Review: Inactivated vaccines provide the greatest protection against influenza in healthy persons

Demicheli V, Rivetti D, Deeks JJ, Jefferson TO. **Vaccines for preventing influenza in healthy adults.** Cochrane Database Syst Rev. 2001;(4):CD001269 (latest version 3 Aug 2001).

QUESTION

What is the effectiveness of vaccines in preventing influenza in healthy adults?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to 1997) with the terms influenza, route (oral), route (parenteral), and vaccine; searching EMBASE/Excerpta Medica (1990 to 1997) and the Cochrane Controlled Trials Register; hand searching the journal *Vaccine* to 1997; scanning the bibliographies of articles; and contacting manufacturers of vaccines and authors of studies in the review.

STUDY SELECTION

Studies were selected if they were quasirandomized or randomized controlled trials (RCTs) that compared influenza vaccines with placebo, control vaccines, or no intervention or doses or schedules of influenza vaccine in healthy persons 14 to 60 years of age and that assessed protection from exposure to naturally occurring influenza.

DATA EXTRACTION

Data were extracted on study quality, participant characteristics, intervention, and outcomes. Outcomes included rates of influenza (clinically defined [unspecified], clinically defined on the basis of specific symptoms or signs [specified], and serologically confirmed), hospital admissions, working days lost, and adverse events.

MAIN RESULTS

20 trials were included (14 RCTs) evaluating 3 types of vaccine: live attenuated aerosol (n = 26 369), inactivated aerosol (n = 1506), and inactivated parenteral (n = 23 628). Live aerosol vaccines were not effective for preventing either type of clinically defined influenza (2 trials). Inactivated vaccines were effective in preventing influenza: Both inactivated aerosol and inactivated parenteral vaccines prevented unspecified clinically defined influenza, and inactivated parenteral vaccines prevented specified clinically defined influenza (Table). Live aerosol and inactivated parenteral vaccines prevented serologically confirmed influenza (Table). No studies of inactivated aerosol reported serologically confirmed influenza. Vaccine and placebo did not differ for working days lost (3 trials), hospitalizations (1 trial), or complications (2 trials). Local tenderness and soreness were increased in patients who received inactivated parenteral vaccine (Table). No increase occurred in systemic myalgia, fever, or fatigue.

CONCLUSION

Inactivated parenteral vaccines are effective in preventing influenza in healthy adults.

Source of funding: Ministry of Defence, UK.

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Vaccines vs placebo for preventing influenza in healthy adults at mean 87 days*

Outcomes	Comparisons	Weighted event rates	Number of trials	RRR (95% CI)	NNT (CI)
CDI unspecified	IA vs placebo	7.2% vs 20%	1	65% (32 to 82)	8 (4 to 63)
	IP vs placebo	17% vs 21%	5	31% (5 to 51)	25 (13 to 250)
CDI specified	IP vs placebo	45% vs 53%	4	26% (1 to 45)	13 (8 to 29)
SCI	LA vs placebo	0.7% vs 8.5%	2	79% (44 to 92)	Not significant
	IP vs placebo	2.9% vs 8.7%	4	65% (44 to 79)	18 (12 to 34)
				RRI (CI)	NNH (CI)
Local adverse events	IP vs placebo	64% vs 35%	4	113% (35 to 236)	4 (3 to 7)

*CDI = clinically defined influenza; IA = inactivated aerosol vaccine; IP = inactivated parenteral vaccine; LA = live aerosol vaccine; SCI = serologically confirmed influenza. Other abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article using random effects.

COMMENTARY

Influenza vaccine is clearly cost-effective in elderly persons and those with chronic cardiac or respiratory disease. It reduces hospitalization, respiratory mortality, and all-cause mortality (1). Important potential benefits also exist in vaccinating healthy adults between 18 and 64 years of age against influenza, including reductions in influenza-like illness (ILI), avoidance of disruption in daily living, decreases in work absenteeism, and reduction in physician visits for ILI (2). From a societal perspective, the average costs range from a net saving of $46.85 per vaccinated person to a net cost of $11.17 per person. The difference depends in part on the factors inserted in the sensitivity analyses and the range of the variable assumptions for vaccine efficacy, infectivity, and cost at different vaccination sites (i.e., private office vs work site) (2, 3). When little or no match exists between the vaccine and epidemic strain, the benefit is small to nil.

Demicheli and colleagues show that an influenza vaccine is effective in reducing serologically confirmed cases of influenza A but is less effective in reducing cases of clinical influenza. However, because clinical influenza is a syndrome caused by several viruses, including respiratory syncytial, parainfluenza, and other viruses, efficacy using the outcome of clinical influenza will typically be underestimated; serologic confirmation is a more reliable outcome.

This review confirms that the inactivated influenza vaccine is an effective method for preventing influenza in healthy adults. When the influenza vaccine supply permits, healthy young adults would benefit by receiving the inactivated influenza vaccine.

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References

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2. **Bridges CB, Thompson WW, Meltzer MI, et al.** Effectiveness and cost-benefit of influenza vaccination of healthy working adults: a randomized controlled trial. JAMA. 2000;284:1655-63.
3. **Nichol KL.** Cost-benefit analysis of a strategyto vaccinate healthy working adults against influenza. Arch Intern Med. 2001;161:749-59.

