

Hepatitis B Virus and Latent Tuberculosis Co-Infection

Understanding Disease Prevalence and Outcomes

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SF Hep B Free - HBV-ECHO

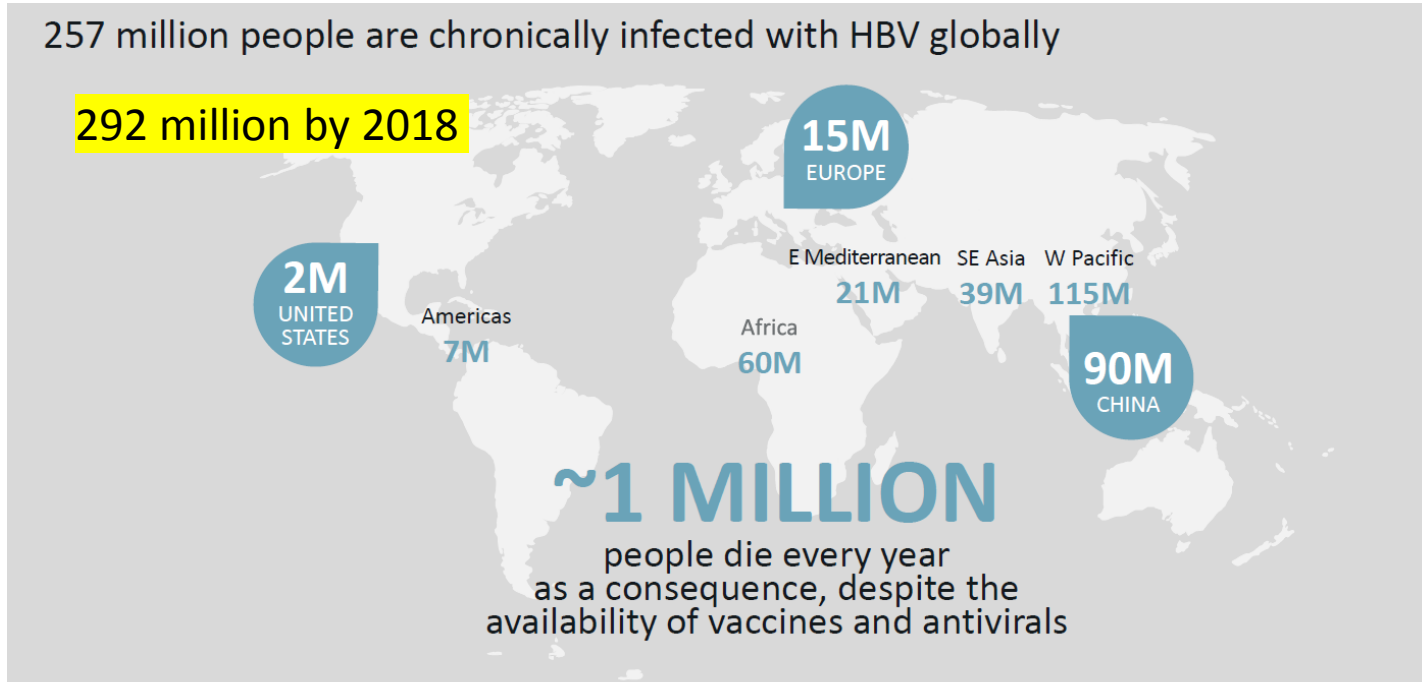
Disclosures

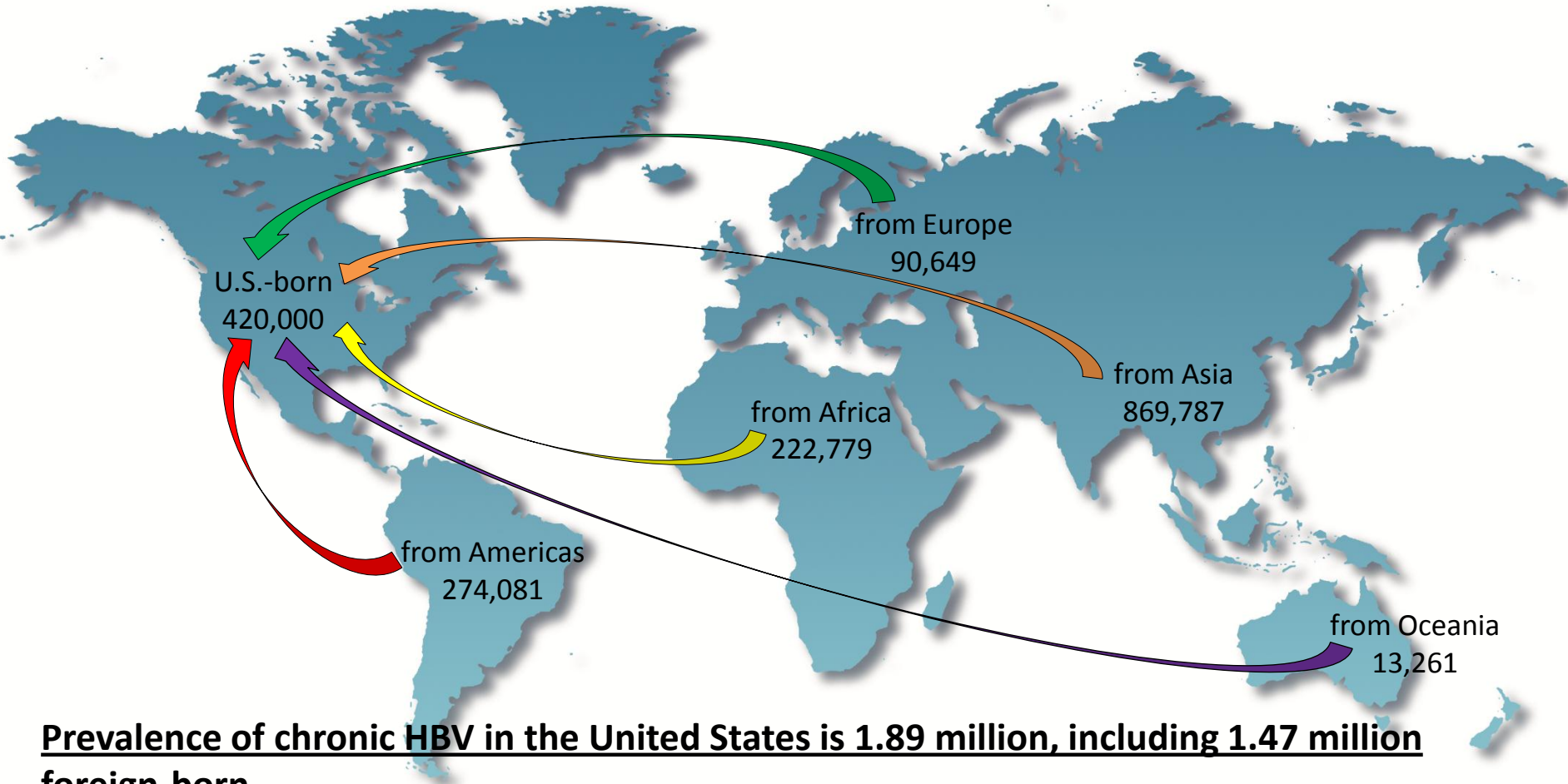
- No relevant disclosures

Objectives

- Understand prevalence of HBV-TB co-infection across world regions
- Identify existing gaps in our understanding of HBV-TB disease epidemiology
- Understand the clinical significance of timely and accurate identification of HBV-TB co-infection

Global Prevalence of HBV Infection





Prevalence of chronic HBV in the United States is 1.89 million, including 1.47 million foreign-born

Global Incidence of TB

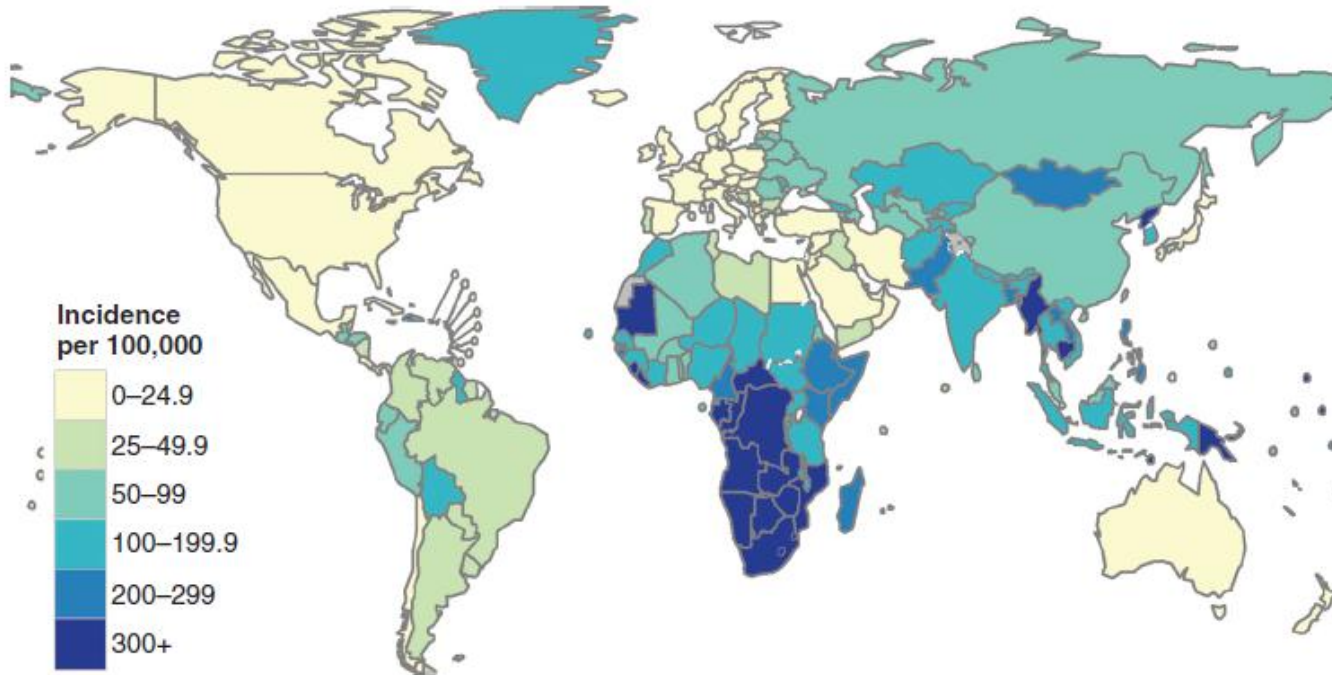
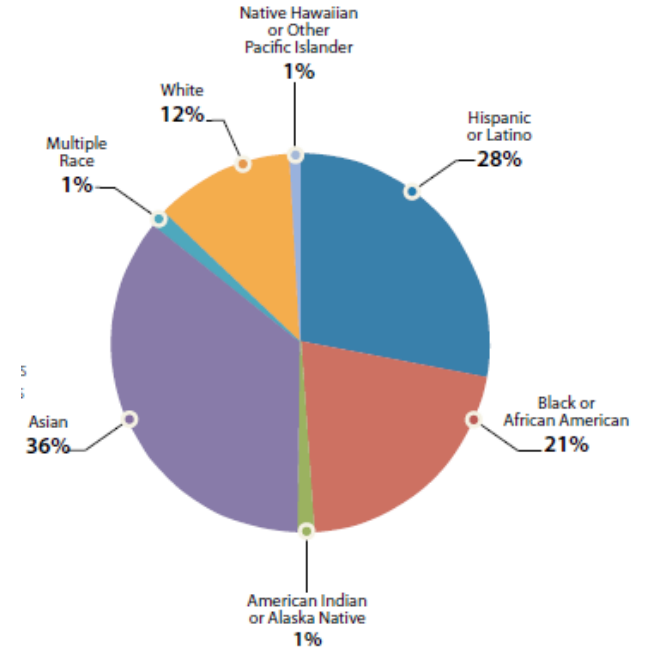
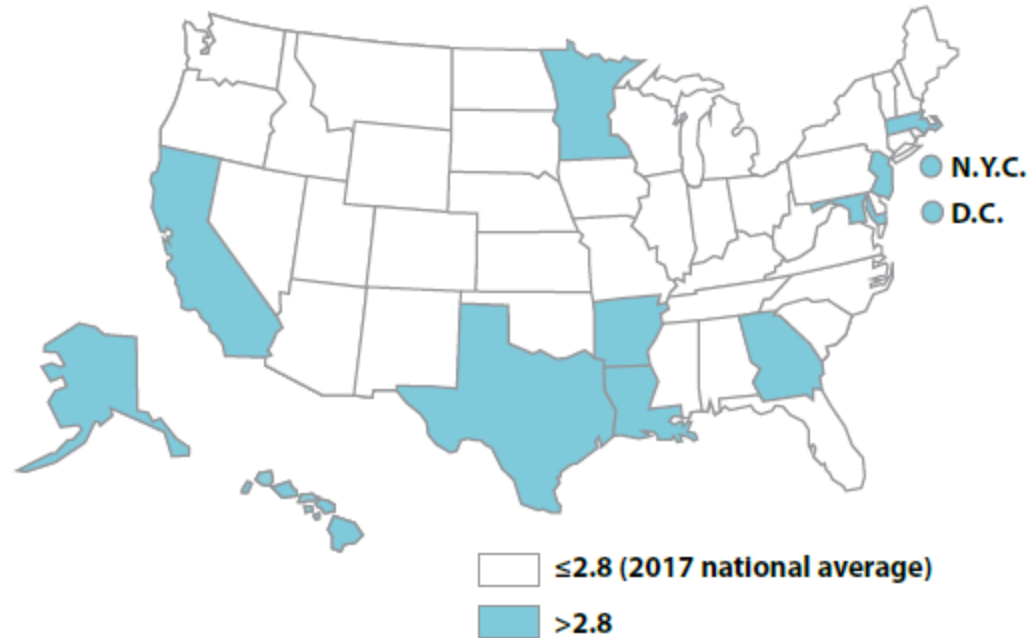


Figure 1. Estimated tuberculosis incidence rates per 100,000 population, 2012.

Epidemiology of TB in the U.S.



*Cases per 100,000

DC, District of Columbia; NYC, New York City (excluded from New York state)

Patients with HBV-TB co-infection are at higher risk of drug induced liver injury

Clinical Infectious Diseases

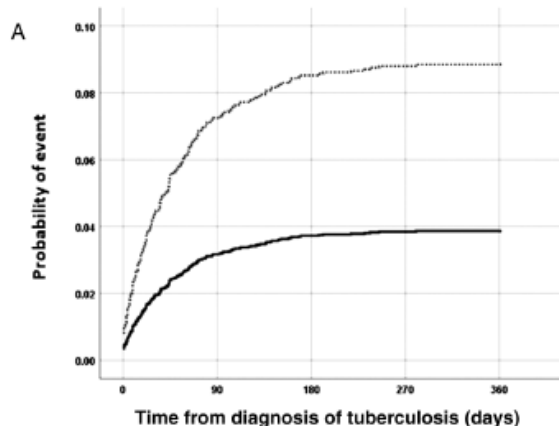
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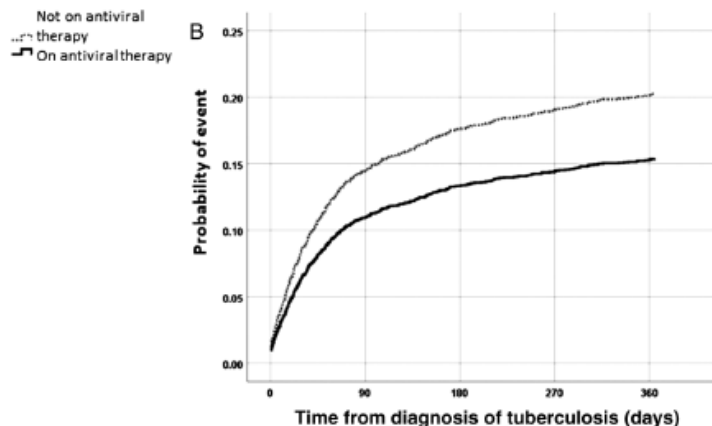
Antiviral Therapy for Hepatitis B Prevents Liver Injury in

Table 1. Baseline Clinical and Biochemical Characteristics of Patients With Tuberculosis–Hepatitis B Virus Coinfection at the Time of Tuberculosis Diagnosis

Characteristic	Patients on Antiviral Therapy (n = 488)	Patients Not on Antiviral Therapy (n = 3210)				
		All Patients Not on Antiviral Therapy (n = 3210)	P Value ^a	Patients Started Antiviral Therapy After Diagnosis of Tuberculosis (n = 446)	Untreated (n = 2764)	P Value ^b
Male	351 (73.7%)	2374 (74.0%)	.894	342 (77.0%)	2032 (73.5%)	.120
Age, y	52.9 ± 14.2	56.1 ± 16.9	<.001	55.1 ± 16.7	56.2 ± 16.9	.195
Presence of other liver disease ^c	21 (4.3%)	69 (2.1%)	.004	5 (1.1%)	64 (2.3%)	.107
Positive hepatitis B e antigen ^d	58 (20.3%)	277 (15.6%)	.045	69 (25.1%)	208 (13.8%)	<.001
Hepatitis B virus DNA (log IU/mL) ^e	2.18 (1.00, 5.68)	3.76 (2.20, 5.94)	<.001	5.47 (3.08, 7.07)	3.14 (1.98, 4.90)	<.001
Alanine transaminase (U/L)	27 (17, 44)	26 (16, 43)	.170	32 (20, 64)	25 (16, 41)	<.001
Total bilirubin (μmol/L)	10 (6, 16)	10 (7, 14)	.518	11 (7, 16)	10 (7, 14)	.005
Albumin (g/L)	34 ± 8	32 ± 7	<.001	33 ± 8	33 ± 7	.723
Platelet (×10 ⁹ /L)	19 (132, 268)	254 (190, 336)	<.001	220 (162, 297)	258 (196, 341)	<.001
Creatinine (μmol/L)	78 (62, 96)	75 (63, 91)	.162	74 (61, 89)	76 (63, 92)	.017



Number at risk	Day 0	Day 90	Day 180	Day 270	Day 360
On antiviral	488	336	315	309	302



Number at risk	Day 0	Day 90	Day 180	Day 270	Day 360
On antiviral	488	319	295	289	278

Table 2. Primary and Secondary Outcomes in Patients on Antiviral Therapy and Patients Not on Antiviral Therapy at the Time of Tuberculosis Diagnosis

Outcome	Patients on Antiviral Therapy (n = 488)	Patients Not on Antiviral Therapy (n = 3210)	Bivariable Cox Proportional Hazards Model			Multivariable Cox Proportional Hazards Model ^a		
	No. (%)	No. (%)	HR	95% CI	PValue	Adjusted HR	95% CI	PValue
Hospitalization due to drug-induced liver injury	18 (3.7)	222 (6.9)	0.53	.33–.86	.01	0.44	.26–.72	.001
Hospitalization due to drug-induced liver injury or alanine transaminase greater than 3 times the upper limit of normal	74 (15.2)	487 (15.2)	1.02	.80–1.30	.88	0.76	.58–.99	.038
Liver-related death	6 (1.2)	30 (0.9)	1.36	.57–3.27	.49	0.94	.36–2.44	.892
Tuberculosis-related deaths	3 (0.6)	53 (1.7)	0.38	.12–1.21	.1	0.48	.15–1.57	.226

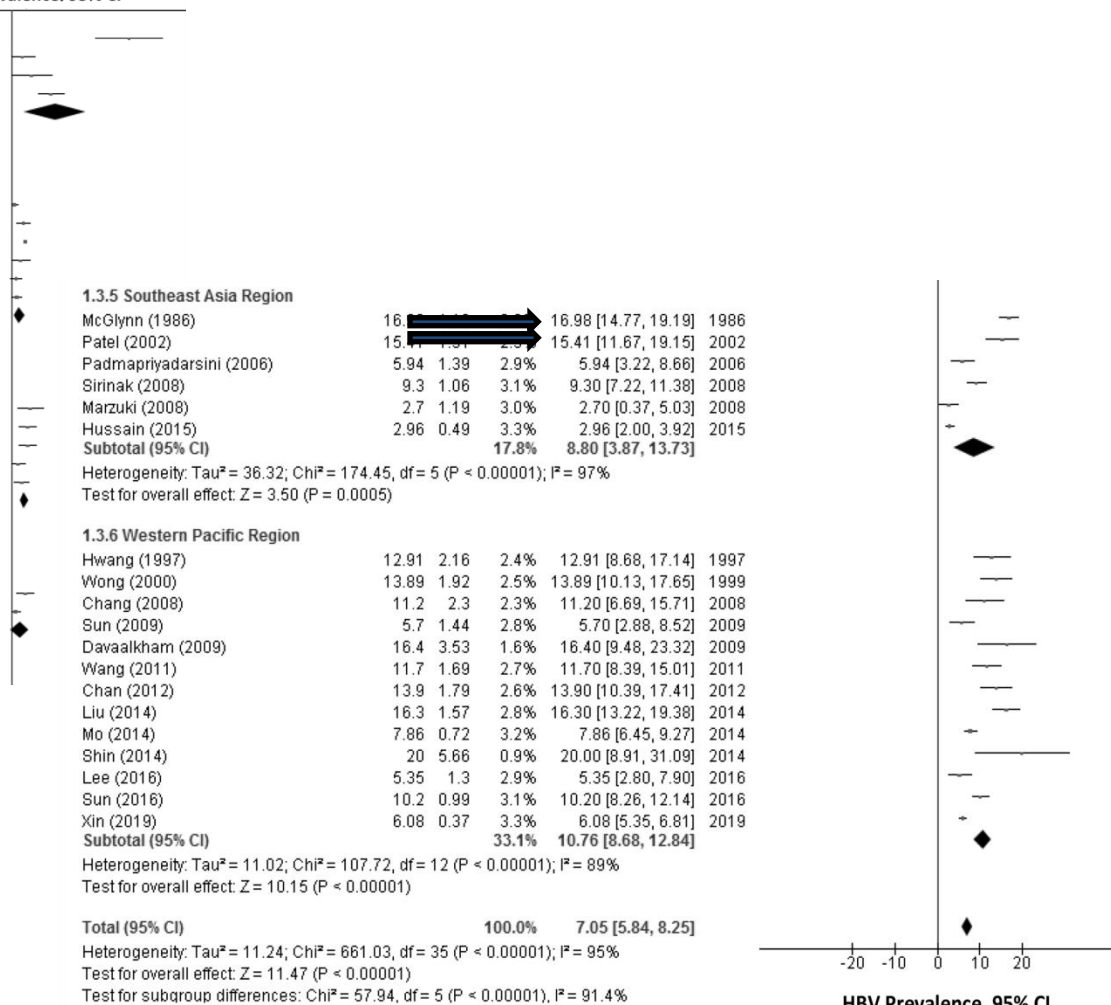
Estimating Global Prevalence of HBV-TB Co-Infection

- Systematic review and meta-analyses
- Pubmed from inception to September 1, 2019
- Aim: To evaluate the prevalence of chronic HBV among adults with latent or active TB infection

HBV Prevalence

Studies by Region	HBV Prevalence	SE	Weight	95% CI	Year
1.3.1 African Region					
Adebajo (1994)	30.63	4.38	1.2%	30.63 [22.05, 39.21]	1994
Makhlouf (2008)	3	1.53	2.8%	3.00 [0.00, 6.00]	2008
Shigidi (2012)	5.26	2.68	2.1%	5.26 [0.01, 10.51]	2012
Makuza (2019)	10.36	1.66	2.7%	10.36 [7.11, 13.61]	2019
Subtotal (95% CI)			8.8%	11.38 [3.45, 19.31]	
Heterogeneity: Tau ² = 58.24; Chi ² = 40.20, df = 3 (P < 0.00001); I ² = 93%					
Test for overall effect: Z = 2.81 (P = 0.005)					
1.3.2 Americas Region					
Cheung (2002)	0.81	0.74	0.0%	0.81 [0.01, 1.61]	2002
Aires (2012)	3.23	0.88	3.1%	3.23 [1.51, 4.95]	2012
Bushnell (2015)	3.68	0.19	2.3%	3.68 [3.31, 4.05]	2015
Araujo-Mariz (2016)	2.41	1.19	3.0%	2.41 [0.08, 4.74]	2016
Pelecias (2016)	1.39	0.71	3.2%	1.39 [-0.00, 2.78]	2016
Pouza (2019)	1.43	0.71	3.2%	1.43 [0.04, 2.82]	2019
Subtotal (95% CI)			19.2%	2.15 [0.78, 3.53]	
Heterogeneity: Tau ² = 2.44; Chi ² = 51.68, df = 5 (P < 0.00001); I ² = 90%					
Test for overall effect: Z = 3.07 (P = 0.002)					
1.3.3 Eastern Mediterranean Region					
Omer (1976)	5	1.72	2.7%	5.00 [1.63, 8.37]	1976
Kuniholm (2008)	4.3	1.17	3.0%	4.30 [2.01, 6.59]	2008
Lomtadze (2013)	4.29	1.12	3.0%	4.29 [2.09, 6.49]	2013
Merza (2016)	1.87	0.93	3.1%	1.87 [0.05, 3.69]	2016
Aljohaney (2018)	2.75	0.96	3.1%	2.75 [0.87, 4.63]	2018
Subtotal (95% CI)			14.9%	3.34 [2.22, 4.45]	
Heterogeneity: Tau ² = 0.37; Chi ² = 5.18, df = 4 (P = 0.27); I ² = 23%					
Test for overall effect: Z = 5.85 (P < 0.00001)					
1.3.4 European Region					
Nooredinvand (2015)	3.7	1.15	3.0%	3.70 [1.45, 5.95]	2015
Sewell (2015)	1.17	0.59	3.3%	1.17 [0.01, 2.33]	2015
Subtotal (95% CI)			6.3%	2.24 [-0.21, 4.69]	
Heterogeneity: Tau ² = 2.37; Chi ² = 3.83, df = 1 (P = 0.05); I ² = 74%					
Test for overall effect: Z = 1.79 (P = 0.07)					

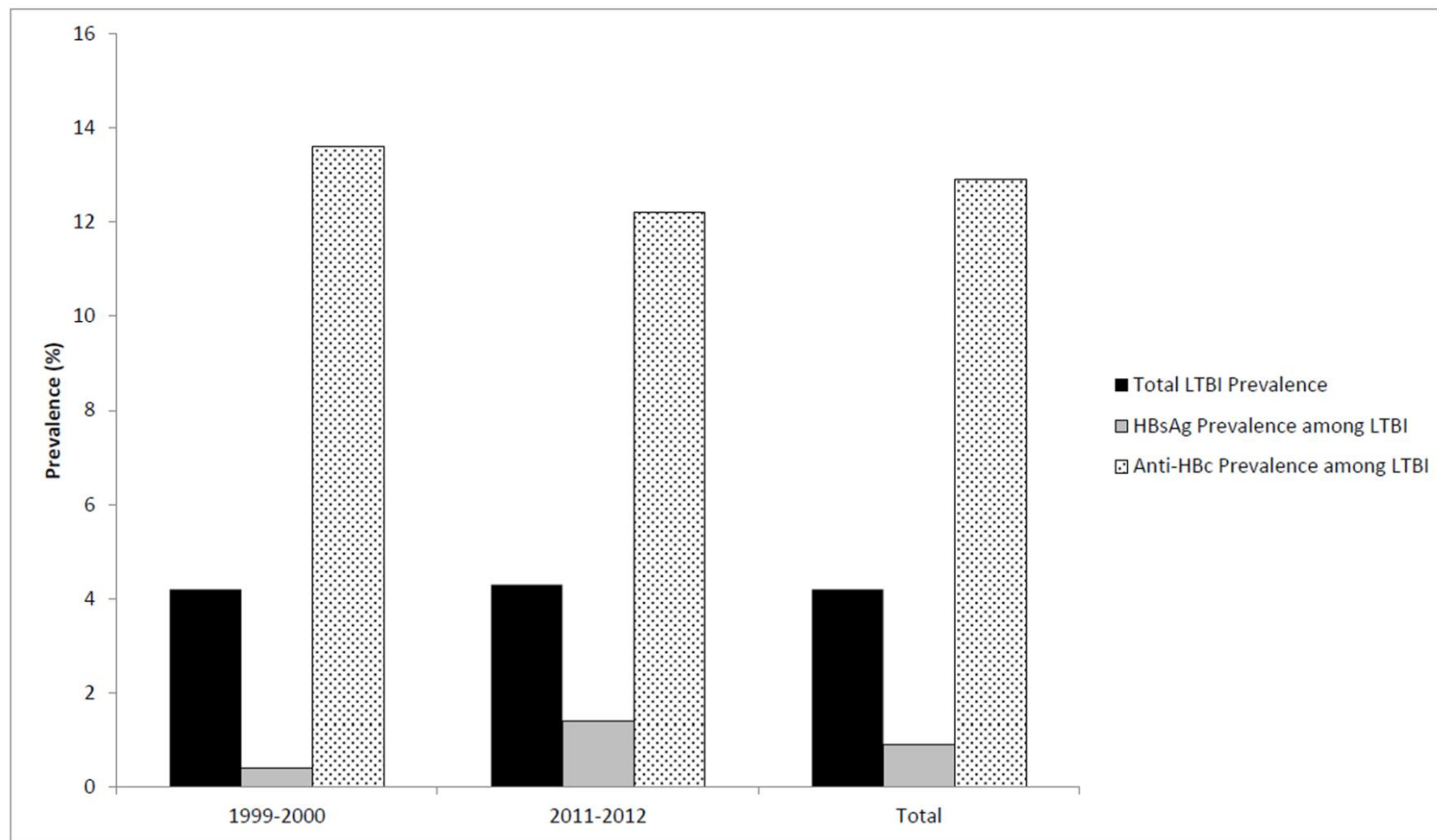
HBV Prevalence. 95% CI



Estimating HBV-TB Co-Infection - NHANES

- U.S. NHANES data
- Retrospective cross sectional study
- TB testing data collected 1999-2000 and 2011-2012
- TB testing included both TST and TB-QTF data
- Aim: Prevalence of HBsAg and anti-HBc among patients with positive TST/TB-QTF testing

Figure 1. Prevalence of HBsAg Positive and Anti-HBc Among Individuals with LTBI



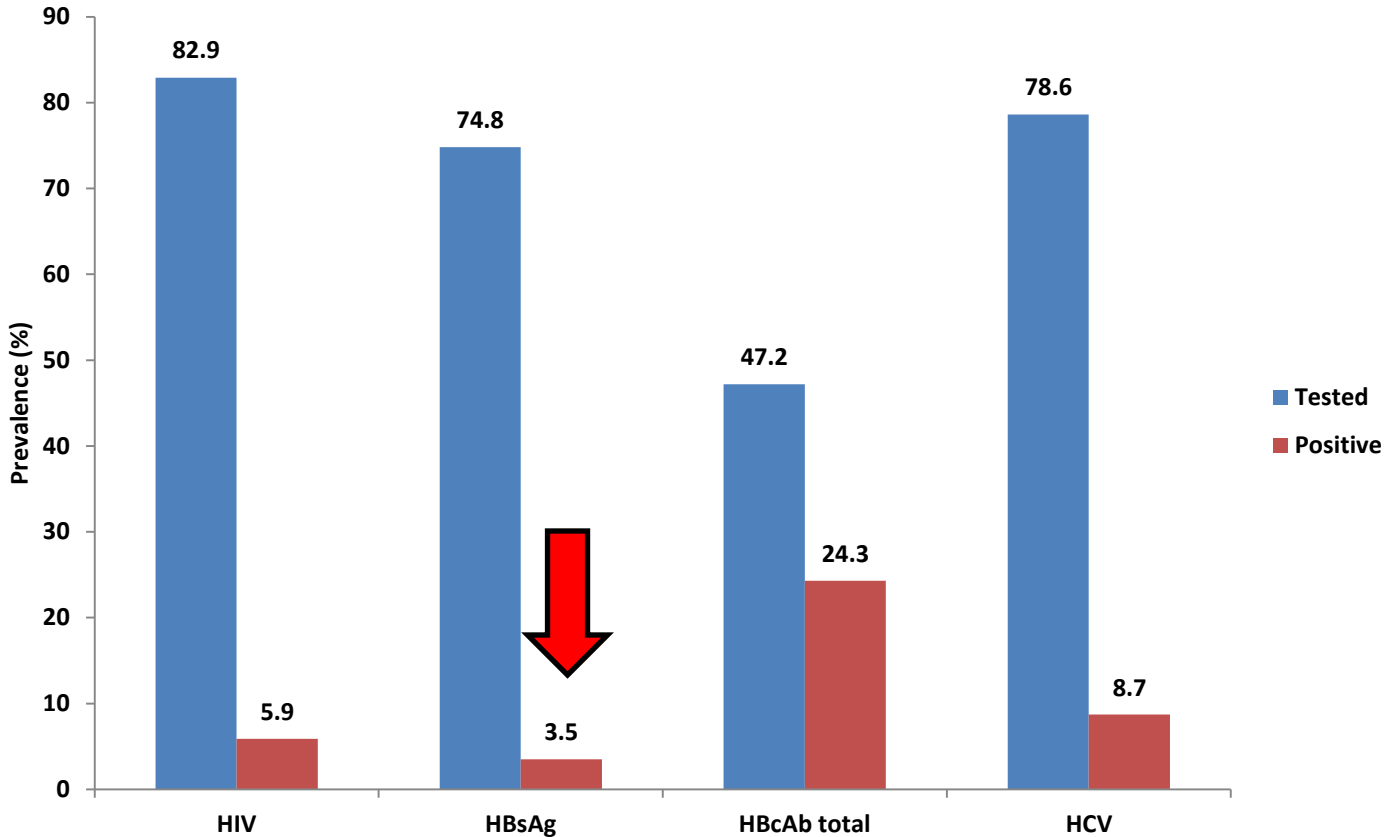
Preliminary Data – Single Center Safety-Net

- Highland Hospital
- Retrospective observational study
- Sept 2016 – May 2019
- Aim: Evaluate prevalence of HBV among patients with positive TB-QTF testing among adults

Results

- 453 adults with positive QFT (12 with active TB and 441 with latent TB)
- 56.5% were female, 43.5% male
- Mean age was 53.6 +/- 14.8 years
- Race/Ethnicity: 40.7% Hispanic, 29.3% African American, 16.6% Asian, 1.6% white, and 11.8% identified as “Other” race/ethnicity

Testing and Prevalence Among TB-QTF Positive Patients



Estimating HBV-TB Co-Infection

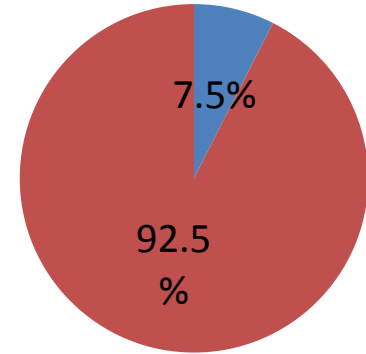
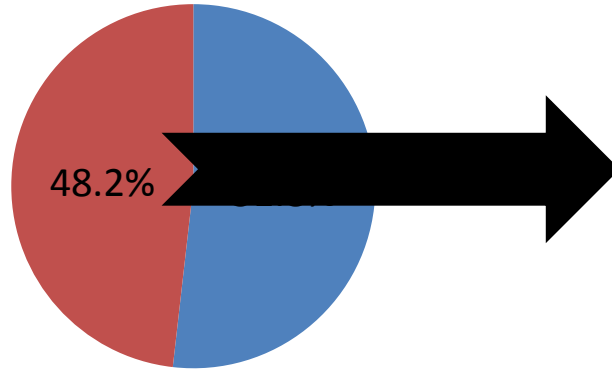
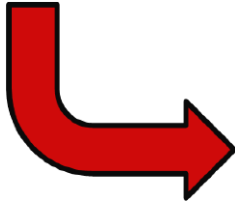
Prevalence in the U.S.

- Preliminary data using U.S. national laboratory data from 2015 – 2020
- Chronic HBV defined as any 2 positive HBV tests (HBsAg, HBV DNA, HBeAg pos) at least 6 months apart
- TB identified by any positive of Quantiferon, T-Spot, positive Mycobacteria culture

■ Tested for HBV ■ Not Tested

■ HBV positive ■ HBV Negative

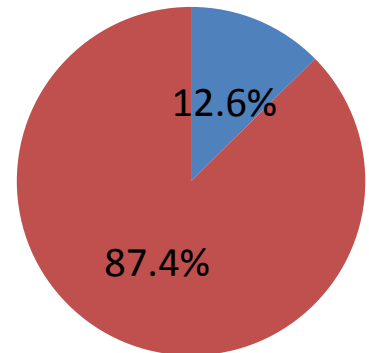
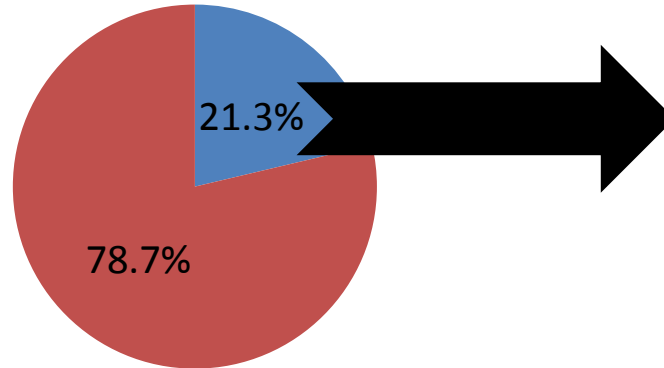
442,646 TB patients



117,684 chronic HBV patients

■ Tested for TB ■ Not Tested

■ TB Positive ■ TB Negative



Take Home Points

- Patients with TB have higher prevalence of HBV than general population
- Sub-optimal screening for HBV-TB co-infection
- Patients with underlying chronic HBV have higher risk of anti-TB medication related drug induced liver injury
- Early identification of HBV-TB co-infection may guide changes in TB and HBV management to reduce risk of drug induced liver injury
- Need to improve awareness of HBV-TB co-infection and improve screening especially given that populations most affected are ethnic minorities and underserved, vulnerable populations.

Thank You