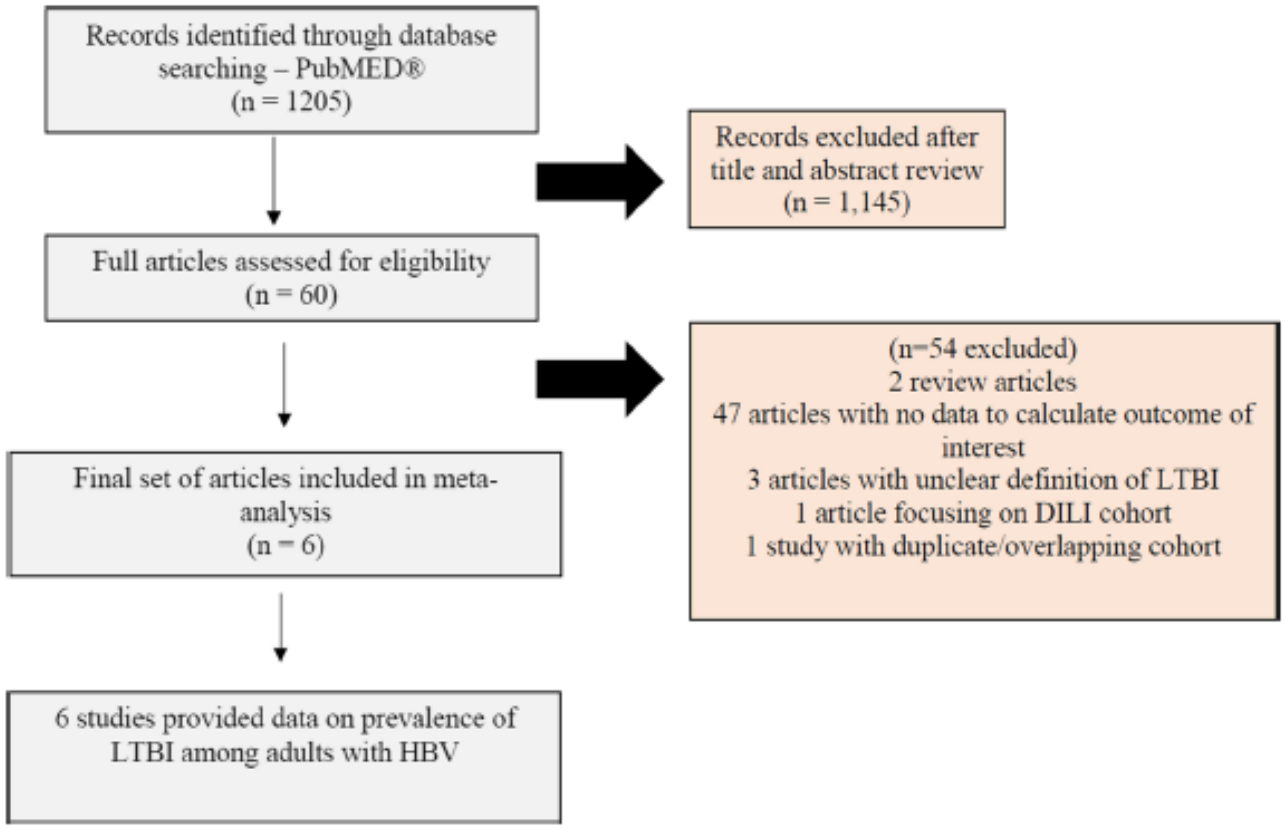
Wong, et al. *J Clin Gastroenterol* 2021

Digestive Diseases and Sciences
https://doi.org/10.1007/s10620-021-07056-5

ORIGINAL ARTICLE

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

Jennie Chen[1,2] · Ashley Hubbard[3] · Laurie Bagley[3,4] · Rita Shiau[5] · Robert J. Wong[6,7] · Amit S. Chitnis[1]



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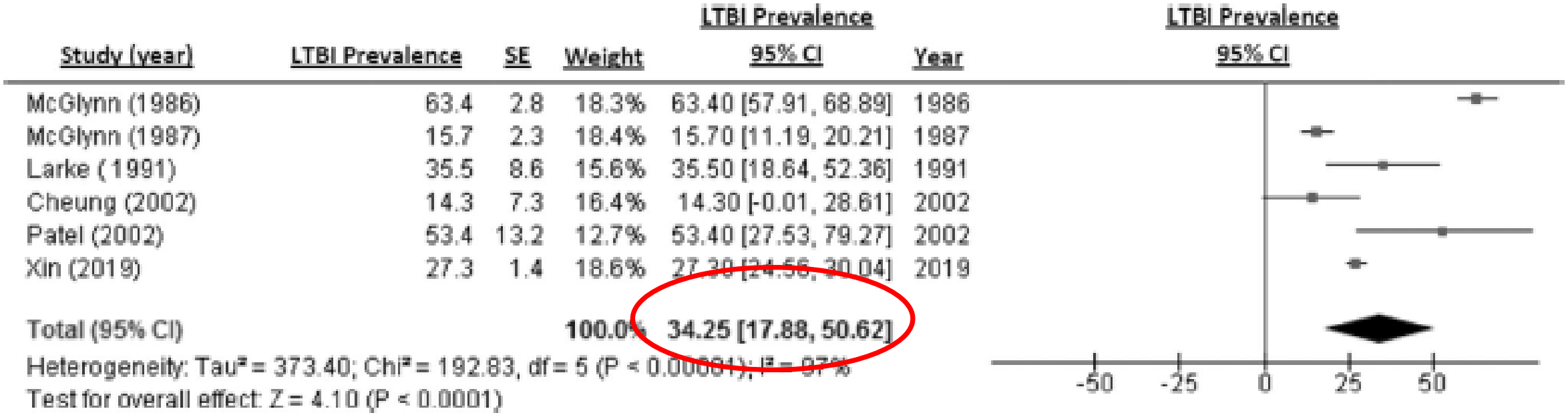

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Prevalence of hepatitis B surface antigen and hepatitis B core antibody among adults with latent tuberculosis infection

Ashley Hubbard[a], Grishma Hirode[b], Amit Chitnis[c] and Robert Wong[d,e]

- Cross sectional study of NHANES data from 1999–2000 and 2011–2012
- Prevalence of hepatitis B surface antigen (HBsAg) and hepatitis B core antibody total (anti-HBc) among US adults aged ≥20 years with LTBI
- LTBI was identified by positive tuberculin skin test (TST) measured 46–76 h after administration (induration >10 mm) or positive QuantiFERON-TB Gold In-Tube test (QFT-GIT).

Hubbard, et al. *Eur J Gastro Hepatol*. 2021

Table 1. Evaluating prevalence of HBsAg among adults with LTBI

	N (%) (95% CI)		
	1999–2000	2011–2012	Total
Total LTBI prevalence	410 (4.2) (3.4–5.1)	442 (4.3) (3.1–5.9)	852 (4.2) (3.5–5.1)
Prevalence of HBsAg			
Total	2 (0.4) (0.1–1.7)	8 (1.4) (0.5–3.8)	10 (0.9) (0.4–2.1)
Men			7 (1.1) (0.4–3.0)
Women			3 (0.7) (0.2–2.3)
Non-Hispanic White			1 (0.5) (0.1–4.4)
Black			3 (1.0) (0.3–4.0)
Hispanic			1 (0.1) (0.01–1.0)
Other			5 (3.1) (0.9–10.3)
Non-US born			8 (1.2) (0.5–2.9)
US-born			2 (0.3) (0.04–2.4)
Age <25			0
Age 25–44			4 (1.2) (0.3–4.4)
Age 45–64			2 (0.4) (0.1–1.8)
Age ≥65			4 (2.1) (0.6–7.1)

CI, confidence interval; HBsAg, hepatitis B surface antigen; LTBI, latent tuberculosis infection.

Table 2. Evaluating prevalence of anti-HBc among adults with LTBI

	N (%) (95% CI)		
	1999–2000	2011–2012	Total
Total LTBI prevalence	410 (4.2) (3.4–5.1)	442 (4.3) (3.1–5.9)	852 (4.2) (3.5–5.1)
Prevalence of anti-HBc			
Total	44 (13.6) (9.1–20.0)	83 (12.2) (8.7–17.0)	127 (12.9) (9.8–16.8)
Men	33 (17.9) (11.3–27.1)	58 (15.7) (10.6–22.6)	91 (16.8) (12.3–22.6)
Women	11 (6.9) (2.6–17.0)	25 (8.6) (5.3–13.7)	36 (7.9) (4.9–12.3)
Non-Hispanic White	4 (8.7) (2.5–26.4)	6 (5.6) (1.9–15.8)	4 (5.9) (1.8–18.3)
Black	23 (27.1) (17.6–39.3)	25 (18.6) (10.6–30.3)	48 (22.9) (16.1–31.4)
Hispanic	12 (2.9) (1.4–6.0)	19 (6.4) (3.5–11.4)	31 (4.8) (3.0–7.7)
Other	5 (44.2)(19.6–71.9)	39 (26.2) (17.8–36.7)	44 (31.4) (20.6–44.8)
Non-US born	26 (16.8) (9.8–27.4)	70 (15.1) (10.7–20.7)	96 (15.9) (11.5–21.4)
US-born	18 (8.6) (5.5–13.3)	13 (5.4) (2.4–11.8)	31 (7.2) (4.7–10.9)
Age <25	4 (20.5) (5.5–53.4)	2 (2.9) (0.4–17.7)	6 (11.8) (3.5–32.9)
Age 25–44	11 (13.0) (6.6–24.0)	12 (6.9) (3.1–14.8)	23 (10.0) (5.8–16.8)
Age 45–64	18 (13.2) (5.9–26.9)	44 (15.2) (9.8–22.9)	68 (13.3) (9.3–18.6)
Age ≥65	11 (11.1) (4.2–26.5)	25 (25.0) (16.4–36.2)	36 (17.5) (10.5–27.8)

CI, confidence interval; HBc, hepatitis B core; LTBI, latent tuberculosis infection.

Hubbard, et al. *Eur J Gastro Hepatol*. 2021

Prevalence of Hepatitis B Virus and Latent Tuberculosis Co-Infection in the United States

- Aim: To evaluate patterns of HBV and LTBI testing and prevalence of HBV-LTBI co-infection in the US

- We retrospectively evaluated 2014–2020 U.S. national clinical laboratory data to analyze testing patterns for chronic HBV and LTBI and prevalence of HBV-LTBI co-infection

- Chronic HBV was defined as any combination of two positive HBV surface antigen, HBV e antigen, or detectable HBV DNA tests at least 6 months apart

- LTBI was defined as a positive QuantiFERON®-TB or T-SPOT®.TB test without evidence of active TB infection

Under Review

Overall LTBI and Chronic HBV Prevalence

- LTBI
  - Overall: 7.6%
  - Men: 8.2%, Women: 7.2%
  - Age < 18: 3.0%, Age 18-29: 4.6%, Age 30-49: 8.7%; Age 50-69: 10.2%, Age 70+: 11.2%
  - Non-Hispanic White: 6.4%, African American: 7.5%; Hispanic: 9.1%, Asian: 9.7%

- Chronic HBV
  - Overall: 0.51%
  - Men: 0.74%, Women: 0.38%
  - Age < 18: 0.15%, Age 18-29: 0.12%, Age 30-49: 0.62%; Age 50-69: 0.87%, Age 70+: 0.59%
  - Non-Hispanic White: 0.41%, African American: 0.45%; Hispanic: 0.50%, Asian: 1.33%

Under Review

	LTBI Testing in Chronic HBV Patients						
	Within 3 Months	Within 6 Months	Within 1 Year	Ever During Study Period	P-Value*	HBV-LTBI Co-Infection	P-Value#
Total (n=89,259)	5,248 (5.9%)	6,126 (6.9%)	7,132(8.0%)	**9,508 (10.7%)**		**1,865 (19.6%)**	
Men (n=46,258)	2,866 (6.2%)	3,353 (7.2%)	3,880 (8.4%)	**4,985 (10.8%)**	0.220	**975 (19.6%)**	0.859
Women (n=42,926)	2,379 (5.5%)	2,770 (6.5%)	3,247 (7.6%)	**4,517 (10.5%)**	Ref	**890 (19.7%)**	Ref
Age < 18 y (n=818)	53 (6.5%)	57 (7.0%)	65 (7.9%)	**83 (10.1%)**	0.002	**6 (7.2%)**	0.146
Age 18-29 y (n=6,606)	547 (8.3%)	622 (9.4%)	704 (10.7%)	**930 (14.1%)**	Ref	**118 (12.7%)**	Ref
Age 30-49 y (n=41,435)	2,471 (6.0%)	2,876 (6.9%)	3,345 (8.1%)	**4,457 (10.8%)**	<0.001	**803 (18.0%)**	<0.001
Age 50-69 y (n=34,784)	1,989 (5.7%)	2,342 (6.7%)	2,739 (7.9%)	**3,650 (10.5%)**	<0.001	**825 (22.6%)**	<0.001
Age ≥ 70 y (n=5,589)	185 (3.3%)	226 (4.0%)	274 (4.9%)	**383 (6.9%)**	<0.001	**113 (29.5%)**	<0.001
Non-Hispanic White (n=35,811)	1,915 (5.3%)	2,252 (6.3%)	2,626 (7.3%)	**3,480 (9.7%)**	Ref	**641 (18.4%)**	Ref
Black/African American (n=11,215)	889 (7.9%)	1,029 (9.2%)	1,186 (10.6%)	**1,515 (13.5%)**	<0.001	**269 (17.8%)**	0.576
Hispanic (n=21,280)	1,356 (6.4%)	1,572 (7.4%)	1,823 (8.6%)	**2,416 (11.4%)**	<0.001	**499 (20.7%)**	0.033
Asian American (n=16,709)	842 (5.0%)	986 (5.9%)	1,164 (7.0%)	**1,651 (9.9%)**	0.557	**377 (22.8%)**	<0.001
Other (n=3,128)	189 (6.0%)	218 (7.0%)	254 (8.1%)	**337 (10.8%)**	0.057	**72 (21.4%)**	0.185

Under Review

	HBV Testing in LTBI Patients						
	Within 3 Months	Within 6 Months	Within 1 Year	**Ever During Study Period**	P-Value	**HBV-LTBI Co-Infection**	P-Value
Total (n=394,817)	88,504 (22.4%)	96,094 (24.3%)	105,975 (26.8%)	**127,414 (32.3%)**		**1,865 (1.5%)**	
Men (n=170,196)	35,596 (20.9%)	38,228 (22.5%)	41,987 (24.7%)	**50,210 (29.5%)**	<0.001	**975 (1.9%)**	<0.001
Women (n=222,853)	52,228 (23.4%)	57,165 (25.7%)	63,261 (28.4%)	**76,441 (34.3%)**	Ref	**890 (1.2%)**	Ref
Age < 18 y (n=18,277)	1,844 (10.1%)	1,908 (10.4%)	2,003 (11.0%)	**2,271 (12.4%)**	<0.001	**6 (0.3%)**	0.054
Age 18-29 y (n=57,568)	14,919 (25.9%)	16,278 (28.3%)	17,680 (30.7%)	**20,387 (35.4%)**	Ref	**118 (0.6%)**	Ref
Age 30-49 y (n=147,099)	34,230 (23.3%)	37,315 (25.4%)	41,159 (28.0%)	**49,509 (33.7%)**	<0.001	**803 (1.6%)**	<0.001
Age 50-69 y (n=132,278)	30,006 (22.7%)	32,549 (24.6%)	36,275 (27.4%)	**44,668 (33.8%)**	<0.001	**825 (1.8%)**	<0.001
Age ≥ 70 y (n=38,681)	6,894 (17.8%)	7,425 (19.2%)	8,230 (21.3%)	**9,942 (25.7%)**	<0.001	**113 (1.1%)**	<0.001
Non-Hispanic White (n=156,344)	32,472 (20.8%)	35,094 (22.4%)	38,639 (24.7%)	**46,495 (29.7%)**	Ref	**641 (1.4%)**	Ref
Black/African American (n=60,036)	12,799 (21.3%)	13,856 (23.1%)	15,394 (25.6%)	**18,751 (31.2%)**	<0.001	**269 (1.4%)**	0.581
Hispanic (n=117,672)	29,446 (25.0%)	32,151 (27.3%)	35,387 (30.1%)	**42,202 (35.9%)**	<0.001	**499 (1.2%)**	0.001
Asian American (n=40,333)	9,607 (23.8%)	10,458 (25.9%)	11,572 (28.7%)	**13,980 (34.7%)**	<0.001	**377 (2.7%)**	<0.001
Other (n=13,678)	3,153 (23.1%)	3,417 (25.0%)	3,761 (27.5%)	**4,522 (33.1%)**	<0.001	**72 (1.6%)**	0.243

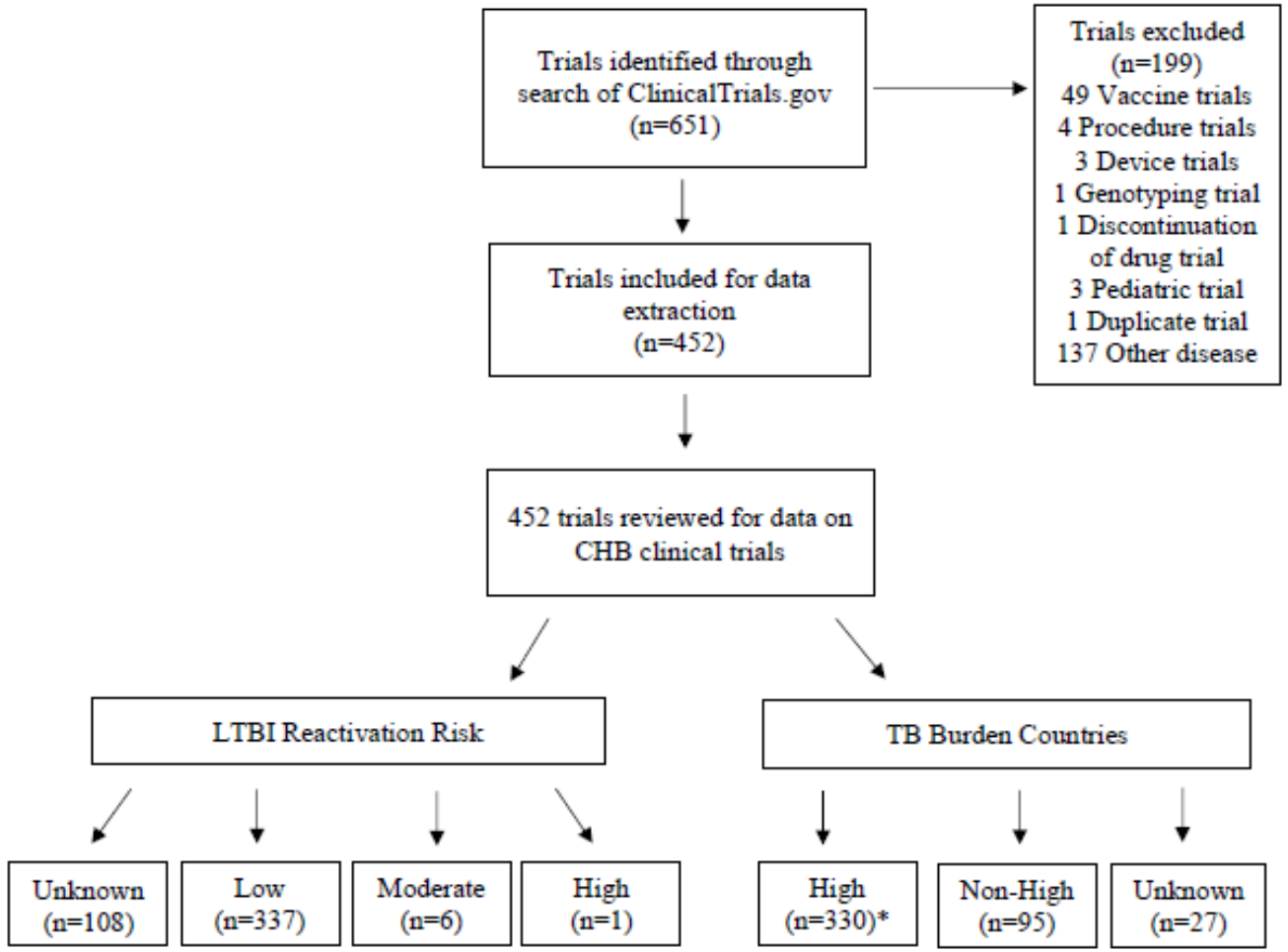
Screening Practices for Latent Tuberculosis Infection in Clinical Trials Evaluating Treatments for Chronic Hepatitis B Virus Infection

- Latent tuberculosis infection (LTBI) and chronic hepatitis B virus (CHB) virus co-infection prevalence is two times higher than LTBI prevalence in the general adult population

- Although newer CHB treatments evaluated in clinical trials modulate the immune system and potentially increase LTBI reactivation risk, it is unknown whether CHB clinical trials are screening for LTBI

- We describe LTBI screening practices in CHB clinical trials

Under Review



Of the 330 trials conducted in high TB burden countries, 252 were low, 5 were medium, 1 was high, and 27 were unknown TB risk for LTBI reactivation. Of the combined 78 trials conducted in a high TB burden country with moderate, high, and unknown LTBI reactivation, 19 were in China, 6 were in Taiwan, 3 were in Hong Kong, 3 were in Korea, 2 were in Bangladesh, 2 were in Moldova, 2 were in Russian Federation, 1 was in Singapore, and 40 were conducted in multiple Asia Pacific and Eastern Europe countries.

- Of 651 CHB clinical trials identified, 452 (69%) were included in the final cohort, among which 337 (75%), 108 (24%), and 7 (1%) evaluated CHB medications with a low, unknown, and moderate LTBI reactivation risk, respectively.
- A total of 330 (73.0%) CHB clinical trials reviewed were conducted in high TB burden countries.
- Three (0.6%) CHB trials reviewed screened for LTBI; one each among CHB treatments with low, moderate, and high LTBI reactivation risk.

Under Review

Main Findings from Review of LTBI Screening in Clinical Trials Evaluating Chronic Hepatitis B Virus Treatments

- Although nearly 75% of all CHB clinical trials were conducted in high TB burden countries and 25% of trials evaluated CHB treatments with an unknown LTBI reactivation risk, *less than 1% of trials screened for LTBI*

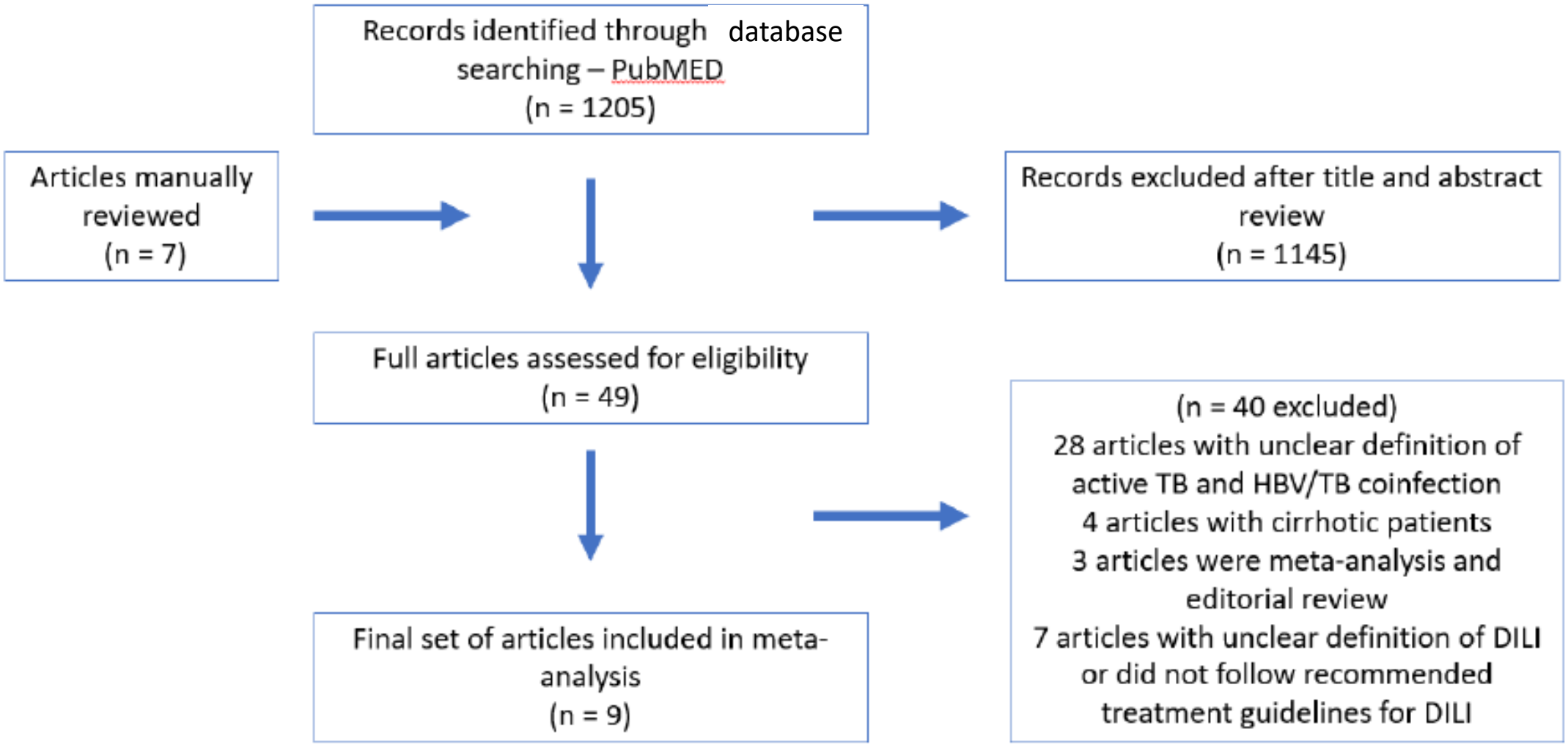
- Consideration should be given to screen for LTBI among CHB clinical trials given high prevalence of co-infection and potential for increased LTBI reactivation risk with CHB treatments evaluated

Risk of Drug-Induced Liver Injury in Patients with Chronic Hepatitis B and Active Tuberculosis Co-infection: A Systematic Review and Meta-Analysis

- Evaluate prevalence of drug-induced liver injury (DILI) among HBV-TB co-infected patients undergoing anti-TB therapy

- Determine whether HBV-TB co-infected patients have a higher risk of DILI compared to TB patients without HBV co-infection

Under Review



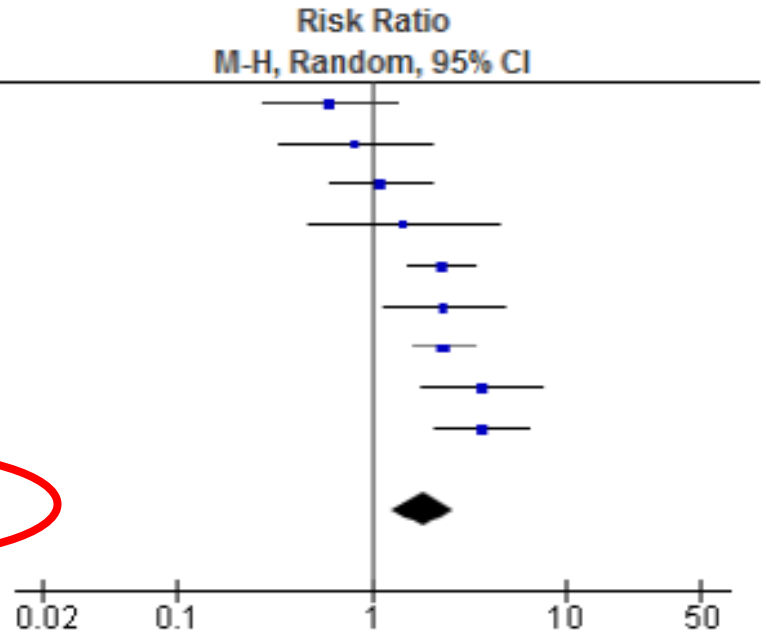
Under Review

Figure 2. Random effects meta-analysis model evaluating risk of DILI in HBV-TB co-infected patients vs. TB patients without HBV co-infection undergoing anti-TB therapies.

Study or Subgroup	HBV/TB Events	HBV/TB Total	TB only Events	TB only Total	Weight	Risk Ratio M-H, Random, 95% CI
Lee (2005)	9	110	13	97	9.6%	0.61 [0.27, 1.37]
Liu (2014)	5	75	32	392	8.5%	0.82 [0.33, 2.03]
Hwang (1997)	9	31	54	208	12.0%	1.12 [0.62, 2.03]
Chien (2009)	3	25	22	270	6.6%	1.47 [0.47, 4.58]
Sun (2016)	25	96	96	842	14.7%	2.28 [1.55, 3.36]
Lomtadze (2013)	5	12	49	276	10.6%	2.35 [1.15, 4.80]
Pan (2005)	26	47	40	170	14.8%	2.35 [1.62, 3.42]
Anand (2006)	9	24	13	128	10.4%	3.69 [1.78, 7.66]
Wong (2000)	15	43	26	276	12.6%	3.70 [2.14, 6.41]
Total (95% CI)		**463**		**2659**	**100.0%**	**1.85 [1.28, 2.68]**
Total events	106		345			

Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 25.99$, $df = 8$ ($P = 0.001$); $I^2 = 69\%$

Test for overall effect: $Z = 3.24$ ($P = 0.001$)



Under Review

Figure 3. Random effects meta-analysis model evaluating risk of DILI in HBV-TB co-infected patients vs. TB patients without HBV co-infection undergoing anti-TB therapies in prospective cohort studies only.

Study or Subgroup	HBV/TB Events	HBV/TB Total	TB only Events	TB only Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hwang (1997)	9	31	54	208	28.7%	1.12 [0.62, 2.03]
Sun (2016)	25	96	96	842	40.2%	2.28 [1.55, 3.36]
Lomtadze (2013)	5	12	49	276	8.4%	2.35 [1.15, 4.80]
Anand (2006)	9	24	13	128	8.4%	3.69 [1.78, 7.66]
Wong (2000)	15	43	26	276	14.3%	3.70 [2.14, 6.41]
Total (95% CI)		**206**		**1730**	**100.0%**	**2.28 [1.79, 2.90]**
Total events	63		238			

Heterogeneity: Chi² = 10.18, df = 4 (P = 0.04); I² = 61%
Test for overall effect: Z = 6.67 (P < 0.00001)

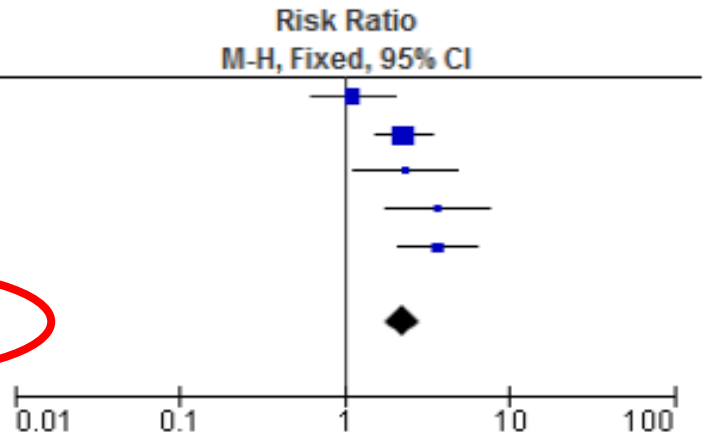
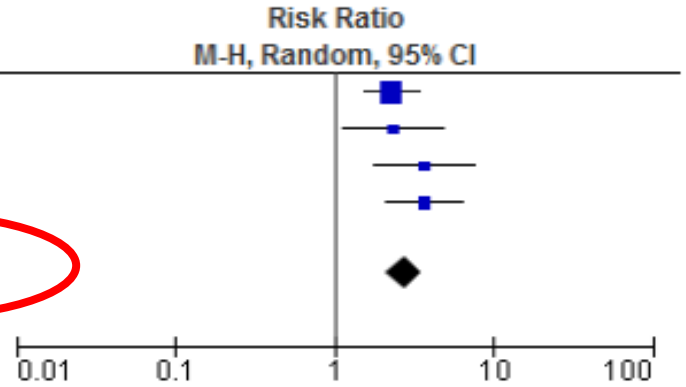


Figure 4. Random effects meta-analysis model evaluating risk of DILI in HBV-TB co-infected patients vs. TB patients without HBV co-infection undergoing anti-TB therapies in prospective cohort studies after year 2000.

Study or Subgroup	HBV/TB Events	HBV/TB Total	TB only Events	TB only Total	Weight	Risk Ratio M-H, Random, 95% CI
Sun (2016)	25	96	96	842	48.4%	2.28 [1.55, 3.36]
Lomtadze (2013)	5	12	49	276	14.1%	2.35 [1.15, 4.80]
Anand (2006)	9	24	13	128	13.6%	3.69 [1.78, 7.66]
Wong (2000)	15	43	26	276	24.0%	3.70 [2.14, 6.41]
Total (95% CI)		**175**		**1522**	**100.0%**	**2.75 [2.10, 3.59]**
Total events	54		184			

Heterogeneity: Tau² = 0.00; Chi² = 2.83, df = 3 (P = 0.42); I² = 0%
Test for overall effect: Z = 7.38 (P < 0.00001)



Ongoing Collaborations and Future Work

- VA and CHeCS HBV cohort to evaluate:
  - LTBI testing patterns among patients with chronic HBV
  - Prevalence of HBV-LTBI co-infection
  - Determine whether HBV-LTBI co-infection is associated with higher risk of TB medication related drug induced liver injury compared to LTBI patients without concurrent chronic HBV

- Kaiser Southern California to evaluate:
  - Chronic HBV cascade of care and treatment patterns
  - HBV-LTBI co-infection testing patterns and co-infection prevalence

- UCSF to utilize large national healthcare claims datasets to evaluate:
  - Testing patterns and prevalence of HBV-LTBI co-infection
  - Determine whether patients with HBV-LTBI co-infection are at increased risk of TB medication related drug-induced liver injury

Summary

- TB and CHB disproportionately impacts non-U.S.-born persons, especially Asians
- Prevalence of TB-CHB and LTBI-CHB is at least 2-fold higher among co-infected patients
- Nearly 33% of LTBI patients are tested for CHB in a large national laboratory database; while only ~11% of CHB patients are tested for LTBI
- Risk of DILI is 2-fold higher among TB-CHB co-infected patients compared to patients with TB only
- Reductions in TB and CHB morbidity and mortality may require healthcare provider-,system-, and policy-level interventions to improve the diagnostic and treatment cascade of care for LTBI and CHB