

**Table 1: Level of clinical protection conferred by a complete primary series of *Haemophilus influenzae* type b (Hib) vaccination**

**(A)**

**Population :** Immunocompetent individuals

**Intervention:** Complete primary series of Hib vaccination ( $\geq 2$  doses)

**Comparison:** No vaccination

**Outcome :** Hib meningitis

<b>PICO Question:</b> What is the level of clinical protection conferred by a complete primary series of Hib vaccination ( $\geq 2$ doses) in preventing Hib meningitis in immunocompetent individuals?				
		Rating	Adjustment to rating	
<b>Quality Assessment</b>	No of studies/starting rating		2 RCT/ 6 observational <sup>1</sup>	4
	Factors decreasing confidence	Limitation in study design	Serious <sup>2</sup>	-1
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	None detected	0
	Factors increasing confidence	Strength of association/ large effect	High <sup>3</sup>	+1
		Dose-response	Not applicable	0
		Antagonistic /mitigated bias and confounding	Not applicable	0
	<b>Final numerical rating of quality of evidence</b>			<b>4</b>
<b>Summary of Findings</b>	<b>Statement on quality of evidence</b>		We are very confident that the true effect lies close to that of the estimate of effect on health outcome	
	<b>Conclusion</b>		We are very confident that a primary series of vaccination against Hib ( $\geq 2$ doses) confers high levels of clinical protection against Hib meningitis. Vaccine efficacy ranged from 67%-95% and effectiveness from 65%-99%.	

<sup>1</sup> Evidence retrieved from two systematic reviews (Jackson et al.2013; Low et al.2013). For 2p+0 vs 0 doses, intention to treat (ITT) vaccine efficacy was 96% (95%CI 37-100%) against Hib meningitis (Santosham 1991). ITT efficacy of a 3p vs 0 dose schedule against meningitis was calculated to be 67% (95%CI 22-86%) (Mulholland 1997). Observational studies confirm vaccine effectiveness against Hib meningitis ranging from 65% (95%CI -190-100%) (Baqui 2007) to 99% (95%CI 92-100%) (Lee 2008) after two or more doses.

<sup>2</sup> Unclear allocation concealment and blinding of participants in the larger of the two RCTs (21490 participants) (Mulholland 1997)

<sup>3</sup> Evidence from RCTs and observational studies suggest vaccine efficacy and effectiveness over 50%

## Reference List

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10. Santosham M et al. The efficacy in Navajo infants of a conjugate vaccine consisting of *Haemophilus influenzae* type b polysaccharide and *Neisseria meningitidis* outer-membrane protein complex. *The New England Journal of Medicine*, 1991. 324(25): 1767-1772.

**(B)****Population :** Immunocompetent individuals**Intervention:** Complete primary series of Hib vaccination ( $\geq 2$  doses)**Comparison:** No vaccination**Outcome : Invasive Hib disease**

<b>PICO Question:</b> What is the level of clinical protection conferred by a complete primary series of Hib vaccination ( $\geq 2$ doses) in preventing invasive Hib disease in immunocompetent individuals?				
		Rating	Adjustment to rating	
<b>Quality Assessment</b>	No of studies/starting rating		5 RCT/ 6 observational <sup>4</sup>	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	None detected	0
	Factors increasing confidence	Strength of association/ large effect	Very high <sup>5</sup>	(+2)
		Dose-response	Not applicable	0
		Antagonistic /mitigated bias and confounding	Not applicable	0
	<b>Final numerical rating of quality of evidence</b>			<b>4</b>
<b>Summary of Findings</b>	<b>Statement on quality of evidence</b>		We are very confident that the true effect lies close to that of the estimate of effect on health outcome	
	<b>Conclusion</b>		We are very confident, that a primary series of vaccination against Hib ( $\geq 2$ doses) confers a high level of clinical protection against invasive Hib disease. Vaccine efficacy ranged from 83%-96% and effectiveness from 86%-100%.	

<sup>4</sup> Evidence retrieved from two systematic reviews (Jackson et al.2013; Low et al.2013). Data from RCTs confirm high vaccine efficacy. For 2p+0 vs 0 doses, intention to treat (ITT) vaccine efficacy (VE) against invasive Hib disease was 95% (95%CI 72-99) (Santosham 1991). For four trials reporting invasive Hib disease for a 3p vs 0 dose schedule (Mulholland 1997, Black 1991, Vadheim 1993, Lagos 1996) the combined ITT VE estimate was 83% (95%CI 72-89) with low between trial heterogeneity (I2 0%). Observational studies confirm high levels of vaccine effectiveness against invasive Hib disease ranging from 86% (95%CI 16-98%) (Jafari 1999) to 100% (95%CI 68-100%) (Vadheim 1994) after two or more doses.

<sup>5</sup> Evidence from RCTs and observational studies suggest vaccine efficacy and effectiveness over 80%

## Reference List

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