



EVIDENCE-BASED REVIEW

Preventing influenza: An overview of systematic reviews[☆]

J.C. van der Wouden^{a,*}, H.J. Bueving^a, P. Poole^b

^aDepartment of General Practice, Erasmus MC, University Medical Center Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands

^bUniversity of Auckland, Auckland, New Zealand

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Summary

Background: Many options are available for preventing people from getting infected by influenza virus, with vaccination being the most widely used.

Methods: We assessed the evidence available in Cochrane systematic reviews. We found nine reviews, five of them addressing influenza vaccination, and four addressing medication.

Results: Vaccination is effective in healthy adults and children, but the effect is modest in adults, and for young children few data are available. In patients with asthma, chronic obstructive pulmonary disease (COPD) and cystic fibrosis, more evidence is needed to determine effectiveness. Vaccination does not result in exacerbation of asthma. Neuraminidase inhibitors may also have a place in limiting the spread of infection, at least in adults. Amantadine and rimantadine seem effective but have unfavourable adverse-effect profiles. The popularity of homoeopathic Oscillocochinum, especially in France, is not supported by current evidence.

Conclusion: In many areas, more clinical trials are needed, as the current evidence is inconclusive. Furthermore, several other measures that may be helpful in preventing influenza that have not been addressed in Cochrane reviews.

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[☆]The following Cochrane reviews have been cited in this evidence-based review: Demicheli V, et al. Vaccines for preventing influenza in healthy adults, Issue 3, 2004; Cates CJ, et al. Vaccines for preventing influenza in people with asthma, Issue 3, 2003; Poole PJ, et al. Influenza vaccine for patients with chronic obstructive pulmonary disease, Issue 3, 2000; Tan A, et al. Vaccines for preventing influenza in people with cystic fibrosis, Issue 1, 2000; Jefferson T, et al. Amantadine and rimantadine for preventing and treating influenza A in adults, Issue 3, 2004; Jefferson T, Demicheli V, Deeks J, Rivetti D. Neuraminidase inhibitors for preventing and treating influenza in healthy adults, Issue 4, 1999; Matheson NJ, Symmonds-Abrahams M, Sheikh A, Shepperd S, Harnden A. Neuraminidase inhibitors for preventing and treating influenza in children, Issue 3, 2003; Vickers AJ, et al. Homoeopathic Oscillocochinum for preventing and treating influenza and influenza-like syndromes, Issue 1, 2004.

*Corresponding author. Tel.: +31 10 408 7611; fax: +31 10 463 21 27.

E-mail address: j.vanderwouden@erasmusmc.nl (J.C. van der Wouden).

Background

Influenza is a disease of viral origin that occurs worldwide, usually in seasonal epidemics. The annual incidence varies from year to year and from region to region. In a typical epidemic season, about 5–15% of adults and children develop symptomatic influenza.¹ To reduce the substantial morbidity and mortality one requires the use of preventive strategies that have proved to be effective.

Several potential strategies can prevent people from getting infected by influenza virus or, once infected, developing illness. Examples are hygienic measures, antiviral medication and vaccination. Vaccination is considered to be the principal measure for preventing influenza and reducing the affect of epidemics. World wide, immunization programmes have been implemented, particularly aimed at elderly people and people with specific chronic disorders. However, the uptake rate varies substantially,^{2,3} and, recently, there have been supply chain problems.⁴

In this paper, we review the available evidence on measures for preventing influenza. We will restrict ourselves to interventions that have been the subject of Cochrane systematic reviews, as these reviews may be considered at the top of the hierarchy of levels of evidence, being restricted to randomized-controlled trials (RCTs) and performed in the most systematic way according to predefined protocols.

Methods

In November 2004, we searched the Cochrane Library for relevant reviews, using “influenza” as a search term. The full text of each of the reviews resulting from this search was screened to verify that the intervention studied, was aimed at preventing influenza.

Results

The search provided 80 completed Cochrane systematic reviews in which the term “influenza” appeared. Eight of these focused on preventing influenza: four of these addressed the effect of vaccination and four the effect of medications, one of them homeopathic. A review addressing influenza vaccination in healthy children, using Cochrane methodology, published in *The Lancet* in February 2005, was also included.⁵ Reviews were excluded if

they did not address interventions for influenza, but were found by the search strategy because the word “influenza” was mentioned for other reasons.

A brief summary of the findings of all reviews is given in [Table 1](#). For each selected review, we will provide details of methods and results. Some of the reviews addressed both the prevention of influenza and reduction of illness when infected with influenza. We will not describe the results relating to the reduction of illness, as this is beyond the scope of this paper.

Methods common to all reviews

All the included Cochrane reviews were conducted after searching the literature in various databases, notably the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE. Some reviews also used specialized databases within the Cochrane Collaboration, such as the Cochrane Airways Group trial register. The date of the most recent search varied between reviews, and is specified in the results of the review. In addition to searching these databases, the authors of the reviews also checked references of relevant articles, wrote to manufacturers of drugs and vaccines, and to authors of studies to ask for additional studies, published or unpublished.

For most of the reviews, extraction of data and assessment of methodological quality were carried out by more than one reviewer independently.

Cochrane review on influenza vaccine in healthy adults

Traditionally, influenza vaccination programmes have targeted elderly people and those at serious risk of complications. Healthy adults may also benefit from vaccination, as influenza may result in loss of working days, and affected employees may spread the disease to others. The authors set out to identify studies that assessed the effectiveness of vaccines in preventing cases of influenza in healthy adults, as well as their adverse effects.⁶

The last search of the literature for this Cochrane review was carried out in 2003. The authors included any randomized or quasi-randomized studies comparing influenza vaccines in humans with placebo, control vaccines or no intervention, or comparing types, doses or schedules of influenza vaccine. All routes of administration of vaccines (i.e. intramuscular, subcutaneous, intranasal) were considered. Only studies assessing protection by vaccination from exposure to naturally occurring influenza in healthy individuals aged 14–60 years

Table 1 Summary of Cochrane systematic reviews on preventing influenza.

Topic of Cochrane review	Most recent search	Number of studies included	Authors' conclusion
Influenza vaccine in healthy adults ⁶	2003	25 RCTs	Effective in reducing serologically confirmed cases. Less effective in reducing cases of clinical influenza or working days lost.
Influenza vaccine in healthy children ⁵	2004	25 (15 RCTs)	Effective in reducing laboratory confirmed influenza in children older than 2 years of age. Less effective in reducing influenza-like illness or influenza complications.
Influenza vaccine in patients with asthma ⁷	2004	14 RCTs	No significant increase in asthma exacerbations after vaccination. Uncertainty about degree of protection by vaccination.
Influenza vaccine in patients with chronic obstructive pulmonary disease ⁹	2001	9 RCTs	Inactivated vaccine may reduce exacerbations.
Influenza vaccine in cystic fibrosis patients ¹²	2001	4 RCTs	No evidence.
Amantadine and rimantadine in adults ¹³	2003	30 RCTs	Amantadine significantly prevents influenza-like illness and influenza A. For rimantadine, no significant reduction was found. Both drugs induce significant adverse effects.
Neuraminidase inhibitors in healthy adults ¹⁴	1999	4 RCTs	Effective in preventing influenza. Overall, they are safe, although oseltamivir causes significant nausea.
Neuraminidase inhibitors in children ¹⁵	2002	3 RCTs	Ability to prevent influenza infection in children remains unproven.
Homeopathic Oscillocochinum ¹⁶	2003	7 RCTs	No support for a preventive effect.

(irrespective of influenza immune status) were considered.

Twenty-five reports of studies involving 59,566 people were included. Live aerosol vaccines reduced the number of cases of serologically confirmed influenza by 48% (95% confidence interval [CI] 24–64%), whereas inactivated parenteral vaccines had a much larger efficacy, reducing the number of serologically proven cases by 70% (95% CI 56–80%). The vaccines had low effectiveness against clinical influenza cases: 15% reduction (95% CI 8–21%) and 25% reduction of clinical cases compared with placebo (95% CI 13–35%), respec-

tively. Overall, the percentage of participants experiencing clinical influenza decreased by 7% (20% vs. 13%: number needed to treat is 14). Use of the vaccine significantly reduced time off work, but only by 0.16 days for each influenza episode (95% CI 0.04–0.29 days).

The authors of this review conclude that influenza vaccines are effective in reducing serologically confirmed cases of influenza. However, they are not as effective in reducing cases of clinical influenza and number of working days lost. One of the reasons is that not all influenza infections that can be detected serologically result in clinical

illness. The authors state that universal immunisation of healthy adults is not supported by the results of their review.

Cochrane review on influenza vaccine in healthy children

Schoolchildren were the focus of influenza vaccination in Japan in the second half of last century, and recently the American Academy of Pediatrics has recommended vaccination of children aged 6–23 months. Various reasons have been put forward to underpin these recommendations but, until recently, thorough assessment of the benefit of vaccinating children was absent.

In their review, part of a forthcoming larger Cochrane review, the authors set out to identify studies that assessed the effectiveness of influenza vaccines in preventing cases of influenza, as well as several other related outcomes in healthy children up to 16 years of age.⁵

The last search of the literature for this Cochrane review was carried out in 2004. The authors included randomized, cohort and case-control studies comparing efficacy of vaccines against influenza (reduction in laboratory-confirmed cases), effectiveness against influenza-like illness (reduction in symptomatic cases), or both, with placebo or no intervention. The authors analyzed the following outcomes: influenza confirmed by viral isolation, serological support or any other type of laboratory testing; influenza-like illness; admissions for influenza or influenza-like illness; death due to influenza or influenza-like illness. Serological outcome data were not considered.

Twenty-five reports of studies were selected, reporting on 15 randomized trials, eight cohort studies and one case-control study. We will focus on the results that were provided by the randomized trials. Live attenuated vaccines reduced the number of cases of laboratory-confirmed influenza by 79% (95% CI 48–92%). No data were available for children below the age of 3 years. Inactivated vaccines reduced the number of cases by 65% (95% CI 47–76%). In children aged 6 years or younger, the reduction was much smaller and did not reach statistical significance. Both types of vaccines had lower effectiveness against influenza-like illness: 38% reduction (95% CI 33–43%) and 28% reduction of cases compared with placebo or no intervention (95% CI 22–33%) for live attenuated and inactivated vaccine, respectively. Overall, the percentage of participants experiencing clinical influenza decreased by 15% (17% vs. 2%: number needed to treat is about 7) in the case of live attenuated

vaccine and 19% (26% vs. 7%: number needed to treat is about 5) in the case of inactivated vaccine.

Few studies provided data on other influenza-related outcomes. Vaccines were somewhat effective in reducing school absence, but they had little effect on other outcomes (secondary cases, lower-respiratory tract disease, acute otitis media, hospital stay), compared with placebo. Death due to influenza or to influenza-like illness was not reported.

The authors conclude that influenza vaccines do reduce influenza infection in children older than 2 years. The reduction of influenza-like illness is much lower. The authors state that if influenza immunization in children is to be recommended as public-health policy, large-scale studies are urgently needed that address important outcomes such as mortality, serious complications and community transmission of influenza.

Cochrane review on influenza vaccine in people with asthma

Influenza vaccination is recommended for asthmatic patients in most Western countries, as influenza infection may trigger asthma exacerbations. However, this is controversial as vaccination may precipitate an asthma attack. The objective of this review was to assess the efficacy and side-effects of influenza vaccination in children and adults with asthma.⁷

The last search of the literature was carried out in 2004. The authors selected randomized trials of influenza vaccination in children (over 2 years of age) and adults with asthma. Studies involving people with chronic obstructive pulmonary disease (COPD) were excluded.

Fourteen trials were included. The included studies covered a wide diversity of populations, settings and types of influenza vaccination. Data from the more recent studies that used similar vaccines were pooled. The pooled results of two trials involving 2306 people with asthma did not demonstrate any increase in asthma exacerbations in the 2 weeks after influenza vaccination (risk difference 0.00; 95% CI –0.02 to 0.02). A recent study of 696 children with asthma did not demonstrate a significant reduction in influenza-related asthma exacerbations (risk difference 0.01; 95% CI –0.02 to 0.04).⁸

The authors conclude that there is no significant increase in asthma exacerbations immediately after vaccination (at least with inactivated influenza vaccination); however, uncertainty remains about the degree of protection vaccination affords

against asthma exacerbations that are related to influenza infection.

Cochrane review on influenza vaccine in people with chronic obstructive pulmonary disease

Influenza vaccinations are currently recommended in the care of people with COPD in many countries, but these recommendations are based largely on evidence from observational studies. Influenza infection causes excess morbidity and mortality in patients; however, in this group, influenza vaccination may cause adverse effects. Moreover, its cost-effectiveness has to be established in this group.

The objective of this review was to evaluate the evidence from RCTs for a treatment effect of influenza vaccination in people with COPD.⁹ Outcomes of interest were exacerbation rates, hospitalizations, mortality, lung function and adverse effects.

The last substantive update to this review was made in 2000. The review included RCTs that compared live or inactivated virus vaccines with placebo, either alone or combined with another vaccine, in people with COPD. Studies of people with asthma were excluded.

Nine trials were included, but only four of these were specifically carried out in people with COPD. The others were conducted on elderly and high-risk individuals, some of whom had COPD. In one study of inactivated influenza vaccine in people with COPD, there was a significant reduction in the total number of exacerbations per vaccinated individual compared with those who received placebo (weighted mean difference [WMD] -0.45 , 95% CI -0.75 to -0.15). This difference was mainly due to the reduction in number of exacerbations occurring in the period beyond 3 weeks after administration (WMD -0.44 ; 95% CI -0.68 to -0.20). The number of patients experiencing exacerbations in this period was also significantly less (OR = 0.13 , 95% CI 0.04 – 0.45). There was no evidence of an effect of intranasal live attenuated virus when this was added to inactivated intramuscular vaccination. In studies of elderly patients (only a minority of whom had COPD), there was a significant increase in the occurrence of local adverse reactions in vaccinees, but the effects were generally mild and transient.

The authors conclude that, on the basis of a limited number of RCTs, inactivated vaccine may reduce exacerbations in people with COPD. In elderly, high-risk people, vaccination caused an increase in adverse effects, but these were seen early and were usually mild and transient.

This review is in the process of being updated, as there have been recent publications resulting from the findings of a large RCT carried out in Thailand that included a cost-effectiveness analysis.^{10,11}

Cochrane review on influenza vaccine in people with cystic fibrosis

Viral respiratory-tract infections in patients with cystic fibrosis have a detrimental effect on lung function and disease progression. Annual influenza vaccination is, therefore, recommended for patients with cystic fibrosis. The objective of this review was to assess the effectiveness and adverse events of influenza vaccination for people with cystic fibrosis.¹²

The date of the most recent search of the literature was November 2001. The authors included all randomized and pseudo-randomized trials (published or unpublished) comparing any influenza vaccine with a placebo or with another type of influenza vaccine.

Four trials enrolling a total of 179 patients with cystic fibrosis (80% of which were children aged 1–16 years) were included in this review. No studies were found comparing a vaccine to a placebo, or a whole virus vaccine to a subunit or split virus vaccine. Two studies compared an intranasal applied live vaccine to an intramuscular inactivated vaccine, and the other two studies compared a split virus with a subunit vaccine, and a virosome to a sub-unit vaccine (all intramuscular). The total adverse event rate ranged from 48 out of 201 (24%) for the intranasal live vaccine to 13 out of 30 (43%) for the split-virus vaccine. No severe adverse events were reported. With the limitation of low statistical power, there was no significant difference in the occurrence of adverse events between the vaccines used. All studied vaccines generated a satisfactory serological antibody response, but other clinically more important benefits were not found.

The conclusion of the review is that there is currently no evidence from randomized studies that influenza vaccine benefits people with cystic fibrosis. There remains a need for a well-constructed clinical study that assesses the effectiveness of influenza vaccination on important clinical outcome measures, such as subsequent *Pseudomonas* infection, lung function, length of hospital stay and nutritional status.

Cochrane review on amantadine and rimantadine in adults

Amantadine hydrochloride and rimantadine hydrochloride have antiviral properties, but these drugs

are not widely used owing to a lack of knowledge of their potential value and concerns about possible adverse effects. The objective of this review was to assess the effectiveness and safety of amantadine and rimantadine in healthy adults.¹³

The last search of the literature was conducted in 2003. The authors included 30 randomized and quasi-randomized studies comparing amantadine, rimantadine, or both, with placebo, control antivirals or no intervention, or comparing doses or schedules of amantadine, rimantadine, or both, in healthy adults. For prevention trials, the numbers of participants with influenza-like-illness or confirmed influenza A, and adverse effects were analysed.

Amantadine prevented 25% of cases of influenza-like illness (95% CI 13–36%), and 61% of influenza A cases (flu symptoms combined with laboratory findings) (95% CI 35–76%). For rimantadine, the results for prevention were not statistically significant. Both amantadine and rimantadine induced significant gastrointestinal adverse effects. Adverse effects of the central nervous system and study withdrawals were significantly more common with amantadine than with rimantadine.

Cochrane review on neuraminidase inhibitors in healthy adults

In the 1990s, neuraminidase inhibitors became available for the prevention and treatment of influenza. Neuraminidase inhibitors act by inhibiting the entry of viral particles into the target and subsequent release of virions from the infected cell, neuraminidase being essential for both functions. Neuraminidase inhibitors are available as a metered dose aerosol (zanamivir) or as oral suspension (oseltamivir).

One of the objectives of this review was to assess the effects of neuraminidase inhibitors in preventing cases of influenza.¹⁴ A further objective was to estimate the frequency of adverse effects associated with neuraminidase inhibitor administration. The last search of the literature was carried out in 1999. The authors included randomized or quasi-randomized placebo-controlled studies of neuraminidase inhibitors in healthy adults.

Studies assessing protection from exposure to naturally occurring and experimental influenza (challenge studies) were considered. The main outcomes were numbers, severity, or both, of influenza cases and the number and seriousness of adverse effects.

Four preventive trials were found. The manufacturers provided additional data. The methodologi-

cal quality of the studies was difficult to assess, owing to a lack of detailed descriptions. Compared with placebo, neuraminidase inhibitors were 74% effective (95% CI 50–87%) in preventing naturally occurring cases of clinically defined influenza, and 60% effective (95% CI 76–33%) in preventing cases of laboratory-confirmed influenza.

Adverse events, especially local nasal irritation, in the group treated with zanamivir, did not differ from that of placebo; odds ratio 1.19 (95% CI 0.39–3.62). Compared with rimantadine as a preventive measure, oseltamivir showed a significantly lower incidence of adverse effects and a significantly higher incidence of nausea.

The reviewers conclude that neuraminidase inhibitors are effective for the prevention of influenza. Overall, neuraminidase inhibitors are safe, although oseltamivir causes significant nausea.

Cochrane review on neuraminidase inhibitors in children

General information on neuraminidase inhibitors and their role in influenza prevention was provided in the previous section. The objective of this review was to assess the efficacy, safety and tolerability of neuraminidase inhibitors in the treatment and prophylaxis of influenza infection in children.¹⁵

The last search of the literature was carried out in 2002. The authors included double-blind, RCTs comparing neuraminidase inhibitors with placebo or other antiviral drugs in children less than 12 years of age. Additional safety and tolerability data from other sources were also included. Data were analysed separately for oseltamivir and zanamivir.

The authors identified three trials of neuraminidase inhibitors in the prevention of influenza in families (including children). However, the companies that performed these trials were not willing to separate out the data for paediatric populations, and so no data from these studies were eligible for inclusion in the review.

The adverse-events profile of zanamivir was no worse than placebo and no reports of zanamivir-induced bronchospasm in children were found. Vomiting was more common in children treated with oseltamivir than in children treated with placebo (14.8 vs. 9.3%).

The authors conclude that the ability of neuraminidase inhibitors to prevent influenza infection in children remains unproven.

Homoeopathic Oscillocochinum

Oscillocochinum is a patented, commercially available homoeopathic medicine. The medicine is manufactured from wild duck heart and liver, which are said to be reservoirs for influenza viruses. Scarcely known in the English-speaking world, it is one of the most widely used and popular homeopathic medicines in France, introduced in the 1930s.

The authors' objective was to determine whether homoeopathic Oscillocochinum or similar medicines are more effective than placebo in the prevention and treatment of influenza and influenza-like syndromes.¹⁶ Here, we will focus on prevention.

The last search of the literature was done in 2003. The authors included placebo-controlled trials of Oscillocochinum or homoeopathically prepared influenza virus, influenza vaccine or avian liver in the prevention and treatment of influenza and influenza-like syndromes.

Of the seven studies that were included in this review, three addressed the prevention of influenza, with a total number of 2265 patients. Two of the prevention trials used prepared-prepared mixtures of inactivated bacteria and influenza viruses. The third used extract of heart and liver of wild duck (similar to that used in the preparation of Oscillocochinum) in a 200C potency (i.e. diluted 1 in 100 repeated 200 times). There was no evidence that homoeopathic treatment can prevent influenza-like syndrome (relative risk 0.64, 95% CI 0.28–1.43).

The authors conclude that current evidence does not support a preventive effect of Oscillocochinum-like homeopathic medicines in preventing influenza and influenza-like syndromes.

Discussion

We found nine Cochrane reviews that specifically focused on the prevention of influenza, five of which addressed vaccination and four medication.

For six reviews, the most recent search of the literature was carried out in 2002–2004. However, the other three reviews have not been updated for several years,^{9,12,14} although this may be due to a lack of new studies. However, the findings for interventions that have become recently available and are widely advised, such as the neuraminidase inhibitors,^{12,14} should be interpreted with caution, as there may be more recent trials that provide evidence to alter the original review's conclusions.

With one exception, all reviews were restricted to controlled trials, although the strictness relating to randomization differed. The review on influenza vaccination in healthy children also included cohort studies and case-control studies, but, for this overview, we only used results from the randomized trials. Some of the reviews allowed pseudo- or quasi-randomization. Similarly, some authors required all studies to be double-blind, whereas others also allowed single-blind studies. In any case, by restricting reviews to controlled trials with some sort of randomization and blinding, it is likely that the best available evidence has been gathered. As the number of studies will increase in the future, restriction to studies of high methodological quality should be considered.

Other strategies that may be helpful in preventing influenza, but are not yet subjects of Cochrane reviews, include restricting circulation of viruses (e.g. by increasing vaccination rates or by vaccinating all children,¹⁷ vaccinating pregnant women,¹⁸ promoting hand washing,^{19,20} not blowing nose,²¹ and taking measures in poultry farms²²).

Other therapies, such as vitamin C and Echinacea, have been reviewed for their effects on preventing the common cold. As it is often difficult to distinguish episodes of influenza illness from illness due to other viruses, it cannot be ruled out that some of these therapies also have a role in preventing influenza. However, as the reviews on the common cold did not look at the causative agents, no data are available on the role of these therapies in preventing influenza.

Influenza vaccination is currently recommended for use in patients with a variety of conditions, including cardiovascular disease, respiratory illness, diabetes, renal disease, immunodeficiencies, children on long-term aspirin, children under the age of 2 years and pregnant women. Other target groups are nursing-home residents, health-care personnel and household contacts of influenza patients.²³ It is clear that the evidence for effectiveness in many of these groups has not yet been covered by individual Cochrane systematic reviews. The most likely reason is that few RCTs have been conducted in these groups. The participants in these groups are often subsets of larger groups (e.g. elderly people). Trials may be old, limiting any ability to obtain data for meta-analysis from the authors. In future RCTs, it may be unethical to conduct a placebo-controlled RCT of influenza vaccine in chronically ill elderly people, where guidelines recommend it universally, as for example in COPD.^{24–26}

Several of the identified gaps may be filled by reviews that will be completed in the near future.

In the Cochrane Library, there are protocols for development of reviews for influenza vaccination in elderly people and in people with HIV/AIDS; influenza vaccination to prevent myocardial infarction; amantadine and rimantadine for influenza A in children and the elderly.

The largest body of evidence to support the recommendations for influenza vaccination in chronically ill elderly people comes from observational studies (e.g. the work of Nichol et al.^{27,28}) A meta-analysis of 20 cohort studies of influenza vaccination in elderly people showed a 56% reduction in respiratory illness, a 53% reduction in pneumonia, a 50% reduction in hospitalization, and a 68% reduction in deaths from all causes during influenza outbreaks.²⁹ A major problem with observational studies is that it is impossible to rule out bias. Reasons why people were vaccinated or were not vaccinated may be related to their health status, which in turn may be related to the chance of getting infected.

Conclusion

A range of options is available for preventing influenza, with some having been studied more extensively than others. Most of the interventions to prevent influenza have unknown or disappointing effects. The evidence from RCTs, accumulated in current Cochrane systematic reviews, supports vaccinating healthy workers, although the effects are small. Antivirals, especially zanamivir and oseltamivir, may also have a place in the prevention of spreading the virus, although this review has not been recently updated. In people with chronic diseases, there is limited evidence in support of vaccination for people with COPD, but no evidence yet of effectiveness in asthma or cystic fibrosis. The reviews do, however, suggest that vaccination is safe in all these groups.

Practice points

- At the moment, Cochrane systematic reviews address only some of the options available for preventing influenza
- Influenza vaccination does not cause exacerbations of chronic respiratory diseases
- There is, as yet, very little RCT evidence of effectiveness of vaccination in preventing exacerbations of chronic respiratory disease
- Vaccinating healthy workers and healthy children is effective, but the effect on the first is modest

- Neuraminidase inhibitors, zanamivir and oseltamivir, may also have a place in limiting the spread of infection, and showed less adverse effects than older antiviral medication (amantadine and rimantadine)
- The popularity of homoeopathic Oscillo-cinum in some parts of the world is not supported by current evidence

Research directions

- Most of the systematic reviews ask for new, well-designed clinical trials, as the current evidence is inconclusive
- New Cochrane reviews are needed for several measures that may be helpful in preventing influenza. Some of these are at the protocol stage; however, other reviews need to be designed and conducted
- Priority should be given to conducting reviews on the effect of influenza vaccination in the high-risk groups mentioned in recommendations worldwide

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