# Reminder through more than one letter for influenza vaccination

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**Palabras clave** Vaccines, Reminder Systems, Primary health care, Epistemonikos, GRADE.

## Abstract

### Introduction

Different interventions have been proposed to reinforce the use of the influenza vaccine. The use of reminders, whether through letters, phone calls, pamphlets or technological applications, among others, has stood out among those aimed at increasing adherence to treatment. However, its effectiveness is not clear. In this summary, which is part of a series of reminder evaluations, we assess the use of multiple mail reminders.

### Methods

We conducted a search in Epistemonikos, the largest database of systematic health reviews, which is maintained by screening multiple sources of information, including MEDLINE, EMBASE, Cochrane, among others. We extracted the data from the identified reviews, analyzed the data from the primary studies, performed a meta-analysis and prepared a summary table of the results using the GRADE method.

### Results and conclusions

We identified eight systematic reviews including 35 primary studies, of which four analyze the use of more than one letter as a reminder. We conclude that the use of multiple mail reminders probably increase adherence to influenza vaccination in patients over 60; while it may make little or no difference in children under 6 years, but the certainty of the evidence is low.

## Problem

Influenza is an acute respiratory disease caused by the influenza virus that can be prevented with a seasonal vaccine. Despite this, it remains an important cause of morbidity and mortality[1] since it is estimated that annual influenza epidemics cause 3-5 million serious cases of the disease and 290 000 to 650 000 deaths[2]. Additionally, these are associated with significant school and work absenteeism, generating significant productivity losses[2].

Various interventions have been proposed to increase the use of the influenza vaccine. Reminders can be provided through different communication channels: letters, phone calls, pamphlets or technological applications, among others. This article is part of a series

of publications aimed at evaluating the use of reminders and will focus on the effects of sending two or more letters, postcards or pamphlet type reminders via traditional mail.

## Key messages

- Multiple mail reminders probably increase adherence to influenza vaccination in people over 60 years.
- Multiple mail reminders may make little or no difference to adherence to influenza vaccination in children under six years.

## About the body of evidence for this question

| | |
|---|---|
| What is the evidence. See evidence matrix in Epistemonikos later | We found eight systematic reviews[3-10] including 35 primary studies reported in 34 references[11-44] of which, 32 are randomized trials reported in 31 references[11-41].<br><br>Five trials were excluded[16,18,21,33,35] because they included co-interventions to increase influenza vaccination.<br><br>Twenty-two trials were excluded[11-15,17,20,22,23,25,26,28-30,32,34,36-41] because the intervention consisted of a single mail reminder, which has already been analysed[45].<br><br>In addition, observational studies[42-44] did not increase the certainty of the evidence, nor provided any additional relevant information.<br><br>This table and the summary in general are based on four randomized trials[19,24,27,31]. |
| What types of patients were included* | The trials included a total of 71 458 participants of all ages, including targeted risk population such as children over six months up to six years and adults over 60 years.<br><br>Two trials included children[19,24] and two trials included older adults[27,31] (over 60 years old).<br><br>In general, the trials excluded patients who had already received the vaccine prior to the start of the trial, with egg allergy or participants living in nursing homes. |
| What types of interventions were included* | All trials evaluated the use of multiple reminders, defined as more than one reminder sent by traditional mail[24,31,19,27].<br><br>All included trials compared against usual medical care. |
| What types of outcomes were measured | This systematic reviews identified only evaluated the adherence to the vaccine (influenza vaccination rate).<br><br>The average follow-up of the trials was seven months, ranging from six to 11 months. |

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

## Methods

We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

## Summary of findings

Information on the effects of multiple mail reminders is based on four randomized trials that included 71 458 patients[19,24,27,31].

Of these, two trials included population under 6 years with a total of 7044 participants[19,24], while the other two included populations over 60 years with a total of 64 414 participants[27,31].

All trials measured the outcome adherence to vaccination.

The summary of findings is the following:

- Multiple mail reminders probably increase adherence to influenza vaccination in people over 60 years.
- Multiple mail reminders may make little or no difference to adherence to influenza vaccination in children under six years.

| **Multiple mail reminders for influenza vaccination** | | | | |
|---|---|---|---|---|
| **Patients** | Population over 60 years and under 6 years old. | | | |
| **Intervention** | Multiple mail reminders (any format). | | | |
| **Comparison** | No reminder (usual medical care). | | | |
| Outcome | Absolute effect* | | Relative effect (95% CI) | Certainty of evidence (GRADE) |
| | WITHOUT **reminders** | WITH **reminders** | | |
| | Difference: participants per 1000 | | | |
| Adherence to vaccination in population over 60 years | 208 per 1000 | 225 per 1000 | RR 1.08 (1.02 a 1.13) | ⨁⨁⨁◯[1] Moderada |
| | Difference: 17 more (Margin of error: 4 to 27 more) | | | |
| Adherence to vaccination in children under 6 years | 558 per 1000 | 754 per 1000 | RR 1.35 (0.86 a 2.12) | ⨁⨁◯◯[2,3] Baja |
| | Difference: 196 more (Margin of error: 78 less to 625 more) | | | |

**Margin of error:** 95% confidence interval (CI).
**RR:** Risk ratio.
**GRADE:** Evidence grades of the GRADE Working Group (see later).

[1] A level of certainty of the evidence for risk of bias was reduced, since the trials presented limitations associated with the generation of the randomization sequence and its concealment.
[2] A level of certainty of inaccuracy of evidence was reduced, since different decisions would be made at each end of the confidence interval.
[3] A level of certainty of the evidence for inconsistency was decreased, since different trials present different conclusions ($I^2$ = 99%).

Follow the link to access the interactive version of this table (Interactive Summary of Findings – iSoF)

## About the certainty of the evidence GRADE)*

⊕⊕⊕⊕
**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.

⊕⊕◯◯
**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
**Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision

## Other considerations for decision-making

### To whom this evidence does and does not apply

The conclusions of this summary are applicable to children and adults over 60 years, and they are also considered to apply to general population.

The evidence presented in this summary should not be extrapolated to participants allergic to influenza vaccine components.

These conclusions can be applied to any type of reminders sent more than once, at different times, combined or not with a postcard.

### About the outcomes included in this summary

The outcomes selected are those considered critical for decision-making according to the opinion of the authors of this summary and generally coincide with those evaluated by the systematic reviews identified.

### Balance between benefits and risks, and certainty of the evidence

Multiple mail reminders probably increase adherence to influenza vaccination in people over 60 years and may make, in children under six years, little or no difference to adherence to influenza vaccination.

However, there are certain limitations associated with the intervention evaluated, since the studies used pamphlets, letters and postcard reminders, varying both in the presentation of the information and its content (not reported). This heterogeneity in the intervention could explain the inconsistency found in the results of children under 6 years ($I^2$ = 99%).

It should be noted that this is an intervention that should not pose any risk to the population.

### Resource considerations

The costs of this intervention are very variable depending on the type of reminder, quantity and context where they are used.

Even though the intervention presents a favorable risk/benefit balance in the older population, the cost-effectiveness could vary according to the format, quantity and channel of delivery of the reminders.

### What would patients and their doctors think about this intervention

In general, the use of reminders to prevent and promote health are well received by the population. Especially, when there are no direct costs associated to the patient.

From the point of view of healthcare workers or providers, the use of reminders would allow to implement a potentially effective preventive measure in the general population or in high-risk populations[8].

However, there may be some concerns regarding the use of vaccines in certain sectors of the population with certain values and preferences (lifestyles, religions, perceived lack of effectiveness, possible adverse effects, among others). This could influence decision making when assessing applicability and effectiveness of the intervention.

### Differences between this summary and other sources

The conclusiones of this summary are consistent with those found in one of the systematic reviews[3], which analyzed the use of multiple mail reminders. Only one systematic review[8] reports that the intervention would be effective with a high certainty of the evidence, but it should be noted that it only included one[27] of the four trials analyzed in this summary.

The Task Force on Community Preventive Services[46] and Standards for immunization practices[47] guidelines recommend the use of reminders to increase adherence, without specifying the type or format of the reminder. The American Academy of Pediatrics[48]

suggests that efforts should be devoted to the scope and infrastructure necessary to achieve optimal distribution of vaccines, so that more people are immunized.

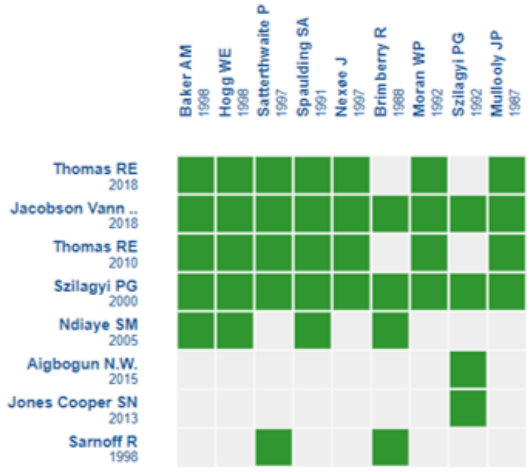
**Could this evidence change in the future?**

The probability that future evidence changes the conclusions presented in this summary regarding older population is low. However, it is likely that the conclusions related to children do so, since the certainty of the evidence is low.

We identified one ongoing systematic review in the PROSPERO database [49] and one clinical trial in the International Clinical Trials Registry Platform[50] of the World Health Organization that could provide additional relevant information.

## How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.




An evidence matrix is a table that compares systematic reviews that answer the same question.
Rows represent systematic reviews, and columns show primary studies.
The boxes in green correspond to studies included in the respective revisions.
The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version** Mail reminders to increase adherence to influenza vaccination

## Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (http://dx.doi.org/10.5867/medwave.2014.06.5997)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database

www.epistemonikos.org.

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