APPENDIX

Search strategy used in Medline

1 exp Haemophilus Vaccines/
2 exp Haemophilus Influenzae type b/
3 exp haemophilus influenzae type b.ab,ti
4 exp hemophilus influenzae type b.ab,ti
5 exp haemophilus influenza type b.ab,ti
6 exp hemophilus influenzae type b.ab,ti
7 2 or 3 or 4 or 5 or 6
8 exp *vaccines/
9 immunization/ or vaccination/
10 exp Immunization Programs/
11 8 or 9 or 10
12 7 and 11
13 1 or 12

Terms used in electronic screening

Titles and abstracts of papers classified as observational following initial screening, and with a title and abstract in English, were searched electronically for the following terms (and variants):

Cohort
Longitudinal
Case-control
Prospective
Retrospective
Matched pair
Comparative
Follow-up
Non-randomised
Observational
Screening method
Case population

Appendix Table 1: Summary of case control studies of Hib vaccine effectiveness against clinically important Hib disease (studies are grouped by outcome).

Country / reference	Year published	Schedule comparisons	Age group in months	Number of cases	Type of control *	Ratio of controls to cases	Length of study	Study timing †	Vaccination history	Type of Hib vaccine	Method of statistical analysis	Method of calculating VE	Factors adjusted for in estimating VE
Invasive Hib disease													
USA [1]	1992	1 or more HbOC vs no Hib vaccine	18-60	16	C	4 to 1	2 years, 2 months	P	Documented only	HbOC [PRP and PRP-D included in paper but not in this review]	Conditional logistic regression	1 - OR	Matching: age (± 1 day), area of residence
USA [2]	1994	1 dose HbOC vs no Hib vaccine 2 doses HbOC vs no Hib vaccine 3 doses HbOC vs no Hib vaccine 4 doses HbOC vs no Hib vaccine 1 dose PRP-OMP vs no Hib vaccine 2 doses PRP-OMP vs no Hib vaccine Intended schedule 2, 4, 6, 15 months (HbOC); 2, 4, 12 months (PRP-OMP)	1.5-35	105	C	7 to 1	2 years	P	Documented only	HbOC, PRP-OMP	Conditional logistic regression	1 - OR	Matching: age (± 2 months), area of residence Analysis: paternal ethnicity, gender, breastfeeding history, number sleeping in room with child, usual source of medical care
USA [3]	1994	1, 2 or 3 doses of Hib conjugate vaccine vs no Hib vaccine	2.5-59	45 in analysis of all conjugate vaccines combined; 39 in analysis of PRP-OMP	C	4 to 1	3 years	P	Documented only	PRP-OMP, HbOC, PRP-D	Conditional logistic regression	1 - OR	Matching: age (as close as possible), area of residence
USA [4]	1991	1 or more HbOC vs no Hib vaccine	18.5-59	59	C	2 to 1	1 year, 5 months	P	Documented only	HbOC [PRP and PRP-D included in paper but not in this review]	Conditional logistic regression	1 - OR	Matching: SES

Country / reference	Year published	Schedule comparisons	Age group in months	Number of cases	Type of control *	Ratio of controls to cases	Length of study	Study timing †	Vaccination history	Type of Hib vaccine	Method of statistical analysis	Method of calculating VE	Factors adjusted for in estimating VE
USA [5]	1999	1, 2, 2 or more, 3, and 3 or more doses of Hib conjugate vaccines vs no Hib vaccine Intended schedule 2, 4, 6 months	2-18	57	C	3 to 1	3 years 6 months	P	Documented only	HbOC (1 case received PRP-OMP and 1 control a vaccine other than HbOC but the type is not stated)	Conditional logistic regression	1 - OR	Matching: age (as close as possible), county of birth Analysis: single mother, household crowding
USA [6]	1991	3 doses of HbOC (intended schedule 2, 4, 6 months, mean ages at receipt 2.6, 4.9 and 7.2 months) vs no Hib vaccine	1.5 - 12	25 total; 13 included in matched analysis	C	≥7 to 1	2 years, 5 months	P	Documented only	HbOC	Conditional logistic regression	1 - OR	Matching: month of birth, sex, zip code Analysis: daycare attendance, ethnicity, family income
USA [7]	2004	1 or more doses vs no Hib vaccine. Intended schedule not stated.	≥18 months	29 total; unclear how many received PRP vaccine so are not included in the analysis of conjugate vaccine.	C	4:1	3 years	P	Documented only	Not stated	Conditional logistic regression	1 - OR	Matching: age (±2 days), town of birth
The Gambia [8]	2005	1, 2 or 3 doses vs no Hib vaccine Intended schedule 2, 3, 4 months but often given later	<72	46	C	10 to 1	4 years 8 months	P	Documented only	PRP-T	Conditional logistic regression	Not stated	Matching: age (± 2 weeks), area of residence
England & Wales [9]	2008	Any Hib vaccine vs no Hib vaccine; 3 doses of Hib-containing vaccine with 0, 1, 2 or 3 administered as DTaP-Hib. Intended schedule 2, 3, 4 months	<51	138 (any Hib vaccine vs none) 95 (doses of DTaP-Hib)	C	5 to 1	5 years	R	Parental report for cases; parental report and computerised records for controls	Not stated	Conditional logistic regression	Not presented	Matching: age (same DOB), region

Country / reference	Year published	Schedule comparisons	Age group in months	Number of cases	Type of control *	Ratio of controls to cases	Length of study	Study timing †	Vaccination history	Type of Hib vaccine	Method of statistical analysis	Method of calculating VE	Factors adjusted for in estimating VE
England & Wales [10]	2003	Any Hib vaccine vs no Hib vaccine; 3 doses of Hib-containing vaccine with 0, 1, 2 or 3 administered as DTaP-Hib. Intended schedule 2, 3, 4 months	Unclear	110	C	35 to 1		R	Documented only	Not stated	Conditional logistic regression	1 – OR	Matching: age (same DOB) Analysis: age at third dose
Hib meningitis													
Australia [11]	1998	1 or more doses vs no Hib vaccine	2-60	8	C	4.8 to 1	2 years	P	Documented only	PRP-OMP	Conditional logistic regression	1 - OR	Matching: age (DOB in same calendar year and month), sex, area of residence Analysis: breastfeeding, exposure to cigarette / tobacco smoke, exposure to campfire smoke
Malawi [12]	2006	1, 2, at least 1, at least 2, or at least 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	2-59	43	H (children with *S. pneumoniae* meningitis)	5 to 1	3 years	Not stated	Not stated	Combined PRP-T, DTP, hep B	Logistic regression	1 - OR	Analysis: age, area of residence (within or outside Blantyre city), HIV status
Uganda [13]	2008	2 or more or 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	3-59	41	C, H (children with conditions other than those potentially related to Hib)	3 to 1	3 years	P / R	Verbal and documented	Combined PRP-T, DTP, hep B	Conditional logistic regression	1 - OR	Matching: age (DOB ± 2, 3, 6 or 12 months for cases aged 3-6, 7-11, 12-23 and 24-59 months, respectively), neighbourhood Analysis: maternal education
Dominican Republic [14]	2008	1, 2, 3 or 2 or more doses vs no Hib vaccine Intended schedule 2, 4, 6 months	2-59	32	C	3 to 1	3 years 2 months	R	Verbal and documented	Combined PRP-T, DTP, hep B	Conditional logistic regression	1 - OR	Matching: age (DOB ± 60 or 180 days for cases aged <1 and 1-4 years, respectively), neighbourhood

Country / reference	Year published	Schedule comparisons	Age group in months	Number of cases	Type of control *	Ratio of controls to cases	Length of study	Study timing †	Vaccination history	Type of Hib vaccine	Method of statistical analysis	Method of calculating VE	Factors adjusted for in estimating VE
Uganda [15]	2008	1, 2, 3 or 2 or more doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks.	0-59	Not stated	H (children with *S. pneumoniae* meningitis)	Not stated	6 years	Unclear	Verbal and documented	Combined PRP-T, DTP, hep B	Logistic regression	1 - OR	Analysis: age
Bangladesh [16]	2007	1 or more, 2 or more or 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	3-23	15	C, H (children with conditions other than pneumonia or meningitis)	Community: 4 to 1 Hospital: 2 to 1	3 years, 3 months	P	Documented only	Combined PRP-T DPT	Conditional logistic regression	Unclear	Matching (community controls only): age (DOB ± 1 month), sex, season, distance from hospital Analysis: age, number of doses; household income
The Gambia [8]	2005	1, 2 or 3 doses vs no Hib vaccine Intended schedule 2, 3, 4 months but often given later	<72	36	C	10 to 1	4 years 8 months	P	Documented only	PRP-T	Conditional logistic regression	Not stated (presumably 1 - OR)	Matching: age (DOB ± 2 weeks), area of residence Analysis: unspecified covariates (data were collected on distance from health centre, overcrowding, mother's education)
Senegal [17]	2011	1 or more or 2 or more doses vs no Hib vaccine. Intended schedule 6, 10, 14 weeks.	1.5-12	24	C	4 to 1	3 years 5 months	P	Verbal and documented	Combined PRP-T or HbOC, DTP, hepatitis B	Not stated	1 - OR	Matching: age (± 28 days), neighbourhood Analysis: maternal education, number of children aged <5 years living in household
Purulent meningitis													
Rwanda [18]	2007	2 or 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	0-59	45	H (children with <20 WBC per μl CSF, non-turbid and negative for Hib)	1.5 to 1	4 years 6 months	R	Not stated	Combined PRP-T, DTP, hepatitis B	Not stated	1 - OR	None stated

Country / reference	Year published	Schedule comparisons	Age group in months	Number of cases	Type of control *	Ratio of controls to cases	Length of study	Study timing †	Vaccination history	Type of Hib vaccine	Method of statistical analysis	Method of calculating VE	Factors adjusted for in estimating VE
Uganda [15]	2008	1, 2, 3 or 2 or more doses vs no Hib vaccine	0-59	Not stated	H (children with <20 WBC per microlitre CSF, of unknown cause)	Not stated	6 years	Unclear	Verbal and documented	Combined PRP-T, DTP, hep B	Logistic regression	1 - OR	Analysis: age
Bangladesh [16]	2007	1 or more, 2 or more or 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	3-23	41	C, H (children with conditions other than pneumonia or meningitis)	Community: 4 to 1 Hospital: 2 to 1	3 years, 3 months	P	Documented only	Combined PRP-T DPT	Conditional logistic regression	Unclear	Matching (community controls only): age (DOB ± 1 month), sex, season, distance from hospital Analysis: age, number of doses; household income
Aetiology negative meningitis (purulent meningitis with no cause identified)													
Uganda [15]	2008	1, 2, 3 or 2 or more doses vs no Hib vaccine	0-59	Not stated	H (children with <20 WBC per microlitre CSF, of unknown cause)	Not stated	6 years	Unclear	Verbal and documented	Combined PRP-T, DTP, hep B	Logistic regression	1 - OR	Analysis: age
Rwanda [18]	2007	2 or 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	0-59	13	H (children with *S. pneumoniae* meningitis)	1.5 to 1	4 years 6 months	R	Not stated	Combined PRP-T, DTP, hepatitis B	Not stated	1 - OR	None stated
Radiologically confirmed (all-cause) pneumonia													
Brazil [19]	2004	2 or 3 doses (or 1 at age >12 months) vs 0 or 1 (at age <12 months) doses Intended schedule 2, 4, 6 months	2-24	427	C	2 to 1	1 year, 4 months	P	Documented only	HbOC	Conditional logistic regression	1 - OR	Matching: age (±4 months), neighbourhood Analysis: age, sex, daycare attendance, previous flu-like illness, smokers at home, home ownership, mother's education

Country / reference	Year published	Schedule comparisons	Age group in months	Number of cases	Type of control *	Ratio of controls to cases	Length of study	Study timing †	Vaccination history	Type of Hib vaccine	Method of statistical analysis	Method of calculating VE	Factors adjusted for in estimating VE
Colombia [20]	2004	1, 2 or 3 doses vs no Hib vaccine Intended schedule 2, 4, 6 months	2-24	389	C	2 to 1	2 years, 7 months	P	Documented only	PRP-T	Conditional logistic regression	1 - OR	Matching: age (±1 month), sex, area of residence, SES Analysis: maternal education, maternal smoking, number of smokers in household, daycare attendance, cooking in the sleeping room, underlying illness, previous hospitalisation, crowding
Bangladesh [16]	2007	1 or more, 2 or more or 3 doses vs no Hib vaccine Intended schedule 6, 10, 14 weeks	3-23	343	C, H (children with conditions other than pneumonia and meningitis)	Community: 4 to 1 Hospital: 2 to 1	3 years, 3 months	P	Documented only	Combined PRP-T DPT	Conditional logistic regression	Unclear	Matching (community controls only): age (DOB ±1 month), sex, season, distance from hospital Analysis: age, number of doses; household income

* C = community; H = hospital
† P = prospective; R = retrospective

Appendix Table 2: Hib vaccine effectiveness (VE) estimates (95% CIs) from case control studies against probable bacterial meningitis and aetiology negative meningitis, by number of Hib vaccine doses received and control type. The intended schedule was 6, 10, 14 weeks in all studies.

	Probable bacterial meningitis					Aetiology negative meningitis (purulent meningitis with no cause identified)				
Country / ref	**1 dose**	**2 doses**	**3 doses**	**≥1 dose**	**≥2 doses**	**1 dose**	**2 doses**	**3 doses**	**≥1 dose**	**≥2 doses**
Vaccine effectiveness (95% CI) using community controls										
Bangladesh [16]			40 (-138 to 85)	54 (-21 to 83)	71 (-1 to 92)					
Vaccine effectiveness (95% CI) using hospital controls										
Bangladesh [16]			74 (-30 to 95)	59 (-18 to 86)	83 (24 to 96)					
Uganda [15]	60 (21 to 80)	36 (-10 to 63)	68 (46 to 81)	38 (23 to 50)	53 (11 to 68)		66 (-10 to 90)	15 (-51 to 52)	31 (3 to 51)	35 (-11 to 62)
Rwanda [18]					52 (5 to 75)					68 (-78 to 94)

Appendix Table 3: Estimates of vaccine effectiveness (95% CI) against Hib meningitis, invasive Hib disease and radiologically confirmed pneumonia, for imprecise numbers of doses from case-control studies.

	Hib meningitis			**Invasive Hib disease**	**Radiologically confirmed pneumonia**	
Country	≥1 dose	≥2 doses	≥3 doses	≥1 dose	≥1 dose	≥2 doses
Studies using community controls						
Uganda[13]		99 (92 to 100)				
Dominican Republic [14]		94 (60 to 100)				
Brazil [19]						31 (-9 to 57)
Colombia [20]					47 (2 to 72)	
USA [1]				100 (-37 to 100)		
USA [3]				95 (66 to 99)		
USA [5]				86 (16 to 98)		
USA [4]				100		
Bangladesh [16]	90 (34 to 100)	89 (28 to 100)			24 (-6 to 43)	34 (6 to 53)
Australia [11]	75 (-266 to 98)					
England [9]				96 (81 to 99)		
USA [7]	95 (56 to 99)					
Senegal [17]	91 (66 to 98)	96 (68 to 99)				
Studies using hospital controls						
Malawi [12]	73 (39 to 88)	92 (72 to 98)	94 (70 to 99)			
Uganda [13]		94 (74 to 99)				
Uganda [15]	65 (41 to 79)	93 (69 to 99)				

Appendix Table 4: Summary of vaccines and schedules in cohort studies of Hib vaccine effectiveness

Country [ref]	Study period	Intended schedule	Hib vaccine	Other vaccines co-administered with Hib
Invasive Hib disease				
Chile [21]	1992-1995	2, 4, 6 mo	PRP-T	DTwP (quadrivalent), OPV
Germany [22]	1998-2002	2, 3, 4 +b11 (or later) mo	Conjugate molecule not stated.	DTaP (quadrivalent) or DTaP-IPV (pentavalent)
Germany[23]	2000-2005	2, 3, 4 +b11-14 mo	PRP-T	DTaP-HBV-IPV (hexavalent)[a]
South Africa [24, 25]	1997-2000[25]; 1998-2004[24]	6, 10, 14 w	PRP-HbOC	DTwP (quadrivalent)[25]; DTwP, OPV and HepB on same schedule; unclear whether any administered in same syringe[24]
Hib meningitis +/- other outcomes				
Denmark[26]	1991-1999	May 1993 - 31 Dec 1995: 5, 6 mo + b16 mo[b]; 1 Jan 1996-31 Dec 1996: 5, 6 mo + b15 mo; 1 Jan 1997 onwards: 3, 5, 12 mo	PRP-T	Not stated.
Denmark[27]	1990-2001	June 1993-1995: 5, 6, b16 mo; 1996: 5, 6, b15 mo; 1997-2001: 3, 5, 12 mo	PRP-T	wP (1990-1996: 0.5 dose with 5 w Hib); DT-IPV (1990-1996; 5, 6, 16 mo); DTaP-IPV (1997-2001; 3, 5, 12 mo)

[a] One of the two hexavalent vaccines in use in Germany at the time of this study was withdrawn in the EU in 2012

[b] Routine Hib vaccination was introduced in May 1993 "with catch-up vaccination offered to all children less than 6 years of age"

Appendix Table 5: Further details of cohort studies of Hib vaccine effectiveness against invasive Hib disease

Country [ref]	Number of participants	Method of ascertainment of exposure	Assessment of clinical outcomes	Method of statistical analysis	Factors adjusted for	Main quality concerns
Invasive Hib disease						
Chile [21]	3 doses of DTP-Hib: 35 264; 3 doses of DTP only: 36 741	EPI clinic databases	Passive surveillance, of laboratory reports from 11 hospitals in study region which would admit pediatric patients, to identify Hib cases among study participants in 17 months following last vaccine administered as part of this study[c]	Rate ratio comparing incidence in vaccinated to unvaccinated cohort	None.	No control for confounding.
Germany [22]	Cases: 36; Non-cases: 667[d]	Cases: unclear.; Non-cases: Parents read from vaccination booklet during phone survey.	Nationwide passive hospital and laboratory surveillance for outcomes in children under 10 years of age	Multivariable Cox regression. Non-cases contribute follow-up time from birth or the start of surveillance period (whichever later). Cases contribute to the analysis cross-sectionally, on date of positive Hib culture, only.[e]	Age at vaccination; changing immunisation status of each non-case over-time	Blinding - lab staff apparently blind to vaccination status of cases, clinicians apparently not. Unclear how vaccination status of cases was ascertained
Germany [23]	Cases: 32; Non-cases: 2893[f]	Cases: vaccination booklets or vaccinating paediatricians.; Non-cases: Parents read from vaccination booklet during phone survey.	Hospital / laboratory surveillance (presumably in children under 10 years of age, as for [22], but not stated)	Multivariable Cox regression. Non-cases contribute follow-up time from birth or the start of surveillance period (whichever later). Cases contribute to the analysis cross-sectionally, on date of positive Hib culture, only.[e]	Age at vaccination; changing immunisation status of each non-case over-time	Blinding - lab staff apparently blind to vaccination status of cases, clinicians apparently not. Possible overestimate of vaccination coverage from telephone survey due to survey population being overrepresentative of wealthier.

[c] The exposures assessed in this study (DTP-Hib vs DTP alone) were given between 1 Nov 1992 and 31 Oct 1993. Surveillance for invasive disease occurred between 1 Nov 1992 and 30 Apr 1995

[d] Cases are all those in Germany between Jan 1998 and Jun 2002, identified through nationwide surveillance, and non-cases are a random sample ("sub-cohort") of all children born in Germany between 1 Jun, 1996 and 31 Dec, 1998 (the sub-cohort was assumed to contain no cases)

[e] Reference for method of statistical analysis: Moulton LH et al AJE 1995; 142 (9): 1000-1006.

[f] Cases are all those in Germany between Aug 2000 and Dec 2004, identified through nationwide surveillance, and non-cases are a random sample ("sub-cohort") of all children born in Germany between 1 Aug, 2000 and 31 Dec, 2004 (the sub-cohort was assumed to contain no cases)

Country [ref]	Number of participants	Method of ascertainment of exposure	Assessment of clinical outcomes	Method of statistical analysis	Factors adjusted for	Main quality concerns
Invasive Hib disease						
South Africa[24, 25]	Vaccinated cohort: 19 267; Unvaccinated cohort: approx. 22000	Not stated, but presumably trial records (this study nested within Phase III trial of 9-valent pneumococcal vaccine)	"Daily laboratory surveillance of culture-confirmed invasive Hib disease was undertaken from January, 1997. There was active case detection during prospective studies evaluating invasive bacterial disease in children between March, 1997, and September,2000" in children under 1 year of age	Risk ratio comparing incidence in vaccinated to unvaccinated cohort[g]	None.	Provenance of unvaccinated cohort is unclear. Unclear how vaccinated children were selected from trial for inclusion in cohort study. Unclear what statistical methods used to estimate incidence; not clear how/if losses to follow-up were accounted for. No adjustment for confounding.
Hib meningitis +/- other outcomes						
Denmark[26]	All children in Denmark who were liveborn between 1 June 1987 and 31 December 1998 (542,100 children)	Immunization register	National Hospital Discharge Registry. All hospitalisations for children up to age 9 years between 1 Jan 1991 and 31 Dec 1999 were extracted	Log-linear multivariable Poisson regression to estimate rate ratio for association of outcome with 1, 2 or 3 doses of vaccine, relative to rate of outcome in pre-vaccination period	Age[h]	Rate of loss to follow-up not reported by exposure group.
Denmark[27]	Unvaccinated: 922480 child years under 5; At least one dose: 1977983 child years under 5	Immunization register	Linkage of information in hospitalization register to immunization register (exposure status) and population register for children under 5 years of age	Log-linear multivariable Poisson regression to estimate rate ratio for association of outcomes with >=1 Hib dose of Hib and per dose among vaccinees[i]	Age, calendar period, and receipt of other vaccines; age and calendar period interaction.[j]	Rate of loss to follow-up not reported by outcome. Estimates of vaccine effectiveness give in figures only.

[g] The calculation of the risk ratio for at least one dose was restricted to children <1; the unvaccinated cohort was restricted to children 6 weeks or older. The calculation of the risk ratio for fully vaccinated included children between 4.1 and 12.0 months of age in the unvaccinated cohort and all cases occurring at least 14 days after having received the third dose of Hib conjugate vaccine in the vaccinated cohort.

[h] The authors checked and there was no evidence for confounding by birth weight, birth method, gestational age, season, birth order or gender.

[i] This study was mainly about adverse effects of vaccines so the authors also presented associations with vaccination 14 d to 3 mo after receipt of any dose and greater than 3 mo after receipt of any dose.

[j] The authors report no confounding by sex, place of birth, birth weight, mother's country of birth, mother's age at birth, birth order, or season.

Appendix Table 6: Estimates of vaccine effectiveness (95% CI) against invasive Hib disease for imprecise numbers of doses, from cohort studies

Country	≥1 dose	1-2 doses
Germany [22]		90 (67 to 97)
Germany [23]		68 (19 to 88)
South Africa (all children) [24, 25]	82 (59 to 92)†	
	79 (66 to 88)‡	
South Africa (HIV-uninfected children only) [24, 25]	97 (76 to 100) †	
	91 (79-96) ‡	

† At age <1 year

‡ At age <2 year

Appendix Table 7: Details of screening studies included in the review. All studies estimated VE against invasive Hib disease.

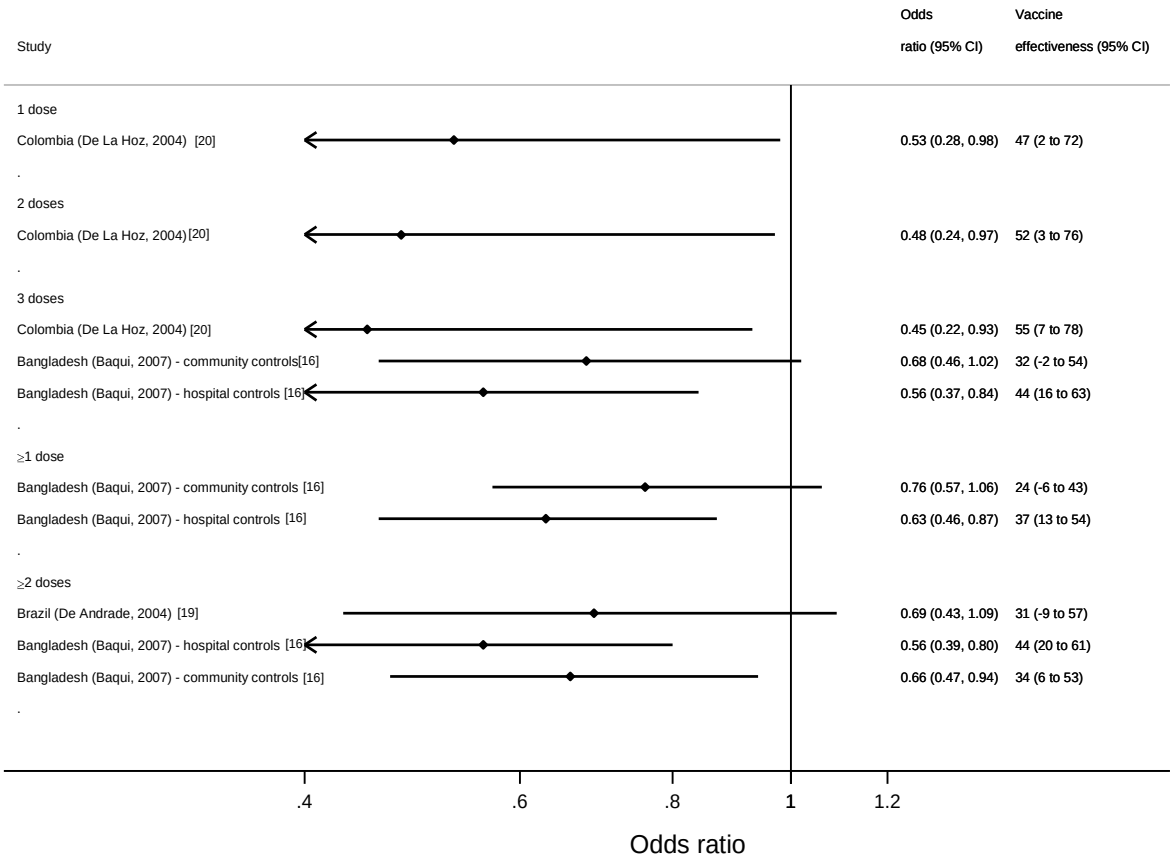
Country	Study period	Hib vaccine	Intended schedule	Number of cases	Method of ascertainment of vaccination status in cases and non-cases	Assessment of clinical outcomes	Factors adjusted for
England & Wales [28]	1993-2002	PRP-T / HbOC in combination with DTaP or DTwP	2, 3, 4 months, plus catch-up campaign for children aged 1-4 years	443	Cases: GP / computerised health records Non-cases: national routine vaccine coverage data; regional vaccination coverage database	Reporting from laboratories; notifications from public health departments; reports from paediatricians; isolates referred to the Haemophilus Reference Unit.	Stratified by period of birth, age and time since vaccination
Germany [29]	1998-99	DTaP/Hib or DTaP-IPV/Hib	2, 3, 4 months; booster at 11-15 months	91	Cases: reported by paediatrician Non-cases: random digit telephone survey	Clinical and laboratory surveillance with active follow-up of paediatricians	None
Australia [30]	1993-96	PRP-T, HbOC, PRP-OMP	Not stated, but the standard schedule in Australia at the time was 2, 4, 6, 18 months for HbOC or 2, 4, 12 months for PRP-OMP [31].	~400	Cases: unclear Non-cases: national vaccine coverage survey [32]	National Notifiable Diseases Surveillance System; Hib Case Surveillance Scheme	None

Country	Study period	Hib vaccine	Intended schedule	Number of cases	Method of ascertainment of vaccination status in cases and non-cases	Assessment of clinical outcomes	Factors adjusted for
Spain [33]	1995-96	Not stated, but both vaccinated cases had received HbOC	Not stated	23	Unclear	Hospital surveillance system	None

VE against radiologically confirmed pneumonia

Three studies reported VE against radiologically confirmed pneumonia (Appendix Figure 1). In Colombia, the intended schedule for PRP-T was 2, 4, 6 months, and the effectiveness of three doses was 55% (95% CI 7-78%) [20]. In Bangladesh, three doses of combined Hib-DTwP vaccine were estimated to be 44% (95% CI 16-63%) or 32% (95% CI -2 to 54%) effective, based on hospital and community controls, respectively [16]. (These estimates from Bangladesh refer to pneumonia diagnosed by both study personnel and an independent paediatrician. If cases were diagnosed by only study personnel or by only the paediatrician, VE estimates are lower than those stated above, e.g. 16% (95% CI -11 to 37%) based on community controls and diagnosis by the paediatrician [16].) One further study, from Brazil, reported the effectiveness of two or more doses against radiologically confirmed pneumonia as 31% (95% CI -9 to 57%), based on an intended schedule of 2, 4, 6 months for HbOC and including children who had received one vaccine dose in the unvaccinated comparison group [19].

Appendix Figure 1: Dose-specific estimates of vaccine effectiveness against radiologically confirmed (all cause) pneumonia. Intended vaccination schedules were 6,10, 14 weeks (Bangladesh [16]); 2, 4, 6 months (Colombia [20], Brazil [19]). Hib vaccine was intended to be given with DTwP in Bangladesh; Colombia and Brazil currently also administer Hib vaccine with DTwP.



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