

Supplementary information

Patient Biochemistry and Treatment Need in Chronic Hepatitis B Virus Infection Across Three

Continents: Retrospective Cross-Sectional Cohort Studies

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Supplementary Methods

United States: The study was a retrospective cross-sectional analysis of electronic health record (EHR) data. Patients with chronic hepatitis B virus (HBV) infection were identified between January 1, 2010 and January 1, 2016 and this period was considered as the disease index date. Characteristics of patients at the disease index date were described, with the baseline period defined as the 1-year (365 days) period prior to the index date (unless stated otherwise).

United Kingdom: The study was a retrospective cross-sectional analysis of EHR data. Patients with chronic HBV infection were identified between January 1, 2015 and December 31, 2015 with the first evidence of chronic HBV infection in 2015 being considered the disease index date for each patient. Characteristics of patients at the disease index date were described, with the baseline period defined as the 1-year (365 days) period prior to the index date.

Hong Kong: The study was a retrospective cross-sectional analysis of EHR data. Patients with chronic HBV infection were identified between January 1, 2017 and December 31, 2017, with first evidence of chronic HBV infection within 2017 being considered the disease index date for each patient. Characteristics of patients at the disease index date were described, with the baseline period defined as the 5-year period prior to the disease index date.

Fuzhou, China: The study was a retrospective cross-sectional analysis of EHR data. Patients with chronic HBV infection were identified between January 1, 2017 and December 31, 2017, with the first record of chronic HBV infection within 2017 being considered as the disease index date for each patient. Characteristics of patients at disease index was described, with a 12-month baseline period prior to the disease index date.

Supplementary Table 1. Patient disposition categorized by age group for US, UK, Hong Kong, and Fuzhou

Age group	United States		United Kingdom	Hong Kong		Fuzhou, China	
	All	Included	Included	All	Included	All	Included
<1 year	0	0	0	<5 (<0.01)	<5 (<0.01)	6 (0.02)	6 (0.03)
1–<2 years	1 (0.01)	1 (0.01)	0	<5 (<0.01)	<5 (<0.01)	5 (0.01)	5 (0.02)
2–<12 years	27 (0.2)	27 (0.2)	3 (0.6)	39 (0.1)	39 (0.1)	188 (0.5)	81 (0.4)
12–<18 years	35 (0.3)	29 (0.2)	1 (0.2)	61 (0.2)	61 (0.2)	305 (0.8)	121 (0.6)
18–<50 years	4,267 (30.5)	3,710 (29.4)	318 (63.2)	11,337 (33.2)	11,337 (33.2)	28,962 (74)	15,182 (70.2)
50–<65 years	4,510 (32.2)	4,036 (32)	143 (28.4)	14,273 (41.8)	14,273 (41.8)	7,804 (19.9)	4,892 (22.6)
≥65 years	5,154 (36.8)	4,811 (38.1)	38 (7.6)	8,419 (24.7)	8,419 (24.7)	1,855 (4.7)	1,327 (6.1)
Total	13,994	12,614	503	34,135	34,135	39,125	21,614

UK, United Kingdom; US, United States.

Supplementary Table 2. Patient characteristics, by patient age and index treatment status, for complete and missing laboratory data. *Ad hoc* analysis

Test	Age/Treatment	US		UK		Hong Kong		Fuzhou, China	
		Complete	Missing	Complete	Missing	Complete	Missing	Complete	Missing
HBsAg	<18 yr - Treated	0	0	0	0	10 (0.1)	0	33 (0.3)	14 (0.2)
	<18 yr - Untreated	37 (0.6)	20 (0.3)	2 (0.6)	2 (1.4)	45 (0.3)	0	91 (0.7)	75 (0.8)
	18-<65 yr - Treated	934 (14.9)	699 (11)	45 (12.5)	24 (16.8)	3573 (22.5)	301 (25.2)	5709 (45.4)	4334 (47.9)
	18-<65 yr - Untreated	3250 (51.8)	2863 (45.2)	286 (79.4)	106 (74.1)	8536 (53.8)	459 (38.4)	6074 (48.3)	3957 (43.8)
	65+ yr - Treated	361 (5.8)	251 (4)	7 (1.9)	4 (2.8)	1317 (8.3)	214 (17.9)	265 (2.1)	357 (3.9)
	65+ yr - Untreated	1692 (27)	2507 (39.5)	20 (5.6)	7 (4.9)	2392 (15.1)	221 (18.5)	402 (3.2)	303 (3.4)
	Total	6274 (49.7)	6340 (50.3)	360 (71.6)	143 (28.4)	15873 (93.0)	1195 (7.0)	12574 (58.2)	9040 (40.8)
HBeAg	<18 yr - Treated	0	0	0	0	10 (0.1)	0	31 (0.3)	16 (0.1)
	<18 yr - Untreated	18 (0.5)	39 (0.4)	2 (0.5)	2 (1.4)	31 (0.3)	14 (0.2)	78 (0.7)	88 (0.8)
	18-<65 yr - Treated	779 (20.1)	854 (9.8)	54 (14.8)	15 (10.8)	3266 (31.4)	608 (9.1)	5606 (52)	4437 (40.9)
	18-<65 yr - Untreated	1878 (48.5)	4235 (48.4)	280 (76.9)	112 (80.6)	4912 (47.3)	4083 (61.1)	4592 (42.6)	5439 (50.2)
	65+ yr - Treated	305 (7.9)	307 (3.5)	8 (2.2)	3 (2.2)	1089 (10.5)	442 (6.6)	249 (2.3)	373 (3.4)
	65+ yr - Untreated	889 (23)	3310 (37.9)	20 (5.5)	7 (5)	1077 (10.4)	1536 (23)	221 (2.1)	484 (4.5)
	Total	3869 (30.7)	8745 (69.3)	364 (72.4)	139 (27.6)	10385 (60.8)	6683 (39.2)	10777 (49.9)	10837 (50.1)
ALT	<18 yr - Treated	0	0	0	0	10 (0.1)	0	39 (0.2)	8 (0.1)
	<18 yr - Untreated	46 (0.4)	11 (2.1)	3 (0.7)	1 (1.9)	44 (0.3)	1 (0.2)	123 (0.8)	43 (0.8)
	18-<65 yr - Treated	1576 (13)	57 (10.9)	63 (14)	6 (11.3)	3849 (23.2)	25 (5.4)	7312 (45.6)	2731 (49.1)
	18-<65 yr - Untreated	5777 (47.8)	336 (64.1)	353 (78.4)	39 (73.6)	8572 (51.6)	423 (92.2)	7661 (47.7)	2370 (42.6)
	65+ yr - Treated	590 (4.9)	22 (4.2)	9 (2)	2 (3.8)	1531 (9.2)	0	428 (2.7)	194 (3.5)
	65+ yr - Untreated	4101 (33.9)	98 (18.7)	22 (4.9)	5 (9.4)	2603 (15.7)	10 (2.2)	484 (3)	221 (4)
	Total	12090 (95.8)	524 (4.2)	450 (89.5)	53 (10.5)	16609 (97.3)	459 (2.7)	16047 (74.2)	5567 (25.8)

Test	Age/Treatment	US		UK		Hong Kong		Fuzhou, China	
		Complete	Missing	Complete	Missing	Complete	Missing	Complete	Missing
DNA	<18 yr - Treated	0	0	0	0	1 (0)	9 (0.1)	34 (0.2)	13 (0.2)
	<18 yr - Untreated	15 (0.2)	42 (0.7)	2 (0.7)	2 (1)	1 (0)	44 (0.3)	106 (0.7)	60 (0.9)
	18-<65 yr - Treated	1349 (21.7)	284 (4.4)	46 (15.1)	23 (11.6)	526 (25.7)	3348 (22.3)	6983 (47.6)	3060 (44.1)
	18-<65 yr - Untreated	2917 (46.9)	3196 (50)	231 (75.7)	161 (81.3)	1189 (58.1)	7806 (52)	6830 (46.5)	3201 (46.1)
	65+ yr - Treated	511 (8.2)	101 (1.6)	9 (3)	2 (1)	142 (6.9)	1389 (9.2)	382 (2.6)	240 (3.5)
	65+ yr - Untreated	1427 (22.9)	2772 (43.3)	17 (5.6)	10 (5.1)	187 (9.1)	2426 (16.1)	340 (2.3)	365 (5.3)
	Total	6219 (49.3)	6395 (50.7)	305 (60.6)	198 (39.4)	2046 (12)	15022 (88)	14675 (67.9)	6939 (32.1)
Any lab	<18 yr - Treated	0	0	0	0	1 (0)	9 (0.1)	26 (0.3)	21 (0.2)
	<18 yr - Untreated	8 (0.3)	49 (0.5)	2 (0.8)	2 (0.8)	1 (0)	44 (0.3)	72 (0.7)	94 (0.8)
	18-<65 yr - Treated	615 (22.8)	1018 (10.3)	27 (10.8)	42 (16.6)	516 (25.7)	3358 (22.3)	5361 (53.4)	4682 (40.4)
	18-<65 yr - Untreated	1276 (47.3)	4837 (48.8)	203 (81.2)	189 (74.7)	1175 (58.4)	7820 (51.9)	4198 (41.8)	5833 (50.4)
	65+ yr - Treated	250 (9.3)	362 (3.7)	4 (1.6)	7 (2.8)	138 (6.9)	1393 (9.3)	228 (2.3)	394 (3.4)
	65+ yr - Untreated	551 (20.4)	3648 (36.8)	14 (5.6)	13 (5.1)	180 (9)	2433 (16.2)	149 (1.5)	556 (4.8)
	Total	9914 (78.6)	2700 (21.4)	253 (50.3)	250 (49.7)	15057 (88.2)	2011 (11.8)	11580 (53.6)	10034 (46.4)

Column percentages for strata; row percentages for totals.

ALT, alanine aminotransferase; DNA, deoxyribonucleic acid; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; UK, United Kingdom; US, United States.

Supplementary Table 3. Selected characteristics of patients excluded from treatment analysis

Exclusion reason	United States		United Kingdom		Hong Kong		Fuzhou, China	
	N	% [95% CI]	N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
HBsAg –ve	2,956	87.4 [86.2–88.5]	0	0	185	74.3 [68.4–79.6]	354	62.8 [58.6–66.8]
<18 years	57	1.7 [1.3–2.2]	4	57.1 [18.4–90.1]	55	22.1 [17.1–27.8]	213	37.8 [33.8–41.9]
HCV+untreated+fibrosis	396	11.7 [10.6–12.8]	2	28.6 [3.7–71.1]	6	2.4 [0.9–5.2]	6	1.1 [0.4–2.3]
HCV+untreated+cirrhosis	595	17.6 [16.3–18.9]	1	14.3 [0.4–57.9]	12	4.8 [2.5–8.3]	5	0.9 [0.3–2.1]
HCV+untreated+ALT ≥2 ULN	92	2.7 [2.2–3.3]	1	14.3 [0.4–57.9]	3	1.2 [0.3–3.5]	0	0
Multiple	495	14.6 [13.5–15.9]	1	14.3 [0.4–57.9]	10	4.02 [1.9–7.3]	14	2.5 [1.4–4.1]
Total	3,383		7		249		564	

ALT alanine aminotransferase; CI, confidence interval; HBsAg -ve, negative for hepatitis B surface antigen; HCV, hepatitis C virus; ULN, upper limit of normal.

Supplementary Table 4. Characteristics of patients with chronic HBV infection according to treatment status at disease index in the a) US, b) UK, c) Hong Kong, and d)

Fuzhou

a) United States

Metric	Value	Treated		Untreated-but-indicated for treatment		Untreated-and-not-indicated for treatment	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
Age Group	18–<50	695	35.75 [33.62–37.93]	433	27.01 [24.85–29.26]	1,857	32.67 [31.45–33.91]
	50–<65	775	39.87 [37.68–42.08]	448	27.95 [25.76–30.21]	1,689	29.71 [28.53–30.92]
	65+	474	24.38 [22.49–26.35]	722	45.04 [42.58–47.51]	2,138	37.61 [36.35–38.89]
Coinfection	Both	41	2.11 [1.52–2.85]	0	0	22	0.39 [0.24–0.59]
	HCV	104	5.35 [4.39–6.45]	14	0.87 [0.48–1.46]	299	5.26 [4.69–5.87]
	HIV	246	12.65 [11.21–14.21]	58	3.62 [2.76–4.65]	158	2.78 [2.37–3.24]
	None	1,553	79.89 [78.03–81.65]	1,531	95.51 [94.38–96.47]	5,205	91.57 [90.82–92.28]
Fibrosis/Cirrhosis	Yes	583	29.99 [27.96–32.08]	1,035	64.57 [62.17–66.91]	0	0
	No	1,361	70.01 [67.92–72.04]	568	35.43 [33.09–37.83]	5,684	100
Treated	INFs	0	0	0	0	0	0
	NAs	1,944	100	0	0	0	0
	NAs+INFs	0	0	0	0	0	0
	None	0	0	1,603	100	5684	100

Metric	Value	Treated		Untreated-but-indicated for treatment		Untreated-and-not-indicated for treatment	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
HBsAg	Positive	994	51.13 [48.88–53.38]	629	39.24 [36.84–41.68]	1,647	28.98 [27.8–30.17]
	Indeterminate	0	0	0	0	0	0
	Missing	950	48.87 [46.62–51.12]	974	60.76 [58.32–63.16]	4,037	71.02 [69.83–72.2]
HBeAg	Positive	274	14.09 [12.58–15.72]	115	7.17 [5.96–8.55]	72	1.27 [0.99–1.59]
	Negative	622	32 [29.93–34.12]	480	29.94 [27.71–32.25]	1,230	21.64 [20.58–22.73]
	Indeterminate	0	0	0	0	0	0
	Missing	1,048	53.91 [51.66–56.14]	1,008	62.88 [60.46–65.25]	4,382	77.09 [75.98–78.18]
HBV DNA	≥20,000 IU/mL	108	5.56 [4.54–6.57]	596	37.18 [34.81–39.55]	0	0
	2,000–<20,000 IU/mL	38	1.95 [1.39–2.67]	61	3.81 [2.92–4.86]	664	11.68 [10.86–12.55]
	<2,000 IU/mL	148	7.61 [6.47–8.88]	102	6.36 [5.22–7.67]	782	13.76 [12.87–14.68]
	Detectable without count	32	1.65 [1.13–2.32]	17	1.06 [0.62–1.69]	41	0.72 [0.52–0.98]
	Undetectable	1,292	66.46 [64.31–68.56]	213	13.29 [11.66–15.05]	864	15.2 [14.28–16.16]
	Uncertain	0	0	0	0	0	0
	Missing	326	16.77 [15.13–18.51]	614	38.3 [35.92–40.73]	3,333	58.64 [57.35–59.92]

Metric	Value	Treated		Untreated-but-indicated for treatment		Untreated-and-not-indicated for treatment	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
ALT ULN	≥5 ULN	13	0.67 [0.36–1.14]	39	2.43 [1.74–3.31]	0	0
	2–<5 ULN	71	3.65 [2.86–4.58]	145	9.05 [7.69–10.56]	0	0
	1–<2 ULN	223	11.47 [10.09–12.97]	236	14.72 [13.02–16.55]	493	8.67 [7.95–9.44]
	≤1 ULN	1,563	80.4 [78.57–82.14]	1,138	70.99 [68.7–73.2]	4,946	87.02 [86.11–87.88]
	Missing	74	3.81 [3–4.76]	45	2.81 [2.05–3.74]	245	4.31 [3.8–4.87]
Total		1,944		1,603		5,684	

b) United Kingdom

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
Age Group	18–<50	46	57.50 [45.94–68.49]	63	70.00 [59.43–79.21]	208	63.80 [58.33–69.03]
	50–<65	23	28.75 [19.18–39.95]	19	21.99 [13.21–30.99]	99	30.37 [25.42–35.68]
	≥65	11	13.75 [7.07–23.27]	8	8.89 [3.92–16.77]	19	5.83 [3.55–8.95]
Coinfection	Both	0	0	0	0	0	0
	HCV	1	1.25 [0.03–6.77]	0	0	0	0
	HIV	1	1.25 [0.03–6.77]	1	1.11 [0.03–6.04]	0	0
	None	78	97.50 [91.26–99.70]	89	98.89 [93.96–99.97]	326	100
Fibrosis/Cirrhosis	Yes	49	61.25 [49.70–71.94]	60	66.70 [55.95–76.26]	0	0
	No	31	38.75 [28.06–50.30]	30	33.33 [23.74–44.05]	326	100
Treated	INFs	3	3.75 [0.78–10.57]	0	0	0	0
	NAs	75	93.75 [86.01–97.94]	0	0	0	0
	NAs+INFs	2	2.50 [0.30–8.74]	0	0	0	0
	None	0	0	23	100	326	100

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
HBsAg	Positive	52	65.00 [53.52–75.33]	67	74.44 [64.16–83.06]	236	72.39 [67.20–77.18]
	Indeterminate	0	0	0	0	0	0
	Missing	28	35.00 [24.67–46.48]	23	25.56 [16.94–35.84]	90	27.61 [22.82–32.8]
HBeAg	Positive	12	15.00 (8.00–24.74)	12	13.33 [7.08–22.13]	13	3.99 [2.14–6.72]
	Negative	50	62.5 (50.96–73.08)	53	58.89 [48.02–69.16]	219	67.18 [61.79–72.25]
	Indeterminate	0	0	0	0	0	0
	Missing	18	22.50 (13.91–33.21)	25	27.78 [18.85–38.22]	94	28.83 [23.98–34.08]
HBV DNA	≥1,000,000 IU/mL	2	2.5 (0.30–8.74)	7	7.78 [3.18–15.37]	0	0
	≥20,000 IU/mL	0	0	0	0	0	0
	20,000–<1000 IU/mL	5	6.25 (2.06–13.99)	13	14.44 [7.92–23.43]	0	0
	2,000–<20,000 IU/mL	7	8.75 (3.59–17.20)	5	5.56 [1.83–12.49]	43	13.19 [9.71–17.35]
	<2,000 IU/mL	39	48.75 (37.41–60.19)	33	36.67 [26.75–47.49]	145	44.48 [39.00–50.06]
	Detectable without count	0	0	0	0	0	0
	Undetectable	2	2.50 (0.30–8.74)	0	0	0	0
	Uncertain	0	0	0	0	0	0
	Missing	25	31.25 (21.35–42.59)	32	35.56 [25.74–46.35]	138	42.33 [36.91–47.9]

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
ALT ULN	≥5 ULN	0	0	3	3.33 [0.69–9.43]	0	0
	2–<5 ULN	5	6.25 (2.06–13.99)	28	31.33 [21.77–41.74]	0	0
	1–<2 ULN	21	26.35 (17.04–37.29)	23	25.56 [16.94–35.84]	65	19.94 [15.74–24.69]
	≤1 ULN	46	57.5 (45.94–68.49)	27	30.00 [20.79–40.57]	226	69.33 [64.01–74.29]
	Missing	8	10.00 (4.42–18.76)	9	4.68 [4.68–18.14]	35	10.74 [7.59–14.61]
Total		80		90		326	

c) Hong Kong

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
Age Group	18–<50	1,383	25.92 (24.75–27.12)	608	28.07 (26.19–30.01)	3,671	39.4 (38.4–40.4)
	50–<65	2,451	45.94 (44.6–47.29)	833	38.46 (36.4–40.54)	3,811	40.9 (39.9–41.91)
	≥65	1,501	28.13 (26.93–29.36)	725	33.47 (31.48–35.5)	1,836	19.7 (18.9–20.53)
Coinfection	Both	0	0	0	0	0	0.03 (0.01–0.09)
	HCV	10	0.19 (0.09–0.34)	0	0	3	0.1 (0.04–0.18)
	HIV	3	0.06 (0.01–0.16)	6	0.28 (0.1–0.6)	9	99.87 (99.78–99.93)
	None	5,322	99.76 (99.58–99.87)	2,160	99.72 (99.4–99.9)	9,306	100
Fibrosis/Cirrhosis	Yes	1,781	33.38 (32.12–34.67)	1,328	61.31 (59.22–63.37)	0	0
	No	3,554	66.62 (65.33–67.88)	838	38.69 (36.63–40.78)	9,318	100
Treated	INFs	8	0.15 (0.06–0.30)	0	0	0	0
	NAs	5,327	99.85 (99.70–99.94)	0	0	0	0
	NAs+INFs	0	0	0	0	0	0
	None	0	0	2,166	100	9,318	100

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
HBsAg	Positive	4,819	90.33 (89.5–91.11)	2,071	95.61 (94.66–96.44)	8,733	93.72 (93.21–94.21)
	Indeterminate	1	0.02 (0–0.01)	0	0	0	0
	Missing	515	9.65 (8.87–10.48)	95	4.39 (3.56–5.34)	585	6.28 (5.79–6.79)
HBeAg	Positive	835	15.65 (14.69–16.65)	237	10.94 (9.66–12.33)	491	5.27 (4.82–5.74)
	Negative	3,482	65.27 (63.97–66.55)	923	42.61 (40.52–44.73)	4,308	46.23 (45.22–47.25)
	Indeterminate	14	0.26 (0.14–0.44)	1	0.05 (0–0.26)	4	0.04 (0.01–0.11)
	Missing	1,004	18.82 (17.78–19.89)	1,005	46.40 (44.28–48.53)	4,515	48.45 (47.44–49.48)
HBV DNA	≥1,000,000 IU/mL	83	1.56 (1.24–1.92)	107	4.94 (4.07–5.94)	0	0
	≥20,000 IU/mL	0	0	0	0	0	0
	20,000–<1000 IU/mL	56	1.05 (0.79–1.36)	136	6.28 (5.29–7.38)	0	0
	2,000–<20,000 IU/mL	37	0.69 (0.49–0.95)	41	1.89 (1.36–2.56)	219	2.25 (2.05–2.68)
	<2,000 IU/mL	273	5.12 (4.54–5.74)	114	5.26 (4.36–6.29)	667	7.16 (6.64–7.7)
	Detectable without count	1	0.02 (0–0.01)	0	0	0	0
	Undetectable	0	0	0	0	0	0
	Uncertain	211	3.96 (3.45–4.51)	22	1.02 (0.64–1.53)	60	0.64 (0.49–0.83)
	Missing	4,674	87.61 (86.70–88.48)	1,746	80.61 (78.88–82.26)	8,372	89.85 (89.22–90.45)

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
ALT ULN	≥5 ULN	135	2.53 (2.13–2.99)	303	13.99 (12.55–15.52)	0	0
	2–<5 ULN	172	3.22 (2.77–3.73)	664	30.66 (28.72–32.65)	0	0
	1–<2 ULN	492	9.22 (8.46–10.03)	311	14.36 (12.91–15.91)	1,384	14.85 (14.14–15.59)
	≤1 ULN	4,511	84.55 (83.56–85.51)	888	41.00 (38.92–43.1)	7,501	80.5 (79.68–81.3)
	Missing	25	0.47 (0.3–0.69)	0	0	433	4.65 (4.23–5.09)
Total		5,335		2,166		9,318	

d) Fuzhou, China

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
Age Group	18–<50	7,298	69.26 (68.37–70.14)	2,066	67.19 (65.5–68.85)	5,580	75.02 (74.02–76)
	50–<65	2,629	24.95 (24.13–25.79)	712	23.15 (21.67–24.69)	1,474	19.82 (18.92–20.74)
	≥65	610	5.79 (5.35–6.25)	297	9.66 (8.64–10.76)	384	5.16 (4.67–5.69)
Coinfection	Both	0	0	0	0	0	0
	HCV	1	0.01 (0–0.05)	0	0	2	0.03 (0–0.10)
	HIV	2	0.02 (0–0.07)	4	0.13 (0.04–0.33)	3	0.04 (0.01–0.12)
	None	10,534	99.97 (99.92–99.99)	3,071	99.87 (99.67–99.96)	7,433	99.93 (99.84–99.98)
Fibrosis/Cirrhosis	Yes	1,534	14.56 (13.89–15.25)	1,949	63.38 (61.65–65.09)	0	0 (0–0.05)
	No	9,003	84.44 (84.75–86.11)	1,126	36.62 (34.91–38.35)	7,438	100
Treated	IFNs	5	0.05 (0.02–0.11)	0	0	0	0
	NAs	10,531	99.94 (99.88–99.98)	0	0	0	0
	NAs+IFNs	1	0.01 (0–0.05)	0	0	0	0
	None	0	0 (0–0.04)	3,075	100	7,438	100
HBsAg	Positive	5,846	55.48 (54.53–56.43)	2,343	76.2 (74.65–77.69)	3,912	52.59 (51.45–53.74)
	Indeterminate	0	44.52 (43.57–45.47)	0	0	0	0
	Missing	4,691	25.29 (24.46–26.13)	732	23.80 (22.31–25.35)	3,526	47.41 (46.26–48.55)

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
HBeAg	Positive	2,665	29.31 (28.44–30.19)	825	26.83 (25.27–28.43)	1,089	14.64 (13.84–15.46)
	Negative	3,088	20.31 (28.44–30.19)	799	25.98 (24.44–27.57)	1,952	26.24 (25.25–27.26)
	Indeterminate	0	0	0	0	0	0
	Missing	4,784	45.4 (44.45–46.36)	1,451	47.19 (45.41–48.97)	4,397	59.12 (57.99–60.24)
HBV DNA	≥1,000,000 IU/mL	186	1.77 (1.52–2.04)	748	24.33 (22.82–25.88)	0	0
	≥20,000 IU/mL	0	0	0	0	0	0
	20,000–<1000 IU/mL	218	2.07 (1.81–2.36)	605	19.67 (18.28–21.12)	0	0
	2,000–<20,000 IU/mL	324	3.07 (2.75–3.42)	139	4.52 (3.81–5.32)	466	6.27 (5.72–6.84)
	<2,000 IU/mL	2,108	20.01 (19.25–20.78)	781	25.4 (23.87–26.98)	1,948	26.19 (25.19v27.2)
	Detectable without count	0	0	0	0	0	0
	Undetectable	4,465	42.37 (41.43–43.32)	451	14.67 (13.43–15.97)	1,900	25.54 (24.56–26.55)
	Uncertain	0	0	0	0	0	0
	Missing	3,236	30.71 (29.83–31.6)	351	11.41 (10.31–12.59)	3,124	42.00 (40.88–43.13)

Metric	Value	Treated		Untreated-but-indicated		Untreated-and-not-indicated	
		N	% [95% CI]	N	% [95% CI]	N	% [95% CI]
ALT ULN	≥5 ULN	38	0.36 (0.26–0.49)	83	2.70 (2.16–3.34)	0	0
	2–<5 ULN	152	1.44 (1.22–1.69)	275	8.90 (7.96–10.01)	0	0
	1–<2 ULN	627	5.95 (5.51–6.42)	506	16.5 (15.16–17.81)	458	6.16 (5.62–6.73)
	≤1 ULN	6,825	64.77 (63.85–65.68)	2,063	67.09 (65.4–68.75)	4,564	61.36 (60.24–62.47)
	Missing	2,895	24.47 (26.62–28.34)	148	4.81 (4.08–5.63)	2,416	32.48 (31.42–33.56)
Total	–	10,537	–	3,075	–	7,438	–

Children and adolescents (<18 years of age) were excluded from assessment of treatment eligibility as they are generally ineligible for treatment; HBsAg-negative patients were also excluded as their status as ‘true’ patients with chronic HBV infection was uncertain.

ALT, alanine aminotransferase; CI, confidence interval; DNA, deoxyribonucleic acid; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INF, interferon; NA, nucleos(t)ide analogue; UK, United Kingdom; ULN, upper limit of normal; US, United States.

Supplementary Table 5. Algorithm classification for complete lab data patients ('Complete') and those originally included in the algorithm ('Original').

Ad hoc analysis

Class	Subclass	US		UK		Hong Kong		Fuzhou, China	
		Complete	Original	Complete	Original	Complete	Original	Complete	Original
Treated		1944 (61)	1944 (21.1)	80 (27.1)	80 (16.1)	5335 (79.8)	5335 (31.7)	10537 (71.2)	10537 (50.1)
Need to be treated		414 (13)	1603 (17.4)	46 (15.6)	90 (18.1)	413 (6.2)	2166 (12.9)	1515 (10.2)	3075 (14.6)
	HBeAg +ve Chronic Hepatitis B ^a	43 (1.4)	62 (0.7)	4 (1.4)	5 (1)	24 (0.4)	164 (1)	489 (3.3)	521 (2.5)
	HBeAg -ve Chronic Hepatitis B ^b	188 (5.9)	1061 (11.5)	31 (10.5)	72 (14.5)	210 (3.1)	1823 (10.8)	568 (3.8)	1639 (7.8)
	HBV DNA ≥20,000 IU/mL	183 (5.7)	480 (5.2)	11 (3.7)	13 (2.6)	179 (2.7)	179 (1.1)	458 (3.1)	915 (4.3)
Not indicated for treatment		827 (26)	5684 (61.6)	169 (57.3)	326 (65.7)	936 (14)	9318 (55.4)	2738 (18.5)	7438 (35.3)
	HBeAg +ve Chronic HBV infection ^c	40 (1.3)	72 (0.8)	9 (3.1)	13 (2.6)	24 (0.4)	495 (2.9)	1011 (6.8)	1089 (5.2)
	HBeAg -ve Chronic HBV infection ^d	787 (24.7)	5612 (60.8)	160 (54.2)	313 (63.1)	912 (13.6)	8823 (52.5)	1727 (11.7)	6349 (30.2)
Total		3185 (34.5)	9231	295 (59.5)	496	6684 (39.7)	16819	14790 (70.3)	21050

Column percentages for strata; row percentages for totals. ^aPhase 2 Immune reactive; ^bPhase 4 Immune reactivation; ^cPhase 1 Immune tolerant; ^dPhase 3 Inactive carrier.

DNA, deoxyribonucleic acid; HBeAg +ve, positive for hepatitis B e antigen; HBeAg -ve, negative for hepatitis B e antigen; HBV, hepatitis B virus; UK, United Kingdom; US, United States.

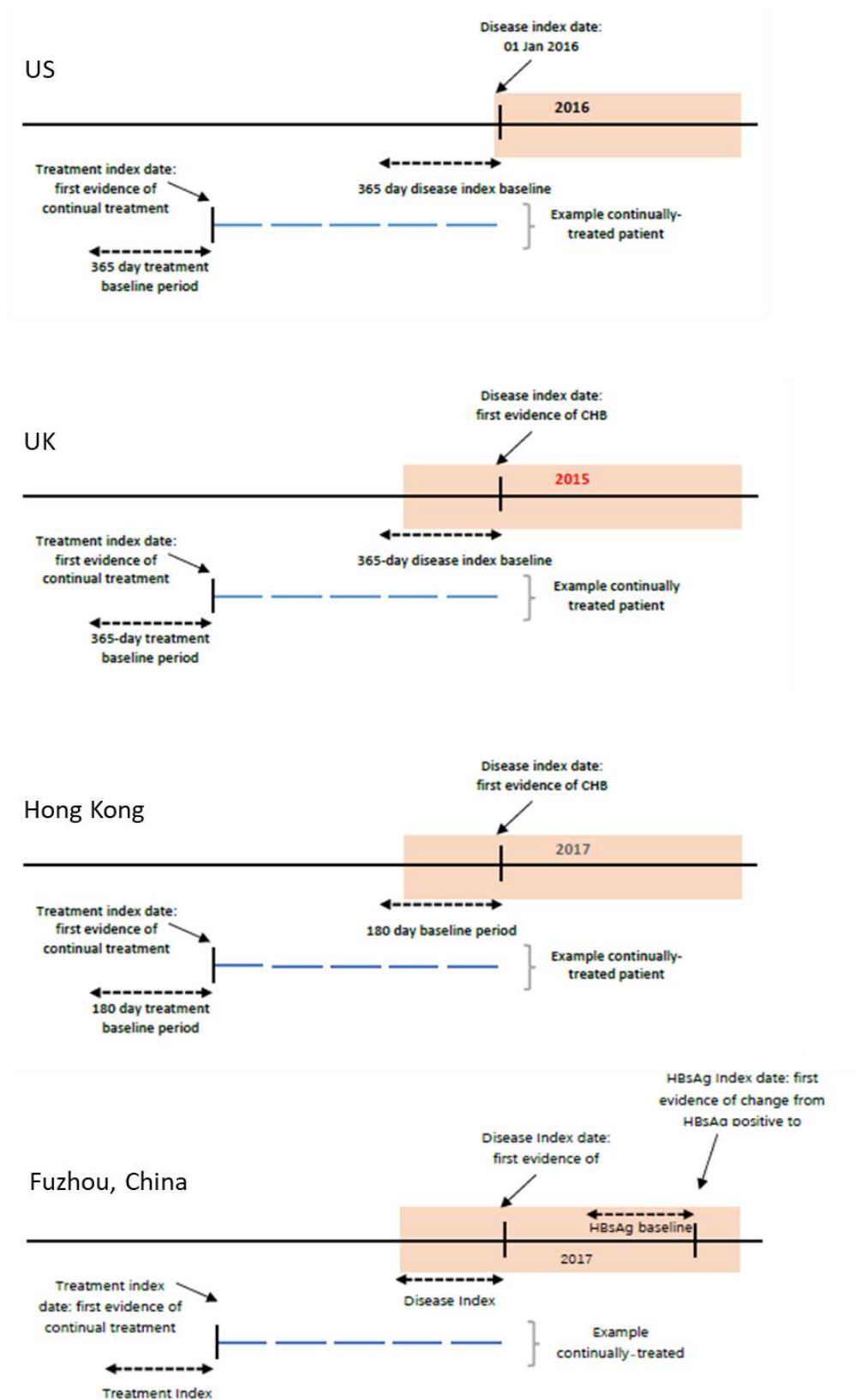
Supplementary Table 6. Algorithm classification for when patients with HBV DNA $\geq 20,000$ IU/mL are recoded ('Recoded') as Untreated-and-not-indicated versus those originally included in the algorithm ('Original'). *Ad hoc* analysis

Classification	US		UK		Hong Kong		Fuzhou, China	
	Complete	Original	Complete	Original	Complete	Original	Complete	Original
<i>Treated</i>	1944 (21.1)	1944 (21.1)	80 (16.1)	80 (16.1)	5335 (31.7)	5335 (31.7)	10537 (50.1)	10537 (50.1)
<i>Untreated-but-indicated for treatment</i>	1123 (12.2)	1603 (17.4)	77 (15.5)	90 (18.1)	1987 (11.8)	2166 (12.9)	2160 (10.3)	3075 (14.6)
HBeAg +ve Chronic Hepatitis B ^a	62 (0.7)	62 (0.7)	5 (1)	5 (1)	164 (1)	164 (1)	521 (2.5)	521 (2.5)
HBeAg -ve Chronic Hepatitis B ^b	1061 (11.5)	1061 (11.5)	72 (14.5)	72 (14.5)	1823 (10.8)	1823 (10.8)	1639 (7.8)	1639 (7.8)
HBV DNA $\geq 20,000$ IU/mL	0	480 (5.2)	0	13 (2.6)	0	179 (1.1)	0	915 (4.3)
<i>Untreated-and-not-indicated for treatment</i>	6164 (66.8)	5684 (61.6)	339 (68.3)	326 (65.7)	9497 (56.5)	9318 (55.4)	8353 (39.7)	7438 (35.3)
HBeAg +ve Chronic HBV infection ^c	72 (0.8)	72 (0.8)	13 (2.6)	13 (2.6)	495 (2.9)	495 (2.9)	1089 (5.2)	1089 (5.2)
HBeAg -ve Chronic HBV infection ^d	5612 (60.8)	5612 (60.8)	313 (63.1)	313 (63.1)	8823 (52.5)	8823 (52.5)	6349 (30.2)	6349 (30.2)
HBV DNA $\geq 20,000$ IU/mL	480 (5.2)	0	13 (2.6)	0	179 (1.1)	0	915 (4.3)	0
Total	9231	9231	496	496	16819	16819	21050	21050

^aPhase 2 Immune reactive; ^bPhase 4 Immune reactivation; ^cPhase 1 Immune tolerant; ^dPhase 3 Inactive carrier.

DNA, deoxyribonucleic acid; HBeAg +ve, positive for hepatitis B e antigen; HBeAg -ve, negative for hepatitis B e antigen; HBV, hepatitis B virus; UK, United Kingdom; US, United States.

Supplementary Figure 1. Study design



CHB, chronic hepatitis B; HBsAg, hepatitis B surface antigen; UK, United Kingdom; US, United States.