Influenza vaccination for healthcare workers who work with the elderly (Review)

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TABLE OF CONTENTS

Influenza vaccination for healthcare workers who work with the elderly

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A B S T R A C T

Background

Healthcare workers' (HCWs) influenza rates are unknown, but may be similar to the general public and they may transmit influenza to patients.

Objectives

To identify studies of vaccinating HCWs and the incidence of influenza, its complications and influenza-like illness (ILI) in individuals ≥ 60 in long-term care facilities (LTCFs).

Search strategy

We searched CENTRAL (*The Cochrane Library* 2009, issue 3), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (1966 to 2009), EMBASE (1974 to 2009) and Biological Abstracts and Science Citation Index-Expanded.

Selection criteria

Randomised controlled trials (RCTs) and non-RCTs of influenza vaccination of HCWs caring for individuals ≥ 60 in LTCFs and the incidence of laboratory-proven influenza, its complications or ILI.

Data collection and analysis

Two authors independently extracted data and assessed risk of bias.

Main results

We identified four cluster-RCTs (C-RCTs) (n = 7558) and one cohort (n = 12742) of influenza vaccination for HCWs caring for individuals ≥ 60 in LTCFs. Pooled data from three C-RCTs showed no effect on specific outcomes: laboratory-proven influenza, pneumonia or deaths from pneumonia. For non-specific outcomes pooled data from three C-RCTs showed HCW vaccination reduced ILI; data from one C-RCT that HCW vaccination reduced GP consultations for ILI; and pooled data from three C-RCTs showed reduced all-cause mortality in individuals ≥ 60.

Authors' conclusions

No effect was shown for specific outcomes: laboratory-proven influenza, pneumonia and death from pneumonia. An effect was shown for the non-specific outcomes of ILI, GP consultations for ILI and all-cause mortality in individuals ≥ 60. These non-specific outcomes are difficult to interpret because ILI includes many pathogens, and winter influenza contributes < 10% to all-cause mortality in individuals ≥ 60. The key interest is preventing laboratory-proven influenza in individuals ≥ 60, pneumonia and deaths from pneumonia, and we cannot draw such conclusions.

The identified studies are at high risk of bias.

Some HCWs remain unvaccinated because they do not perceive risk, doubt vaccine efficacy and are concerned about side effects. This review did not find information on co-interventions with HCW vaccination: hand washing, face masks, early detection of laboratory-proven influenza, quarantine, avoiding admissions, anti-virals, and asking HCWs with ILI not to work. We conclude there is no evidence that vaccinating HCWs prevents influenza in elderly residents in LTCFs. High quality RCTs are required to avoid risks of bias in methodology and conduct, and to test these interventions in combination.

PLAIN LANGUAGE SUMMARY

Influenza vaccination for healthcare workers who work with the elderly

There are no accurate data on rates of laboratory-proven influenza in healthcare workers.

The three studies in the first publication of this review and the two new studies we identified in this update are all at high risk of bias.

The studies found that vaccinating healthcare workers who look after the elderly in long-term care facilities did not show any effect on the specific outcomes of interest, namely laboratory-proven influenza, pneumonia or deaths from pneumonia. An effect was shown for outcomes with a non-specific relationship to influenza, namely influenza-like illness (which includes many other viruses and bacteria than influenza), GP consultations for influenza-like illness, hospital admissions and the overall mortality of the elderly (winter influenza is responsible for less than 10% of the deaths of individuals over 60 and overall mortality thus reflects many other causes).

Healthcare workers have lower rates of influenza vaccination than the elderly and surveys show that healthcare workers who do not get vaccinated do not perceive themselves at risk, doubt the efficacy of influenza vaccine, have concerns about side effects, and some do not perceive their patients to be at risk. This review did not find information on other interventions that can be used in conjunction with vaccinating healthcare workers, for example hand washing, face masks, early detection of laboratory-proven influenza in individuals with influenza-like illness by using nasal swabs, quarantine of floors and entire long-term care facilities during outbreaks, avoiding new admissions, prompt use of anti-virals, and asking healthcare workers with an influenza-like illness not to present for work.

We conclude that there is no evidence that only vaccinating healthcare workers prevents laboratory-proven influenza, pneumonia, and death from pneumonia in elderly residents in long-term care facilities. Other interventions such as hand washing, masks, early detection of influenza with nasal swabs, anti-virals, quarantine, restricting visitors and asking healthcare workers with an influenza-like illness not to attend work might protect individuals over 60 in long-term care facilities and high quality randomised controlled trials testing combinations of these interventions are needed.

BACKGROUND

Description of the condition

Healthcare workers, such as doctors, nurses, other health professionals, cleaners and porters may have substantial rates of clinical and sub-clinical influenza during influenza seasons (Elder 1996; Ruel 2002), but there are no reliable data on rates of laboratory-proven influenza in healthcare workers and whether they differ from those of the general population (Jefferson 2009). Laboratory-proven influenza in the general population on average accounts for 7% to 10% of influenza-like illnesses, and is based on biased or incomplete samples. Data from the control arms of randomised controlled trials (RCTs) could provide data on laboratory-proven influenza rates but is also biased.

Healthcare workers often continue to work when infected with influenza, increasing the likelihood of transmitting influenza to those in their care (Coles 1992; Weingarten 1989; Yassi 1993). Elderly people (aged 60 or older) in institutions such as long-stay hospital wards and nursing homes are at risk of influenza and its complications, especially if affected with multiple pathologies (Fune 1999; Jackson 1992; Muder 1998; Nicolle 1984).

Description of the intervention

One way to prevent the spread of influenza to elderly residents in long-term care facilities may be to vaccinate healthcare workers. The Centers for Disease Control (CDC) Advisory Committee on Immunization Practices (ACIP) recommends vaccination of all healthcare workers (Harper 2004). However, only 36% of healthcare workers in the US (CDC 2003) and 35% of staff in long-term care facilities in Canada were vaccinated in 1999 (Stevenson 2001). Nurses and (in some institutions) physicians, tend to have lower influenza vaccination rates than other healthcare workers. This relatively low uptake may partly be a reflection of doubts as to the vaccine's effectiveness (its ability to prevent influenza-like illness (ILI) and efficacy (its ability to prevent influenza) (Ballada 1994; Campos 2002-3; Ludwig-Beymer 2002; Martinello 2003; Quereshi 2004). The design and execution of campaigns to increase vaccination rates are also important (Doebbeling 1997; NFID 2004; Russell 2003a; Russell 2003b), in order to provide an intervention at minimal risk of bias from inadequate randomisation, concealment of allocation, blinding, attrition, incomplete reporting and inappropriate statistical analysis.

How the intervention might work

Healthcare workers are the key group who enter nursing and long-term care facilities on a daily basis. Immune systems of the elderly are less responsive to vaccination, and vaccinating healthcare workers should reduce the exposure of elderly people to influenza.

Why it is important to do this review

Previous systematic reviews of the effects of influenza vaccines in the elderly are now out of date or do not include all relevant studies. The Gross 1995 review is 14 years old and its conclusions are affected by the exclusion of recent evidence. The Vu 2002 review has methodological weaknesses (excluding studies with denominators smaller than 30 and quantitative pooling of studies with different designs), which are likely to undermine the conclusions. A systematic review by Jordan 2004 of the effects of vaccinating healthcare workers against influenza on high-risk elderly reports significantly lower mortality in the elderly (13.6% versus 22.4%, odds ratio (OR) 0.58, 95% confidence interval (CI) 0.4 to 0.84)

but does not include the latest studies. The Burls 2006 systematic review of effects on elderly people only identified the RCTs by Potter 1997 and Carman 2000, and Anikeeva 2009 does not include the studies by Lemaitre 2009 and Oshitani 2000. It is important to provide accurate information for policy makers, and highlight the need for high quality trials to test combinations of interventions, including healthcare worker vaccination.

There are Cochrane systematic reviews assessing the effects of influenza vaccines in children (Jefferson 2008), the elderly (Rivetti 2006), healthy adults (Demicheli 2007), people affected with chronic obstructive pulmonary disease (Poole 2009), asthma (Cates 2003) and cystic fibrosis (Dharmaraj 2009), and reviews of children (Jefferson 2005a) and the elderly (Jefferson 2005b). The first publication of this review (Thomas 2006) needed updating to search for and assess new literature.

O B J E C T I V E S

To identify all randomised controlled trials (RCTs) and non-RCTs assessing the effects of vaccinating healthcare workers on the incidence of influenza, influenza-like-illness (ILI) and its complications in elderly residents in long-term care facilities.

M E T H O D S

Criteria for considering studies for this review

Types of studies

RCTs and non-RCTs (cohort or case-control studies) reporting exposure and outcomes by vaccine status.

Types of participants

Healthcare workers (nurses, doctors, nursing and medical students, other health professionals, cleaners, porters and volunteers who have regular contact with the elderly) of all ages, caring for elderly residents (aged 60 years or older) in institutions such as nursing homes, long-term care facilities or hospital wards.

Types of interventions

Vaccination of healthcare workers with any influenza vaccine given alone or with other vaccines, in any dose, preparation, or time schedule, compared with placebo or with no intervention. Studies on vaccinated elderly are included in reviews looking at the effects of influenza vaccines in the elderly (Jefferson 2005b; Rivetti 2006).

The review by Demicheli et al (Demicheli 2007) looked at the effects of vaccination in healthy adults such as healthcare workers.

Types of outcome measures

Primary outcomes

Outcomes for the elderly - specific outcome measures for influenza

1. Cases of influenza confirmed by viral isolation and/or serological supporting evidence, plus a list of likely respiratory symptoms.
2. Cases of influenza admitted to hospital.
3. Deaths caused by influenza or its complications.

Studies reporting only serological outcomes in the absence of symptoms were excluded. Outcomes for healthcare workers were not considered.

Secondary outcomes

Non-specific outcome measures related to influenza-like illness and all-cause mortality

1. Cases of influenza-like illness clinically defined from a list of likely respiratory and systemic signs and symptoms within the epidemic period (the six-month winter period if not better specified).
2. Cases of influenza-like illness admitted to hospital.
3. Deaths from all causes.
4. Any other direct or indirect indicator of disease impact (days of illness, resources consumption, complications).

Search methods for identification of studies

Electronic searches

For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, issue 3), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register and the Database of Abstracts of Reviews of Effects (DARE); MEDLINE (January 1966 to Week 3, September 2009); EMBASE (1974 to September 2009); Biological Abstracts (1969 to December 2005) and Science Citation Index-Expanded (1974 to September 2009), which included Science Citation Index-Expanded, Biosis Previews and Current Contents. See Appendix 1 for details of previous searches. There were no language restrictions.

We searched MEDLINE, MEDLINE in-process and CENTRAL using the following search strategy. We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity-maximising version (2008 revision); Ovid format (Lefebvre 2008). We adapted the search strategy to search EMBASE (Appendix 2) and Web of Science (Appendix 3).

We also combined the following search strategy with the SIGN filter (SIGN 2009) for identifying observational studies and ran the searches in MEDLINE and adapted them for EMBASE and Web of Science (see Appendix 4).

1 Influenza Vaccines/
2 Influenza, Human/
3 exp Influenzavirus A/
4 exp Influenzavirus B/
5 influenza.tw.
6 flu.tw.
7 or/2-6
8 exp Vaccines/
9 Vaccination/
10 vaccin*.tw,nm.
11 exp Immunization/
12 (immuniz* or immunis*).tw.
13 or/8-12
14 7 and 13
15 1 or 14
16 exp Health Personnel/
17 ((health or health care or healthcare) adj2 (personnel or worker* or provider* or employee* or staff)).tw.
18 ((medical or hospital) adj2 (staff or employee* or personnel or worker*)).tw.
19 (doctor* or physician* or clinician*).tw.
20 (allied health adj2 (staff or personnel or worker*)).tw.
21 paramedic*.tw.
22 nurse*.tw.
23 (nursing adj2 (staff or personnel or auxiliar*)).tw.
24 exp Hospitals/
25 Long-Term Care/
26 exp Residential Facilities/
27 nursing home*.tw.
28 (institution* adj3 elderly).tw.
29 aged care.tw.
30 or/16-29
31 30 and 15

Searching other resources

We searched bibliographies of retrieved articles and contacted trial authors for further details, if required.

Data collection and analysis

Selection of studies

Two review authors (TJL, RET) independently reviewed the abstracts by using the following inclusion criteria.

1. Elderly people 60 years or older.
2. Long-term care facilities or hospitals.
3. Healthcare workers.
4. Influenza vaccination.
5. Morbidity and mortality of residents.

Disagreements were resolved by a third review author (TOJ).

Data extraction and management

Two review authors (RET, TJL) applied the inclusion criteria to all identified and retrieved articles, and extracted data from included studies into standard Cochrane Vaccines Field forms. We extracted the following data in duplicate.

Methods: purpose; design; period study conducted and statistics.

Participants: country or countries of study; setting; eligible participants; age and gender.

Interventions and exposure: in intervention group and control group.

Outcomes:

1. cases of influenza confirmed by viral isolation and/or serological supporting evidence plus a list of likely respiratory symptoms;
2. cases of influenza admitted to hospital;
3. cases of influenza-like illness clinically defined from a list of likely respiratory and systemic signs and symptoms within the epidemic period (the six-month winter period if not better specified);
4. cases of influenza-like illness admitted to hospital;
5. deaths from all causes;
6. deaths caused by influenza or its complications;
7. any other direct or indirect indicator of disease impact (days of illness, resources consumption, complications).

Two review authors (RET, TJL) independently checked data extraction, and disagreements were resolved by third review author (TOJ).

Assessment of risk of bias in included studies

Assessment of methodological quality for RCTs was carried out using the Cochrane Collaboration's 'Risk of bias' tool (Higgins 2008a). We assessed the quality of non-RCTs in relation to the presence of potential confounders using the appropriate Newcastle-Ottawa Scales (NOS) (Wells 2005). The NOS asks whether all possible precautions against confounding have been taken by the study designers, and links study quality to the answer. We translated the number of inadequately reported or conducted items into categories of risk of bias. We used quality at the analysis stage as a means of interpreting the results. The review authors resolved

disagreements on inclusion or methodological quality of studies by discussion. Two review authors (RET, TOJ) checked quality assessment.

We looked for details of formal ethics approval and informed consent of participants.

Measures of treatment effect

Only the last primary outcome measure (that is, any other direct or indirect indicator of disease impact (days of illness, resources consumption, complications)) allowed a comparison with two studies; for each of the remaining outcomes only data from one study were available. Efficacy (against influenza) and effectiveness (against influenza-like illness) (effects) estimates were summarised as risk ratio (RR) or odds ratio (OR) within 95% confidence intervals (CI). For Hayward 2006 we analysed the data as mean differences of rates. Absolute vaccine efficacy (VE) was expressed as a percentage using the formula: VE = 1 - RR whenever significant. When statistical significance was not achieved we reported the relevant RR or OR.

Unit of analysis issues

All four RCTs were cluster-RCTs. Carman 2000 did not control for clustering and we were not able to adjust his data to do so. We adjusted the precision of the study estimates for the cluster-RCTs based on standard *Cochrane Handbook for Systematic Reviews of Interventions* advice (Higgins 2008b). We contacted trial authors to ascertain the intra-cluster correlation coefficient (ICC), and to confirm statistical analyses.

Dealing with missing data

We did not use any strategies to impute missing outcome data, and recorded missing data in the 'Risk of bias' table. We attributed an ICC to two studies (Carman 2000; Potter 1997), from an assumed intra-cluster variance of 2.3% in Hayward 2006.

Assessment of heterogeneity

We used the X^2 and I^2 statistic to assess heterogeneity, and pooled studies in meta-analysis only if the I^2 statistic was approximately 50%.

Assessment of reporting biases

We reviewed an additional 554 abstracts for potential RCTs and 251 for non-RCTs, and 312 citations from the systematic review by Jefferson 2005b. We identified only four cluster-RCTS and one cohort study. The funnel plot for all-cause mortality (Figure 1), for example, contains only three cluster-RCTs and it is difficult to draw conclusions about bias from such a small number.

Figure 1. Funnel plot of comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design, outcome: 1.7 Deaths from all causes.
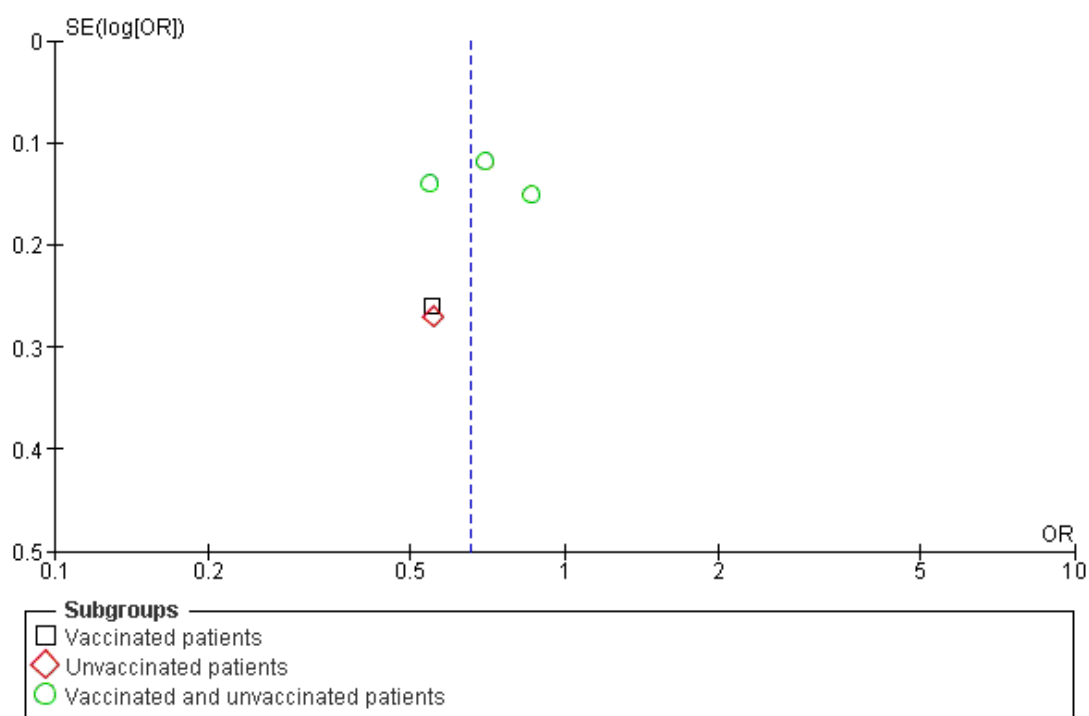
Data synthesis

We meta-analysed RCTs when the I^2 statistic was less than approximately 50%, and used the random-effects model as it could not be assumed that the studies came from similar populations.

Subgroup analysis and investigation of heterogeneity

We structured two comparisons: studies with an experimental design and studies without an experimental design. Whenever data presented in the study allowed it, we carried out subgroup analysis according to elderly residents' vaccination status. We assessed the following outcomes which arose during the influenza season.

1. Influenza-like illness.
2. Laboratory-proven influenza infections (by paired serology, nasal swabs, reverse-transcriptase polymerase chain reaction (RT-PCR), or tissue culture).
3. GP consultations for influenza-like illness.
4. Lower respiratory tract infections.
5. Deaths from pneumonia.
6. All-cause mortality.

Sensitivity analysis

With only four cluster-RCTs, a sensitivity analysis was not feasible.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

This updated search retrieved a total of 554 records in the search for RCTs and 251 records in the search for observational studies. In the first publication of this review we also examined 312 reports for detailed assessment from the review on the effects of influenza vaccines in the elderly (Rivetti 2006).

Due to the comprehensive nature of the Cochrane Review on the effects of influenza vaccines in the elderly (Rivetti 2006), we carried

out a review with a very focused study question and benefited from extensive searches which generated a large number of 'hits' but a relatively low yield of studies to include.

Only four cluster-RCTs were found. The funnel plot (Figure 1) does not suggest publication bias, but the number of studies is small.

Included studies

We identified four cluster-RCTs (n = 7558) meeting our inclusion criteria (Carman 2000; Hayward 2006; Lemaitre 2009; Potter 1997) and one cohort study (n = 12742) (Oshitani 2000).

Excluded studies

We excluded 22 studies. The abstract appeared appropriate, but after examining the full text, the studies were excluded because they either did not have influenza vaccination outcome data for the elderly or healthcare workers or both, or reported only influenza antibody levels.

Risk of bias in included studies

See the 'Risk of bias' tables and Figure 2 and Figure 3.

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.
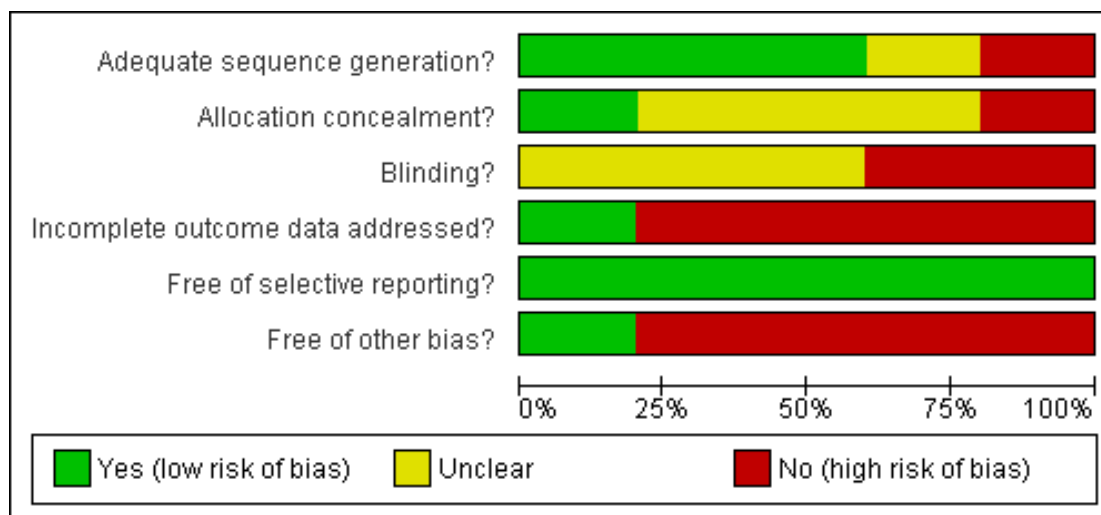
Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

Oshitani 2000 was assessed (Appendix 5) using the 'Newcastle-Ottawa scale for assessment of quality of non-randomised studies' and the entries in the 'Risk of bias' table for sequence generation and allocation concealment do not apply to this non-RCT.

Allocation

There was adequate sequence generation in three studies (Carman 2000 and Hayward 2006 by a random number table; and Lemaitre 2009 by centralised random-number generator) but uncertainty in one study (Potter 1997 "Hospital sites were stratified by unit policy for vaccination, then randomized for their healthcare workers to be routinely offered either influenza vaccination and patients

unvaccinated..."). There was allocation concealment in one study (Hayward 2006 by a researcher blinded to the homes' identity and characteristics).

Blinding

No RCT used blinding of participants or study personnel. In Carman 2000, Potter 1997 and Hayward 2006 there is no statement that any researcher, assessor, data analyst, healthcare worker or participant was blinded. In Hayward 2006 lead nurses "were trained to promote influenza vaccination to staff". In Carman 2000 the study nurses "took additional opportunistic nose and

throat swabs from non-randomised patients who the ward nurses thought had an influenza-like illness". In Potter 1997 ward nurses paged the research nurses "if any patients under their care developed clinical symptoms suggestive of upper respiratory tract viral illness, influenza, or lower respiratory tract infection," and in Lemaitre 2009 "Influenza vaccination was further recommended during face-to-face interviews with each member of staff ... The study team individually met all administrative staff, technicians, and caregivers to invite them to participate, and volunteers were vaccinated at the end of the interview."

Incomplete outcome data

Incomplete data were not addressed in four studies (Carman 2000; Hayward 2006; Oshitani 2000; Potter 1997).

Selective reporting

No study appeared to report results selectively.

Other potential sources of bias

For Potter 1997 potential sources of bias were as follows.

1. Selection bias: the total number of long-term care hospitals in West and Central Scotland is not stated. There were inconsistencies in outcome gradients (see Table 1). In the population under observation, Potter 1997 reported 216 cases of suspected viral illness, 64 cases of influenza-like illness, 55 cases of pneumonia, 72 deaths from pneumonia and 148 deaths from all causes; in the sub-population of both vaccinated staff and patients, Potter 1997 reported 24 cases of suspected viral illness, two cases of influenza-like illness, seven cases of pneumonia, 10 deaths from pneumonia and 25 deaths from all causes. As these gradients are not plausible (one would expect a greater proportion of cases of influenza-like illness to be caused by influenza during a period of high viral activity), the effect on all-cause mortality is likely to reflect a selection bias rather than a real effect of vaccination.

Table 1. Potter 1997

	SVPV	SVP0	S0PV	S0P0
Suspected viral illness	24	58	75	59
Influenza-like illness	2	20	19	23
Pneumonia	7	14	16	18
Deaths from pneumonia	10	15	24	23

Table 1. Potter 1997 *(Continued)*

All deaths	25	25	56	42

S0P0: staff and patients not vaccinated
S0PV: staff not vaccinated, patients vaccinated
SVPV: staff and patients vaccinated
SVP0: staff vaccinated and patients not vaccinated

1. Performance bias: 67% of staff in active arm 1 and 43% in active arm 2 were vaccinated.

2. There is no description of the vaccines administered, vaccine matching or background influenza epidemiology.

For Carman 2000 potential sources of bias were as follows.

1. Selection bias: the total number of long-term care hospitals in West and Central Scotland is not stated. In the long-term care hospitals in which healthcare workers were offered vaccination, residents had higher Barthel scores.

2. Performance bias: only 51% of healthcare workers in the Lemaitre 2009 arm received vaccine in the long-term care hospitals where vaccine was offered, and 4.8% where it was not; 48% of patients received vaccine in the arm where healthcare workers were offered vaccination, and 33% in the arm where healthcare workers were not.

3. Statistical bias: the analysis was not corrected for clustering, unlike the Potter 1997 pilot; in the long-term care hospitals where healthcare workers were offered vaccination, the patients had significantly higher Barthel scores and were more likely to receive influenza vaccine (no significance level stated), and due to missing data these differences could not be adjusted for other than by estimation. Statistical power may also have been a problem as the detection rate of 6.7% was lower than the estimated rate of 25% used in the power calculation.

The Potter 1997 and Carman 2000 cluster-RCTs can be regarded as investigations in the same geographical area with a modest possible but unknown overlap of staff and residents. Only three of the long-term care hospitals in the Potter study (Potter 1997) were included in the Carman cluster-RCT (Carman 2000) because some of the homes were closed down (e-mail communication from Dr. Stott), but the continuity of staff between the institutions is unknown.

We assessed Oshitani 2000 with the Newcastle-Ottawa scale for assessing the quality of non-RCTs (see Appendix 5). It is at a high risk of bias due to problems in the following.

1. Selection: lack of clear definition of vaccine coverage rates among healthcare workers, and unclear ascertainment of vaccination status and comparability of hemicohorts (the government mandated surveys but there is no description of the surveys, how they were administered or completeness).

2. Comparability: there was no ascertainment of health status or co-morbidities in the hemicohorts, and the study mixed two types of healthcare facilities, one which is for elderly patients and the other for elderly with severe health conditions. Also, facilities with higher vaccination rates might have practised other preventive measures, such as hand washing, limitation of visitors during influenza epidemics or isolation of patients. These practices may have had an impact on the outcome but are not reported.

3. Outcomes: demographic inconsistencies in reporting of denominators, differential criteria for diagnosing influenza-like illness, and the lack of laboratory confirmation.

Ethics approval: Carman 2000, Hayward 2006, Lemaitre 2009 and Potter 1997 received formal ethics approval. Carman 2000 and Potter 1997 obtained written informed consent from healthcare workers and witnessed verbal consent from participants for nose swabs to be taken and Potter 1997 for blood samples. The long-term care facilities already had policies for opting in or opting out of influenza vaccination. Lemaitre 2009 obtained face-to-face informed consent from healthcare workers and Hayward 2006 trained nurses to promote vaccination to healthcare workers, and neither had an intervention for the elderly.

Effects of interventions

The data analysis tables show two pieces of information for each study: (1) the average (central tendency of the results) as a diamond (if only one study is in the group) and as a box (if more than one

study is in the group), and (2) the possible range or dispersion of the results. The convention is to show the 95% confidence interval (CI) as a horizontal bar, and the interpretation is that it shows the maximum range of results statistically possible in 95 experiments if the study were repeated 100 times, and thus 2.5% of times the result could be lower than the lower end and 2.5% of times higher then the upper end of the CI bar. For an entire set of studies the average is shown by a diamond. The legend at the bottom of each graph shows whether the placement of the boxes and diamonds favours the intervention or the control group.

Specific effects of interventions

Effects of healthcare worker vaccination on influenza

Carman 2000 reported data on influenza cases among vaccinated and unvaccinated patients combined (OR 0.80, 95% CI 0.39 to 1.64, P = 0.54). Potter 1997 reported outcomes only for unvaccinated patients (OR 1.37, 95% CI 0.22 to 8.36, P = 0.73). We were able to pool the results and we computed an overall OR of 0.86 (95% CI 0.44 to 1.68, P = 0.66). The pooled OR which was adjusted for clustering was 0.87 (95% CI 0.38 to 1.99, P = 0.74).

Effects of healthcare worker vaccination on pneumonia

The Potter 1997 study reported data separately for vaccinated patients and for vaccinated we computed an OR of 0.59 (95% CI 0.25 to 1.40, Z = 1.20, P = 0.23) and for unvaccinated we computed OR 0.78 (95% CI 0.40 to 1.54, P = 0.47). For vaccinated we computed an adjusted OR of 0.59 (95% CI 0.13 to 2.63), Z = 0.69 (P = 0.49) and for unvaccinated an adjusted OR of 0.78 (95% CI 0.26 to 2.33), Z = 0.45 (P = 0.66). The combined adjusted OR was 0.71 (0.29 to 1.71), Z = 0.77 (P = 0.44).

Effects of healthcare worker vaccination on deaths from pneumonia

Potter 1997 reported data separately for vaccinated patients and we computed OR 0.56 (95% CI 0.27 to 1.14, Z = 1.59, P = 0.11) and for unvaccinated we computed OR 0.65 (95% CI 0.35 to 1.23, Z = 1.32, P = 0.19). Lemaitre 2009 reported results for vaccinated and unvaccinated patients combined and we computed OR 1.54 (95% CI 0.75 to 3.17, Z = 1.18, P = 0.24). We were able to pool the results (Tau^2 = 0.16, X ^{2} = 4.56, P = 0.10, I ^{2} statistic = 56%) and computed OR 0.82 (95% CI 0.45 to 1.49, Z = 0.66, P = 0.51). Adjusted estimates gave a pooled OR 0.87 (95% CI 0.47 to 1.64, Z = 0.42, P = 0.67) with a lower level of statistical heterogeneity (X^2 = 2.06, P = 0.36, I^2 statistic = 3%).

Non-specific effects of interventions

Effects of healthcare worker vaccination on influenza-like illness

Potter 1997, Hayward 2006 and Lemaitre 2009 defined influenza-like illness from a list of likely respiratory and systemic signs and symptoms.

Potter 1997 reported the data separately for vaccinated patients (RR 0.14, 95% CI 0.03 to 0.60, P = 0.008) and unvaccinated patients (RR 0.87, 95% CI 0.49 to 1.55, P = 0.64).

Hayward 2006 and Lemaitre 2009 reported results for vaccinated and unvaccinated patients combined. We were able to pool the results for Hayward 2006, Lemaitre 2009 and Potter 1997, which favoured vaccination (RR 0.71, 95% CI 0.55 to 0.90, P = 0.005, I^2 statistic 46%). When the analyses were adjusted for clustering the amount of statistical heterogeneity was greatly reduced (I^2 statistic = 0%) although the pooled RR was similar at 0.71 (95% CI 0.58 to 0.88, P = 0.002).

Oshitani 2000 did not define influenza-like illness. His cohort study shows a significant effect apart from the vaccination of residents (overall vaccine efficacy (VE) 61%, 95% CI 54% to 68%), but the study had a high risk of bias.

Effects of healthcare worker vaccination on GP consultations for influenza-like illness

Hayward 2006 provided data and we computed an adjusted OR of 0.48 (95% CI 0.33 to 0.69, Z = 3.98, P < 0.0001).

Effects of healthcare worker vaccination on deaths from influenza-like illness

Hayward 2006 provided data and we computed an adjusted OR of 0.72 (95% CI 0.31 to 1.70, Z = 0.75, P = 0.45).

Effects of healthcare worker vaccination on admissions to hospital

Hayward 2006 and Lemaitre 2009 provided data, and we were able to pool their data (X ^{2} = 1.30, P = 0.25, I ^{2} statistic = 65%) and we computed OR 0.89 (95% CI 0.75 to 1.06, Z = 1.29, P = 0.20). Adjusted estimates gave a pooled OR of 0.90 (95% CI 0.66 to 1.21, Z = 0.73, P = 0.47) with a lower level of statistical heterogeneity (X^2 = 1.36, P = 0.24, I^2 statistic = 26%).

Effects of healthcare worker vaccination on deaths from all causes

Potter 1997 reported outcomes separately for vaccinated patients and we computed OR 0.55 (95% CI 0.33 to 0.91, Z = 2.32, P = 0.02) and for unvaccinated patients we computed OR 0.55 (95%

CI 0.33 to 0.94, Z = 2.19, P = 0.03). Carman 2000, Hayward 2006 and Lemaitre 2009 reported data for vaccinated and unvaccinated patients combined. We were able to pool the results (Tau^2 = 0.03; X^2 = 4.90, P = 0.09, I^2 statistic = 59%) and we computed OR 0.69 (95% CI 0.54 to 0.87, Z = 3.07, P = 0.002).

We were able to pool the results for Carman 2000, Hayward 2006, Lemaitre 2009 and Potter 1997 (Tau^2 = 0.01; X^2 = 6.05, P = 0.2, I^2 statistic = 34%) and we computed OR 0.66 (95% CI 0.55 to 0.79, Z = 4.55, P = 0.00001). Based on adjusted estimates there was lower statistical heterogeneity (X^2 = 2.69, P = 0.61, I^2 statistic = 0%) and a similar pooled OR 0.68 (95% CI 0.55 to 0.84, Z = 3.54, P = 0.0004).

DISCUSSION

We identified four cluster-RCTs and one cohort study to answer the question of whether vaccinating healthcare workers against influenza protects elderly residents in long-term care facilities. For the four cluster-RCTs adequate allocation was achieved in three, concealment of allocation in one, blinding in none and incomplete data were addressed in one. Carman 2000 and Oshitani 2000 did not adjust results for the effect of clustering.

Pooled data from three cluster-RCTs (Hayward 2006; Lemaitre 2009; Potter 1997) showed no effect on specific outcomes: laboratory-proven influenza, lower respiratory tract infections, admissions to hospital and deaths from pneumonia, with the 95% CI in each case including unity. Pooled data from three cluster-RCTs (Hayward 2006; Lemaitre 2009; Potter 1997) showed for non-specific outcomes that vaccination of healthcare workers reduced influenza-like illness and resident all-cause mortality; and data from one RCT (Hayward 2006) showed that healthcare worker vaccination reduced GP consultations for influenza-like illness.

A survey of 301 nursing home directors in one chain of nursing homes in the US found that homes with more than 55% of staff and more than 89% of residents vaccinated had a 60% lower risk of influenza-like illness clusters than all others.

One question is what is the maximum contribution that influenza vaccination of elderly people could make in reducing total annual mortality. A population study by Simonsen 2006 used data from the US national multiple-cause-of-death databases from 1968 to 2001 and found that for those aged 65 years or older, the mortality attributable to pneumonia or influenza never exceeded 10% of all deaths during those winters. The study by Vila-Córcoles 2007 of 11,240 Spanish community-dwelling elderly, conducted between January 2002 to April 2005 found the attributable mortality risk in individuals not vaccinated against influenza was 24 deaths/100,000 person-weeks within influenza periods. Vaccination prevented 14% of these deaths for the population, and one death was prevented for every 239 annual vaccinations (ranging

from 144 in winter 2005 to 1748 in winter 2002). It should be noted that these data are not for residents of long-term care facilities. A mathematical model (van den Dool 2008) predicted that for a 30-bed unit, an increase in healthcare worker vaccination rates from 0% to 100% would decrease resident influenza infections by 60%.

Summary of main results

We identified four cluster-RCTs. Pooled data from three cluster-RCTs (Hayward 2006; Lemaitre 2009; Potter 1997) showed that there was no effect on laboratory-proven influenza, lower respiratory tract infections, admissions to hospital and deaths from pneumonia, with the 95% CI in each case including unity. Pooled data from three cluster-RCTs (Hayward 2006; Lemaitre 2009; Potter 1997) showed that vaccination of healthcare workers reduced influenza-like illness; data from one cluster-RCT (Hayward 2006) showed that healthcare worker vaccination reduced GP consultations for influenza-like illness; pooled data from three cluster-RCTs (Hayward 2006; Lemaitre 2009; Potter 1997) showed a reduction in resident all-cause mortality. Pooled data from two cluster-RCTs, Hayward 2006 and Lemaitre 2009, did not show an effect on hospital admissions.

Overall completeness and applicability of evidence

The four cluster-RCTs focused directly on the question of the effect of healthcare worker vaccination on the mortality and morbidity of long-term care facility residents aged 60 years or older. The four cluster-RCTs contributed data from a total of 10,137 participants, and the cohort study by Oshitani 2000 contributed data from 12,742 participants.

Quality of the evidence

The Cochrane Collaboration recommends assessment of study quality by independent assessment by two authors of six risks of bias. We found the following.
(1) Adequate sequence generation in three studies (Carman 2000 and Hayward 2006 by a random number table; and Lemaitre 2009 by centralised random-number generator) but uncertainty in one study (Potter 1997 "Hospital sites were stratified by unit policy for vaccination, then randomized for their healthcare workers to be routinely offered either influenza vaccination and patients unvaccinated...").
(2) Allocation concealment in one study (Hayward 2006 by a researcher blinded to the homes' identity and characteristics).
(3) No RCT used blinding of participants or study personnel. In Carman 2000, Potter 1997 and Hayward 2006 there is no statement that any researcher, assessor, data analyst, healthcare worker

or participant was blinded. In Hayward 2006 lead nurses "were trained to promote influenza vaccination to staff." In Carman 2000 the study nurses "took additional opportunistic nose and throat swabs from non-randomised patients who the ward nurses thought had an influenza-like illness." In Potter 1997 ward nurses paged the research nurses "if any patients under their care developed clinical symptoms suggestive of upper respiratory tract viral illness, influenza, or lower respiratory tract infection," and in Lemaitre 2009 "Influenza vaccination was further recommended during face-to-face interviews with each member of staff ... The study team individually met all administrative staff, technicians, and caregivers to invite them to participate, and volunteers were vaccinated at the end of the interview.

In cluster-RCTs where the intervention is delivered to a group and there is an attempt to change both individual attitudes and behaviour and group perceptions and willingness to participate, it is a good question how much blinding can be achieved. Blinding is intended to avoid effects of interventions other than the study intervention, but when sharing of ideas and motivations is a key idea in the intervention then blinding is not achievable.

(4) Incomplete data were not addressed in four studies: Carman 2000, Hayward 2006, Oshitani 2000 and Potter 1997. Nursing homes vary in the numbers of admissions and departures both of residents and staff, and a complete account of the sample requires maintaining a flow-sheet of resident admissions and discharges and staff arrivals and departures. Only Lemaitre 2009 made a full inventory of residents: "The analyses included all residents who were present on at least one day in a participating nursing home between the beginning and end of the primary study period." In Hayward 2006 "The rates were measures based on person time where the denominator was the average number of residents during the period of interest (calculated as the number of occupied bed days during the period divided by the number of days in the period) and the numerator was the number of events in these residents during the period." Potter 1997 noted that "many patients refused a blood sample, and paired samples were only available from survivors..."

(5) None were selective in reporting data.

(6) (a) Two (Carman 2000 and Potter 1997) were at risk of selection bias.

(b) All four cluster-RCTs and Oshitani 2000 were at risk of performance bias, with inadequate provision of influenza vaccine to some or all participants. In Carman 2000, in the long-term care facilities where vaccination was offered 48% of patients (range 0% to 94% for 10 long-term care facilities) and 50.9% of healthcare workers were vaccinated, and in those where it was not offered 33% of patients (range 0% to 70% for 10 long-term care facilities) and 4.9% of healthcare workers were vaccinated. The results for healthcare workers were based on the questionnaire data for nurses (with a 68% return rate in hospitals that offered vaccine to 49% in hospitals which did not offer vaccine). In Potter 1997, in the arm where both healthcare workers and participants were offered

vaccination, 67% of the healthcare workers and 88.8% of the patients were vaccinated. In the arm where only healthcare workers were offered vaccination, 57% of the healthcare workers and 0.4% of the patients were vaccinated. In the arm where only patients were offered vaccination, 91.9% of participants were vaccinated and the percentage of healthcare workers was not stated. Lastly, in the arm where neither were offered vaccination, 0% of patients were vaccinated and the percentage for healthcare workers was not stated.

In Hayward 2006 78.2% of patients in intervention homes were vaccinated in 2003 to 2004 (70.5% in 2004 to 2005), and 71.4% in control homes in 2003 to 2004 (71.1% in 2004 to 2005). For healthcare workers in intervention homes 48.2% were vaccinated in 2003 to 2004 and 43.2% in 2004 to 2005, compared to 5.9% and 3.5% in control homes. In Lemaitre 2009 the average patient vaccination rate was 84.3% in the intervention and 82.5% in the control arm; and the staff vaccination rate was 69.9% (range 48.4% to 89.5% for 20 homes) in the intervention arm and 31.8% (range 0% to 69% for 20 homes) in the control arm. Thus the vaccination rates and the ranges of vaccination rates between homes vary widely, and this varying and incomplete uptake affects the conclusions that can be drawn, as clearly the interventions had no or minimal effect on vaccination rates in some homes.

Pooled data from three cluster-RCTs showed no effect on the key specific outcomes of laboratory-proven influenza, pneumonia and deaths from pneumonia, with the 95% confidence interval (CI) in each case including unity. For the non-specific outcomes pooled data from three cluster-RCTs showed that vaccination of healthcare workers reduced influenza-like illness; data from one cluster-RCT revealed that healthcare worker vaccination reduced GP consultations for influenza-like illness; pooled data from three cluster-RCTs showed a reduction in resident all-cause mortality, and pooled data from two cluster-RCTs showed no effect on hospital admissions.

The effect of the clustered design was not addressed in Carman 2000 and Oshitani 2000. All five studies are at high risk of bias.

Potential biases in the review process

We imposed no language restrictions on the search, and all studies were independently assessed by two review authors. The intra-cluster correlation coefficients (ICCs) we used for two of the four studies were based on the estimate provided by Hayward 2006. Although the recalculation of the standard errors was done in accordance with recommended procedures (Higgins 2008a), we have assumed that the adjustment required is the same across the outcomes extracted for each study. Rather than increase uncertainty around the pooled effect size, adjustment of the standard errors for the studies reduced the statistical heterogeneity between the study effect estimates. If the ICCs we used as the basis for these calculations were too large, our adjusted analyses may underestimate the true amount of variation between the study results.

Agreements and disagreements with other studies or reviews

Other reviews addressing similar study questions do not include all the studies that we found.

AUTHORS' CONCLUSIONS

Implications for practice

All five studies are at high risk of bias. Pooled data from three cluster-randomised controlled trials (cluster-RCTs) (Hayward 2006; Lemaitre 2009; Potter 1997) found no effect on the outcomes of direct interest, namely laboratory-proven influenza, lower respiratory tract infections, admissions to hospital and deaths from pneumonia, with the 95% confidence interval (CI) in each case including unity. Pooled data from three cluster-RCTs (Hayward 2006; Lemaitre 2009; Potter 1997) showed that vaccination of healthcare workers reduced influenza-like illness and resident all-cause mortality; and data from one RCT (Hayward 2006) showed that healthcare worker vaccination reduced GP consultations for influenza-like illness. However, there was no effect on the outcomes of direct interest, namely laboratory-proven influenza, lower respiratory tract infections, admissions to hospital and deaths from pneumonia, with the 95% CI in each case including unity, and we conclude that there is an absence of high quality evidence to guide medical care and public health practitioners to mandate influenza vaccination for healthcare workers who care for the elderly in long-term care facilities. Because influenza-like illness encompasses many pathogens other than influenza, and because winter influenza contributes to less than 10% of all-cause mortality in the elderly, the most likely explanation for our findings is residual confounding from pathogens other than influenza, differential uptake of vaccine affected by socio-economic status, and varying belief on the part of healthcare workers regarding vulnerability to influenza, vaccine effectiveness and side effects. We conclude that there is no evidence from this research that vaccinating healthcare workers against influenza protects elderly people in their care.

Implications for research

There are currently only four cluster-RCTS providing data about the impact on elderly residents of vaccinating their healthcare workers against influenza, all at high risk of bias. RCTs are needed with minimal risk of bias from allocation, failure to conceal allocation, selection, performance, attrition and detection and these should be adequately powered for the key outcomes of laboratory-proven influenza, hospitalisation for pneumonia and death from

pneumonia. They should carefully define and measure outcomes including influenza-like illness, laboratory-proven influenza, cause of hospitalisation, deaths from pneumonia and all-cause mortality. They should carefully consider the degree to which they must, to adequately assess outcomes, obtain proof of diagnosis for all participants by laboratory testing all participants with appropriate symptoms for influenza and all other likely viruses, performing blood cultures, white blood cell counts and other laboratory investigations and chest X-rays if pneumonia is suspected, and following the course of all hospitalised patients by scrutinising individual records so that they can definitively assess all outcomes and co-morbidities.

The area of interest is the elderly in long-term care facilities, therefore if the existing long-term care facilities' organisational structure is to be used to implement the interventions, these will need to be given to clusters of elderly residents and healthcare workers, which will make blinding difficult. An important ethical issue is informed consent by the elderly and healthcare workers. It is not ethical to blind participants or healthcare workers, but the researchers, data assessors and statisticians could all be blinded.

The elderly are much keener to be vaccinated than healthcare workers, and there is an extensive literature about the group of healthcare workers who say they do not feel vulnerable to influenza, do not believe the vaccine is effective and are afraid of side effects, and some of these do not perceive risk for their patients. Persistence of these beliefs may limit uptake by healthcare workers, and make it difficult to test conclusively the effect of very high levels of healthcare worker influenza vaccination.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Carman 2000

Methods	Purpose: to assess the effects of staff vaccination against influenza on resident mortality in long-term care hospitals Design: cluster-randomised study (C-RCT) conducted in Scotland during the 1996 to 1997 influenza season. The study identified 10 long-term care geriatric hospitals in West and Central Scotland with a policy of vaccinating all patients against influenza if they had no contraindications, and then only on the request of the patients or their relatives. Pairs of hospitals in each of these clusters were matched on patient enrolment and then in a Latin square design were randomised by a table of random numbers for the HCWs to be offered influenza vaccination or not Anonymous questionnaires were sent to ward nurses on 31 March 1997 to ask if they had received influenza vaccination, and these data were used to estimate vaccine acceptance for all HCWs in hospitals where influenza vaccine had not been offered to HCWs. In each hospital a random sample chosen by computer of 50% patients was selected for virological monitoring Data from the Scottish Centre for Infection and Epidemiological Health and from GPs were used to define the start of the influenza season. Combined nasal and throat swabs were taken from patients every 2 weeks from 14 December 1996 to 14 February 1997. Opportunistic samples were also taken from patients whom the ward nurses thought had influenza. Samples were taken within 12 hours of death of any patient who died. Samples were analysed by RT-PCR analysis Results were summarised for the 2 groups of LTCFs. Hospitals were not well-matched for patient vaccination rates and Barthel scores (Wikipedia 2009) and post-hoc statistical adjustments could not be made because of missing data. The outcome was the empirical logic of mortality for each cluster (= natural logarithm of the odds on death) Statistics: the power calculation was based on the previous study by Potter 1997, and the authors computed that with 1600 patients in 20 hospitals they would have ≥ 80% power to detect a decrease in mortality from 15% to 10% with alpha = 0.05 (2-tailed), allowing for the clustered design. The power calculation for virological sampling showed that 500 patients would be required to give 80% power at 5% significance (2-tailed) to detect a decrease in influenza infection from 25% to 15% Mortality rates were compared in the 2 groups with the Mann-Whitney test. "Incomplete data for patient-level covariates meant that a full multilevel approach to the analysis was not possible without making strong, implausible, and untestable assumptions about the mechanisms that led to the incomplete data. Instead, we calculated summary statistics to describe the mix of patients in each hospital, and these values were included in a multiple linear-regression analysis. The response variable in these analyses was the empirical logit of each hospital's mortality rate that is, the natural logarithm of the odds on death."
Participants	Country: Scotland Setting: 20 long-term care hospitals in Glasgow Eligible participants: 749 participants were residents of facilities in the arm in which 1217 HCWs were offered vaccination (620 accepted) and 688 in the arm in which HCWs were not offered vaccination. Day and night nurses, doctors, therapists, porters and ancillary staff (including domestic staff and ward cleaners) were offered influenza

	vaccination Age: 82 Gender: 70% F
Interventions	Intervention: Influenza vaccination. The type, dosage and route are not described. A good match in the study year between the prevailing strain and the vaccine strains was reported Control: no influenza vaccination
Outcomes	1. RT-PCR and tissue culture for influenza A or B. A random sample of 50% of patients in each hospital was selected for virological monitoring of influenza infections by nose and throat swabs every 2 weeks, which were sent for RT-PCR analysis and tissue culture. "At the times when study nurses took routine samples, they took additional opportunistic nose and throat swabs from non-randomised patients who the ward nurses thought had an influenza-like illness. The ward staff were asked to take routine nasal swabs within 12 hours of death for any patient who died." 2. Mortality (all causes) (N.B. clinical outcomes were not reported, but were used to investigate the viral circulation in the facility)
Notes	The situation that 10 long-term care hospitals had a policy of routinely vaccinating residents for influenza vaccination and 10 did not, permitted a Latin square design RCT of offering influenza vaccination or not to HCWs within each of these clusters Analysis was not according to intention-to-treat Design effect: 2.6; source: intra-cluster variance of 2.3% reported in Hayward 2006 Despite no difference in isolation of influenza viruses between clusters, the authors conclude that vaccines are protective. In addition, they fail to comment on the implausibility of the vaccines' effect on aspecific outcomes (ILI) and lack of effect on influenza

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"Hospitals were randomly allocated ... by random-numbers table."
Allocation concealment?	Unclear	Not stated
Blinding? All outcomes	Unclear	Not stated
Incomplete outcome data addressed? All outcomes	No	In the 10 hospitals where HCWs were offered vaccination 749 patients were included and "a random sample of 375 patients was offered virological screening by nose/throat swab"; 258 accepted. In the 10 hospitals where HCW were not offered vaccination 688 patients were included and a random sample of 344 were offered vi-

Carman 2000   (*Continued*)

		rological screening by nose/throat swab; 269 accepted. Note comments by authors in the Description section above on incomplete data. Polymerase chain reaction (PCR) samples were obtained from only 17% of deaths. Four samples from each patient surveyed were planned from protocol: 1798 samples were obtained from 719 patients (2.5 samples/patient)
Free of selective reporting?	Yes	
Free of other bias?	No	1. Selection bias: the total number of long-term care hospitals in West and Central Scotland is not stated. In the long-term care hospitals in which HCWs were offered vaccination, residents had higher Barthel scores 2. Performance bias: only 51% of HCWs in the arm received vaccine in the long-term care hospitals where vaccine was offered, and 4.8% where it was not; 48% of patients received vaccine in the arm where HCWs were offered vaccination, and 33% in the arm where HCWs were not 3. Statistical bias: the analysis was not corrected for clustering, unlike the Potter 1997 pilot; in the long-term care hospitals where HCWs were offered vaccination, the patients had significantly higher Barthel scores and were more likely to receive influenza vaccine (no significance level stated), and due to missing data these differences could not be adjusted for other than by estimation. Statistical power may also have been a problem as the detection rate of 6.7% was lower than the estimated rate of 25% used in the power calculation

Hayward 2006

Methods	Purpose: to increase staff vaccination rates in care homes by adoption of a policy to encourage staff to be vaccinated against influenza and providing vaccination clinics Design: C-RCT; 48 nursing homes were placed in matched pairs (by size of home, % of high dependency, and mortality of residents) within 3 regions (northern, central and southern England), then the 25 homes which most closely matched were selected and randomised by a researcher, blinded to the home's identity and characteristics, using a table of random numbers Data from the Royal College of General Practitioners sentinel surveillance scheme were used to divide the study into periods of influenza activity and no influenza activity Duration of study: 3 November 2003 to 28 March 2004, and 1 November 2004 to 27 March 2005 Interval between intervention and when outcome was measured: 3 November 2003 to 28 March 2004, and 1 November 2004 to 27 March 2005 Power computation: to detect reduction in all-cause mortality of residents from 15% to 10% (intra-cluster variance = 2.3%) with 90% power and alpha = 0.05% level required 20 pairs of homes each with an average of 20 residents (based on findings from pilot study) Statistics: outcomes were analysed using aggregate data for each cluster, and "to take account of the matched clustered design we used a random-effects meta-analysis. This treated the results from each pair of homes as a separate study and provided a pooled estimate of effect weighted for the size of homes and the size of the effects and their standard errors." "When significant protection of residents was observed we calculated the number of staff vaccinations needed to prevent one event in residents (number needed to treat) as number of vaccinations given in all intervention homes divided by the average number of residents in all intervention homes multiplied by the weighted rate difference."
Participants	Country: UK Setting: private chain of nursing homes, whose policy was not to offer influenza vaccination to staff Eligible participants: (health status): 1 intervention and 1 control home were unable to provide data so they and their matched home were excluded, leaving 44 homes for analysis; eligible staff were all staff in intervention homes (full-time: n = 844 in both 2003 to 2004 and in 2004 to 2005), and (part-time: n = 766 in 2003 to 2004 and n = 882 in 2004 to 2005) Age: Avg 83 Gender: 71% F
Interventions	Intervention 1: Adoption of policy in intervention homes of vaccinating staff against influenza, including a lead nurse in each home was trained to promote vaccination of staff; distribute leaflets and posters, and liaise to provide three vaccination clinics for staff in each home. Staff were sent a letter explaining the study and the potential benefits of influenza vaccination Control: staff in control homes received a letter describing the study and the Department of Health recommendation that those with chronic illnesses should receive influenza vaccination No attempt to influence vaccination of residents in any home

Outcomes	Primary outcome of the study: to assess effect of vaccinating staff on all-cause mortality of residents
	Secondary outcomes: ILI (defined as fever $\geq$ 37.8 °C measured orally, or an acute deterioration in physical or mental ability, plus either new onset or one or more respiratory symptoms or acute worsening of a chronic condition involving respiratory symptoms) , mortality with ILI, admission to hospital from any cause, admission to hospital with ILI, and consultations with a GP for ILI
	Other outcomes measured: % of staff vaccinated
	Time points from the study that are considered in the review or measured or reported in the study: 3 November 2003 to 28 March 2004 and 1 November 2004 to 27 March 2005
	% of staff vaccinated: by 28 March 2004 for first year of study and by 27 March 2005 for second year of study: Full time staff: intervention group 407/844 vaccinated; control group 51/859
	Part-time staff: intervention group 163/766 vaccinated; control group 33/815
Notes	Funding: UK Department of Health
	Design effect: 2.3; source: calculation based on reported intra-cluster variance (2.3%) in the published paper
	Vaccine content was not reported. No conclusions on matching can be drawn

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"A researcher blinded to the home's identity and characteristics carried out randomisation within those pairs using random number tables"
Allocation concealment?	Yes	"A researcher blinded to the home's identity and characteristics carried out randomisation..."
Blinding? All outcomes	No	
Incomplete outcome data addressed? All outcomes	No	"No outcome data were available for the excluded homes so an intention to treat analysis was not possible"
Free of selective reporting?	Yes	
Free of other bias?	Yes	

Lemaitre 2009 *(Continued)*

Methods	Purpose: to assess the effect of staff and resident influenza vaccination on resident all-cause mortality Design: C-RCT. A written invitation was sent to the 376 nursing homes with 50 to 200 elderly people (out of a total 1105 nursing homes) in the Paris area, and 88 responded. Of these 40 with staff influenza coverage < 40% during the 2005 to 2006 winter season were selected. Each institution was pair-matched on size, staff vaccination coverage 2005 to 2006, and Group Iso Resources (GIR) weighted average disability score (which ranges from 1 = severe disability to 6 = total autonomy). Randomisation was centrally based using a random-number generator Statistics: it was assumed that the influenza epidemic would last 2 months, mortality would be 8% in the control arm, and resident mortality would be reduced 40% after staff vaccination to 4.8% in the intervention arm. 20 pairs of nursing homes with 2000 residents in each group were required to obtain 80% power with 2-tailed hypothesis testing. Analysis was by intention-to-treat. "Odds ratios were calculated using alternating logistic regression, with one-nested log odds ratios to model the association between the responses of the same pair and the same nursing home within the pair." "In secondary analyses, multivariate estimates were adjusted for the residents' age, vaccination status, GIR disability score, and Charlson comorbidity index."
Participants	Country: France Setting: 40 nursing homes near Paris Eligible participants: 3483 patients in the 40 nursing homes In the intervention arm there were 1592 residents at the beginning, and 130 entered the homes during the study period (total = 1722); 989 staff were present at recruitment, and 678 (68.6%) were vaccinated. In the control arm there were 1558 residents at the beginning and 120 entered the homes during the study period (total = 1678); there were 1015 staff at recruitment, and 323 (31.8%) were vaccinated 1452 (84.3%) of patients in the intervention and 1385 (82.5%) in the control group were vaccinated during the 2005 to 2006 winter season Age: 86 Gender: 77.% F
Interventions	Intervention: 　1. Promotional campaign with posters, leaflets and an information meeting with the study team to sensitise staff to the benefits of influenza vaccination for oneself and residents 　2. Face-to-face interviews with each member of staff present in nursing homes between 6 November and 15 December 2006 　3. The study team met all administrative staff, technicians and caregivers to invite them to participate, and those who volunteered were vaccinated at the end of the interview. The vaccine was inactivated Influvac (Solvay Pharma Laboratories), with 15 mcg of each of A/Wisconsin/67/2005-like (H3N2), A/New Caledonia/20/99 (H1NH1) and B/Malysia/2506/2004 Control: routine information on influenza vaccination
Outcomes	Primary: all-cause mortality Secondary: 　1. Influenza, measured when clusters of ILI occurred in residents, using the Quick View Influenza Test 　2. ILI ("defined as a fever of ≥ 37.8 °C and onset of respiratory symptoms or

Lemaitre 2009 (*Continued*)

	worsening of chronic respiratory conditions" 3. Proportion of staff who reported ≥ 1 day of sick leave
Notes	Design effect: 1.9; source: reported in published paper and confirmed by Magali Lemaitre Choice of main outcome is inappropriate

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"Randomisation was centrally based using a random-number generator"
Allocation concealment?	Unclear	Not stated
Blinding? All outcomes	Unclear	Not stated
Incomplete outcome data addressed? All outcomes	Yes	
Free of selective reporting?	Yes	
Free of other bias?	No	

Oshitani 2000

Methods	Purpose: to assess the effect of staff and resident influenza vaccination rates on resident influenza-like illness (ILI) Design: prospective cohort study assessing the effectiveness of influenza vaccination levels in patients of long-term nursing care facilities (LTCFs) by vaccination coverage rates of HCWs (less than 10 or more than 10 vaccinated HCWs per facility), in Niigata, Japan. Niigata Prefecture and Niigata City conducted mandatory surveys of influenza vaccine status and occurrence of ILI every 2 weeks from January to March 1999. During this period more than 20% of facilities had outbreaks, and more than 10% of residents experienced ILI during an influenza A (H3N2) epidemic All LTCFs in Niigata Prefecture provided reports. Information (assumed questionnaires) included number of residents in each institution, number of vaccinated residents and staff and weekly ILI in residents. No ILI definition is reported An influenza outbreak was defined as 10% of more of the residents in a home reporting ILI symptoms during a week Two types of LTCFs, special nursing homes for the elderly and geriatric health services facilities were used. Both are for the elderly who need constant care, special nursing homes are for the elderly who have more severe conditions Statistics: X^2 and Fisher's Exact test for univariate analysis. X^2 for linear trend and Mantel-Haenszel ORs for different categories of resident vaccination rates. Logistic regression for multivariate analysis of outbreak status
Participants	Country: Japan Setting: 149 long-term care facilities in Niigata Prefecture and Niigata City Eligible participants: the text reports 12,784 residents in 149 facilities were included in the study with 3933 (30.8%) vaccinated and 7459 staff with 1532 (20.5%) vaccinated However, table 2 shows 8669 residents living in homes where less than 10 staff were vaccinated and 4073 living in homes with ≥10 staff vaccinated, for a total of 12,742. The totals for residents living in homes with less than 10 staff vaccinated is given as 8699, but the subcategories add to 8669, and for the homes where ≥10 staff were vaccinated the total is given as 4085 but the subcategories add to 4073 Age: not stated Gender: not stated
Interventions	Intervention: trivalent influenza vaccine containing A/Beijing/262/95 (H1N1), A/Sydney/5/97 (H3N2), and B/Mie/1/93, which was a good match against the circulating strain. No mention of pneumococcal vaccination is made Control: no control group
Outcomes	ILI (no case definition). During the period of surveying the number of ILI cases per week exceeded 10% of the residents in 34 (22.8%) of facilities
Notes	Choice of outcome is inappropriate (ILI is an aspecific outcome)

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	No	See Appendix 5 'Newcastle-Ottawa scale for assessment of quality of non-ran-

Oshitani 2000 (*Continued*)

		domised studies'
Allocation concealment?	No	
Blinding? All outcomes	No	
Incomplete outcome data addressed? All outcomes	No	
Free of selective reporting?	Yes	
Free of other bias?	No	

Potter 1997

Methods	Purpose: to assess the effect of staff and patient vaccination against influenza on resident 1. Serologically proven influenza 2. ILI 3. Lower respiratory tract infection 4. Deaths (from all causes) 5. Deaths (from pneumonia) Design: 6 geriatric long-stay hospitals in Glasgow in 1994 had an "opt-out" policy in which patients were routinely given influenza vaccine unless they refused it or had a major contraindication, and 6 had an "opt-in" policy in which patients were given vaccine only if they or their relatives requested it following advertisement on the ward that it was available Hospitals were stratified by policy on vaccination then randomised for their HCWs to be "routinely offered either influenza vaccination or no vaccination." Study conducted in Scotland, during the 1994 to 1995 influenza season, in the community. Follow-up period was 1 October 1994 to 31 March 1995. 12 hospitals were randomly allocated to offer vaccination of HCWs or not; facilities were grouped according to the vaccination policy. The vaccination of staff and patients was voluntary. The study thus presents data on four sub-populations: - staff and patients not vaccinated (S0P0) - staff not vaccinated, patients vaccinated (S0PV) - staff and patients vaccinated (SVPV) - staff vaccinated and patients not vaccinated (SVP0) Statistical analysis: "Baseline characteristics, morbidity and mortality in the 4 groups of hospitals were compared using the X^2 test, unpaired Student's test, and Wilcoxon rank sum test as appropriate. Odds ratios and 95% CIs were calculated for the effects of staff and patient vaccination. Survival analysis was by Kaplan-Meier product limit estimates, using the Tarone Ware test for statistical significance. Cluster analysis, examining mortality rates and other outcomes by hospital site, was also done."
Participants	Country: Scotland Setting: 12 geriatric medical long-term care hospitals in Glasgow Eligible participants: 1059 hospital residents. All 1078 HCWs (day and night nurses and nursing auxiliaries, ward cleaners, doctors, therapists and porters) in SVPV and SVP0

Potter 1997   (*Continued*)

hospitals were offered vaccination, but "voluntary workers, patients' friends and relatives and other casual or occasional ward visitors were not offered vaccine." Observed units were hospitals and not patients

654 (61%) of the 1078 agreed to participate; vaccination was contraindicated in 34 (3%) and 47 (4%) were on long-term sick leave and unavailable

The physical dependency level of patients was measured on the 20-point Barthel scale. The hospitals where patients were routinely offered vaccination (S0PV and SVPV) had lower Bartel scores (P = 0.003) than those not offered vaccination, but there were no differences between hospitals where HCWs were vaccinated and those where they were not

Age: 77

Gender: 71% F

Interventions	Vaccination of patients and HCWs began October 1994 ("4 weeks before the earliest likely start date of the annual influenza outbreak") Parenteral influenza vaccine. Vaccine strains probably matched the circulating strain
Outcomes	1. Serologically proven influenza (paired sera in 225 consenting patients in the "patients not vaccinated" arms)

   1. Serologically proven influenza (paired sera in 225 consenting patients in the "patients not vaccinated" arms)

   2. ILI (defined as a temperature of $\geq$ 37 °C, "plus one of the following symptoms: new-onset cough, coryza, sore throat, malaise, headache, or muscle aches" - reported singly or within the ILI outcome), and was monitored from the end of October 1994 to the end of March 1995

   3. LRTI ("was identified by the presence of (1) pulmonary crackles, wheeze or tachypnoea plus temp $\geq$ 37 °C or WBC > 10 x 10^9/L or (2) a positive sputum culture" and was monitored from the end of October 1994 to the end of March 1995

   4. Deaths (from all causes)

   5. Deaths (from pneumonia)

All deaths and discharges and admissions to the wards were recorded

Ward staff notified the research nurse of any patient who developed clinical symptoms of upper respiratory tract viral illness, influenza or lower respiratory tract infection, and the research nurse visited the patient within 24 hours to record symptoms, clinical signs and investigations on standardised forms. "Chest radiographs were not included as part of the routine assessment of suspected lower respiratory tract infection, as for many of the peripheral hospitals, it would have required an ambulance journey for the patient." "Patients with suspected viral illness who gave verbal consent had a nasopharyngeal aspirate (NPA) sample obtained within 48 hours of notification of symptoms. IFA for influenza A and B, respiratory syncytial virus (RSV), *Chlamydia psittaci*, and adenovirus antigens" were obtained

Antibody levels to *Mycoplasma pneumoniae (M. pneumoniae)* were ascertained by complement fixation in consenting patients who had not received influenza vaccination

Notes	Staff vaccination was incomplete and variable; results were presented by hospital group and not by vaccination status of patients. The authors concluded that vaccination of HCWs was associated with lower mortality and ILI. These benefits were not evident vaccinating patients alone

Design effect: 3.0; source: intra-cluster variance of 2.3% reported in Hayward 2006

Risk of bias

Potter 1997 *(Continued)*

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Hospital sites were stratified by unit policy for vaccination, then randomized for their HCWs to be routinely offered either influenza vaccination and their patients unvaccinated (S0P0), staff vaccinated and patients unvaccinated (SVP0), staff unvaccinated and patients vaccinated (S0PV), and both staff and patients vaccinated (SVPV)" (N.B. the phrase "either influenza vaccination and their patients unvaccinated (S0P0)" is an error and should read: "neither staff nor patients vaccinated (S0P0)")
Allocation concealment?	Unclear	Not stated
Blinding? All outcomes	Unclear	Not stated
Incomplete outcome data addressed? All outcomes	No	Only 654 (61%) of the 1078 HCWs agreed to participate and receive influenza vaccination, and 478 (88.8%) of the 538 patients in the "routine vaccination of patients" arms. Serologically proven influenza was ascertained in paired sera in only 225 consenting patients in the "patients not vaccinated" arms. The numbers of influenza or ILI infections in HCWs were not reported
Free of selective reporting?	Yes	
Free of other bias?	No	1. Selection bias: the total number of long-term care hospitals in West and Central Scotland is not stated. There were inconsistencies in outcome gradients (see Table 1). In the population under observation, Potter 1997 reported 216 cases of suspected viral illness, 64 cases of ILI, 55 cases of pneumonia, 72 deaths from pneumonia and 148 deaths from all causes; in the sub-population of both vaccinated staff and patients, Potter 1997 reported 24 cases of suspected viral illness, 2 cases of ILI, 7 cases of pneumonia, 10 deaths from pneumonia and 25 deaths from all causes. As these gradients are not plausible, the effect on all-cause mortality

Potter 1997 *(Continued)*

		is likely to reflect a selection bias rather than a real effect of vaccination
		2. Performance bias: 67% of staff in active arm 1 and 43% in active arm 2 were vaccinated
		3. There is no description of the vaccines administered, vaccine matching or background influenza epidemiology.

Avg: average
C-RCT: cluster-randomised controlled trial
F: female
HCWs: healthcare workers
ILI: influenza-like illness
LRTI: lower respiratory tract infection
LTC: long-term care
PCR: polymerase chain reaction
RCT: randomised controlled trial
RT-PCR: reverse-transcriptase polymerase chain reaction
S0P0: staff and patients not vaccinated
S0PV: staff not vaccinated, patients vaccinated
SVPV: staff and patients vaccinated
SVP0: staff vaccinated and patients not vaccinated
WBC: white blood cell

Characteristics of excluded studies *[ordered by study ID]*

Bellei 2007	Surveillance study of influenza and rhinovirus infections among HCWs; no vaccination data; no data for elderly people
Bertin 2007	Intranet assessment of HCW vaccination status; no vaccination or outcome data for elderly people
Carusone 2007	Study of pneumonia and lower respiratory infections in nursing home residents as predictors of hospitalisation and mortality; based on previous RCT; influenza vaccination status of patients; no HCW vaccination data
Chicaíza-Becerra 2008	Economic evaluation of influenza vaccination of HCWs; no vaccination or outcome data for elderly people
Chittaro 2009	Influenza vaccination campaign for HCWs; no data on elderly people
del Villar-Belzunce 2007	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people

Doratotaj 2008	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Hood 2009	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Isaacs 1997	Data were not presented by HCW vaccine coverage; only 21% of staff were vaccinated; amantadine was a confounder as it was given to patients and not staff; a flow sheet of admissions and discharges was not presented
Isahak 2007	Programme to increase influenza vaccination among elderly people in long-term care homes; no vaccination data for HCWs
Kheok 2008	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Kimura 2007	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Landi 2006	Prospective observational study of influenza vaccination in elderly people; no HCW data
Lee 2008	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Looijmans-van den Akker	Survey of effect of national policy on influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Mangtani 2004	Historical cohort study of individuals older than 64 years in the UK General Practice Research Database 1989 to 1999 in England and Wales. No intervention for HCWs
Munford 2008	Campaign to increase influenza vaccination among elderly people and HCWs; no outcome data for elderly people
Sato 2005	Study of antibody levels in elderly people and HCWs in response to influenza vaccination
Shugarman 2006	Retrospective cross-sectional study of 344 nursing homes (310 replied) from one chain in the US, with reports of staff and resident vaccination rates and whether the home had an ILI cluster ($\geq$ 3 residents with ILI within 72 hours)
Yang 2007	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people
Yassi 1993	Data were not presented by HCW vaccine coverage. Vaccine and amantadine were used to control outbreak: amantadine acts as confounder
Zimmerman 2009	Programme to increase influenza vaccination among HCWs; no vaccination or outcome data for elderly people

HCW: healthcare worker
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1.   HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Influenza-like iIlness	3	7031	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.55, 0.90]
1.1 Vaccinated patients	1	538	Risk Ratio (M-H, Random, 95% CI)	0.14 [0.03, 0.60]
1.2 Unvaccinated patients	1	521	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.49, 1.55]
1.3 Vaccinated and unvaccinated patients	2	5972	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.62, 0.84]
2 Mean rate of influenza-like iIlness per participant	1		Mean Difference (Fixed, 95% CI)	-0.09 [-0.15, -0.03]
3 Influenza	2	752	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.44, 1.68]
3.1 Unvaccinated patients	1	225	Odds Ratio (M-H, Fixed, 95% CI)	1.37 [0.22, 8.36]
3.2 Vaccinated and unvaccinated patients	1	527	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.39, 1.64]
4 Pneumonia	1	1059	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.41, 1.20]
4.1 Vaccinated patients	1	538	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.25, 1.40]
4.2 Unvaccinated patients	1	521	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.40, 1.54]
5 GP consultations for influenza-like illness	1	2572	Odds Ratio (M-H, Fixed, 95% CI)	0.48 [0.38, 0.61]
6 Mean rate of GP consultations for influenza-like illness per participant	1		Mean Difference (Fixed, 95% CI)	-0.07 [-0.12, -0.02]
7 Admission to hospital	2	5972	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.75, 1.06]
7.1 Vaccinated and unvaccinated patients	2	5972	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.75, 1.06]
8 Mean rate of admission to hospital per participant	1		Mean Difference (Fixed, 95% CI)	-0.02 [-0.04, -0.00]
9 Deaths from pneumonia	2	4459	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.45, 1.49]
9.1 Vaccinated patients	1	538	Risk Ratio (M-H, Random, 95% CI)	0.56 [0.27, 1.14]
9.2 Unvaccinated patients	1	521	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.35, 1.23]
9.3 Vaccinated and unvaccinated patients	1	3400	Risk Ratio (M-H, Random, 95% CI)	1.54 [0.75, 3.17]
10 Deaths from all causes	4	8468	Odds Ratio (M-H, Random, 95% CI)	0.66 [0.55, 0.79]
10.1 Vaccinated patients	1	538	Odds Ratio (M-H, Random, 95% CI)	0.55 [0.33, 0.91]
10.2 Unvaccinated patients	1	521	Odds Ratio (M-H, Random, 95% CI)	0.55 [0.33, 0.94]
10.3 Vaccinated and unvaccinated patients	3	7409	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.54, 0.87]
11 Mean rate of deaths from all causes	1		Mean Difference (Fixed, 95% CI)	-0.05 [-0.08, -0.02]
12 Deaths from influenza-like illness	1	2572	Odds Ratio (M-H, Fixed, 95% CI)	0.72 [0.35, 1.47]

Comparison 2. ≥Vaccinated HCWs per home versus < 10 vaccinated HCWs per home - cohort study; data for periods of high influenza activity: Oshitani = 90 days

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Influenza-like illness	1	12742	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.26, 0.36]
1.1 Vaccinated and unvaccinated patients	1	12742	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.26, 0.36]

Comparison 3. Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Influenza-like illness	3		Risk Ratio (Random, 95% CI)	0.71 [0.58, 0.88]
1.1 Vaccinated patients	1		Risk Ratio (Random, 95% CI)	0.14 [0.01, 1.88]
1.2 Unvaccinated patients	1		Risk Ratio (Random, 95% CI)	0.87 [0.32, 2.36]
1.3 Vaccinated and unvaccinated patients	2		Risk Ratio (Random, 95% CI)	0.72 [0.58, 0.89]
2 Influenza	2		Odds Ratio (Random, 95% CI)	0.87 [0.38, 1.99]
2.1 Vaccinated patients	0		Odds Ratio (Random, 95% CI)	Not estimable
2.2 Unvaccinated patients	1		Odds Ratio (Random, 95% CI)	1.37 [0.16, 11.86]
2.3 Vaccinated and unvaccinated patients	1		Odds Ratio (Random, 95% CI)	0.80 [0.32, 1.97]
3 Pneumonia	1		Risk Ratio (Random, 95% CI)	0.71 [0.29, 1.71]
3.1 Vaccinated patients	1		Risk Ratio (Random, 95% CI)	0.59 [0.13, 2.63]
3.2 Unvaccinated patients	1		Risk Ratio (Random, 95% CI)	0.78 [0.26, 2.33]
4 GP consultations for influenza-like illness	1		Odds Ratio (Random, 95% CI)	0.48 [0.33, 0.69]
5 Admission to hospital	2		Odds Ratio (Random, 95% CI)	0.90 [0.66, 1.21]
5.1 Vaccinated and unvaccinated patients	2		Odds Ratio (Random, 95% CI)	0.90 [0.66, 1.21]
6 Deaths from pneumonia	2		Risk Ratio (Random, 95% CI)	0.87 [0.47, 1.64]
6.1 Vaccinated patients	1		Risk Ratio (Random, 95% CI)	0.56 [0.16, 1.95]
6.2 Unvaccinated patients	1		Risk Ratio (Random, 95% CI)	0.65 [0.23, 1.80]
6.3 Vaccinated and unvaccinated patients	1		Risk Ratio (Random, 95% CI)	1.54 [0.57, 4.16]
7 Deaths from all causes	4		Odds Ratio (Random, 95% CI)	0.68 [0.55, 0.84]
7.1 Vaccinated patients	1		Odds Ratio (Random, 95% CI)	0.55 [0.23, 1.33]
7.2 Unvaccinated patients	1		Odds Ratio (Random, 95% CI)	0.55 [0.24, 1.29]
7.3 Vaccinated and unvaccinated patients	3		Odds Ratio (Random, 95% CI)	0.70 [0.55, 0.89]
8 Deaths from influenza-like illness	1		(Random, 95% CI)	0.72 [0.31, 1.70]

Analysis 1.1. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 1 Influenza-like illness.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 1 Influenza-like illness

Study or subgroup	Vaccine n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Vaccinated patients					
Potter 1997	2/230	19/308		2.7 %	0.14 [0.03, 0.60]
Subtotal (95% CI)	**230**	**308**		**2.7 %**	**0.14 [0.03, 0.60]**
Total events: 2 (Vaccine), 19 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.65 (P = 0.0080)					
2 Unvaccinated patients					
Potter 1997	20/260	23/261		13.9 %	0.87 [0.49, 1.55]
Subtotal (95% CI)	**260**	**261**		**13.9 %**	**0.87 [0.49, 1.55]**
Total events: 20 (Vaccine), 23 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.46 (P = 0.64)					
3 Vaccinated and unvaccinated patients					
Hayward 2006	142/1249	203/1323		43.5 %	0.74 [0.61, 0.90]
Lemaitre 2009	116/1722	163/1678		39.9 %	0.69 [0.55, 0.87]
Subtotal (95% CI)	**2971**	**3001**		**83.4 %**	**0.72 [0.62, 0.84]**
Total events: 258 (Vaccine), 366 (Control)					
Heterogeneity: Tau² = 0.0; Chi² = 0.18, df = 1 (P = 0.67); I² =0.0%					
Test for overall effect: Z = 4.28 (P = 0.000019)					
Total (95% CI)	**3461**	**3570**		**100.0 %**	**0.71 [0.55, 0.90]**
Total events: 280 (Vaccine), 408 (Control)					
Heterogeneity: Tau² = 0.02; Chi² = 5.55, df = 3 (P = 0.14); I² =46%					
Test for overall effect: Z = 2.81 (P = 0.0049)					

```
        0.05   0.2    1    5    20
     Favours vaccine      Favours control
```

Analysis 1.2.   Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 2 Mean rate of influenza-like illness per participant.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 2 Mean rate of influenza-like illness per participant

Study or subgroup	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hayward 2006	-0.09 (0.03157)	▅	100.0 %	-0.09 [-0.15, -0.03]
Total (95% CI)		◆	**100.0 %**	**-0.09 [-0.15, -0.03]**
Heterogeneity: not applicable				
Test for overall effect: Z = 2.85 (P = 0.0044)				

-0.5   -0.25   0   0.25   0.5

Favours experimental   Favours control

Analysis 1.3. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 3 Influenza.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 3 Influenza

Study or subgroup	Vaccine n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Unvaccinated patients					
Potter 1997	3/118	2/107		10.9 %	1.37 [0.22, 8.36]
Subtotal (95% CI)	**118**	**107**		**10.9 %**	**1.37 [0.22, 8.36]**
Total events: 3 (Vaccine), 2 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.34 (P = 0.73)					
2 Vaccinated and unvaccinated patients					
Carman 2000	14/258	18/269		89.1 %	0.80 [0.39, 1.64]
Subtotal (95% CI)	**258**	**269**		**89.1 %**	**0.80 [0.39, 1.64]**
Total events: 14 (Vaccine), 18 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.61 (P = 0.54)					
Total (95% CI)	**376**	**376**		**100.0 %**	**0.86 [0.44, 1.68]**
Total events: 17 (Vaccine), 20 (Control)					
Heterogeneity: Chi² = 0.29, df = 1 (P = 0.59); I² =0.0%					
Test for overall effect: Z = 0.44 (P = 0.66)					

```
        0.1   0.2   0.5    1    2    5    10
        Favours vaccine      Favours control
```

Analysis 1.4.   Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 4 Pneumonia.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 4 Pneumonia

Study or subgroup	Vaccine n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Vaccinated patients					
Potter 1997	7/230	16/308		37.6 %	0.59 [0.25, 1.40]
Subtotal (95% CI)	**230**	**308**		**37.6 %**	**0.59 [0.25, 1.40]**
Total events: 7 (Vaccine), 16 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.20 (P = 0.23)					
2 Unvaccinated patients					
Potter 1997	14/260	18/261		62.4 %	0.78 [0.40, 1.54]
Subtotal (95% CI)	**260**	**261**		**62.4 %**	**0.78 [0.40, 1.54]**
Total events: 14 (Vaccine), 18 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.72 (P = 0.47)					
Total (95% CI)	**490**	**569**		**100.0 %**	**0.70 [0.41, 1.20]**
Total events: 21 (Vaccine), 34 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.26, df = 1 (P = 0.61); I^2 =0.0%					
Test for overall effect: Z = 1.30 (P = 0.19)					

0.1 0.2   0.5   1   2   5   10

Favours vaccine   Favours control

Analysis 1.5.   Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 5 GP consultations for influenza-like illness.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 5 GP consultations for influenza-like illness

Study or subgroup	Vaccine	Control	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H,Fixed,95% CI		M-H,Fixed,95% CI
Hayward 2006	125/1249	247/1323		100.0 %	0.48 [0.38, 0.61]
Total (95% CI)	**1249**	**1323**		**100.0 %**	**0.48 [0.38, 0.61]**

Total events: 125 (Vaccine), 247 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 6.15 (P < 0.00001)

0.01   0.1   1   10   100

Favours experimental   Favours control

Analysis 1.6.   Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 6 Mean rate of GP consultations for influenza-like illness per participant.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 6 Mean rate of GP consultations for influenza-like illness per participant

Study or subgroup	Mean Difference (SE)	Mean Difference	Weight	Mean Difference
		IV,Fixed,95% CI		IV,Fixed,95% CI
Hayward 2006	-0.07 (0.02621)		100.0 %	-0.07 [-0.12, -0.02]
Total (95% CI)			**100.0 %**	**-0.07 [-0.12, -0.02]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.67 (P = 0.0076)

-0.2   -0.1   0   0.1   0.2

Favours experimental   Favours control

Analysis 1.7. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 7 Admission to hospital.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 7 Admission to hospital

Study or subgroup	Vaccine n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Vaccinated and unvaccinated patients					
Hayward 2006	105/1249	144/1323		49.2 %	0.75 [0.58, 0.98]
Lemaitre 2009	150/1722	143/1678		50.8 %	1.02 [0.81, 1.30]
Total (95% CI)	**2971**	**3001**		**100.0 %**	**0.89 [0.75, 1.06]**
Total events: 255 (Vaccine), 287 (Control)					
Heterogeneity: Chi^2 = 2.89, df = 1 (P = 0.09); I^2 =65%					
Test for overall effect: Z = 1.29 (P = 0.20)					

0.01 0.1 1 10 100

Favours experimental   Favours control
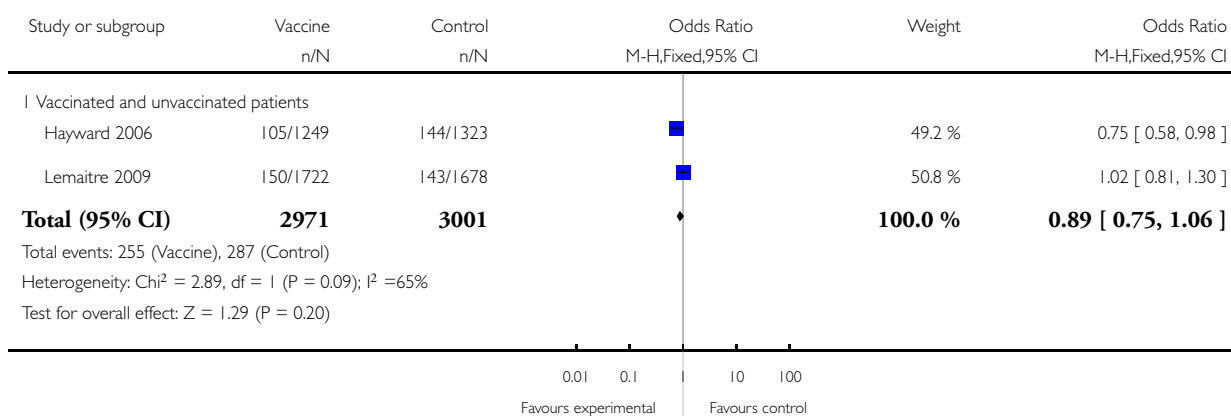
Analysis 1.8. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 8 Mean rate of admission to hospital per participant.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 8 Mean rate of admission to hospital per participant

Study or subgroup	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hayward 2006	-0.02 (0.00769)		100.0 %	-0.02 [-0.04, 0.00]
Total (95% CI)			**100.0 %**	**-0.02 [-0.04, 0.00]**
Heterogeneity: not applicable				
Test for overall effect: Z = 2.60 (P = 0.0093)				

-0.05 -0.03 0 0.03 0.05

Favours experimental   Favours control

Analysis 1.9. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 9 Deaths from pneumonia.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 9 Deaths from pneumonia

Study or subgroup	Vaccine n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Vaccinated patients					
Potter 1997	10/230	24/308		32.1 %	0.56 [0.27, 1.14]
Subtotal (95% CI)	**230**	**308**		**32.1 %**	**0.56 [0.27, 1.14]**
Total events: 10 (Vaccine), 24 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.59 (P = 0.11)					
2 Unvaccinated patients					
Potter 1997	15/260	23/261		36.0 %	0.65 [0.35, 1.23]
Subtotal (95% CI)	**260**	**261**		**36.0 %**	**0.65 [0.35, 1.23]**
Total events: 15 (Vaccine), 23 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.32 (P = 0.19)					
3 Vaccinated and unvaccinated patients					
Lemaitre 2009	19/1722	12/1678		32.0 %	1.54 [0.75, 3.17]
Subtotal (95% CI)	**1722**	**1678**		**32.0 %**	**1.54 [0.75, 3.17]**
Total events: 19 (Vaccine), 12 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.18 (P = 0.24)					
Total (95% CI)	**2212**	**2247**		**100.0 %**	**0.82 [0.45, 1.49]**
Total events: 44 (Vaccine), 59 (Control)					
Heterogeneity: Tau^2 = 0.16; Chi^2 = 4.56, df = 2 (P = 0.10); I^2 =56%					
Test for overall effect: Z = 0.66 (P = 0.51)					

0.1 0.2 0.5 1 2 5 10

Favours vaccine   Favours control

Analysis 1.10. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 10 Deaths from all causes.

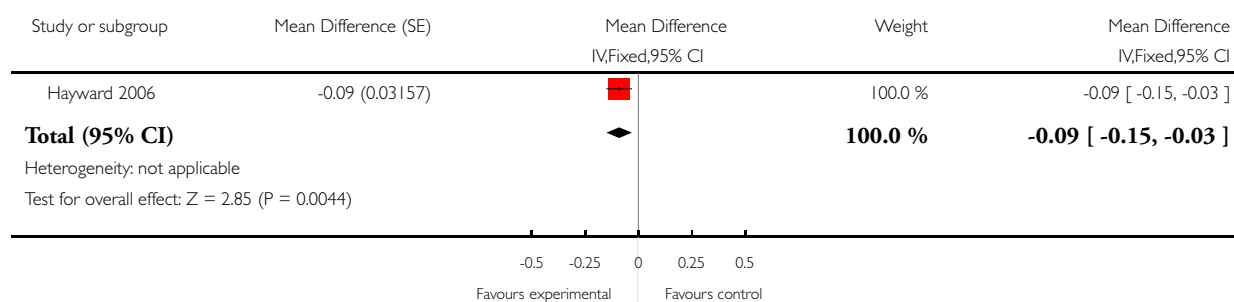Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 10 Deaths from all causes

Study or subgroup	Vaccine n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 Vaccinated patients					
Potter 1997	25/230	56/308		10.6 %	0.55 [0.33, 0.91]
Subtotal (95% CI)	**230**	**308**		**10.6 %**	**0.55 [0.33, 0.91]**
Total events: 25 (Vaccine), 56 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.32 (P = 0.020)					
2 Unvaccinated patients					
Potter 1997	25/260	42/261		9.9 %	0.55 [0.33, 0.94]
Subtotal (95% CI)	**260**	**261**		**9.9 %**	**0.55 [0.33, 0.94]**
Total events: 25 (Vaccine), 42 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.19 (P = 0.029)					
3 Vaccinated and unvaccinated patients					
Carman 2000	102/749	154/688		25.4 %	0.55 [0.42, 0.72]
Hayward 2006	140/1249	203/1323		30.6 %	0.70 [0.55, 0.88]
Lemaitre 2009	89/1722	100/1678		23.4 %	0.86 [0.64, 1.15]
Subtotal (95% CI)	**3720**	**3689**		**79.5 %**	**0.69 [0.54, 0.87]**
Total events: 331 (Vaccine), 457 (Control)					
Heterogeneity: Tau² = 0.03; Chi² = 4.90, df = 2 (P = 0.09); I² =59%					
Test for overall effect: Z = 3.07 (P = 0.0022)					
Total (95% CI)	**4210**	**4258**		**100.0 %**	**0.66 [0.55, 0.79]**
Total events: 381 (Vaccine), 555 (Control)					
Heterogeneity: Tau² = 0.01; Chi² = 6.05, df = 4 (P = 0.20); I² =34%					
Test for overall effect: Z = 4.55 (P < 0.00001)					

0.1 0.2 0.5 1 2 5 10
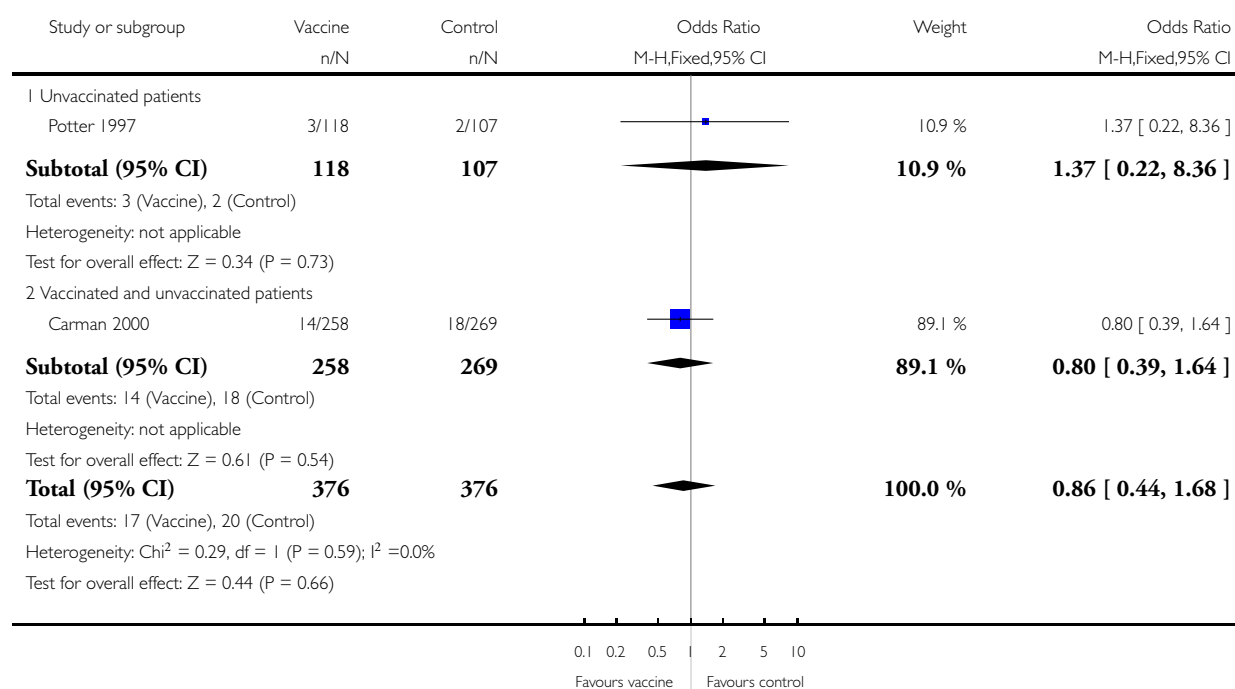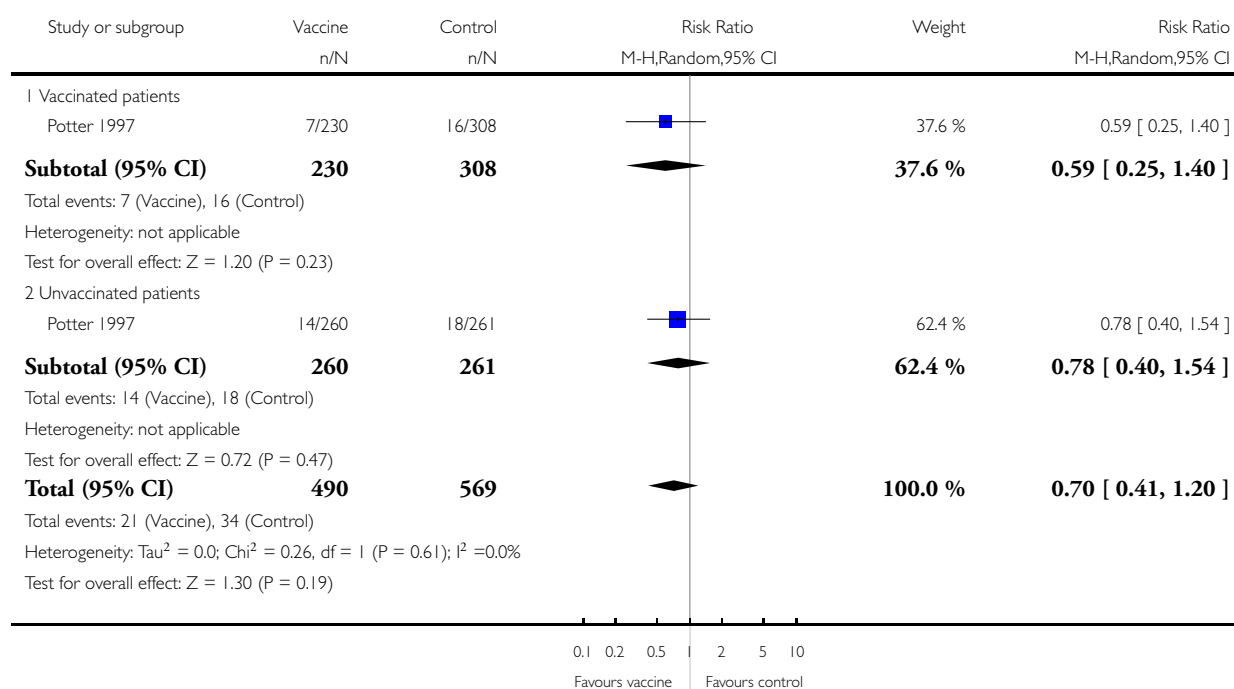
Favours vaccine   Favours control

Analysis 1.11. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 11 Mean rate of deaths from all causes.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 11 Mean rate of deaths from all causes

Study or subgroup	Mean Difference (SE)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hayward 2006	-0.05 (0.0161)		100.0 %	-0.05 [-0.08, -0.02]
Total (95% CI)			**100.0 %**	**-0.05 [-0.08, -0.02]**

Heterogeneity: not applicable
Test for overall effect: Z = 3.11 (P = 0.0019)

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        -0.1   -0.05    0    0.05    0.1
        Favours experimental    Favours control
```
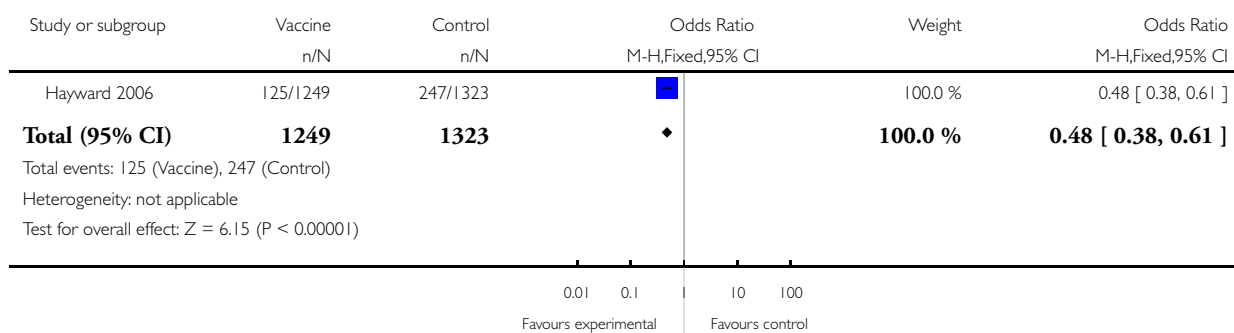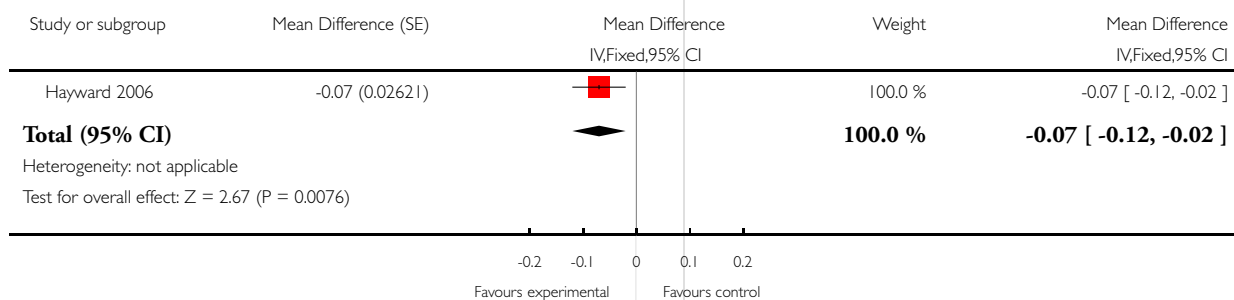
Analysis 1.12. Comparison 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days), Outcome 12 Deaths from influenza-like illness.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (Carman and Potter 152; Hayward 145, Lemaitre 118 days)

Outcome: 12 Deaths from influenza-like illness

Study or subgroup	Vaccine n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Hayward 2006	13/1249	19/1323		100.0 %	0.72 [0.35, 1.47]
Total (95% CI)	**1249**	**1323**		**100.0 %**	**0.72 [0.35, 1.47]**

Total events: 13 (Vaccine), 19 (Control)
Heterogeneity: not applicable
Test for overall effect: Z = 0.90 (P = 0.37)

```
      0.01    0.1    1    10    100
      Favours experimental    Favours control
```
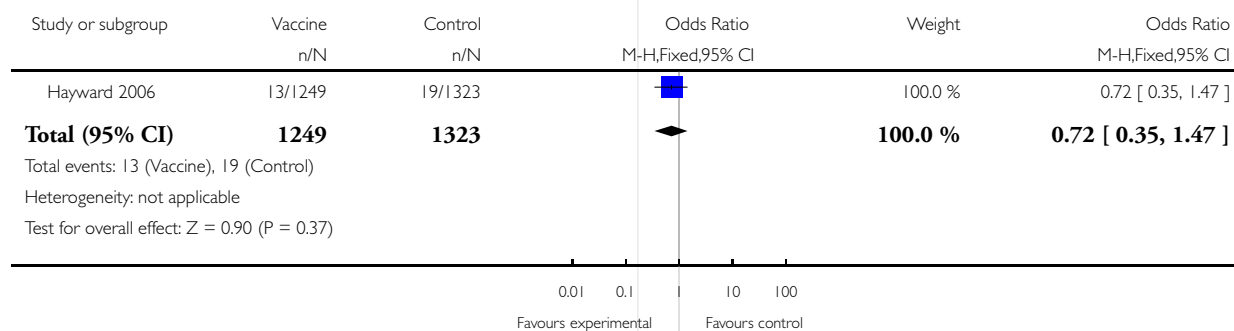
Analysis 2.1. Comparison 2 ≥Vaccinated HCWs per home versus < 10 vaccinated HCWs per home - cohort study; data for periods of high influenza activity: Oshitani = 90 days, Outcome 1 Influenza-like illness.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 2 ≥Vaccinated HCWs per home versus < 10 vaccinated HCWs per home - cohort study; data for periods of high influenza activity: Oshitani = 90 days

Outcome: 1 Influenza-like illness

Study or subgroup	Vaccine n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Vaccinated and unvaccinated patients					
Oshitani 2000	182/4073	1260/8669	■	100.0 %	0.31 [0.26, 0.36]
Total (95% CI)	**4073**	**8669**	◆	**100.0 %**	**0.31 [0.26, 0.36]**
Total events: 182 (Vaccine), 1260 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 15.32 (P < 0.00001)					

```
         0.1  0.2  0.5   1   2    5   10
           Favours vaccine    Favours control
```

Analysis 3.1. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 1 Influenza-like illness.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome: 1 Influenza-like illness

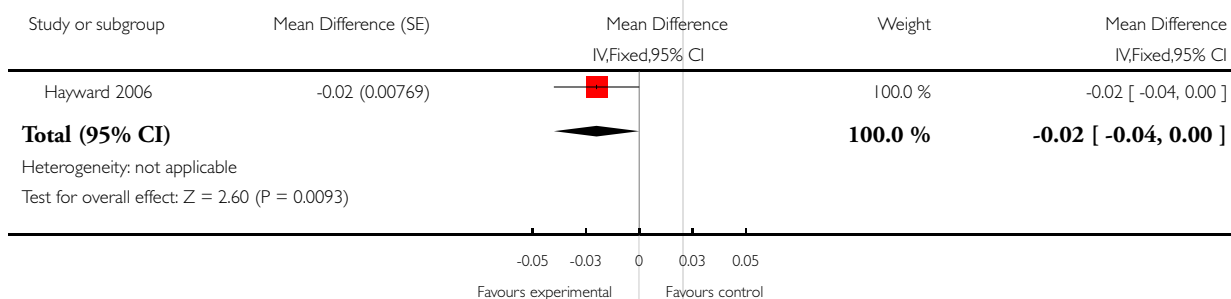| Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Vaccinated patients				
Potter 1997	-1.96611286 (1.32515168)	├──────┤	0.7 %	0.14 [0.01, 1.88]
Subtotal (95% CI)		◆	**0.7 %**	**0.14 [0.01, 1.88]**
Heterogeneity: not applicable				
Test for overall effect: Z = 1.48 (P = 0.14)				
2 Unvaccinated patients				
Potter 1997	-0.13926207 (0.50940836)	├─┤	4.5 %	0.87 [0.32, 2.36]
Subtotal (95% CI)		◆	**4.5 %**	**0.87 [0.32, 2.36]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.27 (P = 0.78)				
3 Vaccinated and unvaccinated patients				

```
        0.01   0.1    1    10   100
      Favours experimental   Favours control
```

(*Continued* . . .)

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Hayward 2006	-0.30110509 (0.15171587)		50.3 %	0.74 [0.55, 1.00]
Lemaitre 2009	-0.37106368 (0.16125049)		44.6 %	0.69 [0.50, 0.95]
Subtotal (95% CI)			**94.9 %**	**0.72 [0.58, 0.89]**
Heterogeneity: Tau² = 0.0; Chi² = 0.10, df = 1 (P = 0.75); I² =0.0%				
Test for overall effect: Z = 3.02 (P = 0.0025)				
Total (95% CI)			**100.0 %**	**0.71 [0.58, 0.88]**
Heterogeneity: Tau² = 0.0; Chi² = 1.76, df = 3 (P = 0.62); I² =0.0%				
Test for overall effect: Z = 3.12 (P = 0.0018)				

```
        0.01   0.1    I    10   100
      Favours experimental   Favours control
```

Analysis 3.2.   Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 2 Influenza.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)
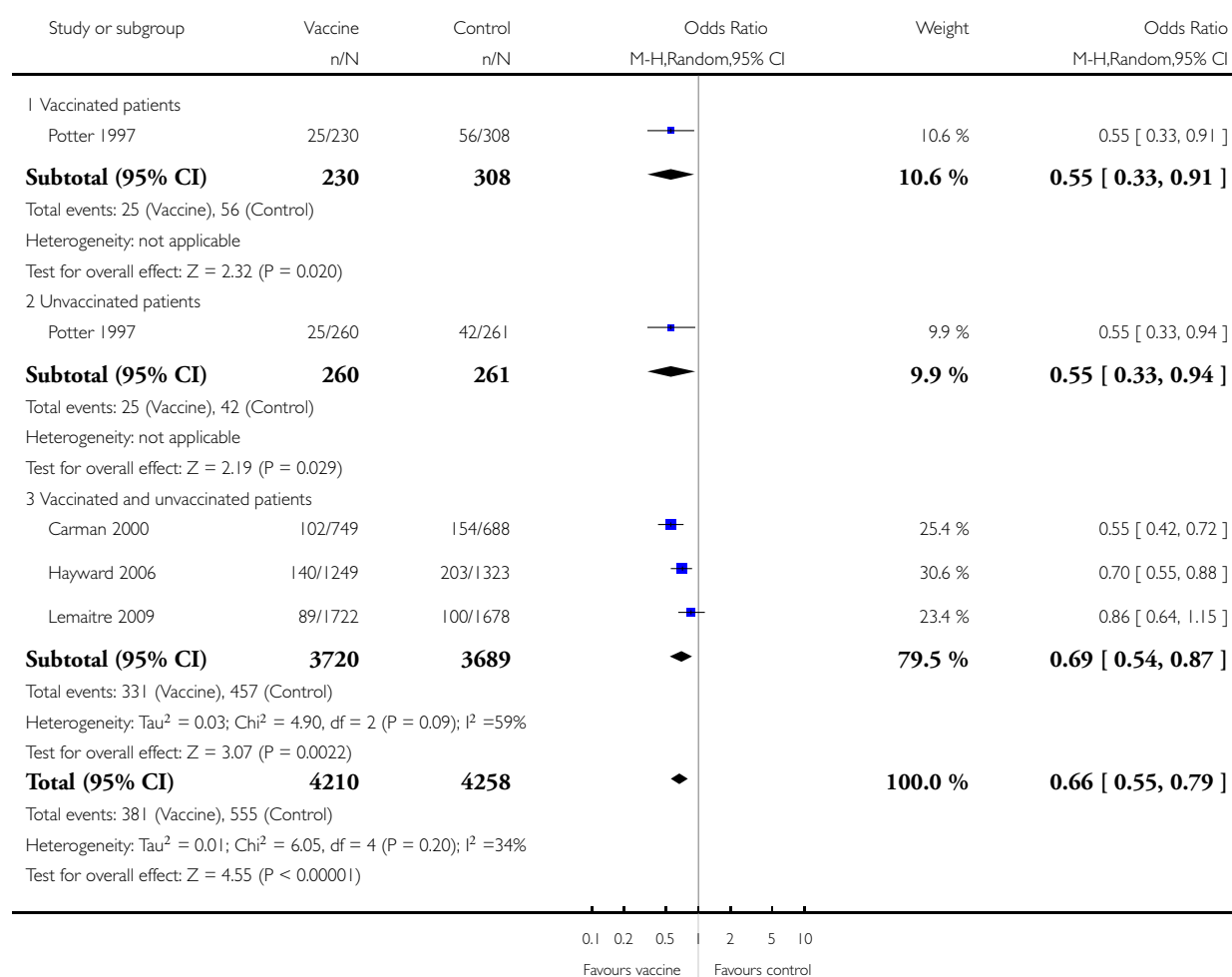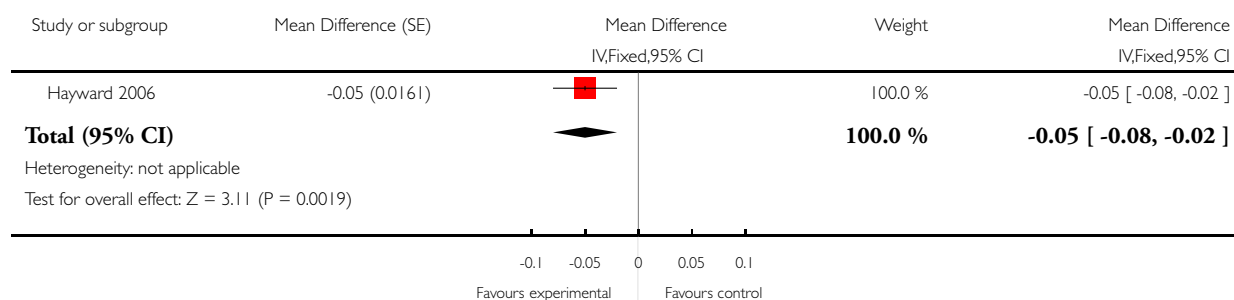
Outcome: 2 Influenza

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
1 Vaccinated patients				
Subtotal (95% CI)			**0.0 %**	**0.0 [0.0, 0.0]**
Heterogeneity: not applicable				
Test for overall effect: not applicable				
2 Unvaccinated patients				
Potter 1997	0.31481074 (1.10120228)		14.9 %	1.37 [0.16, 11.86]
Subtotal (95% CI)			**14.9 %**	**1.37 [0.16, 11.86]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.29 (P = 0.77)				
3 Vaccinated and unvaccinated patients				
Carman 2000	-0.22314355 (0.46100736)		85.1 %	0.80 [0.32, 1.97]
Subtotal (95% CI)			**85.1 %**	**0.80 [0.32, 1.97]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.48 (P = 0.63)				
Total (95% CI)			**100.0 %**	**0.87 [0.38, 1.99]**
Heterogeneity: Tau² = 0.0; Chi² = 0.20, df = 1 (P = 0.65); I² =0.0%				
Test for overall effect: Z = 0.34 (P = 0.74)				

```
   0.001 0.01  0.1    I   10   100  1000
      Favours experimental   Favours control
```

Analysis 3.3. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 3 Pneumonia.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)
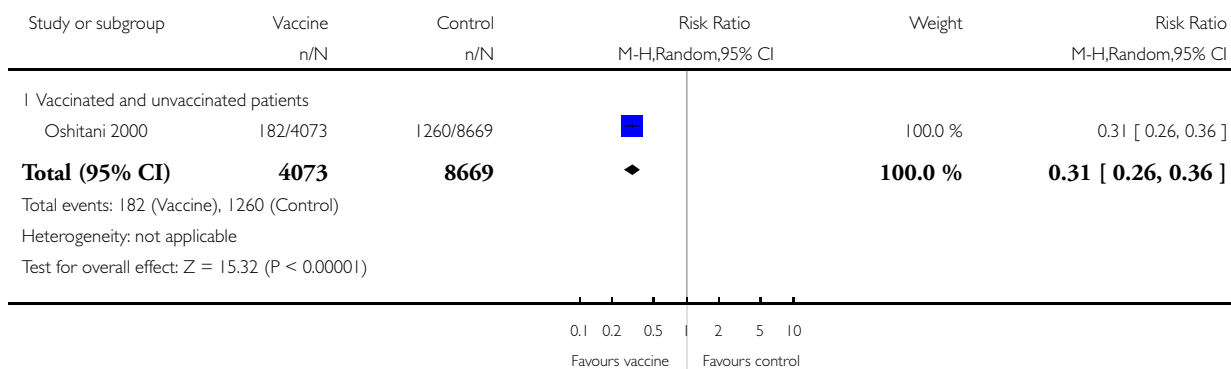
Outcome: 3 Pneumonia

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Vaccinated patients				
Potter 1997	-0.52763274 (0.76205977)	■	34.9 %	0.59 [0.13, 2.63]
Subtotal (95% CI)		◆	**34.9 %**	**0.59 [0.13, 2.63]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.69 (P = 0.49)				
2 Unvaccinated patients				
Potter 1997	-0.24846136 (0.55765822)	■	65.1 %	0.78 [0.26, 2.33]
Subtotal (95% CI)		◆	**65.1 %**	**0.78 [0.26, 2.33]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.45 (P = 0.66)				
Total (95% CI)		◆	**100.0 %**	**0.71 [0.29, 1.71]**
Heterogeneity: Tau² = 0.0; Chi² = 0.09, df = 1 (P = 0.77); I² =0.0%				
Test for overall effect: Z = 0.77 (P = 0.44)				

```
        0.01   0.1    1    10   100
        Favours experimental   Favours control
```
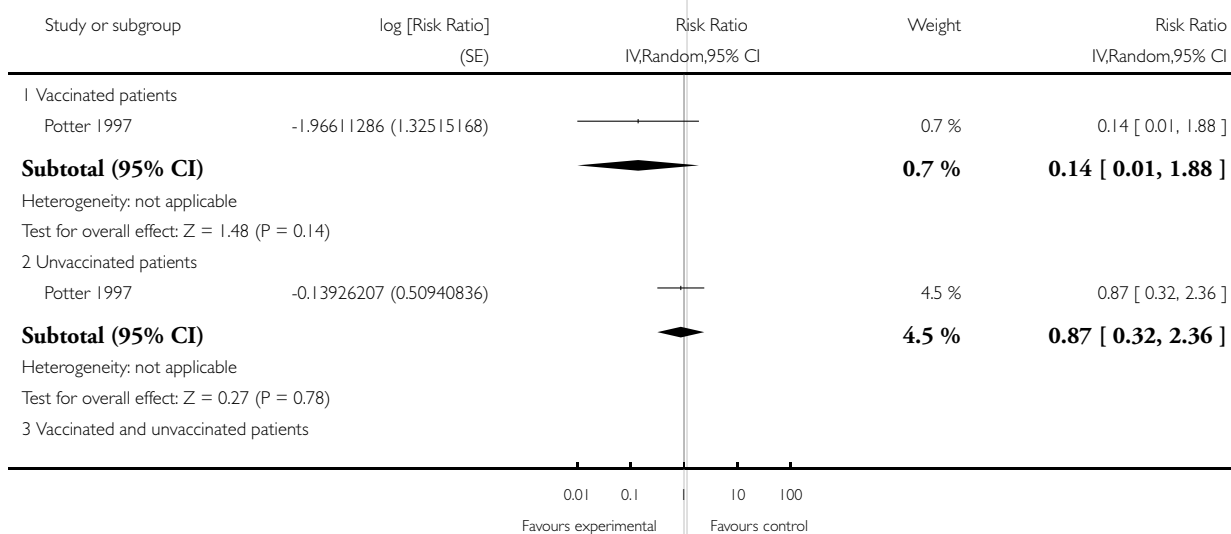
Analysis 3.4. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 4 GP consultations for influenza-like illness.

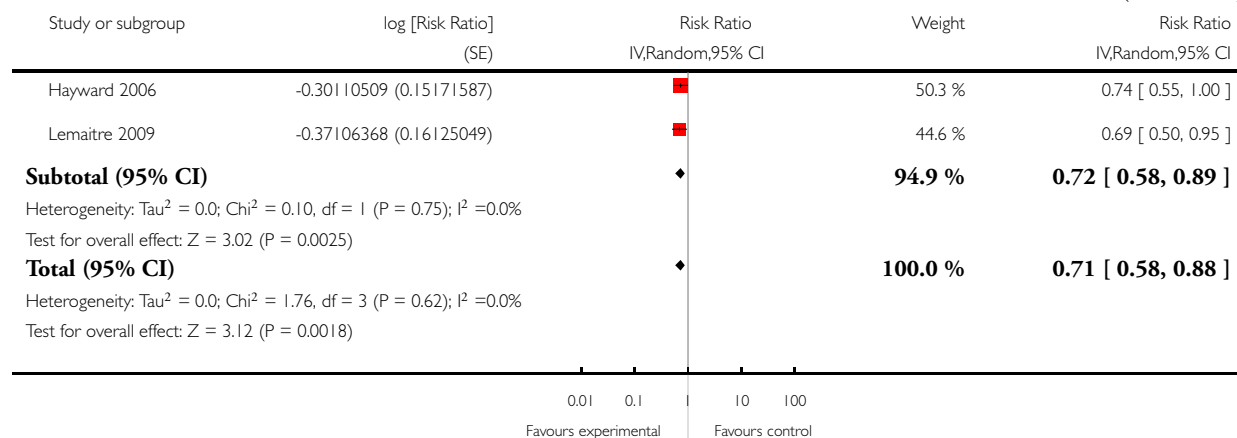Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome: 4 GP consultations for influenza-like illness

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
Hayward 2006	-0.73396918 (0.18461981)		100.0 %	0.48 [0.33, 0.69]
Total (95% CI)			**100.0 %**	**0.48 [0.33, 0.69]**

Heterogeneity: not applicable
Test for overall effect: Z = 3.98 (P = 0.000070)

$$0.01 \quad 0.1 \quad 1 \quad 10 \quad 100$$

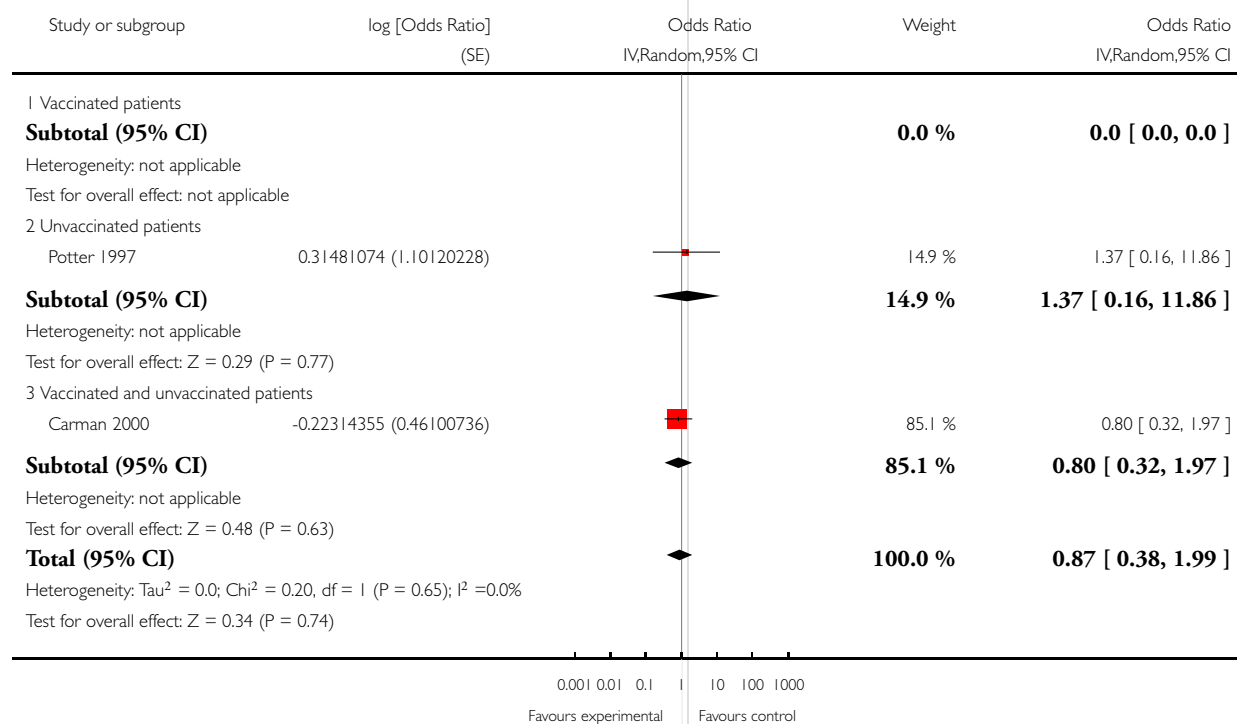Favours experimental   Favours control

Analysis 3.5. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 5 Admission to hospital.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome: 5 Admission to hospital

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
1 Vaccinated and unvaccinated patients				
Hayward 2006	-0.28768207 (0.20460622)		42.5 %	0.75 [0.50, 1.12]
Lemaitre 2009	0.01980263 (0.16635283)		57.5 %	1.02 [0.74, 1.41]
Total (95% CI)			**100.0 %**	**0.90 [0.66, 1.21]**

Heterogeneity: Tau^2 = 0.01; Chi^2 = 1.36, df = 1 (P = 0.24); I^2 =26%
Test for overall effect: Z = 0.73 (P = 0.47)

$$0.01 \quad 0.1 \quad 1 \quad 10 \quad 100$$

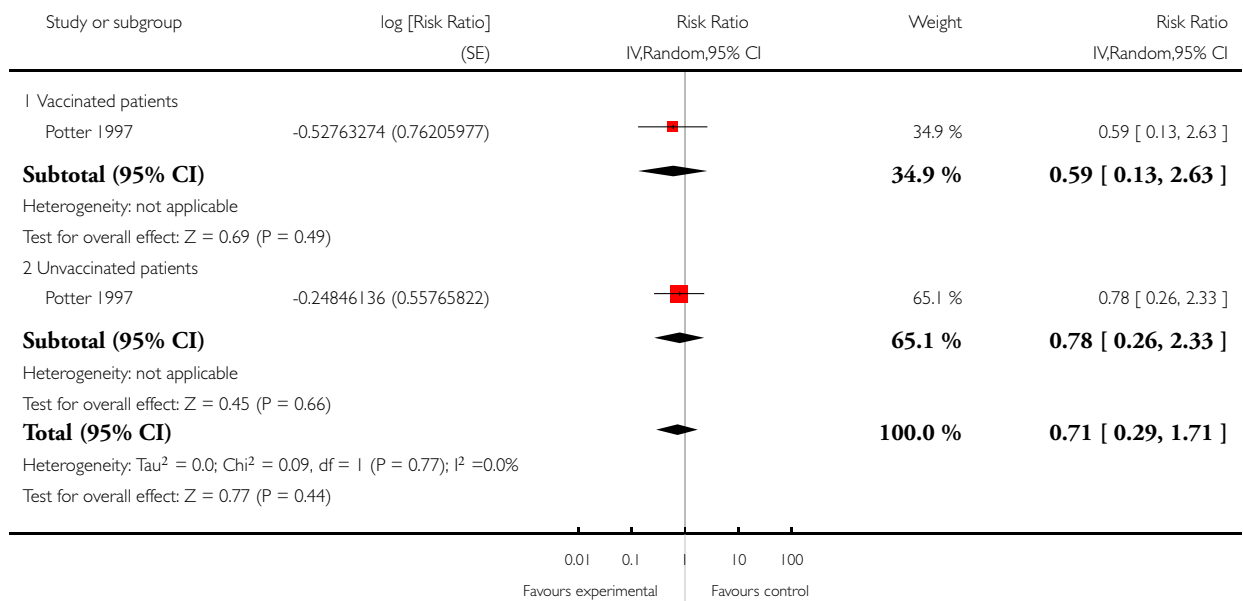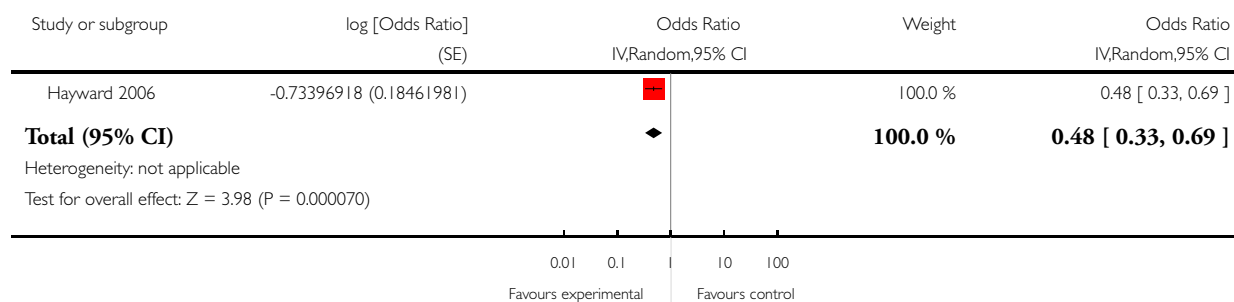Favours experimental   Favours control

Analysis 3.6. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 6 Deaths from pneumonia.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome: 6 Deaths from pneumonia

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Vaccinated patients				
Potter 1997	-0.5798185 (0.6371389)		24.7 %	0.56 [0.16, 1.95]
Subtotal (95% CI)			**24.7 %**	**0.56 [0.16, 1.95]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.91 (P = 0.36)				
2 Unvaccinated patients				
Potter 1997	-0.43078292 (0.51991622)		36.7 %	0.65 [0.23, 1.80]
Subtotal (95% CI)			**36.7 %**	**0.65 [0.23, 1.80]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.83 (P = 0.41)				
3 Vaccinated and unvaccinated patients				
Lemaitre 2009	0.43178242 (0.5068499)		38.6 %	1.54 [0.57, 4.16]
Subtotal (95% CI)			**38.6 %**	**1.54 [0.57, 4.16]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.85 (P = 0.39)				
Total (95% CI)			**100.0 %**	**0.87 [0.47, 1.64]**
Heterogeneity: Tau² = 0.01; Chi² = 2.06, df = 2 (P = 0.36); I² =3%				
Test for overall effect: Z = 0.42 (P = 0.67)				

```
        0.002   0.1    1    10    500
      Favours experimental   Favours control
```
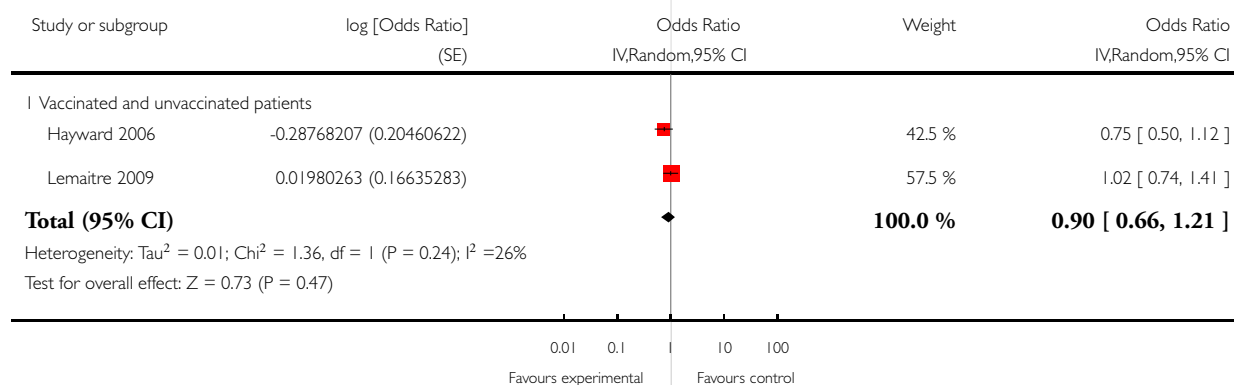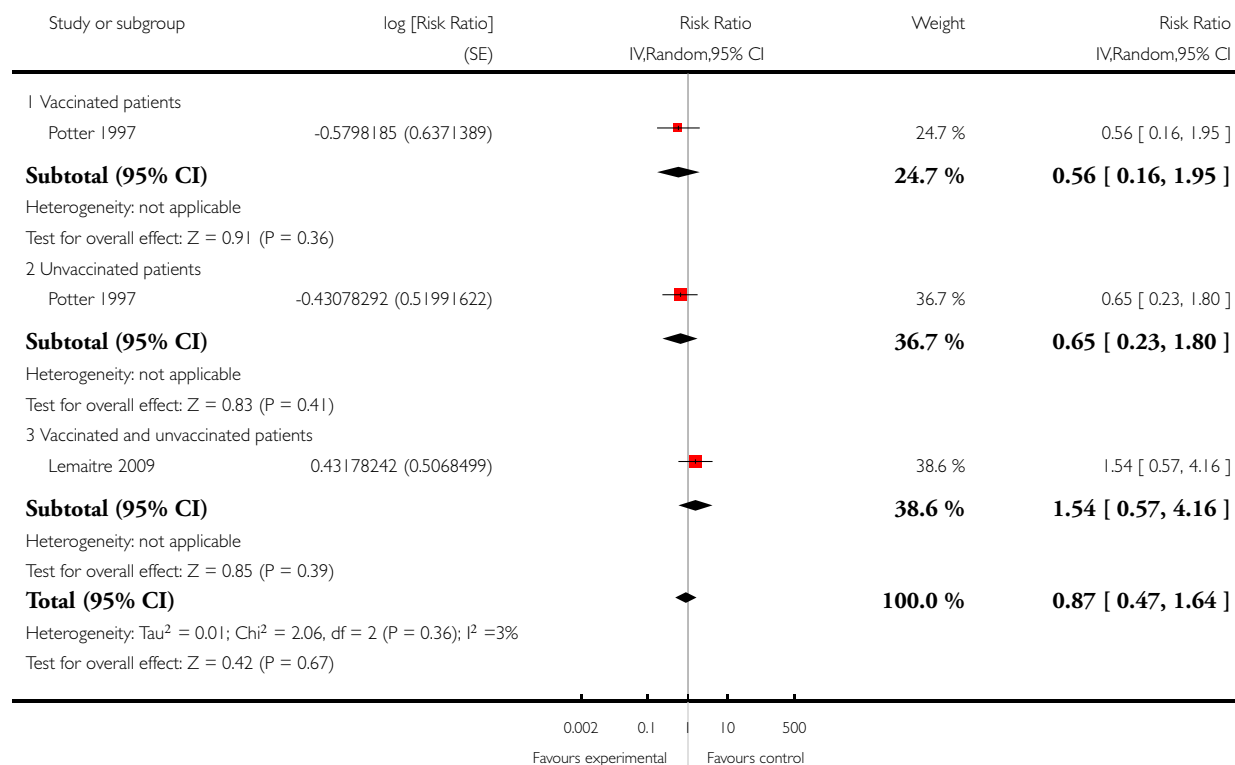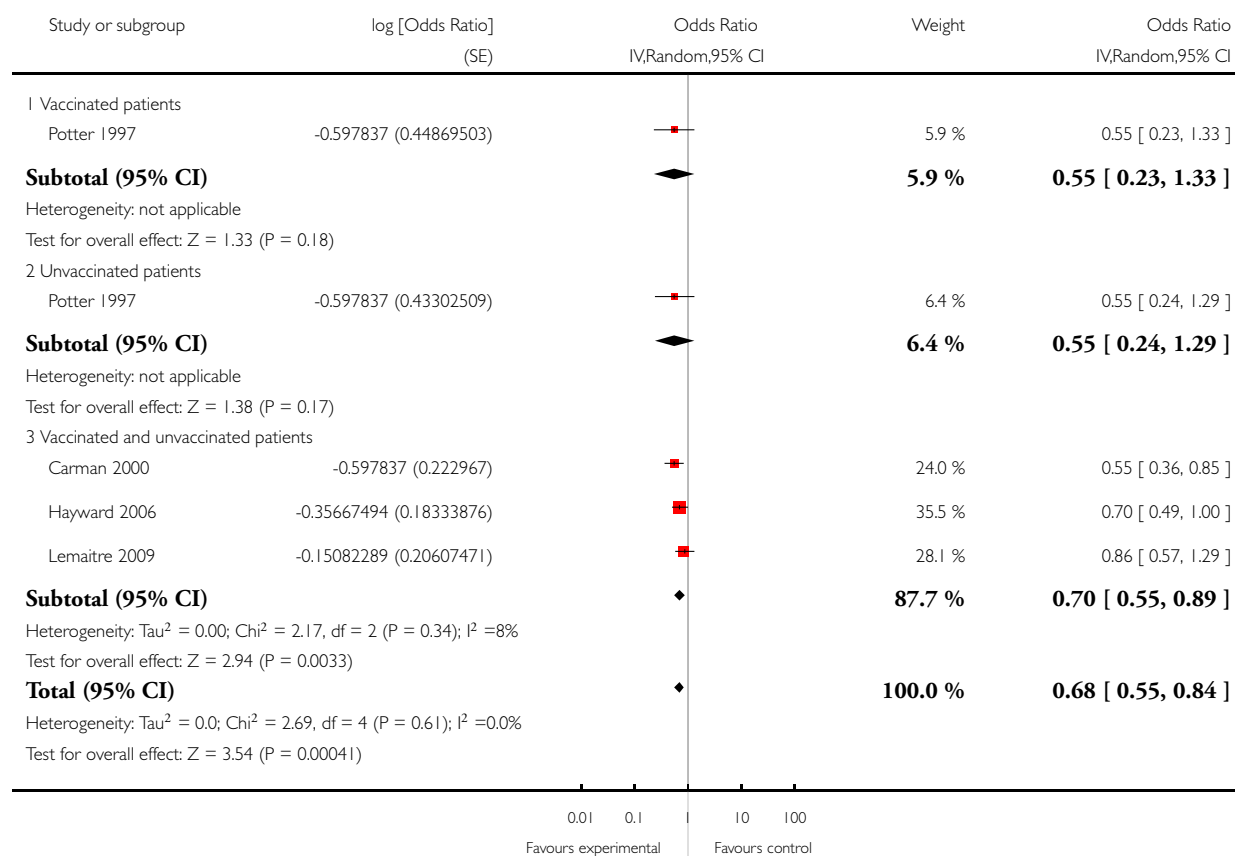
Analysis 3.7. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 7 Deaths from all causes.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome: 7 Deaths from all causes

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
1 Vaccinated patients				
Potter 1997	-0.597837 (0.44869503)		5.9 %	0.55 [0.23, 1.33]
Subtotal (95% CI)			**5.9 %**	**0.55 [0.23, 1.33]**
Heterogeneity: not applicable				
Test for overall effect: Z = 1.33 (P = 0.18)				
2 Unvaccinated patients				
Potter 1997	-0.597837 (0.43302509)		6.4 %	0.55 [0.24, 1.29]
Subtotal (95% CI)			**6.4 %**	**0.55 [0.24, 1.29]**
Heterogeneity: not applicable				
Test for overall effect: Z = 1.38 (P = 0.17)				
3 Vaccinated and unvaccinated patients				
Carman 2000	-0.597837 (0.222967)		24.0 %	0.55 [0.36, 0.85]
Hayward 2006	-0.35667494 (0.18333876)		35.5 %	0.70 [0.49, 1.00]
Lemaitre 2009	-0.15082289 (0.20607471)		28.1 %	0.86 [0.57, 1.29]
Subtotal (95% CI)			**87.7 %**	**0.70 [0.55, 0.89]**
Heterogeneity: Tau² = 0.00; Chi² = 2.17, df = 2 (P = 0.34); I² =8%				
Test for overall effect: Z = 2.94 (P = 0.0033)				
Total (95% CI)			**100.0 %**	**0.68 [0.55, 0.84]**
Heterogeneity: Tau² = 0.0; Chi² = 2.69, df = 4 (P = 0.61); I² =0.0%				
Test for overall effect: Z = 3.54 (P = 0.00041)				

```
        0.01    0.1     1      10    100
     Favours experimental    Favours control
```
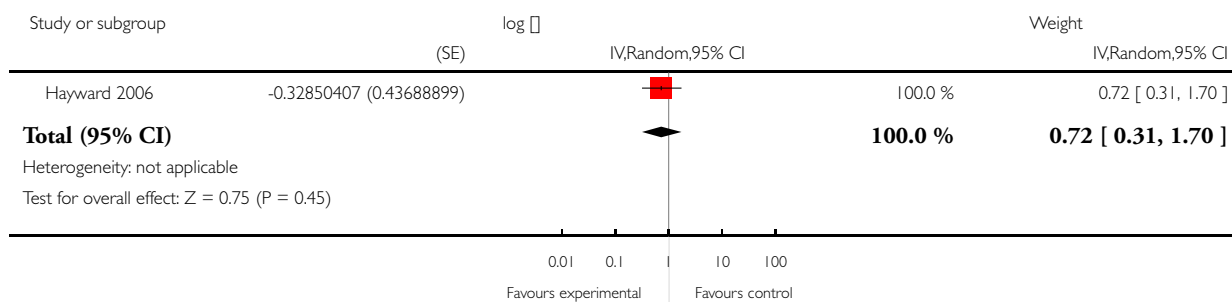
Analysis 3.8. Comparison 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days), Outcome 8 Deaths from influenza-like illness.

Review: Influenza vaccination for healthcare workers who work with the elderly

Comparison: 3 Analyses adjusted for clustering; data for periods of high influenza activity (Carman and Potter 152, Hayward 145, Lemaitre 118 days)

Outcome: 8 Deaths from influenza-like illness

Study or subgroup	log [] (SE)	IV,Random,95% CI	Weight	IV,Random,95% CI
Hayward 2006	-0.32850407 (0.43688899)		100.0 %	0.72 [0.31, 1.70]
Total (95% CI)			**100.0 %**	**0.72 [0.31, 1.70]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.75 (P = 0.45)				

0.01 0.1 1 10 100

Favours experimental   Favours control

A P P E N D I C E S

Appendix 1. Previous search

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Database of Systematic Reviews and the NHS Database of Abstracts of Reviews of Effects (DARE) (*The Cochrane Library* 2006, issue 1); MEDLINE (January 1966 to Week 1, February 2006); EMBASE (1974 to March 2006); Biological Abstracts (1969 to December 2005) and Science Citation Index-Expanded (1974 to March 2006).

MEDLINE was searched using the following search terms in combination with stages I, II and III of the highly sensitive search strategy defined by the Cochrane Collaboration and detailed in Appendix 5b of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2005).

MEDLINE (OVID)

1 exp INFLUENZA/
2 influenza.mp.
3 or/1-2
4 exp VACCINES/
5 exp VACCINATION/
6 (immuniz$ or immunis$).mp.
7 vaccin$.mp.
8 or/4-7
9 3 and 8
10 exp Influenza Vaccine/
11 (influenz$ adj (vaccin$ or immun$)).mp.
12 or/10-11
13 9 or 12
14 exp Health Personnel/
15 (health personnel or healthcare personnel or health care personnel).mp.
16 (health worker$ or healthcare worker$ or health care worker$).mp.
17 (healthcare provider$ or health care provider$).mp.

18 (health practitioner$ or healthcare practitioner$ or health care practitioner$).mp.
19 health employee$.mp.
20 medical staff.mp.
21 (doctor$ or physician$).mp.
22 (allied health adj (staff or personnel)).mp.
23 paramedic$.mp.
24 nursing staff.mp.
25 nurse$.mp.
26 nursing auxiliar$.mp.
27 hospital personnel.mp.
28 hospital staff.mp.
29 hospital worker$.mp.
30 exp HOSPITALS/
31 exp Long-Term Care/
32 exp Residential Facilities/
33 nursing home$.mp.
34 (institution$ adj3 elderly).mp.
35 or/14-34
36 13 and 35

This strategy was adapted to search the other electronic databases. See below for the EMBASE search strategy. There were no language or publication restrictions. The search of CENTRAL included trial reports identified in the systematic search by hand of the journal *Vaccine*. To identify additional published and unpublished studies the Science Citation Index-Expanded was used to identify articles that cite the relevant studies. The relevant studies were also keyed into PubMed and the Related Articles feature used.

Bibliographies of all relevant articles were obtained, and any published review and proceedings from relevant conferences were assessed for additional studies. We explored Internet sources in December 2005: NHS National Research Register (http://www.update-software.com/national/); the metaRegister of Clinical Trials (http://www.controlled-trials.com/) the digital dissertations website (http://wwwlib.umi.com/dissertations). The Vaccine Adverse Event Reporting System website was searched (http://www.vaers.org). We contacted first or corresponding authors of relevant studies to identify further published or unpublished trials.

EMBASE (WebSPIRS)

#1 explode 'influenza-' / all subheadings in DEM,DER,DRM,DRR
#2 (influenza in ti) or (influenza in ab)
#3 #1 or #2
#4 explode 'vaccine-' / all subheadings in DEM,DER,DRM,DRR
#5 explode 'vaccination-' / all subheadings in DEM,DER,DRM,DRR
#6 (immuniz* in ti) or (immuniz* in ab)
#7 (immunis* in ti) or (immunis* in ab)
#8 (vaccin* in ti) or (vaccin* in ab)
#9 #4 or #5 or #6 or #7 or #8
#10 #3 and #9
#11 explode 'influenza-vaccine' / all subheadings in DEM,DER,DRM,DRR
#12 explode 'influenza-vaccination' / all subheadings in DEM,DER,DRM,DRR
#13 (influenz* adj (vaccin* or immun*)) in ti
#14 (influenz* adj (vaccin* or immun*)) in ab
#15 #10 or #11 or #12 or #13 or #14
#16 explode 'health-care-personnel' / all subheadings in DEM,DER,DRM,DRR
#17 (health personnel or healthcare personnel or health care personnel) in ti
#18 (health personnel or healthcare personnel or health care personnel) in ab
#19 (health worker* or healthcare worker* or health care worker*) in ti
#20 (healthcare provider* or health care provider*) in ti
#21 (healthcare provider* or health care provider*) in ab
#22 (health practitioner* or healthcare practitioner* or health care practitioner*) in ti

#23 (health practitioner* or healthcare practitioner* or health care practitioner*) in ab

#24 (health employee* in ti) or (health employee* in ab)

#25 explode 'hospital-personnel' / all subheadings in DEM,DER,DRM,DRR

#26 explode 'hospital-physician' / all subheadings in DEM,DER,DRM,DRR

#27 explode 'medical-personnel' / all subheadings in DEM,DER,DRM,DRR

#28 (medical staff in ti) or (medical staff in ab)

#29 explode 'physician-' / all subheadings in DEM,DER,DRM,DRR

#30 (doctor* or physician*) in ti

#31 (doctor* or physician*) in ab

#32 (allied health adj (staff or personnel)) in ti

#33 explode 'paramedical-personnel' / all subheadings in DEM,DER,DRM,DRR

#34 (paramedic* in ti) or (paramedic* in ab)

#35 explode 'nursing-staff' / all subheadings in DEM,DER,DRM,DRR

#36 (nursing staff in ti) or (nursing staff in ab)

#37 (nurse* in ti) or (nurse* in ab)

#38 (nursing auxiliar* in ti) or (nursing auxiliar* in ab)

#39 (hospital staff in ti) or (hospital staff in ab)

#40 (hospital worker* in ti) or (hospital worker* in ab)

#41 explode 'hospital-' / all subheadings in DEM,DER,DRM,DRR

#42 explode 'long-term-care' / all subheadings in DEM,DER,DRM,DRR

#43 explode 'residential-care' / all subheadings in DEM,DER,DRM,DRR

#44 explode 'residential-home' / all subheadings in DEM,DER,DRM,DRR

#45 (nursing home* in ti) or (nursing home* in ab)

#46 (institution* adj elderly) in ti

#47 (institution* adj elderly) in ab

#48 #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47

#49 #15 and #48

Appendix 2. EMBASE search strategy

Embase.com

27. #23 AND #26

26. #24 OR #25

25. random*:ab,ti OR placebo*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR 'cross over':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*;ti,ab OR ((singl* OR doubl*) NEAR/2 (blind* OR mask*)):ab,ti

24. 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp

23. #11 AND #22

22. #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21

21. 'aged care':ab,ti OR 'nursing home':ab,ti OR 'nursing homes':ab,ti

20. (institution* NEAR/3 elderly):ab,ti

19. 'hospice'/exp OR 'assisted living facility'/exp OR 'hospital'/exp OR 'nursing home'/exp OR 'residential home'/exp

18. (nursing NEAR/2 (staff OR personnel OR auxiliar* OR assistant*)):ab,ti

17. paramedic*:ab,ti OR nurse*:ab,ti

16. 'allied health staff':ab,ti OR 'allied health personnel':ab,ti OR 'allied health worker':ab,ti OR 'allied health workers':ab,ti

15. doctor*:ab,ti OR physician*:ab,ti OR clinician*:ab,ti

14. (medical OR hospital) NEAR/2 (staff OR employee* OR personnel OR worker*)

13. ((health OR healthcare) NEAR/3 (personnel OR worker* OR provider* OR employee* OR staff)):ab,ti

12. 'health care personnel'/exp

11. #1 OR #10
10. #6 AND #9
9. #7 OR #8
8. vaccin*:ab,ti OR immunis*:ab,ti OR immuniz*:ab,ti
7. 'vaccine'/exp OR 'vaccination'/exp OR 'immunization'/exp
6. #2 OR #3 OR #4 OR #5
5. influenza:ab,ti OR flu:ab,ti
4. 'influenza virus b'/exp
3. 'influenza virus a'/exp
2. 'influenza'/exp
1. 'influenza vaccine'/exp

Appendix 3. Web of Science search strategy

Results	Topic=((flu* or influenza*) and (vaccin* or immunis* or immuniz* or inoculat*)) AND Topic=(((health or healthcare or health care or allied health or hospital or medical) and (personnel or worker* or provider* or employee* or staff)) or doctor* or physician* or clinician* or paramedic* or nurse* or (nursing and (staff or personnel or auxiliar* or assist*)) or long term care or residential care or nursing home* or (hospital* and (aged or elderly or old or geriatric*)))
	Refined by: Topic = (random* or placebo* or rct or single blind* or double blind*)
	Timespan = 2006 to 2009. Databases = SCI-EXPANDED, CPCI-S

Appendix 4. SIGN search strategy for observational studies

1 epidemiologic studies/
2 exp case-control studies/
3 exp Cohort Studies/
4 case control.tw.
5 (cohort adj (study or studies)).tw.
6 cohort analy*.tw.
7 (follow up adj (study or studies)).tw.
8 (observational adj (study or studies)).tw.
9 longitudinal.tw.
10 retrospective.tw.
11 cross sectional.tw.
12 Cross-Sectional Studies/
13 or/1-12

Appendix 5. Assessment of Oshitani 2000 using the Newcastle-Ottawa Scale for non-RCTs (Wells 2005)

Selection

1. Representativeness of the exposed cohort:

    i) **truly representative of the average Long Term Care Facilities in Niigata Prefecture and City (mandatory surveys of influenza vaccination status and influenza-like illness occurrence every 2 weeks January to March 1999) in the community**

    ii) somewhat representative of the average ·········· in the community

    iii) selected group of users (e.g. nurses, volunteers)

    iv) no description of the derivation of the cohort

2. Selection of the non-exposed cohort:

    i) **drawn from the same community as the exposed cohort**

    ii) drawn from a different source

    iii) no description of the derivation of the non-exposed cohort

3. Ascertainment of exposure to influenza vaccine:

    i) secure record (e.g. surgical records)

    ii) structured interview. **"Mandatory survey." "Influenza vaccine had been given to 3933 residents (30.8%). No resident had received vaccine in 75 facilities (50.3%). Vaccines had also been given to 1532 of 7459 staff, and 10 or more staff had been vaccinated in 47 facilities (31.5%)." No description of survey or how administered or how completeness ascertained.**

    iii) written self-report

    iv) no description

4. Demonstration that outcome of interest was not present at start of study:

    i) **yes "An influenza outbreak was defined when the number of ILI per week exceeded 10% of the residents"**

    ii) no

Comparability

1. Comparability of cohorts on the basis of the design or analysis:

    i) study controls for differences in demographic characteristics and co-morbidities of residents who were vaccinated, and characteristics of homes where residents received vaccination (select the most important factor) **No**

    ii) study controls for any additional factor: geriatric health services facilities compared to special nursing homes for those with more severe conditions (this criteria could be modified to indicate specific control for a second important factor) **No**

Outcome

1. Assessment of outcome:

    i) independent blind assessment

    ii) record linkage

    iii) self-report **"Mandatory survey every 2 weeks January to March 1999"**

    iv) no description

2. Was follow up long enough for outcomes to occur (select an adequate follow-up period for outcome of interest):

    i) **yes - January to March 1999**

    ii) no

3. Adequacy of follow up of cohorts:

    i) complete follow up - all subjects accounted for

    ii) subjects lost to follow up unlikely to introduce bias - small number lost (> ··· % (select an adequate %) follow up, or description of those lost))

    iii) follow-up rate < ···% (select an adequate %) and no description of those lost

    iv) no statement **No statement of admissions, deaths or separations from homes during study period. Total number of residents in Table 2 in homes where < 10 staff vaccinated is listed as 8699 but subcategories add to 8669, and in homes where ≥ 10 staff vaccinated listed as 4085 but subcategories add to 4073**

FEEDBACK

Influenza vaccination for healthcare workers who work with the elderly, 5 May 2008

Summary

Feedback: The below is not an article in Journal of Infectious Diseases 1997; 175 (1) as cited. Indeed I've not been able to locate the the study in any other journal, though the study has been cited many times in other studies as well.

Potter J, Stott DJ, Roberts MA, Elder AG, O'Donnell B, Knight PV, et al. Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients. Journal of Infectious Diseases 1997;175(1):1-6

Submitter agrees with default conflict of interest statement:

I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

Reply

We thank Thomas Kristiansen for his comment. The article was in fact published in the Journal of Infectious Diseases (volume 175), issue 1 in 1997. It is available for purchase or download at: http://www.jstor.org/pss/30129986.

Contributors

Thomas Birk Kristiansen
Feedback comment added 21 June 2008

Influenza vaccination for healthcare workers who work with the elderly, 1 December 2009

Summary

In the table and list of included studies, you have reported Hayward 2006 (BMJ Des 2006), but this study is not included in the analyses or mentioned in the text. The outcomes of this study do not seem to be adequately reported in the table.

Submitter agrees with default conflict of interest statement: I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

Reply

We thank Signe Flottorp for his comment, which we received as we were updating the review. His comment has now been addressed.

Contributors

Signe Flottorp

WHAT'S NEW

Last assessed as up-to-date: 27 September 2009.

10 December 2009	Feedback has been incorporated	Feedback comment and reply added.
4 December 2009	New citation required and conclusions have changed	The conclusions have changed with the incorporation of new evidence in this review. All four cluster-randomised controlled trials were at high risk of bias. There is thus insufficient evidence to support routine vaccination of healthcare workers to reduce the risk of serologically confirmed influenza cases in elderly populations in long-term care facilities. A new author, Toby Lasserson, joined the authors to update this review.
28 September 2009	New search has been performed	Searches conducted. We included two new studies (Hayward 2006; Lemaitre 2009) and excluded 20 new studies.

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 3, 2006

21 June 2008	Feedback has been incorporated	Feedback comment added.
13 May 2008	Amended	Converted to new review format.
23 May 2006	New search has been performed	Review first published, Issue 3, 2006.

CONTRIBUTIONS OF AUTHORS

Responsible for the design of the review: Roger Thomas (RET), Tom Jefferson (TOJ).

Responsible for data extraction: all authors.

Responsible for the assessment of study quality and outcomes: RET and TOJ.

Responsible for the first draft: RET.

Responsible for the final draft: RET, TOJ, TJL (Toby Lasserson).

DECLARATIONS OF INTEREST

TOJ received fees for consultancies, research and speaking engagements from Glaxo SmithKline Ltd., Roche Ltd., Chiron Ltd. and Sanofi Synthelabo Ltd.

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- No sources of support supplied

External sources

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- National Health and Medical Research Council (NHMRC), Australia.

Competitive grant to Chris Del Mar and Tom Jefferson, 2009

INDEX TERMS

Medical Subject Headings (MeSH)

*Health Personnel; Homes for the Aged; Infectious Disease Transmission, Professional-to-Patient [*prevention & control]; Influenza, Human [prevention & control; *transmission]; Influenza Vaccines [*administration & dosage]; Randomized Controlled Trials as Topic; Vaccines, Inactivated [administration & dosage]

MeSH check words

Adult; Aged; Humans; Middle Aged