Supplementary Table 1 Characteristics of included studies

Study	Year	Country/Region	Study Design	Median Age	Male/ Female	Total No. of Patients	No. of Patients Treated	No. of SVR	No. of HBV Reactivation	No. of Hepatitis	Reason of Hepatitis	HBV Marker Status at Baseline	Baseline HBV DNA Level	Treatment Regimen	Treatment Duration
Chronic HBV infection															
Gane	2016	New Zealand	Prospective cohort study	53 (6.9)	6(2)	8	8	8	3	0		HBsAg+, HBeAg-	NR	SOF + LDV	12 weeks
Wang	2017	China	Prospective cohort study	51(41–61)	7(3)	10	10	10	3	3	HBV reactivation	HBsAg+, HBeAg-,anti-HBe+	3.2 (2.0) log10 IU/mL	SOF+LDV, SOF+DCV	8-12weeks
Yeh	2017	Taiwan	Retrospective cohort study	57(41–66)	4(3)	7	7	6	3	1	HBV reactivation	HBsAg+	3 (42.9) log10 IU/mL	≥3 DAA regimens	8-12weeks
Loggi	2017	Italy	Retrospective cohort study	58	2(0)	2	1	1	1	0		HBsAg+	NR	≥3 DAA regimens	12 weeks
Calvaruso	2017	Italy	Retrospective cohort study	58.6±7.2	7(1)	8	4	4	1	0		HBsAg+, HBeAg-,anti-HBe+	<20	≥3 DAA regimens	12-24weeks
Belperio	2017	US	Retrospective cohort study	60.6 (34.7-77.0)	367(10)	377	48	NR	9	1	HBV reactivation	HBsAg+	128 (1,203) IU/mL	≥3 DAA regimens	8-12weeks
Liu	2017	Taiwan	Prospective cohort study	55 (9)	6(6)	12	12	12	2	0		HBsAg+	UD-2000	≥3 DAA regimens	8-12weeks
Tamori	2017	Japan	Retrospective cohort study	69 (44–88)	13(9)	22	22	22	3	0		HBsAg+	UD-2000	≥3 DAA regimens	8-12weeks
Londoño	2017	Spain	Prospective cohort study	NR	NR	10	6	6	1	0		HBsAg+	UD-3433	≥3 DAA regimens	8-12weeks
Liu	2017	Taiwan	Randomized control trial	55 (32-76)	77(34)	111	111	111	24	4	HBV reactivation	HBsAg+, HBeAg-,anti-HBe+	2.1 (1.3-5.8) log10 IU/mL	SOF + LDV	12 weeks
Doi	2017	Japan	Prospective	NR	NR	4	4	4	0	0		HBsAg+	UD-<20	SOF + LDV ,	12 weeks

			cohort study											SOF+RBV	
Mücke	2017	Germany	Retrospective cohort study	NR	NR	7	7	7	1	1	HBV reactivation	HBsAg+	UD->170000000	≥3 DAA regimens	8-12weeks
Macera	2017	Italy	Prospective cohort study	61	NR	13	13	NR	5	3	HBV reactivation	HBsAg+	UD-570	≥3 DAA regimens	8-12weeks
Preda	2017	Romania	Retrospective cohort study	58	11(3)	14	11	11	4	1	HBV reactivation	HBsAg+, HBeAg-,anti-HBe+	0-134	≥3 DAA regimens	8-12weeks
Weltman	1995	Australia	Retrospective cohort study	31(19-63)	14(5)	19	8	5	NR	1	NR	HBsAg+	NR	Interferon alpha-2b	6 month
Liaw	1997	Taiwan	Randomized control trial	NR	NR	15	15	0	0	1	HCV reactivation	HBsAg+	NR	Interferon alpha-2a	12-14weeks
Guptan	1999	India	Retrospective cohort study	34±15	6(1)	7	7	2	NR	NR		HBsAg+	NR	Interferon alpha-2a, Interferon alpha-2b	6 month
Villa	2001	Italy	Prospective cohort study	18-65	22(8)	30	30	5	1	NR		HBsAg+	NR	Interferon alpha-2a	6 month
Yalcin	2002	Turkey	Retrospective cohort study	47 (41-59)	4(1)	5	5	2	1	1	HBV reactivation	HBsAg+, HBeAg-,anti-HBe+	NR	Interferon alpha-2b+ ribavirin	12 month
Chuang	2005	Taiwan	Case-control study	45	31(11)	42	42	29	14	0		HBsAg+	49.7	Interferon alpha-2b+ ribavirin	24 weeks
Saitta	2006	Italy	Prospective cohort study	45.9 (34-64)	8(1)	9	9	3	2	0		HBsAg+	NR	Interferon alpha-2a/ Interferon alpha-2b +	12 month

													ribavirin	
													Interferon alpha-2a/	
			Retrospective								HBsAg+,		Interferon	48
Senturk	2008	Turkey	cohort study	47±12	28(8)	36	36	2	0	0	HBeAg-,anti-HBe+	NR	alpha-2b + ribavirin	weeks/24 weeks
			Retrospective										PEG-IFN-alpha2b+	
Potthoff	2008	Germany	cohort study	37 (24-65)	15(4)	19	19	10	4	0	HBsAg+	25.8-12000	ribavirin	48 weeks
													Interferon	
			Retrospective							HBV			alpha-2a+	
Yu	2009	China	cohort study	44.9±9.6	40(10)	50	50	27	11	1 reactivation	HBsAg+	6864 ±1.4	ribavirin	48 weeks
			Retrospective										Peg-IFN +	
Erol	2009	Turkey	cohort study	43.9±11.5	7(2)	9	6	1	2	0	HBsAg+	UD-689655	ribavirin	48 weeks
													PEG-IFN-alpha2a/	48
			Retrospective										PEG-IFN-alpha2b	weeks/24
Liu	2009	Taiwan	cohort study	51	105(56)	161	161	161	28	0	HBsAg+	UD-72758	+ ribavirin	weeks
													PEG-IFN-alpha2a/	48
			Retrospective								HBsAg+,		PEG-IFN-alpha2b	weeks/24
Vigano	2009	Italy	cohort study	52 (32-66)	16(6)	32	22	9	4	2	HBeAg-,anti-HBe+	NR	+ ribavirin	weeks
													PEG-IFN-alpha2a/	
			Retrospective										PEG-IFN-alpha2b	
Hung	2011	Taiwan	cohort study	53.0±11.2	82(53)	135	135	96	4	0	HBsAg+	UD- >20000	+ ribavirin	12-48weeks
													PEG-IFN-alpha2a/	48
			Retrospective							HBV			PEG-IFN-alpha2b	weeks/24
Kim	2011	Korea	cohort study	44.1±9.5	12(6)	18	18	13	2	1 reactivation	HBsAg+	NR	+ ribavirin	weeks
			Randomized							HBV			Peg-IFN +	48
Yeh	2015	Taiwan	control trial	52	130(73)	203	203	150	18	3 reactivation	HBsAg+	63-79482823	ribavirin	weeks/24

														weeks
Kawagishi	2017	Japan	Retrospective cohort study	59(33- 74)	NR	3	3	NR	0	0		HBsAg+	NR	IFN-based	24-48weeks
Aygen	2017	Turkey	Retrospective cohort study	44.3±14.7	39(43)	82	27	17	7	3	HBV reactivation	HBsAg+	$1.55x10^7$±$4.83x10^7$	Peg-IFN + ribavirin	NR
Previous HBV infection															
Sulkowski	2016	US	Retrospective cohort study	58 (36-75)	44 (59)	103	103	NR	0	0		HBsAg- anti-HBc+	UD	SOF + LDV	12 weeks
Wang	2017	China	Prospective cohort study	54 (20-75)	86(38)	124	124	124	0	0		HBsAg- anti-HBc+	UD	SOF+LDV, SOF+DCV	8-12weeks
Yeh	2017	Taiwan	Retrospective cohort study	63.0 (35.0,81.0)	13(44）	57	57	56	0	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	8-12weeks
Ogawa	2017	Japan	Retrospective cohort study	71 (60-77)	26(37）	63	63	59	1	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	12 weeks
Mücke	2017	Germany	Retrospective cohort study	57 (18-86)	160 (103)	263	263	247	0	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	8-12weeks
Loggi	2017	Italy	Retrospective cohort study	62 (48–86)	31(13)	44	42	NR	0	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	12 weeks
Kawagishi	2017	Japan	Retrospective cohort study	69(44–87)	NR	84	84	NR	1	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	12-24weeks
Calvaruso	2017	Italy	Retrospective cohort study	65.1±9.5	24(13)	37	37	NR	3	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	12-24weeks
Belperio	2017	US	Retrospective cohort study	63.4(35.6-90.8)	NR	146	146	NR	4	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	8-12weeks
Liu	2017	Taiwan	Prospective cohort study	55 (8)	24(22)	46	46	NR	0	0		HBsAg- anti-HBc+	UD	≥3 DAA regimens	8-12weeks
Tamori	2017	Japan	Retrospective	70 (22–92)	361(404)	765	765	756	1	0		HBsAg-	UD	≥3 DAA regimens	8-12weeks

			cohort study								anti-HBc+			
			Prospective								HBsAg-			
Londoño	2017	Spain	cohort study	61 (20–84)	NR	64	64	NR	1	0	anti-HBc+	UD	≥3 DAA regimens	8-12weeks
			Prospective								HBsAg-		SOF+RBV，SOF +	
Doi	2017	Japan	cohort study	72 (54–75)	NR	143	143	NR	3	0	anti-HBc+	UD	LDV	12 weeks
			Retrospective								HBsAg-			
Tang	2017	US	cohort study	62.5	NR	192	174	NR	0	0	anti-HBc+	UD	≥3 DAA regimens	8-12weeks
			Retrospective								HBsAg-,		Interferon	
Zignego	1997	Italy	cohort study	49.5(33-63)	13(1)	14	14	0	NR	NR	NR	anti-HBc+	NR	alpha-2a	12 month
													Interferon alpha-2a/ Interferon	
			Retrospective								HBsAg-,		alpha-2b ±	
Myers	2003	France	cohort study	36-58	29(22)	51	51	9	NR	NR	NR	anti-HBc+	NR	ribavirin	6 month
			Retrospective								HBsAg-,			
Hasegawa	2005	Japan	cohort study	54.6±8.0	47(17)	64	64	16	NR	NR	NR	anti-HBc+	18-49	IFN-based	NR
			Retrospective								HBsAg-		Peg-IFN +	
Pasternak	2016	Poland	cohort study	48.78 ± 9.51	59(40)	99	99	49	0	0	anti-HBc+	UD	ribavirin	24-48weeks
			Retrospective								HBsAg-			
Kawagishi	2017	Japan	cohort study	NR	NR	69	69	NR	0	0	anti-HBc+	UD	IFN-based	24-48weeks

NR: not report

Supplementary Table 2 Quality Assessment

Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group

Author	Year	Was the study question or objective clearly state	Were eligibility/selection criteria for the study population prespecified and clearly described?	Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Were all eligible participants that met the prespecified entry criteria enrolled?	Was the sample size sufficiently large to provide confidence in the findings?	Was the test/service/intervention clearly described and delivered consistently across the study population?	Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Were the people assessing the outcomes blinded to the participants' exposures/interventions?	Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determin	Quality assessment

													e effects at the group level?	
Gane	2016	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	Y	Y	Good
Wang	2017	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	N	Good
Yeh	2017	Y	Y	N	Y	N	Y	Y	NR	Y	Y	Y	Y	Fair
Loggi	2017	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	Y	Fair
Calvaruso	2017	Y	N	Y	Y	N	Y	Y	NR	Y	Y	Y	Y	Fair
Belperio	2017	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	N	Y	Good
Tamori	2017	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	Y	Y	Fair
Londoño	2017	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	Y	Fair
Liu	2017	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Doi	2017	Y	Y	Y	Y	N	Y	Y	NR	N	N	Y	Y	Fair
Mücke	2017	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Macera	2017	Y	Y	N	Y	N	Y	Y	NR	N	Y	NR	Y	Fair
Preda	2017	Y	Y	Y	Y	N	Y	Y	NR	N	Y	NR	Y	Fair
Weltman	1995	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	Y	Fair
Guptan	1999	Y	Y	Y	Y	N	Y	Y	NR	N	Y	N	Y	Fair
Villa	2001	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	N	Y	Good
Yalcin	2002	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	Y	Fair
Saitta	2006	Y	Y	Y	Y	N	Y	Y	NR	N	Y	N	Y	Fair
Senturk	2008	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Potthoff	2008	Y	Y	Y	Y	N	Y	Y	NR	N	Y	N	Y	Fair
Yu	2009	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	N	Y	Good

Erol	2009	Y	Y	Y	Y	N	Y	Y	NR	N	Y	N	Y	Fair
Liu	2009	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Vigano	2009	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	N	Y	Good
Hung	2011	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Kim	2011	Y	Y	Y	Y	N	Y	N	NR	Y	Y	N	Y	Fair
Kawagishi	2017	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	Y	Y	Fair
Aygen	2017	Y	Y	Y	Y	N	Y	Y	NR	N	Y	Y	Y	Fair
Sulkowski	2016	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Ogawa	2017	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Tang	2017	Y	Y	Y	Y	N	Y	Y	NR	N	Y	NR	Y	Fair
Zignego	1997	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	Y	Fair
Myers	2003	Y	Y	Y	Y	N	Y	N	NR	Y	Y	Y	Y	Fair
Hasegawa	2005	Y	Y	Y	Y	N	Y	Y	NR	Y	N	Y	Y	Fair
Pasternak	2016	Y	Y	Y	Y	N	Y	Y	NR	N	Y	Y	Y	Fair

Quality Assessment of Case-Control Studies

Author	Year	Was the research question or objective in this pap	Was the study population clearly specified and defined?	Did the authors include a sample size justification?	Were controls selected or recruited from the same or similar population that gave rise to the	Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify	Were the cases clearly defined and differentiated from controls?	If less than 100 percent of eligible cases and/or controls were selected for the study,	Was there use of concurrent controls?	Were the investigators able to confirm that the exposure/risk occurred prior to the development of the	Were the measures of exposure/risk clearly defined, valid, reliable, and implemented	Were the assessors of exposure/risk blinded to the case or control status of participants?	Were key potential confounding variables measured and adjusted statistically in the analyses? If	Quality assessment

		er clea rly stat ed and app ropr iate ?			cases (includin g the same timefram e)?	or select cases and controls valid, reliable, and implemen ted consistent ly across all study participan ts?		were the cases and/or controls randoml y selected from those eligible?		condition or event that defined a participan t as a case?	consistent ly (includin g the same time period) across all study participan ts?		matching was used, did the investiga tors account for matching during study analysis?			
Chuang	2005	Y	Y	N	Y	Y	Y	NR	N	Y	Y	NA	NR	N	Fair	

Quality Assessment of Controlled Intervention Studies

Author	Year	Was the stud y desc ribe d aran do miz ed clini	Was the method of randomization adequate (i.e., use of randomly generated assignment)?	Was the treatment allocation concealed (so that assignments could not be predicted)?	Were study participa nts and provider s blinded to treatmen t group assignme nt?	Were the people assessing the outcomes blinded to the participan ts' group assignme nts?	Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated	Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	Was there high adherence to the interventi on protocols for each treatment group?	Were other interventi ons avoided or similar in the groups (e.g., similar backgrou nd	Were outcomes assessed using valid and reliable measures, implemen ted consistent ly across all study	Did the authors report that the sample size was sufficie ntly large to be able to detect a	Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	Were all rand omiz ed parti cipan ts analy zed in the grou	Quality assessm ent

		cal trial , or an RCT ?						to treatmen t?			treatment s)?	participan ts?	differen ce?		p ?	
Yeh	2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Good
Liaw	1997	Y	Y	Y	Y	Y	Y	Y	NR	Y	NR	Y	Y	N	Y	Good
Liu	2017	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Good

NR: not report