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A meta-analysis of the impact of individual correspondence on flu vaccination rates: considerations for COVID-19 vaccination

A research paper produced for the COVID-19 Communications and Behavioural Advisory Group, 2021

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Executive Summary

To curb the COVID-19 pandemic it is imperative to maximise uptake of available vaccines and effective communications have a vital role to play in this. An important consideration for public health authorities is whether mass communications can be enhanced by directly contacting potential recipients.

To answer that question, this literature review compiles evidence of the effectiveness of sending a single written message to an individual to encourage flu vaccination, compared to mass communications.

Mass Communications (control condition) =	v.	Mass Communications + Direct correspondence
Public service announcements Notices to healthcare providers News coverage Media campaigns		

The key findings of this review are as follows:

1. **Sending a single written message directly to an individual increase flu vaccine uptake more than mass communication alone.** Of 37 such interventions reviewed, 32 (86%) report an increase in flu vaccination rates. A formal meta-analysis shows that sending a single written message increases flu vaccine uptake by 18% relative to the no contact comparator group. Subgroup analysis shows that the intervention is effective across correspondence type, age group, period of publication, and location.

2. **The five most common elements of correspondence that increases uptake are**:

   a) a recommendation to get the vaccine, including yearly vaccination;
   b) statements that the vaccine is safe and effective (e.g. does not cause the flu), has minimal side effects, and helps avoid serious complications;
   c) a statement of the seriousness of the flu and its possible complications;
   d) information on how and where to get the vaccine, including scheduling information;
   e) a statement that the vaccine is free.

3. Of the six studies with multiple arms that compare different types of written messages, four studies find a particular message to be most effective. The **most effective written message in each of the four respective studies** was:

a) The message with the most personal mode of contact.
b) A message based on the Health Belief Model (emphasizing severity of influenza, susceptibility of at-risk persons, and benefits of vaccination; addressed to “Dear Patient”).
c) A message including the exact time and place of vaccination clinics.
d) An educational brochure emphasizing the severity of influenza, that it is very contagious and can be passed to friends and family, that the vaccine is safe, effective and free, and that the patient’s doctor recommends vaccination.

This review supports the use of direct correspondence to increase the uptake of COVID-19 vaccines across the wider community.

In the design of correspondence to support the uptake of COVID-19 vaccines it is advised to take the following into account: the content of this review; randomised control trials (RCTs) of the impact of messaging design on vaccine uptake and attendance at healthcare appointments; and factors shown to influence intentions to get COVID-19 vaccinations.

Implications for Practice

Direct written correspondence to individuals to invite them to attend a clinic or to make an appointment for flu vaccination is effective in increasing vaccination rates.

Content included in effective written messages include:

- A clear and strong recommendation to be vaccinated
- Information about vaccine effectiveness
- Information on the seriousness of the flu and how vaccination can help avoid complications
- A statement that the flu vaccine is safe
- Information on cost
- Clear instructions on how to get vaccinated.

1. Introduction

1.1 Background and Purpose

To curb the COVID-19 pandemic it is imperative to maximise uptake of available vaccines and effective communications have a vital role to play in achieving this. An important consideration for public health authorities is whether mass communications can be enhanced by directly contacting potential recipients. Past experience in promoting influenza vaccines is relevant to answering this question. It is relevant not only for the length of public health experience in the mass vaccination of adults for an annual basis, but also for the relative similarity of influenza as a droplet-spread virus with potentially serious complications for at-risk groups.

This review is not only relevant to the COVID-19 vaccination programme but also the enhanced vaccination programme to prevent influenza as referred to in "Resilience and Recovery 2020-2021, Plan for Living with COVID-19".

Therefore, this literature review compiles evidence of the effectiveness of sending a single written message to an individual to encourage flu vaccination. The questions asked are:

1. Does sending a single written message directly to an individual increase flu vaccine uptake?
2. What content is included in tested correspondence encouraging flu vaccine uptake?
3. Has the effectiveness of content or design elements been tested against each other?

The studies extracted for this review are those which measure actual behaviour (i.e., vaccine uptake rather than intention) and which trial single health messages sent to individuals in the general population (i.e., excludes studies of mass communications only, and multiple reminders).

1.2 Method

Information search and screening

A systematic search was undertaken of Web of Science (all databases), PsycINFO (empirical studies) and PubMed (no restrictions) on the 24th of February 2021 using the search string below. We also searched the references of eight systematic reviews found in the above search: Frascella et al. (2020), Atkinson et al. (2019), Sanftenberg et al. (2019), Jacobson et al. (2018), Thomas et al. (2018), Odone et al. (2015), MacDonald et al. (2013), Ward et al. (2012); one meta-analysis, Zhou et al. (2020); and a rapid systematic review identified by a member of the advisory group: Lawes-Wickwar et al. (2020).

((vaccine OR *immunis*) AND (flu OR influenza) AND (letter* OR email* OR SMS OR text OR postcard* OR brochure* OR reminder* OR invitation* OR "portal message") AND (vaccinated OR vaccination rate* OR uptake OR take-up OR effectiveness) AND (RCT OR trial OR quantitative OR experiment*))*

Studies were included if they met the following criteria: compared the effect on flu vaccination rates for a single direct correspondence compared to no direct correspondence; was a randomised controlled trial with an appropriate control group; was published in English in a peer-reviewed journal; was not specific to health care workers; and was conducted in an OECD country.

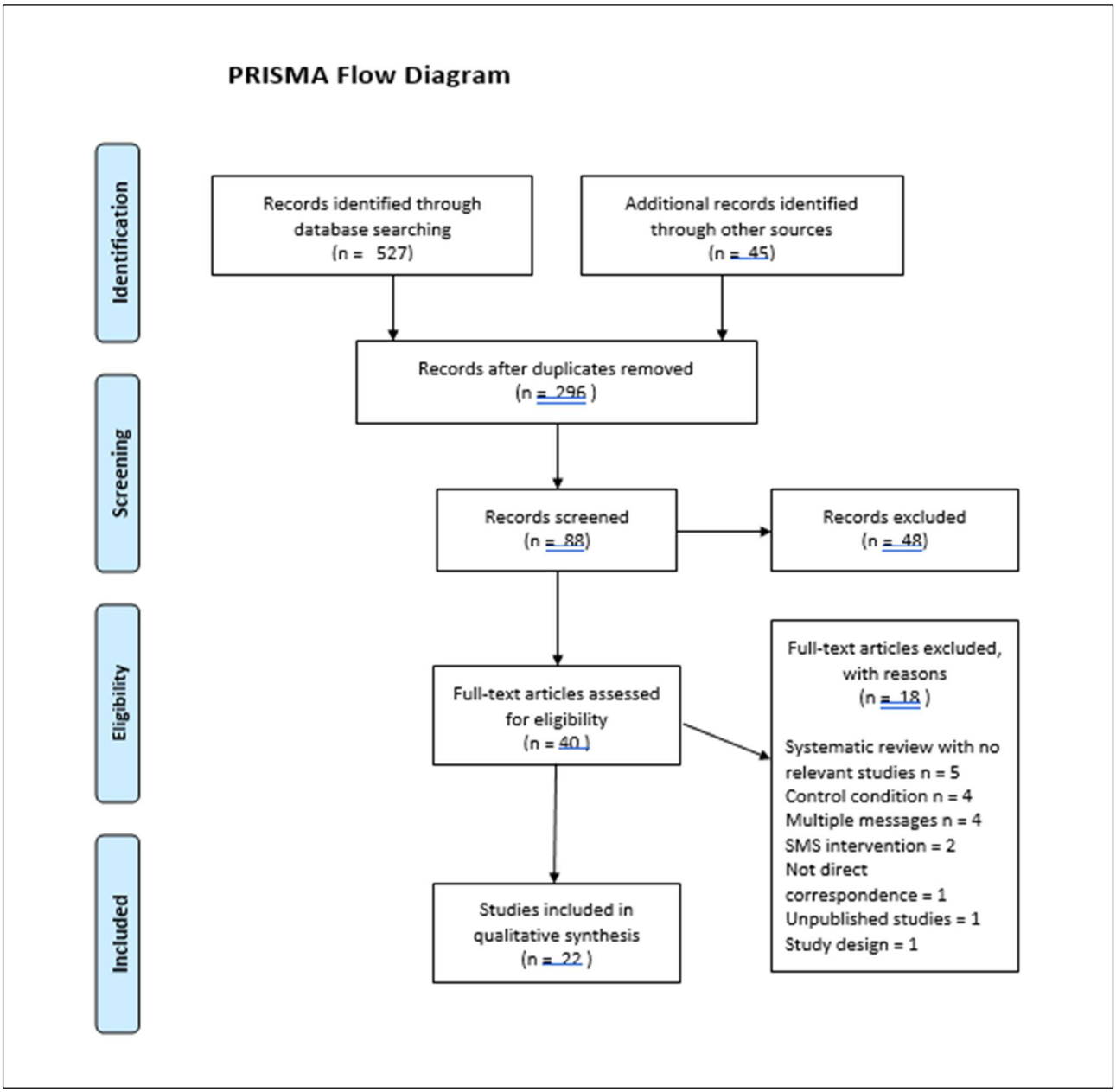
In all, ten systematic reviews were consulted for relevant studies. None of these reviews addressed our specific research question: whether the effectiveness of mass communications can be enhanced by sending a single direct correspondence to potential vaccine recipients.

Zhou et al. (2020) studies educational methods that are effective at improving influenza vaccine uptake, while MacDonald et al. (2013) reviews interventions to increase influenza vaccination uptake primarily in healthcare workers and the elderly. Three reviews explore the use of new technologies in improving vaccine uptake: Frascella et al. (2020) reviews the use of email reminders; Atkinson et al. (2019) studies the use of digital technologies to push vaccine information and reminders; Odone et al. (2015) explores the effectiveness of new media (e.g., YouTube videos, Facebook, smartphone apps, emails) to improve vaccination rates. Lawes-Wickwar et al. (2020) examines public responses to health messages encouraging vaccination against infectious diseases in a pandemic, and Ward et al. (2012) reviews interventions in Australia only.

Three of the ten reviews consulted included papers that met our inclusion criteria; these were Sanftenberg et al. (2019), Jacobson et al. (2018) and Thomas et al. (2018). Sanftenberg et al. (2019) identifies interventions to increase influenza vaccination uptake in people aged 18 years and older; some of its studies were not included here as they compare sending two reminders to one reminder. Jacobson et al. (2018) studies patient reminder and recall interventions to improve immunisation rates generally. Thomas et al. (2018) includes interventions to increase influenza vaccination uptake in people aged 60 years and older; some of the studies in that review were not included here because they did not compare a single correspondence to no correspondence, included a telephone intervention or multiple reminders, or were not published in English

The screening profile is shown in Figure 1.1.

Figure 1.1



Where possible, we try to categorise the direct interventions into personalised or mass communication. MacDonald et al. (2013) defines mass communication as "distribution of universally targeted information to undifferentiated or large segments of the population at the same time" and personalised communication as that "which aims to make a personally relevant appeal to individuals by, for example, using direct contact or individually addressed correspondence". It is not easy to do this for all studies, and the basis for our categorisation is explained.

Meta-Analysis

The events of vaccination and total events (i.e. subsample size, inclusive of events and non-events) from the intervention and control groups were inputted into Review Manager v5.4 to generate risk ratio effect sizes. This was calculated as (SI / NI) / (SC / NC), where SI / NI = the number of 'success' events (vaccination) divided by the total events in the intervention group and SC / NC = the number of 'success' events (vaccination) divided by the total events in the control group. When only the % vaccination rate for both the intervention and control groups was reported, the absolute risk was derived, according to recommended practice (Deeks et al., 2021), from this percentage using the relevant denominator (i.e. subsample size of the intervention group or control group) reported in the respective study.

To determine the mean risk ratio across the included studies inverse-variance weighted, random-effects modelling was conducted. A random-effects model was selected to account for variability between studies which can likely be explained by factors other than sampling error (Borenstein et al., 2009), for example, variance in the sample characteristics and the intervention components between studies. The risk ratio effect size contributed by each study was weighted by its inverse variance so that studies with a larger sample size were given more weight in the analyses to ensure precision in the mean, weighted effect size estimate (Borenstein et al., 2009). Each study contributed only one effect size to the meta-analysis per written correspondence intervention; this avoided weighting individual studies by the number of subsamples reported (e.g. if vaccination was reported by age group for the respective intervention) and also to ensure statistical independence of effect sizes (Lipsey & Wilson, 2001).

For the meta-analysis a mean weighted effect size and 95% confidence intervals were generated and presented visually in a Forest plot along with the study-level effect sizes. To test the null hypothesis that the mean weighted effect size was 0 the Z statistic was interpreted against a .05 alpha level; a significant Z statistic indicated that the mean, weighted effect was significantly different from 0. Heterogeneity, resulting from differences between the study-level effect sizes that contributed to the mean weighted estimate, was evaluated with the Q statistic Chi-square test. Due to low power in a meta-analysis with a small number of studies, the alpha level was set to .10, as recommended by Deeks et al. (2021). The I2 index was applied to quantify the amount of heterogeneity between studies that could be explained by true heterogeneity rather than chance. This was interpreted in accordance with the recommended criteria: 25-49% = small, 50-74% = moderate, and 75%+ = large heterogeneity (Borenstein et al., 2009).

Categorical variables such as the characteristics of the sample (age group), intervention (type of written correspondence) and study (location (continent), year of publication (decades)) were considered for subgroup analyses. A minimum of two studies were required per category in the

subgroup analyses to ensure sufficient power to determine whether the categorical variable was a significant moderator of effect size (Borenstein et al., 2009).

Quality Assurance

Robert Murphy and Carol Taaffe carried out the information search, descriptive and content analysis for this report; the meta-analysis was conducted by Elayne Ahern. In preparing the report, the authors followed the Irish Government Economic and Evaluation Service (IGEES) quality assurance process, seeking feedback on the analysis format (structure); clarity (quality of writing); accuracy (reliability of data); robustness (methodological rigour); and consistency (between evidence and conclusions). The report was circulated for review to the following:

- Internal/ Departmental
  - Line management – Research Services and Policy Unit
- Internal/ External
  - COVID-19 Communications and Behavioural Advisory Group.

1.3 Report Structure

The findings of the individual studies are summarised as follows:

- impact on flu vaccination rates (see Chapter 2),
- content used in tested correspondence (see Chapter 3),
- effectiveness of different content or design elements (see Chapter 4).

A description of the interventions is provided in Table 1. The type of correspondence most frequently sent in the studies was a letter, followed by a postcard, and to a lesser degree by patient portal messages (a patient portal is a secure online application for healthcare correspondence and information; in this instance, the correspondence sent was in letter format). From the information provided it was not possible to determine for all studies whether the correspondence was personalised or generic. It appears that most correspondence was personalised in the sense that it was addressed to the recipient, was signed by a named healthcare professional, or did not form part of mass correspondence as it included information that was specific to the patient (i.e., it was addressed to the patient as a member of an at-risk group). The studies included here were conducted in the USA, Canada, Spain, Denmark, New Zealand and Australia.

Table 1 Description of Studies and Interventions

Studies	Interventions
Klassing et al, 2017 USA n = 311	Control: No contact Intervention: (1) standardized letter, or (2) phone call. A phone call script was utilized for the phone call intervention; patient specific questions were fielded on an individual basis. This second intervention is not discussed further in this review. The letter intervention group received a standardized letter addressed to each specific patient. Both the phone call script and letter referenced the 2014 CDC immunization schedule and guidelines Category and basis: PL = Personalized Letter (addressed to each patient)
McCaul et al, 2002 USA n = 23,733	Control: No reminder Intervention: (1) Reminder letter from state peer review organisation (PRO), or (2) reminder letter with loss or gain frame from PRO, or (3) action letter from county public health office with date, time and place of vaccination clinics. The reminder letter highlighted four main points: (a) “You should have a flu shot every year,” (b) “Medicare will pay for your flu shot this fall,” (c) “The flu shot is safe,” and (d) “You should have your shot soon.” In addition, the framing letter stated, “As a person 65 or older, you are at risk for getting a serious case of flu.” The framing letter was accompanied by one of two inserts. The gain insert featured the picture and testimonial of a North Dakota woman who had received a flu shot the previous year and had not gotten the flu; the loss insert featured the picture and testimonial of another North Dakota woman who had not received a flu shot last year and had spent several days in bed, sick with the flu. More detail on the arms is provided in Chapter 4. Category and basis: PL = Personalised letter (reference to age; addressed to individual; signature of doctor)
McDowell et al, 1986 Canada n = 939	Control: No reminder Intervention: (1) A personal reminder by the physician, **or** (2) a telephone reminder by the nurse, **or** (3) a letter reminder. Only the latter intervention (i.e., 3) is discussed here. The letter was signed by the patient's physician and the practice nurse. The letter read: "As you know, each fall we recommend immunization against influenza for our patients who are 65 years of age or older. The vaccine is now available and if you would like to be immunized, please call to schedule an appointment."

	Category and basis: PL = Personalised Letter (addressee selected by age, signed by physician and practice nurse)
Moran et al, 1992 USA n = 409	Control: Usual Care Intervention: (1) Reminder letter offering free vaccination with an appointment, or (2) two sequential reminder letters, offering the same. The sequential reminder intervention is not discussed further in this review. The reminder letters were written at fifth-grade reading level and emphasized that: 1) immunization was medically indicated, 2) immunization did not cause influenza, 3) immunization could result in minor side effects, and 4) immunization was free and available without an appointment. Category and basis: PL = Personalised Letter (advising high risk patient that immunisation is medically indicated)
Mullooly et al, 1987 USA n = 2217	Control: Did not receive the mailed cue. Intervention: Personalized letter stressing the importance of influenza vaccination for high-risk elderly individuals who had been hospitalized during the past year. It was explained that immunization could help to avoid serious complications from the bout of flu and that the CDC and their personal Kaiser Permanente doctors recommend that they get a flu shot each year. Information about how and where to obtain a vaccination was also provided. Category and basis: PL = Personalised Letter (described as personalised by author, letter also makes reference to people discharged from hospital in last year)
Nexøe et al, 1997 Denmark n = 585	Control: No letter Intervention: (1) Patients were invited for vaccination and had to pay the GP's usual fee, or (2) patients were invited for free vaccination. The second intervention is not discussed further in this review. Category and basis: PL = Personalised Letter. Letter included patient's name and GP's signature in print.
Roca et al, 2012 Spain n = 2402	Control: No intervention Intervention: A personalized letter including basic information about the clinical manifestations and possible complications of influenza, and about the efficacy of the vaccine to prevent the disease, according to recommendations of the Centers for

	Disease Control and Prevention and the local authorities of the Comunidad Valenciana. The letter addressed common concerns about the flu shot and was written in easy-to-understand language. Category and basis: PL = Personalized Letter (described as personalized by author, paper also makes reference to where patients' postal addresses were obtained from)
Satterthwaite et al, 1997 New Zealand n = 2791	Control: No reminder Intervention: (1) Personalised letter recommending vaccination, or (2) personalised letter recommending visit to receive vaccine at no charge. Both letters were signed by principal. The second intervention is not discussed further in this review. Category and basis: PL = Personalised Letter.
Terrell-Perica et al, 2001 USA n = 6528	Control: No letter. During the study period, the State of Hawaii Department of Health conducted routine promotional activities for influenza immunization, including press releases, immunization clinics held at pharmacies and retail stores, and health education at a large annual senior fair. In addition, pneumococcal education kits produced by the National Institute on Aging were mailed to physicians. Intervention: (1) A letter encouraging recipients to take advantage of their new Medicare benefits to receive influenza immunization, or (2) a letter encouraging them to take advantage of their new Medicare benefits to receive influenza *and* pneumococcal immunizations – this intervention is not discussed further in this review. The one-page influenza immunization reminder letter was formatted in an easy-to-read, 14-point font with two prominent bullets: "Have you had your FLU shot this year?" and "Medicare covers FLU shots!" Category and basis: PL = Personalized Letter (did not apply to all households, new Medicare members)
Yokum et al, 2018 USA n = 228,000	Control: No letter Intervention: (1) A letter with vaccination information + picture of National Vaccine Program Officer, or (2) a letter with vaccination information + picture of Acting US Surgeon General, or (3) a letter with implementation intention prompt + picture of Acting US Surgeon General, or (4) a letter with enhanced active choice implementation prompt + picture of Acting US Surgeon General (more details in Chapter 4). Category and basis: PL = Personalised Letter (addressed to recipient's first name)

CDC 1995 USA n = 190,000	Control: No letter. Measures to increase influenza vaccination coverage including public service announcements and notices to health-care providers Intervention: (1) A personalized letter and informational brochure from the Montana-Wyoming Foundation for Medical Care (MWFMC) medical director encouraging vaccination, or (2) a form letter and informational brochure from the MWFMC encouraging vaccination. Category and basis: (1) PL + B, (2) GL + B = Personalised Letter and Brochure, and Generic Letter and Brochure (described as such by authors, also from named medical director)
Minor et al, 2010 USA n = 1371	Control: Standard clinical practice Intervention: (1) A letter addressed from the clinic and signed by the clinic pharmacist and physician medical director and a copy of the Centers for Disease Control and Prevention (CDC) Influenza Vaccine Information Statement, or (2) a telephone reminder. The latter is not discussed further in this review. Category and basis: PL + B = Personalised Letter and Brochure (letter signed by the clinic pharmacist and physician medical director)
Brimberry et al, 1988 USA n = 787	Control: No reminder Intervention: (1) Patients received a reminder letter or, (2) a personal telephone reminder. The second intervention is not discussed further in this review. The letter emphasized that, because of “certain medical problems (for example, diabetes or heart disease),” influenza can be a serious threat to health, and that the patient’s physician had recommended that the patient be vaccinated. As a form letter was used, each patient’s personal diagnosis could not be mentioned, and the signature of a designated “influenza vaccination director” was used because of the difficulty of obtaining the signature of each patient’s personal physician. To make the vaccination convenient for the patient, no appointment was necessary, and the patient was informed of the cost. Category and basis: GL = Generic Letter.
Buchner et al, 1987 USA	Control: No reminder Intervention: Postcard reminder; short message on 3-inch by 5-inch card, mailed in business envelope with physician’s return address; message indicated flu season was coming, some people are at greater risk for influenza and complications, flu shots

n = 655	can decrease risks with minimal side effects, and it is needed each year; also provided instructions for where to obtain flu shots. By having the physician sign the cue and by using the physician's business envelope, the cue emphasised that the physician recommended the flu shot. Category and basis: PP = Personalised Postcard (signed by physician)
Puech et al, 1998 Australia n = 325	Control: Usual care, considered to be an ad hoc approach, influenced by news coverage of potential epidemics, media campaigns by vaccine manufacturers, opportunistic reminders and other secular events. Intervention: A postcard encouraging patients to attend the practice for an influenza vaccination before the end of the month. The postcard stressed the seriousness of influenza as opposed to the effectiveness and safety of influenza vaccine; it also gave availability and cost information. For ease of reading, the postcard was large (A5 format) and had clear, black-on-white large print. The postcard had a Flesch readability score of 68,14 requiring a minimum IQ of 90 to understand it (75% of the general population would understand it). Postcards had the practice logo and were mailed in a handwritten, personally addressed envelope also printed with the practice logo. Category and basis: PP = Personalised Postcard (personally addressed envelope)
Spaulding et al, 1991 USA n = 1068	Control: No postcard and received routine care. Intervention: A reminder postcard advising patients that their physician had determined that they were at high risk of complications should they catch the "flu," and strongly urging them to come to the Family Practice Clinic for immunization. Category and basis: PP = Personalised Postcard (the letter stated that their physician had determined that they were at high risk of complications should they catch the flu)
Clayton et al, 1999 USA n = 5278	Control: Standard member educational materials sent by mail. Intervention: Postcard reminder mailed in addition to standard materials. Category and basis: P = Postcard (unclear if generic or personalised as no information given in paper)
Larson et al, 1982	Control: No reminder

USA n = 395	Intervention: (1) Patients sent a neutral postcard mentioned influenza vaccine now available; listed telephone number for nurse appointments; addressed to "Dear Patient"; or (2) health belief model postcard, emphasizing severity of influenza, susceptibility of at-risk persons to influenza, and benefits of vaccination; addressed to "Dear Patient", or (3) personal postcard; addressed to patient's name and signed by clinician; postcard mentioned that influenza season is approaching and recommended the patient come in for flu shot; it listed telephone number to call and make appointment with nurse (more details in Chapter 4). Category and basis: (1) GP = Generic Postcard (2) HBP = Health Belief Model Postcard (3) PP = Personalised Postcard
Moran et al, 1996 USA n = 797	Control: No intervention Intervention: (1) A large print, illustrated educational brochure emphasizing factors important to patients in making a decision about influenza immunization, or (2) a lottery-type incentive announcing that all patients receiving influenza immunization would be eligible for grocery gift certificates, or (3) both educational brochure and incentive. Category and basis: (1) GEB; (2) Lottery; (3) GEB + Lottery. Generic Educational Brochure and financial incentive (gift certificate lottery)
Baker et al, 1998 USA n = 24,743	Control: Did not receive a postcard or letter Intervention: (1) A generic postcard that included a standard message, (2) a personalized postcard from the primary care physician, addressed to the patient at risk and containing the standard message, (3) a personalized letter from the primary care physician, addressed to the patient at risk, and contained a message tailored to the patient's risk factors for influenza. The standard message of these materials included a description of who is at risk of contracting influenza, a statement that influenza can be serious, and assurance that the vaccine is safe and effective. The printed materials also advised individuals to get the influenza vaccine and listed the influenza clinic locations and operating hours. Category and basis: (1) GP = Generic Postcard; (2) PP = Personalised Postcard; (3) PL = Personalised Letter (described as such by authors, also personalised correspondence signed by physician and/ or tailored to the patient's risk factors.)
Cutrona et al, 2018 USA	Control: Usual care Intervention: (1) A portal message promoting influenza vaccines, or (2) an Interactive Voice Reminder (IVR) call. This second intervention is not discussed further in this review.

n = 89,930	Portal messages appeared in letter format; the signature line contained the name of the patient's PCP. Messages were delivered through standard channels. A generic message (without personal health information or reference to vaccines) was delivered to the patient's email account, prompting login to the secure portal via a hyperlink. Once logged in, patients clicked on a message labelled "Brief Flu Questionnaire" to view. Message included access to direct online scheduling of influenza vaccination appointments. Information about CDC vaccine website(s) appeared within the body of the message as a hyperlink. Message also included opportunities to report community-administered influenza vaccinations, barrier questions, and targeted information dispelling misconceptions. Category and basis: PPM= Patient Portal Message
Szilagyi et al, 2020 USA n = 164,205	Control: No reminder Intervention: (1) One patient portal reminder letter, or (2) two reminders, or (3) three reminders on the importance and safety of influenza vaccination. The sequential reminders (2) and (3) are not discussed further in this review. The letter included (a) information that influenza season was coming, the disease can cause substantial morbidity and the vaccine is the best way to protect against influenza, (b) recommendation to receive an influenza vaccine by calling for an office appointment or going to a pharmacy or other setting, (c) a website link to input influenza vaccinations received elsewhere into the UCLA Health System record, and (d) another website link to a UCLA webpage containing information about influenza vaccine and video testimonials about influenza vaccination. Letters were in English, included the name of the patient's primary care physician, and had a below seventh grade reading level per Flesch-Kincaid analysis. Category and basis: PPM = Patent Portal Message

2. Impact on Flu Vaccination Rates

2.1 Descriptive Analysis

Table 3 summarises the results of the 22 studies; these studies include 37 interventions. Of the 37 interventions, 32 (86%) are reported to have significantly increased flu vaccination rates (i.e., where the odds ratio exceeds one or the *p* value is below 0.05). Table 2 shows the impact across the 32 effective interventions.

Table 2 Impact Across Interventions

	Mean	Median	IQR
Absolute difference, percentage points	7.3	4.9	6.6
Relative difference, %	43.4	21	36.8

Two interventions showed no effect and one showed an effect for men only. Sending a postcard to older people who had previously received a vaccine was not effective (Clayton et al, 1999). Combining an educational brochure with a financial incentive (a lottery to receive a gift certificate) was also not effective compared to sending either a brochure or the incentive alone (Moran et al, 1996). A personalised postcard raised vaccination rates in men but not women and did not raise rates overall (Puech et al, 1998).

In two studies the intervention showed a negative effect on vaccination rates: in the first, pharmacists sent a personalised letter to asthma and COPD patients (Klassing et al, 2017); in the second, a generic reminder letter slightly decreased vaccination rates compared to the control (Brimberry et al, 1988).

The intervention most frequently used across the 22 studies was a personalised letter, followed by a generic letter, personalised postcard, and educational brochure. Patient portal messages, used in two studies, showed only a small positive impact.

Table 3 Summary of Interventions

Studies	Intervention Category	Target group	Vaccination Rate			RR/ OR	95% CI
			Control	Intervention	Abs. Difference		
Klassing et al, 2017	PL	Asthma and COPD patients	88.6%	83.7%	-4.9%	$p = 0.02$	
McCaul et al, 2002[1]	PL (Action)	≥65 years Medicare recipients	19.6%	28.2%	8.6%	z = 12.01, $p = 0.01$	
	PL (PRO)			24.4%	4.8%	not given	
	PL (Loss)			24.5%	4.9%	not given	
	PL (Gain)			23.5%	3.9%	not given	
McDowell et al, 1986	PL	≥ 65 years	9.8%	35.1%	25.3%	not given	
Moran et al, 1992	PL	High risk patients	38.2	40%	1.8%	$p > 0.01$	
Mullooly et al, 1987	PL	≥65 years	30.1%	38.9%	8.8%	RR=1.29	[1.15;1.45]
Nexøe et al, 1997	PL	≥65 years high risk patients	25%	49%	24%	$p < 0.01$	
Roca et al, 2012	PL	≥60 years	39.5%	43.8%	4.3%	OR=6.33	[1.15;1.45]
Satterthwaite et al, 1997	PL	>65 years	17%	27%	10%	RR = 1.55	[1.28; 1.88]
Terrell-Perica et al, 2001	PL	Medicare recipients	17.1%	19.8%	2.7%	$p = 0.023$ [2.70; 3.40]	
CDC 1995a (Wyoming)	GL + B	Medicare recipients	33.1%	40.4%	7.3%	OR=1.91	[1.81; 2.02]
	PL + B			42.7%	9.6%	OR=1.79	[1.69; 1.90]
CDC 1995b (Montana)	GL + B	Medicare recipients	46.7%	52.5%	5.8%	OR=1.51	[1.42; 1.61]
	PL + B			49.9%	3.2%	OR=2.07	[1.45; 2.20]
Minor et al, 2010	PL + B	Hypertension clinic	33%	46%	13%	OR=1.8	[1.3; 2.5]
Yokum et al, 2018[2]	PL (NVPR)	Medicare recipients	25.9%	26.6%	0.7%	$p = 0.01$ [1.01–1.07]	
	PL (USSG)			26.8%	0.9%	$p < 0.001$ [1.02; 1.08]	
	PL (Imp)			26.4%	0.5%	$p < 0.001$ [1.02; 1.07]	
	PL (Active)			26.3%	0.4%	$p < 0.001$ [1.02; 1.07]	
Brimberry et al, 1988	GL	High risk patients	11.4%	10.6%	-0.8%	$p < 0.05$	
Buchner et al, 1987	PP	≥65 years	54%	55%	1%	$p = 0.001$	
Puech et al, 1998	PP	≥65 years	46% [men only]	64% [men only]	18% [men only]	OR=3.75	[1.87;7.56]
Spaulding et al, 1991	PP	Military family practice	9.1%	25.2%	16.1%	RR=2.77	[2.05; 3.75]
Clayton et al, 1999	P	≥65 Received	77.2%	78.6%	1.4%	$p = 0.222$	

		vaccine previous year					
Moran et al, 1996	GEB	High risk patients	20%	36%	16%	OR=2.29	[1.45; 3.61]
	Lottery			29%	9%	OR=1.68	[1.05; 2.68]
	GEB + Lottery			26%	6%	OR=1.41	[0.88; 2.27]
Baker et al, 1998	GP	≥65 years <65 years	40.6%	43.5%	2.9%	----	[1.22; 4.79]
	PP			44.7%	4.1%	----	[2.43; 5.98]
	PL			45.2%	4.6%	----	[2.97; 6.53]
Larson et al, 1982	GP	>65 years or various diagnoses	20.2%	25%	4.8%	*p*<0.1	
	PP			41%	20.8%	*p*<0.025	
	HBP			51.5	31.3%	*p*<0.001	
Cutrona et al, 2018	PPM	≥18 years	11.6%	13.4%	1.8%	OR=1.20	[1.06; 1.35]
Szilagyi et al, 2020	PPM	Adults and children >6 months	37.5%	38%	0.5%	*p* = 0.008	

Key

PL = Personalised Letter; GL = Generic Letter; L = Letter; PL + B = Personalised Letter + Brochure; GL + B = Generic Letter + Brochure; PP = Personalised Postcard; P = Postcard; GEB = Generic Educational Brochure; GP = Generic Postcard; HBP = Health Belief Model Postcard; PPM = Patient Portal Message

1 McCaul et al tested four letter types: Action = letter on when and where to get a flu shot; PRO = letter from state peer review organisation (PRO); Loss = PRO letter with loss frame; Gain = PRO letter with gain frame.

2 Yokum et al tested four letter types: NVPR = letter + picture of National Vaccine Program Officer; USSG = letter + picture of US Surgeon General; Imp = letter + picture of US Surgeon General + implementation intention prompt; Active = letter + picture of US Surgeon General + active choice implementation prompt.

2.2 Meta-analysis

2.2.1 Overall meta-analytical results

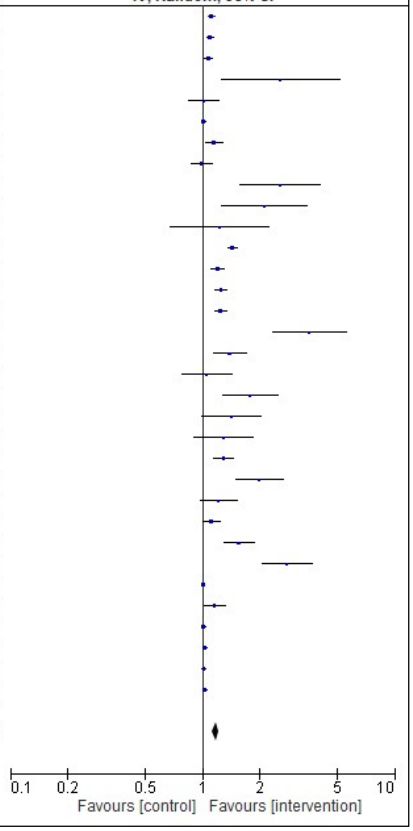
Sending a single written message increases flu vaccine uptake by 18%, relative to the no contact comparator group (RR = 1.18, 95%CI [1.13-1.22], Z = 8.56, p < .00001). The main analysis included 33 subsamples (intervention arms) across 21 studies (see Table 4). There was substantial heterogeneity among the included 33 samples ((n = 21 studies), χ2 (32) = 390.95, p < .0001, I2 = 92%) which warranted further subgroup analyses to determine the influence of patient and/or intervention characteristics on the effect size measure. The subgroups analysed are correspondence type, age group, year of publication and location.

Table 4 – Overall results of meta-analysis

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Baker et al. (1998; personal letter)	2780	6151	2505	6171	5.1%	1.11 [1.07, 1.16]
Baker et al. (1998; personal postcard)	2795	6252	2505	6171	5.0%	1.10 [1.06, 1.15]
Baker et al. (1998; postcard)	2684	6169	2505	6171	5.0%	1.07 [1.03, 1.12]
Brimberry et al. (1988; total sample)	26	267	10	262	0.3%	2.55 [1.26, 5.18]
Buchner et al. (1987; total sample)	108	196	105	194	2.4%	1.02 [0.85, 1.22]
Clayton et al. (1999; total sample)	2068	2631	2043	2647	5.2%	1.02 [0.99, 1.05]
Cutrona et al. (2018; total sample)	669	5000	582	5000	3.8%	1.15 [1.04, 1.28]
Klassing et al. (2017)	55	63	62	70	3.3%	0.99 [0.87, 1.12]
Larson et al. (1982; HBM postcard)	36	70	17	84	0.5%	2.54 [1.57, 4.11]
Larson et al. (1982; personal postcard)	26	61	17	84	0.5%	2.11 [1.26, 3.52]
Larson et al. (1982; postcard)	17	68	17	84	0.4%	1.24 [0.68, 2.23]
McCaul et al. (2002; Action Letter)	1708	6057	1548	7896	4.7%	1.44 [1.35, 1.53]
McCaul et al. (2002; PRO Gain Frame)	766	3260	1548	7896	4.4%	1.20 [1.11, 1.29]
McCaul et al. (2002; PRO Loss Frame)	799	3262	1548	7896	4.4%	1.25 [1.16, 1.35]
McCaul et al. (2002; PRO Reminder)	795	3258	1548	7896	4.4%	1.24 [1.15, 1.34]
McDowell et al. (1986; total sample)	84	239	21	215	0.6%	3.60 [2.31, 5.59]
Minor et al. (2010; total sample)	150	325	104	313	2.1%	1.39 [1.14, 1.69]
Moran et al. (1992; total sample)	54	135	52	137	1.2%	1.05 [0.78, 1.42]
Moran et al. (1996; brochure)	71	198	41	202	1.0%	1.77 [1.27, 2.46]
Moran et al. (1996; lottery)	57	198	41	202	0.9%	1.42 [1.00, 2.01]
Moran et al. (1996; lottery + brochure)	52	199	41	202	0.9%	1.29 [0.90, 1.84]
Mullooly et al. (1987; total sample)	430	1105	335	1112	3.5%	1.29 [1.15, 1.45]
Nexoe et al. (1997; total sample)	95	195	48	195	1.3%	1.98 [1.49, 2.63]
Puech at al. (1998; total sample)	84	154	77	171	1.9%	1.21 [0.97, 1.51]
Roca et al. (2012; total sample)	501	1201	449	1201	3.9%	1.12 [1.01, 1.23]
Satterthwaite et al. (1997; total sample)	247	931	159	930	2.4%	1.55 [1.30, 1.85]
Spaulding et al. (1991; total sample)	131	519	50	549	1.2%	2.77 [2.05, 3.75]
Szilagyi et al. (2020; total sample)	15601	41055	15401	41070	5.3%	1.01 [1.00, 1.03]
Terrell-Perica et al. (2001; total sample)	438	2213	367	2144	3.3%	1.16 [1.02, 1.31]
Yokum et al. (2018; letter active choice)	8940	33992	29520	113977	5.3%	1.02 [1.00, 1.04]
Yokum et al. (2018; letter AUSG)	6163	22997	29520	113977	5.3%	1.03 [1.01, 1.06]
Yokum et al. (2018; letter imp)	8975	33995	29520	113977	5.3%	1.02 [1.00, 1.04]
Yokum et al. (2018; letter NVPO)	6116	22994	29520	113977	5.3%	1.03 [1.00, 1.05]
Total (95% CI)		**205410**		**563073**	**100.0%**	**1.18 [1.13, 1.22]**
Total events	63521		151826			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 390.95$, df = 32 (P < 0.00001); $I^2 = 92\%$

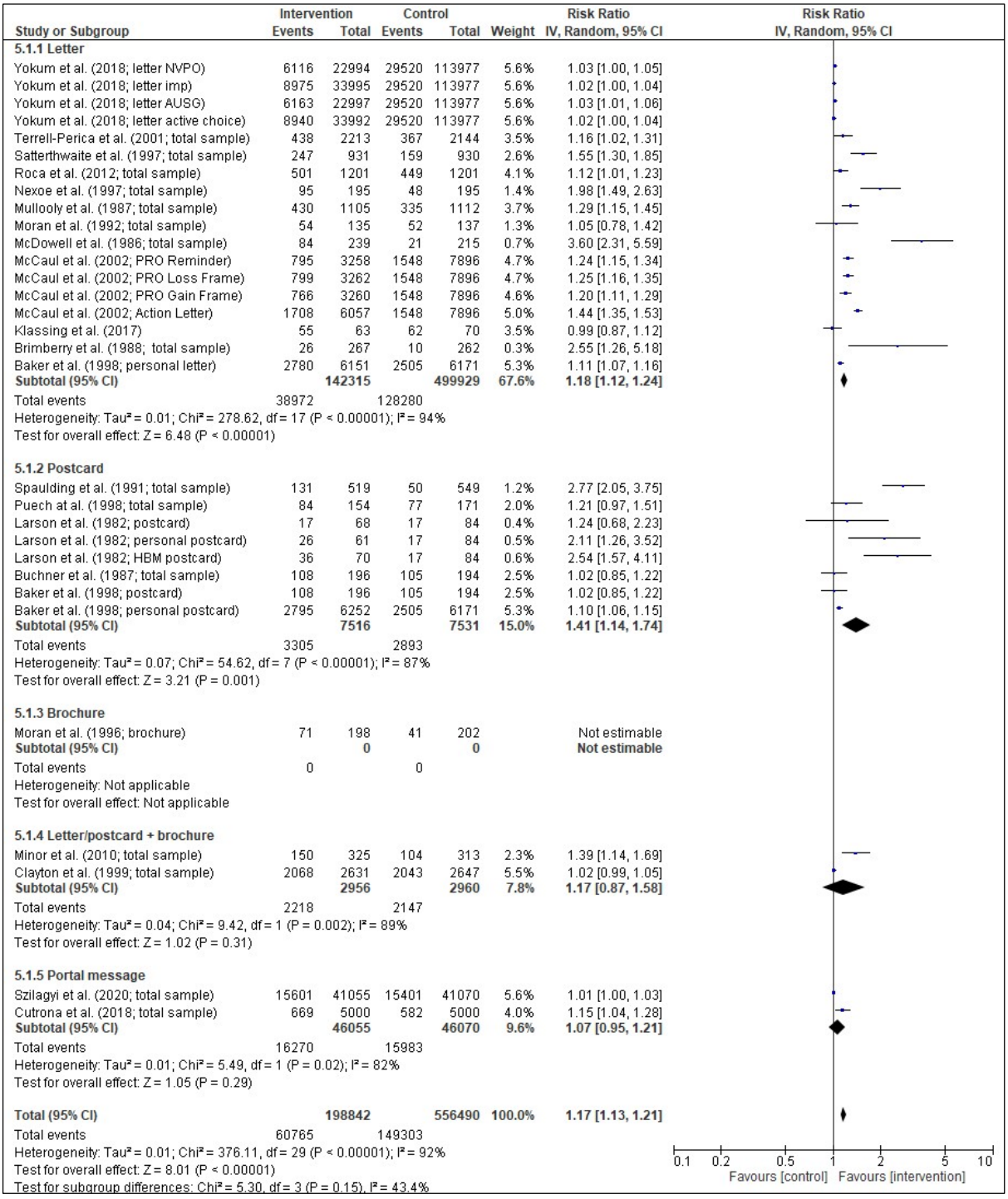
Test for overall effect: Z = 8.56 (P < 0.00001)



2.2.2 Subgroup analysis by correspondence type

No significant differences were observed in the effectiveness of messaging on vaccine uptake based on the type of correspondence message (letter, postcard, letter/postcard + brochure, portal message), $\chi 2$ (3) = 5.30, p = .15.

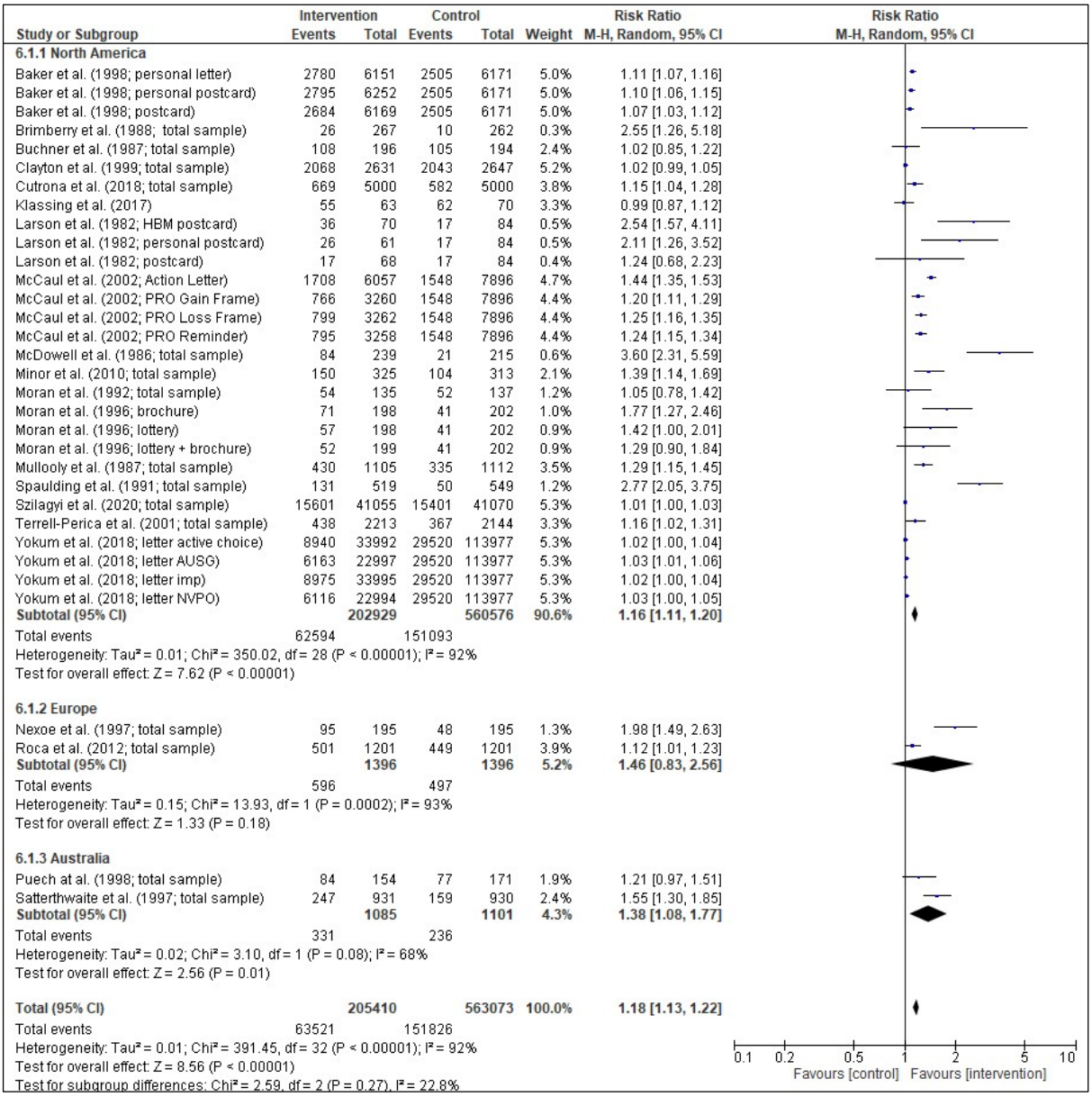
Table 5 – Subgroup analysis by correspondence type



2.2.3 Subgroup analysis by location

No significant differences were observed in the effectiveness of messaging on vaccine uptake based on study location (continent: North America, Europe, Australia), $\chi 2\ (2) = 2.59$, $p = .27$.

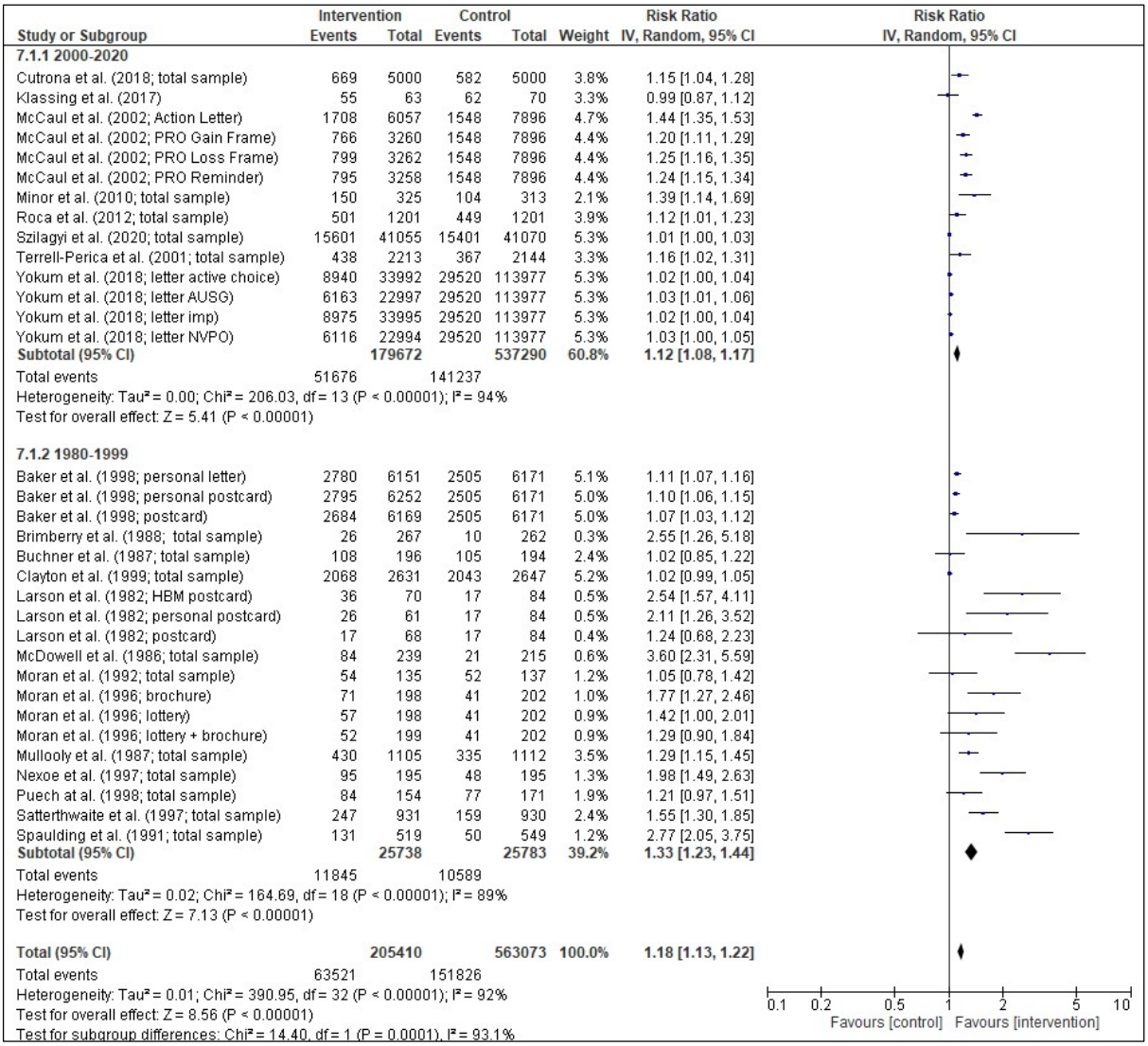
Table 6 – Subgroup analysis by location



2.4 Subgroup analysis by year of publication

The subgroup analysis by year of publication was carried out in two-decade intervals, i.e. 1980-1999 and 2000-2020. The effect of sending correspondence holds over both periods but was higher in the earlier period. Studies published in 1980-1999 saw a 33% increase on control (RR = 1.33, 95% CI[1.23, 1.44]) while the increase was 12% in those published from 2000-2020 (RR = 1.12, 95% CI[1.08, 1.17]), $\chi 2$ (1) = 14.40, p = .0001.

Table 7 – Subgroup analysis by year of publication



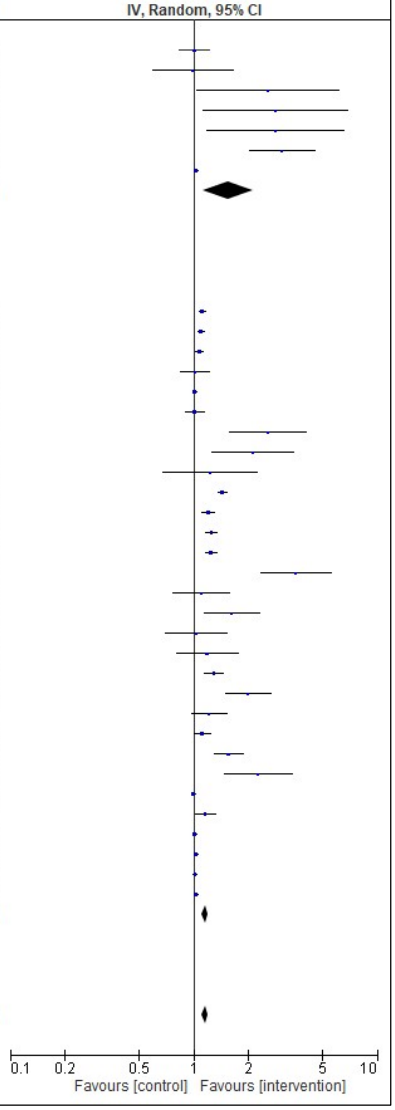
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
7.1.1 2000-2020						
Cutrona et al. (2018; total sample)	669	5000	582	5000	3.8%	1.15 [1.04, 1.28]
Klassing et al. (2017)	55	63	62	70	3.3%	0.99 [0.87, 1.12]
McCaul et al. (2002; Action Letter)	1708	6057	1548	7896	4.7%	1.44 [1.35, 1.53]
McCaul et al. (2002; PRO Gain Frame)	766	3260	1548	7896	4.4%	1.20 [1.11, 1.29]
McCaul et al. (2002; PRO Loss Frame)	799	3262	1548	7896	4.4%	1.25 [1.16, 1.35]
McCaul et al. (2002; PRO Reminder)	795	3258	1548	7896	4.4%	1.24 [1.15, 1.34]
Minor et al. (2010; total sample)	150	325	104	313	2.1%	1.39 [1.14, 1.69]
Roca et al. (2012; total sample)	501	1201	449	1201	3.9%	1.12 [1.01, 1.23]
Szilagyi et al. (2020; total sample)	15601	41055	15401	41070	5.3%	1.01 [1.00, 1.03]
Terrell-Perica et al. (2001; total sample)	438	2213	367	2144	3.3%	1.16 [1.02, 1.31]
Yokum et al. (2018; letter active choice)	8940	33992	29520	113977	5.3%	1.02 [1.00, 1.04]
Yokum et al. (2018; letter AUSG)	6163	22997	29520	113977	5.3%	1.03 [1.01, 1.06]
Yokum et al. (2018; letter imp)	8975	33995	29520	113977	5.3%	1.02 [1.00, 1.04]
Yokum et al. (2018; letter NVPO)	6116	22994	29520	113977	5.3%	1.03 [1.00, 1.05]
Subtotal (95% CI)		**179672**		**537290**	**60.8%**	**1.12 [1.08, 1.17]**
Total events	51676		141237			
Heterogeneity: Tau² = 0.00; Chi² = 206.03, df = 13 (P < 0.00001); I² = 94%						
Test for overall effect: Z = 5.41 (P < 0.00001)						
7.1.2 1980-1999						
Baker et al. (1998; personal letter)	2780	6151	2505	6171	5.1%	1.11 [1.07, 1.16]
Baker et al. (1998; personal postcard)	2795	6252	2505	6171	5.0%	1.10 [1.06, 1.15]
Baker et al. (1998; postcard)	2684	6169	2505	6171	5.0%	1.07 [1.03, 1.12]
Brimberry et al. (1988; total sample)	26	267	10	262	0.3%	2.55 [1.26, 5.18]
Buchner et al. (1987; total sample)	108	196	105	194	2.4%	1.02 [0.85, 1.22]
Clayton et al. (1999; total sample)	2068	2631	2043	2647	5.2%	1.02 [0.99, 1.05]
Larson et al. (1982; HBM postcard)	36	70	17	84	0.5%	2.54 [1.57, 4.11]
Larson et al. (1982; personal postcard)	26	61	17	84	0.5%	2.11 [1.26, 3.52]
Larson et al. (1982; postcard)	17	68	17	84	0.4%	1.24 [0.68, 2.23]
McDowell et al. (1986; total sample)	84	239	21	215	0.6%	3.60 [2.31, 5.59]
Moran et al. (1992; total sample)	54	135	52	137	1.2%	1.05 [0.78, 1.42]
Moran et al. (1996; brochure)	71	198	41	202	1.0%	1.77 [1.27, 2.46]
Moran et al. (1996; lottery)	57	198	41	202	0.9%	1.42 [1.00, 2.01]
Moran et al. (1996; lottery + brochure)	52	199	41	202	0.9%	1.29 [0.90, 1.84]
Mullooly et al. (1987; total sample)	430	1105	335	1112	3.5%	1.29 [1.15, 1.45]
Nexoe et al. (1997; total sample)	95	195	48	195	1.3%	1.98 [1.49, 2.63]
Puech at al. (1998; total sample)	84	154	77	171	1.9%	1.21 [0.97, 1.51]
Satterthwaite et al. (1997; total sample)	247	931	159	930	2.4%	1.55 [1.30, 1.85]
Spaulding et al. (1991; total sample)	131	519	50	549	1.2%	2.77 [2.05, 3.75]
Subtotal (95% CI)		**25738**		**25783**	**39.2%**	**1.33 [1.23, 1.44]**
Total events	11845		10589			
Heterogeneity: Tau² = 0.02; Chi² = 164.69, df = 18 (P < 0.00001); I² = 89%						
Test for overall effect: Z = 7.13 (P < 0.00001)						
Total (95% CI)		**205410**		**563073**	**100.0%**	**1.18 [1.13, 1.22]**
Total events	63521		151826			
Heterogeneity: Tau² = 0.01; Chi² = 390.95, df = 32 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 8.56 (P < 0.00001)						
Test for subgroup differences: Chi² = 14.40, df = 1 (P = 0.0001), I² = 93.1%						

2.2.5 Subgroup analysis by age group

A single direct message is shown to be effective across all age groups, but the size of the effect significantly differs, $\chi 2$ (1) = 3.21, p = .07. Following a message, vaccination is less likely in older adults (typically ≥65 years; 16% increase in vaccine uptake, relative to control) compared to young and middle-aged adults (typically 18-64 years; 54% increase in vaccine uptake, relative to control).

Table 8 – Subgroup analysis by age group

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
8.1.1 Adult						
Klassing et al. (2017; -65 years)	41	49	33	40	2.1%	1.01 [0.84, 1.23]
Moran et al. (1992; -65 years)	21	69	21	68	0.5%	0.99 [0.60, 1.63]
Moran et al. (1996; brochure -65 years)	14	59	6	64	0.2%	2.53 [1.04, 6.15]
Moran et al. (1996; lottery + brochure -65 years)	12	46	6	64	0.2%	2.78 [1.13, 6.87]
Moran et al. (1996; lottery -65 years)	17	65	6	64	0.2%	2.79 [1.18, 6.62]
Spaulding et al. (1991; -65 years)	78	403	28	441	0.7%	3.05 [2.02, 4.59]
Szilagyi et al. (2020; 18 - 64 years)	9952	30340	9699	30310	5.3%	1.03 [1.00, 1.05]
Subtotal (95% CI)		**31031**		**31051**	**9.0%**	**1.54 [1.13, 2.11]**
Total events	10135		9799			
Heterogeneity: Tau² = 0.11; Chi² = 40.79, df = 6 (P < 0.00001); I² = 85%						
Test for overall effect: Z = 2.71 (P = 0.007)						
8.1.2 Older Adult						
Baker et al. (1998; personal letter)	2780	6151	2505	6171	5.0%	1.11 [1.07, 1.16]
Baker et al. (1998; personal postcard)	2795	6252	2505	6171	5.0%	1.10 [1.06, 1.15]
Baker et al. (1998; postcard)	2684	6169	2505	6171	5.0%	1.07 [1.03, 1.12]
Buchner et al. (1987; total sample)	108	196	105	194	2.2%	1.02 [0.85, 1.22]
Clayton et al. (1999; total sample)	2068	2631	2043	2647	5.2%	1.02 [0.99, 1.05]
Klassing et al. (2017; 65+ years)	14	14	29	30	3.3%	1.02 [0.90, 1.15]
Larson et al. (1982; HBM postcard)	36	70	17	84	0.5%	2.54 [1.57, 4.11]
Larson et al. (1982; personal postcard)	26	61	17	84	0.4%	2.11 [1.26, 3.52]
Larson et al. (1982; postcard)	17	68	17	84	0.3%	1.24 [0.68, 2.23]
McCaul et al. (2002; Action Letter)	1708	6057	1548	7896	4.7%	1.44 [1.35, 1.53]
McCaul et al. (2002; PRO Gain Frame)	766	3260	1548	7896	4.3%	1.20 [1.11, 1.29]
McCaul et al. (2002; PRO Loss Frame)	799	3262	1548	7896	4.3%	1.25 [1.16, 1.35]
McCaul et al. (2002; PRO Reminder)	795	3258	1548	7896	4.3%	1.24 [1.15, 1.34]
McDowell et al. (1986; total sample)	84	239	21	215	0.6%	3.60 [2.31, 5.59]
Moran et al. (1992; 65+ years)	33	66	31	68	0.8%	1.10 [0.77, 1.56]
Moran et al. (1996; brochure 65+ years)	57	139	35	138	0.9%	1.62 [1.14, 2.29]
Moran et al. (1996; lottery + brochure 65+ years)	40	153	35	138	0.7%	1.03 [0.70, 1.52]
Moran et al. (1996; lottery 65+ years)	40	133	35	138	0.7%	1.19 [0.81, 1.74]
Mullooly et al. (1987; total sample)	430	1105	335	1112	3.4%	1.29 [1.15, 1.45]
Nexoe et al. (1997; total sample)	95	195	48	195	1.2%	1.98 [1.49, 2.63]
Puech at al. (1998; total sample)	84	154	77	171	1.8%	1.21 [0.97, 1.51]
Roca et al. (2012; total sample)	501	1201	449	1201	3.8%	1.12 [1.01, 1.23]
Satterthwaite et al. (1997; total sample)	247	931	159	930	2.3%	1.55 [1.30, 1.85]
Spaulding et al. (1991; +65 years)	53	116	22	108	0.6%	2.24 [1.47, 3.42]
Szilagyi et al. (2020; 65+ years)	4062	7636	12736	23985	5.2%	1.00 [0.98, 1.03]
Terrell-Perica et al. (2001; total sample)	438	2213	367	2144	3.2%	1.16 [1.02, 1.31]
Yokum et al. (2018; letter active choice)	8940	33992	29520	113977	5.3%	1.02 [1.00, 1.04]
Yokum et al. (2018; letter AUSG)	6163	22997	29520	113977	5.2%	1.03 [1.01, 1.06]
Yokum et al. (2018; letter imp)	8975	33995	29520	113977	5.3%	1.02 [1.00, 1.04]
Yokum et al. (2018; letter NVPO)	6116	22994	29520	113977	5.2%	1.03 [1.00, 1.05]
Subtotal (95% CI)		**165708**		**539671**	**91.0%**	**1.16 [1.11, 1.20]**
Total events	50954		148365			
Heterogeneity: Tau² = 0.01; Chi² = 338.13, df = 29 (P < 0.00001); I² = 91%						
Test for overall effect: Z = 7.54 (P < 0.00001)						
Total (95% CI)		**196739**		**570722**	**100.0%**	**1.16 [1.12, 1.20]**
Total events	61089		158164			
Heterogeneity: Tau² = 0.01; Chi² = 380.95, df = 36 (P < 0.00001); I² = 91%						
Test for overall effect: Z = 7.99 (P < 0.00001)						
Test for subgroup differences: Chi² = 3.21, df = 1 (P = 0.07), I² = 68.9%						



3. Content Used in Tested Correspondence

Of the studies with intervention arms showing an effect, 14 provided information on the content of correspondence. The typical message content is summarised in Table 9. The most commonly reported content elements were: a recommendation to get the vaccine, including yearly vaccination; statements that the vaccine is safe and effective (e.g. does not cause the flu), has minimal side effects, and helps avoid serious complications; a statement of the seriousness of the flu and its possible complications; information on how and where to get the vaccine, including scheduling information; and a statement that the vaccine is free.

Table 9 Typical Message Content

Content[1]	**Studies (N=14)**
Recommend that the recipient gets the vaccine	10
Statement that the vaccine helps avoid serious complications/ is effective	7
Statement on the seriousness of the flu/ possible complications from the flu	6
Information on how and where to get the vaccine/ scheduling information	6
Advice to get the vaccine every year	5
Statement that the vaccine is free	5
Statement that the vaccine is safe/ has minimal side effects	4
Addresses common concerns about the vaccine	4
Statement of who is at high risk of complications from the flu	3
Clinic operating hours	2
Clinic locations	2
Information on the availability of the vaccine	2
Statement the recipient is at high risk of complications/a serious case of the flu	2
Statement on the importance of the flu vaccine for high-risk people	2
Statement that the vaccine can cause minor side effects	1
Advice to get the vaccine soon	1
Information about the clinical manifestations of the flu	1
Access to online scheduling	1

Note: Additional content added in studies with multiple arms is discussed in the next section.

1 The content of brochures is not included in this table as the studies concerned did not include information on the content of the brochures.

4. Effectiveness of Design Elements

Four of six studies found a difference in results between intervention arms. The most effective interventions in these studies highlight design elements that might influence vaccine uptake.

In Baker et al (1998) the effectiveness of the intervention increased with more personal modes of contact: 'the reminder postcard from the patient's primary care physician was more effective than the generic postcard and the personalized tailored letter was more effective than either postcard intervention'.

Larson et al (1982) tested three postcard types and found that all were more effective than no reminder. A postcard designed according to the Health Belief Model was most effective (32.1% increase), followed by a personalised postcard (20.8% increase), while a 'neutral' reminder postcard showed a comparably small increase in vaccine uptake (4.8% increase).

In testing four different letter designs, McCaul et al (2002) found that only the action letter (giving the exact time and places of vaccination clinics) was markedly more effective than the others: 'First, differential framing was no more effective than providing a simple reminder. Second, providing action instructions had a powerful incremental effect on vaccination rates.'

Moran et al (1996) found that sending an educational brochure alone was more effective than either a financial incentive or sending both brochure and incentive: 'the educational brochure more than doubled the likelihood of influenza immunization (odds ratio [OR] = 2.29, 95% confidence interval [CI] 1.45 to 3.61), whereas the incentive had less of an effect on immunization (OR = 1.68, 95% CI 1.05 to 2.68). Immunization for the group mailed both interventions was not significantly different from control.'

Two studies did not find a difference between intervention arms. The CDC (1995) found no difference in sending a personalised letter or generic letter: 'The likelihood of vaccination was similar for persons who received a personal letter and for those who received a form letter.' Yokum et al (2018) tested four letter types and 'found that a single mailed letter significantly increased influenza vaccination rates compared with no letter. However, there was no difference in vaccination rates across the four different letters tailored with behavioural science techniques.'

Table 10 Studies with multiple intervention arms

Baker et al, 1998
(1) A generic postcard that included a standard message (2) A personalized postcard from the primary care physician, addressed to the patient at risk and containing the standard message (3) A personalized letter from the primary care physician, addressed to the patient at risk, and contained a message tailored to the patient's risk factors for influenza.
CDC 1995
(1) A personalized letter from the Montana-Wyoming Foundation for Medical Care (MWFMC) medical director encouraging vaccination (2) A form letter from the MWFMC encouraging vaccination.
Larson et al, 1982
(1) A neutral postcard mentioned influenza vaccine now available; listed telephone number for nurse appointments; addressed to "Dear Patient". "Dear Patient Influenza vaccine is now available at FMC. You can make an appointment with your nurse. Call 545-0555. Family Medical Center Staff University of Washington Hospital" (2) Health belief model postcard, emphasizing severity of influenza, susceptibility of at-risk persons to influenza, and benefits of vaccination; addressed to "Dear Patient". "Dear Patient The influenza season is approaching. Persons with certain medical diseases and persons over 65 years old are especially likely to get influenza. Influenza is also more serious in such persons. We have just received this year's vaccine which will decrease your risk of developing influenza with almost no chance of any adverse side effects. You can make an appointment with your nurse at your convenience. Call 545-0555. Sincerely yours, Family Medical Center University of Washington Hospital." (3) Personalised postcard; addressed to patient's name and signed by clinician; postcard mentioned that influenza season is approaching and recommended the patient come in for flu shot; it listed telephone number to call and make appointment with nurse. "Dear Mr Smith [name handwritten] Influenza season is approaching and I think it would be a good idea if you came in for a flu shot. You can make an appointment with your nurse. Call 545-0555 Charles Reid MD [handwritten signature]"

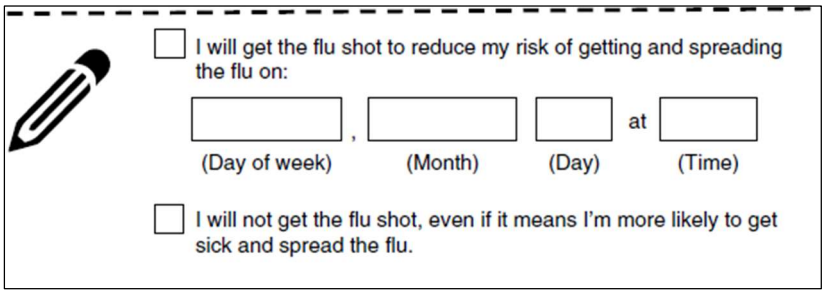
McCaul et al, 2002
(1) Reminder letter from state peer review organisation (PRO). The reminder letter highlighted four main points: (a) "You should have a flu shot every year," (b) "Medicare will pay for your flu shot this fall," (c) "The flu shot is safe," and (d) "You should have your shot soon." The letter included a perforated reminder card with the message, "Get the Flu Shot. Not the Flu." (2) Reminder letter with loss frame from PRO. In addition to the above, the framing letter stated, "As a person 65 or older, you are at risk for getting a serious case of flu." The framing letter was accompanied by one of two inserts. The loss insert featured the picture and testimonial of another North Dakota woman who had not received a flu shot last year and had spent several days in bed, sick with the flu. In addition, the insert displayed information about three costs "if you don't get your flu shot soon" ("You will be more likely to get the flu this fall"; "If you do get the flu, you will probably be more sick"; and "You will be more likely to enter the hospital because of the flu"). The bottom of the framing inserts included a colourful 6.5 mm 10.0mm reminder card that could be separated from the insert on a perforated line. For the loss frame, the card read, "Don't Get Sick. Get the Flu Shot." (3) Reminder letter with gain frame from PRO. As above, but the gain insert featured the picture and testimonial of a North Dakota woman who had received a flu shot the previous year and had not gotten the flu. In addition, the insert displayed information about three benefits of getting "your flu shot soon" ("You will be less likely to get the flu this fall"; "If you do get the flu, you will probably not be as sick"; and "You will be less likely to enter the hospital because of the flu"). For the gain frame, the reminder card read, "Stay Healthy. Get the Flu Shot." (4) Action letter from county public health office. The letters were printed on public health facility letterhead and were addressed to "Dear [county name] resident." Each letter began as follows: "The flu season will soon be upon us, and it's time for you to make arrangements to get your flu shot. Flu, or influenza, is an easily spread virus, and flu shots are for anyone who wants to reduce the risk of catching the disease and avoid illness and hospitalization." The letter went on to indicate the exact times and places during which the health units would be holding flu shot clinics. The list included the town, date, time, and place where the shot could be obtained. The letter concluded by stating, "Medicare B pays for flu shots. Please bring your Medicare card with you to the flu clinic." The director of nursing signed the letter.
Moran et al, 1996
(1) A large print, illustrated educational brochure emphasizing factors important to patients in making a decision about influenza immunisation (2) A lottery-type incentive announcing that all patients receiving influenza immunization would be eligible for grocery gift certificates (3) Both educational brochure and incentive.
Yokum et al, 2018
(1) A letter with vaccination information + picture of National Vaccine Program Officer. All of the letters were printed on US Department of Health and Human Services letterhead, addressed to the recipient's first name and included the bolded first sentence 'Protect yourself and those you love—get your free flu shot!' The subsequent four, brief paragraphs describe the risks associated

with the influenza virus (for example, '36,000 Americans die every year'; 'more than 200,000 hospitalizations annually'), that adults ≥ 65 years of age are at special risk, how yearly vaccination mitigates that risk, and that the flu shot is freely covered by Medicare and widely available at 'your local pharmacy, senior centre, hospital or doctor's office'. The sender manipulation is reflected in typical letter components indicating sender, namely, a top letterhead of the office and a bottom signature line (hand-written name together with position title); in addition, a photo headshot is included.

(2) A letter with vaccination information + picture of Acting US Surgeon General

(3) A letter with implementation intention prompt + picture of Acting US Surgeon General. The bottom of the letter stated, 'Many people find it helpful to make a plan for getting their flu shot. Write yours below, and stick it on your refrigerator so you don't forget!'; it provided space for subjects to write down their intended plan.

(4) A letter with enhanced active choice implementation prompt + picture of Acting US Surgeon General. The bottom of the letter stated, 'Many people find it helpful to decide now on a plan for getting their flu shot. Mark your decided plan below, and stick it on your refrigerator so you don't forget!' and asked subjects to select one of two option boxes designed to make more salient that receiving the vaccine reduces the risk of getting and spreading the flu to their friends and family members (see figure below).



6. Conclusions

Key Findings

1. Sending a single written message directly to an individual increases flu vaccine uptake in comparison to relying on mass communication alone. Of 37 such interventions reviewed, 32 (86%) report an increase in flu vaccination rates. A formal meta-analysis shows that sending a single written message increases flu vaccine uptake by 18% relative to the no contact comparator group. Subgroup analysis shows that the intervention is effective across correspondence type, age group, period of publication, and location.

2. The most common elements of correspondence that increases uptake of flu vaccination are: a recommendation to get the vaccine, including yearly vaccination; statements that the vaccine is safe and effective (e.g. does not cause the flu), has minimal side effects, and helps avoid serious complications; a statement of the seriousness of the flu and its possible complications; information on how and where to get the vaccine, including scheduling information; and a statement that the vaccine is free.

3. Of the six studies with multiple arms that compare different types of written messages four studies find a particular message to be most effective. The most effective written message in each of the respective studies was: (a) the message with the most personal mode of contact, (b) a message based on the Health Belief Model (emphasizing severity of influenza, susceptibility of at-risk persons, and benefits of vaccination; addressed to “Dear Patient”), (c) a message including the exact time and place of vaccination clinics, and (d) an educational brochure emphasizing the severity of influenza, that it is very contagious and can be passed to friends and family, that the vaccine is safe, effective and free, and that the patient’s doctor recommends vaccination.

Implications for Practice

Direct written correspondence to individuals to invite them to attend a clinic or to make an appointment for flu vaccination is effective in increasing vaccination rates.

Content included in effective written messages include:

- A clear and strong recommendation to be vaccinated
- Information about vaccine effectiveness
- Information on the seriousness of the flu and how vaccination can help avoid complications
- A statement that the flu vaccine is safe
- Information on cost
- Clear instructions on how to get vaccinated

This review supports the use of direct correspondence to increase the uptake of COVID-19 vaccines across the wider community.

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