

**Table 5a. Efficacy of influenza vaccine in health care workers**

Is influenza vaccine versus placebo or non-influenza vaccine in health care worker effective to prevent influenza infection of health care worker themselves?				
		Rating	Adjustment to rating	
Quality Assessment	No of studies/starting rating		1 RCT <sup>1,2</sup>	4
	Factors decreasing confidence	Limitation in study design	None serious <sup>3</sup>	0
		Inconsistency	None serious	0
		Indirectness	None serious <sup>4</sup>	0
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Strength of association/ large effect	Not applicable <sup>5</sup>	0
		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>
Summary of Findings	<b>Statement on quality of evidence</b>		Our confidence in the estimate of effect of influenza vaccination of health care worker on influenza incidence is high.	
	<b>Conclusion</b>		Influenza vaccination of HCW prevents serologically-confirmed <b>influenza infection among HCWs with an efficacy of 88%</b> (95% CI: 59 to 96, p=0.0005).	

**NOTES**

<sup>1</sup> Wilde et al. 1999 studied 264 healthy hospital-based staff up to the age of 50 years during a 3-year period. The trial used a four-unit block randomization process to allocate HCW to influenza vaccine (TIV), (n=181) or to one of the three control groups (meningococcal vaccine, pneumococcal vaccine, placebo) (n=180). Match between vaccine strains and circulating virus varied by year and was good in the second year but only partially in the first and third years.

This trial was the only study that reported influenza infection in HCW confirmed by laboratory. Nevertheless, the demonstrated efficacy of TIV and LAIV against influenza infection in healthy adults has been used as a proxy for HCWs given the assumption that the majority of HCWs are in good health.

<sup>2</sup> There were additional publications identified measuring health outcomes after HCW vaccination (including days of ILI absence, ILI episodes, absenteeism due to respiratory infections) (Kheok et al. 2008, Saxén and Virtanen 1999, Weingarten et al. 1988). Two of these studies (Saxén and Virtanen 1999, Weingarten et al. 1988) were also included in a review (Ng, Lai 2011) that did not provide meaningful results since pooling of data was not possible based on different reporting and definitions of ILI and non-reporting of standard deviations (e.g. for mean number of days of ILI symptoms).

Saxén and Virtanen (1999) considered the effect of inactivated influenza vaccine on the number of ILI episodes and on absenteeism due to respiratory infections among HCW (absenteeism and reduction of influenza-associated working days lost is often used as surrogate indicator for the effectiveness of influenza vaccine among HCWs). Specific ILI with fever was not separately registered and assessed and there were serious methodological issues including the lack of information on sequence generation, allocation concealment, and the blinding of investigators and outcome assessors. Methodological limitations were also prominent in the study by Weingarten et al. (1998), that reported on impacts of vaccination of self-reported ILI without viral or serological confirmation. Although the risk of bias for allocation concealment and blinding was lower in Weingarten et al. (1998), both studies did not apply any laboratory test and the effectiveness measures can be biased since symptoms can be caused by other pathogens. Therefore, these studies were not used for evidence grading. Similar limitations apply to an observational study (Kheok et al. 2008) that based the outcome measure (ILI) on self-reported symptoms and failed to blind the study group.

<sup>3</sup> Low drop out rate, clinical follow-up obtained for all subjects, appropriate sequence generation process, adequate blinding of participants and investigators. Serologic data were obtained for 99.4% of subjects with only 1% of data on major outcomes missing. Minimal risk of selective reporting but adequacy of allocation concealment and blinding of outcome assessor remain unclear.

<sup>4</sup> No significant differences between intervention and control group in terms of demographic characteristics. Missed cases are likely to be similar in control and intervention group.

<sup>5</sup> Despite the vaccine effectiveness estimated from this study, no upgrading was applied since the retrospective design does not allow the assessment of vaccine carryover effect, which may affected the effectiveness measurement.

## References

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Saxen, H. and M. Virtanen, *Randomized, placebo-controlled double blind study on the efficacy of influenza immunization on absenteeism of health care workers*. *The Pediatric Infectious Disease Journal*, 1999. **18**:779-83.

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