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A rapid global review of strategies to improve influenza vaccination uptake in Australia

Hassen Mohammed ^{a,b}, Mark McMillan ^{a,b}, Prabha H. Andraweera ^{a,b}, Salenna R. Elliott^a, and Helen S. Marshall ^{a,b}

^aVaccinology and Immunology Research Trials Unit, Women's and Children's Health Network, Adelaide, Australia; ^bRobinson Research Institute, Adelaide Medical School, University of Adelaide, Adelaide, Australia

ABSTRACT

This study aimed to identify effective strategies for improving the uptake of influenza vaccination and to inform recommendations for influenza vaccination programs in Australia. A rapid systematic review was conducted to assimilate and synthesize peer-reviewed articles identified in PubMed. The National Health and Medical Research Council (NHMRC) Hierarchy of Evidence was used to appraise the quality of evidence. A systematic search identified 4373 articles and 52 that met the inclusion criteria were included. The evidence suggests influenza vaccination uptake may be improved by interventions that (1) increase community/patient demand and access to influenza vaccine and overcome practice-related barriers; (2) reinforce the critical role healthcare providers play in driving influenza vaccination uptake. Strategies such as standing orders, reminder and recall efforts were successful in improving influenza vaccination rates. Community pharmacies, particularly in regional/remote areas, are well positioned to improve influenza vaccine coverage. The findings of this rapid review can be utilized to improve the performance of influenza immunization programs in Australia and other countries with comparable programs; and recommend priorities for future evaluation of interventions to improve influenza vaccination uptake.

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Introduction

Most high-income countries have a national influenza vaccination policy with programmes targeting specific WHO-defined risk groups and yet uptake of the recommended influenza vaccinations among high-risk groups has been suboptimal.¹ In Australia, annual seasonal influenza vaccination is funded under the National Immunization Program (NIP) and State funded influenza programs for individuals in the following specific high-risk groups; pregnant women, people aged 6 months and older with medical risk factors, all children aged 6 months to less than 5 years of age, all Aboriginal and Torres Strait Islander people and everyone aged 65 years and over.² In South Australia, adults and children who are homeless and are not eligible for free flu vaccines under the National Immunization Programs are eligible for free flu vaccine under the state funded influenza Program.²

The global coronavirus disease (COVID-19) pandemic has increased demand for seasonal influenza vaccination.³ Many countries, including Australia, have begun rolling out COVID-19 vaccination, which may complicate the delivery of seasonal influenza vaccination programs. Moreover, ongoing changes to influenza vaccination recommendations and policy changes have complicated program delivery at all levels of government and for all immunization providers. This rapid review aimed to identify effective strategies to improve influenza vaccine uptake, coordination and delivery of influenza vaccine programs and make recommendations for successful influenza vaccination programs in Australia by summarizing the

literature evaluating strategies or influenza vaccination programs. Medical settings (hospital or primary setting) to venue-based and community-based approaches were included, in an effort to identify the features of such programs that are most successful and may guide efforts to increase the performance of influenza vaccination programs in Australia and similar high-income countries.

Materials and methods

Search strategy

A search was conducted of the English language literature in the PubMed/MEDLINE (PubMed delivers a publicly available search interface for MEDLINE as well) from 1st January 2011 through 1st August 2021. Keywords and terms used for the search included primarily the following: influenza, vaccination, uptake, intervention, strategies and program (Supplementary table 1).

Inclusion and exclusion criteria

This rapid review is limited to studies that were explicitly, at least in part, concerned with evaluating an intervention or influenza vaccine program aimed at increasing influenza vaccine rates among individuals at high risk/vulnerable cohorts. Both systematic reviews and primary studies published in English were sought. Studies were included based on the methodological quality of their design and if they met the following

Table 1. The inclusion and exclusion criteria for the rapid review followed the PICOS format.

Criteria	Included
Participants/ population	Including but not limited to high-risk groups for more severe influenza outcomes (I) children aged 6 months to <5 years. (II) adults aged ≥65 years (III) Aboriginal and Torres Strait Islander people (IV) people with medical conditions that increase their risk of influenza (V) pregnant women (VI) homeless people
Interventions	Studies that report on interventions to improve influenza vaccine rates in universal or targeted influenza immunization programs
Comparison	Compare to no intervention, another intervention, standard care
Outcomes	Influenza vaccination uptake (interventions VS. comparison groups)
Exclusion criteria	Interventions/influenza vaccination programs in low and lower-middle income countries – healthcare system vastly different from Australia's (e.g. sub-Saharan Africa, South East Asia).

criteria: were systematic reviews/meta-analyses or primary studies that used one of the following designs: (1) individual or cluster randomized controlled trials (RCTs) and quasi-randomized controlled trials; (2) controlled or uncontrolled before and after studies where participants were allocated to control and intervention groups using non-randomized methods; (3) interrupted time series with before and after measurements (Table 1). RCTs included in the eligible systematic reviews or meta-analyses were not individually included in this rapid review to avoid replication of any study findings.

The National Health and Medical Research Council (NHMRC) Level of Evidence table was used to appraise the quality of evidence found (Table 2).⁴ Studies generating NHMRC levels V evidence or lower such as systematic reviews of descriptive and qualitative studies (levels V), a single descriptive or qualitative study or gray literature (levels VI), expert opinion or commentaries (levels VII) were excluded. The authors accept that the best available evidence is that which is least susceptible to bias, such as that provided by Levels I and II of the NHMRC levels of evidence (Table 2). However, a broader search strategy included studies more prone to bias (Levels III and IV) given most studies in this area are observational reflective of real-world data.

Organization of evidence

Each study was classified by the level of evidence it represented (Table 2). Levels of evidence start with a hierarchy of research designs that range from the greatest to least ability to reduce bias. Level I evidence is supported by the results of two or more RCTs (including meta-analysis of all relevant RCTs) producing the strongest and most definitive evidence.⁴ Level II evidence produces tentative conclusions drawn from at least one good quality RCT or high-quality systematic reviews of RCTs and observational studies. Levels III produces limited evidence supported by at least one cohort study or single group interventions. Conflicting evidence is classified as disagreements between the findings of at least two RCTs or where RCTs are not available between two non-RCTs.⁴ The recommendations were based on the majority of the studies, unless the study with conflicting results was of higher quality design.⁴

Data collection

One reviewer (HM) independently reviewed identified titles and abstracts. Studies were sought in full text if they appeared eligible for inclusion against the criteria. Two reviewers (HM and PA) reviewed the identified relevant full text papers to determine eligibility. Detailed characteristics of included systematic reviews were captured and descriptively summarized in Table 3 identifying study design, population, setting, measured outcomes and their main findings. A table of individual eligible studies (not included in the systematic reviews) is presented in Supplementary table 1, describing relevant information.

Results

The initial search generated 4373 published studies. After removing duplicates and screening titles, 187 relevant articles were identified for full review. Two members of the research team (HM & PA) read each relevant article for eligibility, utilizing the inclusion and exclusion criteria of the rapid review. Of the final included 52 studies that met the selection criteria, 14 were systematic literature reviews/meta-analyses, 22 were RCTs and 16 were observational studies (Figure 1). No additional studies were obtained from the reference lists of the included studies. Differences in opinion were resolved by discussion.

Table 2. NHMRC levels of evidence criteria.

Level	Intervention
Level I	Evidence obtained from a systematic review or meta-analysis of all relevant randomized controlled trials (level II studies)
Level II	Evidence obtained from at least one properly-designed randomized controlled trial
Level III-1	Evidence obtained from well-designed pseudorandomised controlled trial (i.e. alternate allocation or some other method)
Level III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls (i) Non-randomized, experimental trial (ii) Cohort study (iii) Case-control study (iv) Interrupted time series with a control group
Level III-3	Evidence obtained from a comparative study without concurrent controls: (i) Historical control study (ii) Two or more single arm study (iii) Interrupted time series without a parallel control group
Level IV	Evidence from well-designed case series with either posttest or pre-test/posttest outcomes
Level V	Expert opinion without explicit critical appraisal

Source: Adapted from NHMRC⁴.

Table 3. Overall description and characteristics of the included systematic reviews.

Authors, year	Location/ country	Aims/ target group	Study type	Included primary studies	Settings in the populations in the included studies	Intervention and outcome(s)	Authors reported key findings	NHMRC evidence Level I
Thomas et al. ⁵ (2018)	High-income countries	To assess access, provider, system, and societal interventions to increase the uptake of influenza vaccination in people aged 60 years and older	Systematic review/ meta-analyses of RCTs	Included 61 RCTs A total of 1,055,337 participants	Hospital/tertiary-care Primary-care Community settings	Increasing community demand (client reminders, recalls by letter plus leaflet, nurses or pharmacists educating and nurses vaccinating patients) Enhancing vaccination access (Free vaccine, home visits by nurses, physician care plan) System-based interventions (Reminder systems for GPs, vaccine champion, educational reminders, outreach plus feedback to team)	Interventions that shown significant positive effects of low (postcards; odds ratio (OR) 1.11, 95% confidence interval (CI) 1.07–1.15; 3 RCTs), medium (personalized phone calls), and high (home visits OR 1.30, 95% CI 1.05–1.61); 2 RCTs, facilitators) intensity that increase community demand for vaccination, enhance access, and improve provider/system response. Some interventions could not be meta-analyzed due to significant heterogeneity	Level I
Zhou et al. ⁶ (2020)	High-income countries	To evaluate the effectiveness of educational interventions in improving influenza vaccination rates	Systematic review/ meta-analyses of RCTs	Included 8 RCTs A total of 21523 participants	Hospital/tertiary-care Primary-care settings	Patient focused interventions Educational interventions evaluated in the included studies are pamphlets & poster (n = 1 study), face to face (n = 2 studies), text messages (n = 2 study), letters (n = 3)	Pooled analysis from the 8 RCTs shows there is no difference in influenza vaccination rates between educational intervention group and control group (OR = 1.16, 95%CI: 0.95–1.41). In subgroup analysis, influenza vaccination rates were significantly higher in messages and letters intervention group (OR = 1.30, 95%CI: 1.05–1.61)	Level I
Sanftenberg et al. ⁷ (2019)	Several	To identify measures in primary care medicine that can be used to increase influenza vaccination rates among the chronically ill population Target group: chronically ill population	Systematic review of RCTs	Included 15 RCTs 7 cluster RCTs, and 8 RCTs	Primary-care settings	Healthcare provider (HCP) focused interventions (Training programs for office teams, reminder systems for physicians & extension of competence for HCPs) Patient focused interventions (Reminder system (e.g. text, postcard, letter), educational brochure and financial incentives such as a lottery-type incentive) Outcome Influenza vaccination rates	Training programs for HCPs focusing on a particular disease improved the uptake of influenza vaccination by 22%. A financial incentive (a lottery-type incentive) (Risk ratio [RR]: 2.79; 95% CI: 1.18–6.62) and reminders via text message (3.8% absolute increase) were effective interventions in improving vaccination rates. Simple interventions were found to be the most effective ones in the heterogeneous population of chronically ill persons.	Level I

(Continued)

Table 3. (Continued).

Authors, year	Location/ country	Aims/ target group	Study type	Included primary studies	Settings included in the studies	Intervention and outcome(s)	Authors reported key findings	NHMRC evidence Level I
Norman et al. ⁹ (2021)	Included studies were conducted in several countries	To evaluate interventions targeting influenza vaccine uptake in children with comorbidities Target group: high-risk pediatric populations	Systematic review/ meta-analyses	Included 35 studies (26 included for meta-analyses) 5 RCTs 4 Cohort studies Quasi-experimental 20 before and after intervention studies 6 quality improvement (QI) studies	Hospital/tertiary-care Primary-care settings Pediatric community clinics	Vaccination reminders targeting patients' parents or guardian Education directed at either patients' parents or providers Vaccination-related clinic process changes Outcome Influenza vaccination rates	Overall, interventions improved influenza vaccine uptake by an average 60% (risk ratio (RR): 1.60; 95% CI: 1.47–1.74). Superiority of single or multicomponent interventions for improving influenza vaccination was not established. RCTs showed simple vaccination reminders (Mailed letters) targeting patients' parents moderately improve influenza vaccine uptake by an average 49% (RR: 1.49; 95% CI: 1.07–2.08). Effect estimates of other study methods (i) cohort RR 1.44 (CI 1.16–1.78) (ii) Quasi-experimental RR 1.71 (1.53–1.91)	Level I
Aigbogun et al. ⁹ (2014)	Several	To examine interventions aimed at improving influenza vaccination in children with high risk conditions Target group: high-risk pediatric populations	Systematic review	Included 18 studies 7 RCTs, 6 before-and-after studies, 1 non-RCT, 1 retrospective study, 1 quasi-experimental posttest study & 1 letter to editors	Hospital/tertiary-care Primary-care Community settings	Multi-component strategies, letter reminders, telephone recall, letters plus telephone calls, an asthma education tool. Outcome Influenza vaccination rates	There is sufficient evidence showing that reminder letters improve influenza vaccination rates in children with high-risk conditions. However, the evidence that telephone recall or a combination of letter reminder and telephone recall will improve uptake is poor.	Level II
Balzarini et al. ¹⁰ (2020)	Included studies were conducted in the USA (n = 7) and Australia (n = 1)	To systematically retrieve and critically appraise all available data on the effectiveness of Personal Electronic Health Records (PEHR) use to increase vaccination uptake. Target group: the general population (n = 4 studies), older adults (n = 1), adults with diabetes mellitus (n = 1), university students (n = 1) and parents of 2 year-old children (n = 1)	Systematic review	Included 8 studies 4 RCTs focused on Influenza vaccine and 1 RCT on Herpes Zoster vaccine) 3 Observational studies (two studies focused on Pneumococcus and Herpes Zoster vaccine)	Hospital/tertiary-care Primary-care settings	Personal Electronic Health Records (PEHR) based interventions Access/delivery of educational messages. Access to an e-journal, reminders and scheduling features. Outcome Influenza vaccination rates	Participants with access to PEHR were 6.7% more likely than those with no access to receive influenza vaccine (p = .008). Parents who accessed their children PEHR at least once over the study period were more likely to have children vaccinated at two years of age (OR 1.2, 95% CI: 1.0–1.3, p-value <0.001). Two RCTs have shown that PEHR with digital communication features promoting vaccines (OR 1.20, 95% CI: 1.06–1.35) or active vaccine reminder (22.0% vs 14.0%, p = .018) had improved influenza vaccine uptake compared to PEHR access alone.	Level II
Julio et al. ¹¹ (2020)	Several	The study aimed to evaluate multiple mail reminders Target group: the general population	A review of systematic reviews and primary studies	Identified 8 Systematic reviews that included 35 primary studies and of these 4 RCTs were included in the review (a total of 71,458 patients of all ages)	Hospital/tertiary-care Primary-care	The use of multiple mail reminders Outcome Influenza vaccination rates	The authors concluded multiple mail-in reminders are likely increase adherence to influenza vaccination in people over 60 years of age. However, it could make little or no difference in adherence to influenza vaccination in children under six years of age.	Level II

(Continued)

Table 3. (Continued).

Authors, year	Location/ country	Aims/ target group	Study type	Included primary studies	Settings in the included studies	Intervention and outcome(s)	Authors reported key findings	NHMRC evidence
Okoli et al. ¹² (2021)	Several	To evaluate the effectiveness of health care provider focused interventions in improving influenza vaccination rates. Target group: the general population	Systematic review/ meta-analyses	Included 39 studies 7 RCTs 32 Non-randomized (NRS) studies	Hospital/tertiary-care Primary-care	Patient focused interventions 6 studies examined the use of team-based training/education sessions, 6 the use of one-off provision of guidelines/information. 11 studies examined the use of reminders (9 using electronic prompts, one using paper-based prompt and one using letters), 2 studies examined the use of incentives (pay-for-performance) whereas 9 studies examined the use of multiple interventions.	Pooled estimates: evidence from two RCTs (20.1% (95% CI 7.5–32.7%) and two NR studies (13.4% (8.6–18.1%)) showed that team-based training/education of physicians significantly increased influenza vaccination rates in adult patients and in pediatric patients (7% (0.1–14%); two NRS). Educational interventions on physicians and nurses marginally (though significantly) increased influenza vaccination rates in adult patients: 0.9% (0.2–1.5%); four NRS). Evidence from NRS showed that one-off provision of information to physicians, and to both physicians and nurses, significantly increased influenza vaccination rates in adult patients: 23.8% (15.7–31.8%); three studies) and pediatric patients: 24% (8.1–39.9%); two studies).	Level II
Jacobson et al. ¹³ (2018)	Several	To evaluate and compare the effectiveness of various types of patient reminder and recall interventions to improve receipt of immunizations. Target group: the general population including infants and children, adolescents and adults	Systematic review/ meta-analyses	Included 75 studies 70 RCTs 5 studies used a controlled before and after design.	Hospital/tertiary-care Primary-care Community settings	Patient reminder or recall interventions considered in this systematic review included telephone, letter, postcard, text message, automated electronic telephone calls (autodialer), patient portal-based interventions, in person outreach, and several combinations of reminder-recall	Reminders increase uptake of vaccinations for childhood influenza (RR 1.51, 95% CI 1.14 to 1.99; risk difference of 22%; five studies; 9265 participants) and adult influenza (RR 1.29, 95% CI 1.17 to 1.43; risk difference of 9%; 15 studies; 59,328 participants).	Level II
Ison et al. ¹⁴ (2016)	Several	To evaluate the impact of pharmacists as educators, facilitators, and administrators of vaccines on vaccination rates	Systematic review	Included 38 studies 27 non-RCTs, 3 cluster RCTs, and 6 RCTs	Practice sites including inpatient, ambulatory clinics, nursing care facilities, and community pharmacies	Other non-influenza vaccinations Pharmacists as educators, facilitators/administrators of vaccines. Outcomes: Influenza, pneumococcal vaccination rates	Pharmacist participation in vaccination as educators, facilitators, or administrators of vaccines, yielded in increased influenza vaccination rates.	Level II
Jones et al. ¹⁵ (2013)	Several	To examine the effectiveness of reminder/recall systems in improving influenza vaccination	Systematic review	Included 11 studies 5 level I (RCT or meta-analysis of RCT) 6 level II (quasi experimental)	Hospital/tertiary-care (Asthma & immunization clinics) Primary-care (Pediatric practices)	Reminder and recall systems that alert patients of the need for vaccination and encourage compliance Outcomes: Influenza vaccination rates	Improvements have been seen in influenza vaccination rates with the implementation of reminder/recall systems; however, most have been modest.	Level II

(Continued)

Table 3. (Continued).

Authors, year	Location/ country	Aims/ target group	Study type	Included primary studies	Settings populations in the included studies	Intervention and outcome(s)	Authors reported key findings	NHMRC evidence Level II
Wong et al. ¹⁶ (2016)	High-income countries	To evaluate interventions used to increase the uptake of seasonal influenza vaccination among pregnant women	Systematic review	Included 11 studies 4 RCTs 7 Cohort studies	Tertiary maternity hospital Primary care outpatient clinic / Antenatal outpatient clinic Venue-based settings	Provider focused interventions Electronic reminder, a provider-focused standing orders, provider education, feedback Pregnant women focused Gain and loss-framed messages targeting pregnant women, influenza education pamphlets and a verbalized benefit statement Multi-components Multicomponent education campaign involving provider education, provider reminders, pregnant woman-focused education	The authors recommend that HCPs provide influenza pamphlets to pregnant women with a verbalized statement about the benefits of maternal influenza vaccine to newborns. Implementing standing orders authorizing nursing staff to administer the vaccine to expecting mothers have improved influenza vaccination rates. Further high-quality RCTs are needed to develop successful maternal influenza vaccination programs.	Level II
McFadden & Seale ¹⁷ (2021)	High-income countries (the USA, Australia, Canada)	A narrative review of hospital-based strategies in acute care settings aimed at improving influenza vaccination rates for adult inpatients.	Systematic review	Included 31 studies 6 RCTs 6 non-RCTs 11 pre-post studies 8 cross-sectional	Hospital settings	7 standing order protocols (SOP); 4 reminders; 4 assessment/administration programs; 1 patient education program; 1 organizational-based program; 7 multi-component strategies and 8 studies comparing SOPs with other strategies.	SOPs were significantly more effective than other individual interventions, but multi-component interventions (which included an SOP) were more effective than SOPs alone. Three articles reported no significant increase in uptake attributed mainly to patient refusals, even with a strategy involving patient education. Only three studies tested provider-level strategies including hospital campaigns, hospital reward programs and interdepartmental competitions, and showed success.	Level II
Bisset et al. ¹⁸ (2018)	High income countries	To identify effective strategies in increasing the uptake of vaccination in pregnancy	Systematic review	18/22 of the included studies focused on influenza vaccination 9 RCTs 9 Observational studies	Tertiary maternity hospital Primary care outpatient clinic / Antenatal outpatient clinic Venue-based settings	Increased availability of vaccines, midwives providing vaccine alerts/reminders for HCP on medical record Education and information for staff for providers and clinical staff and pregnant women Patient antenatal appointment and information pamphlet/ booklet or paper for patient and Posters in clinics Outcomes: Maternal influenza and pertussis vaccination rates	Strategies such as reminders about vaccination on antenatal healthcare records, midwives providing vaccination, and education and information provision for healthcare staff and patients have been found to be effective.	Level II

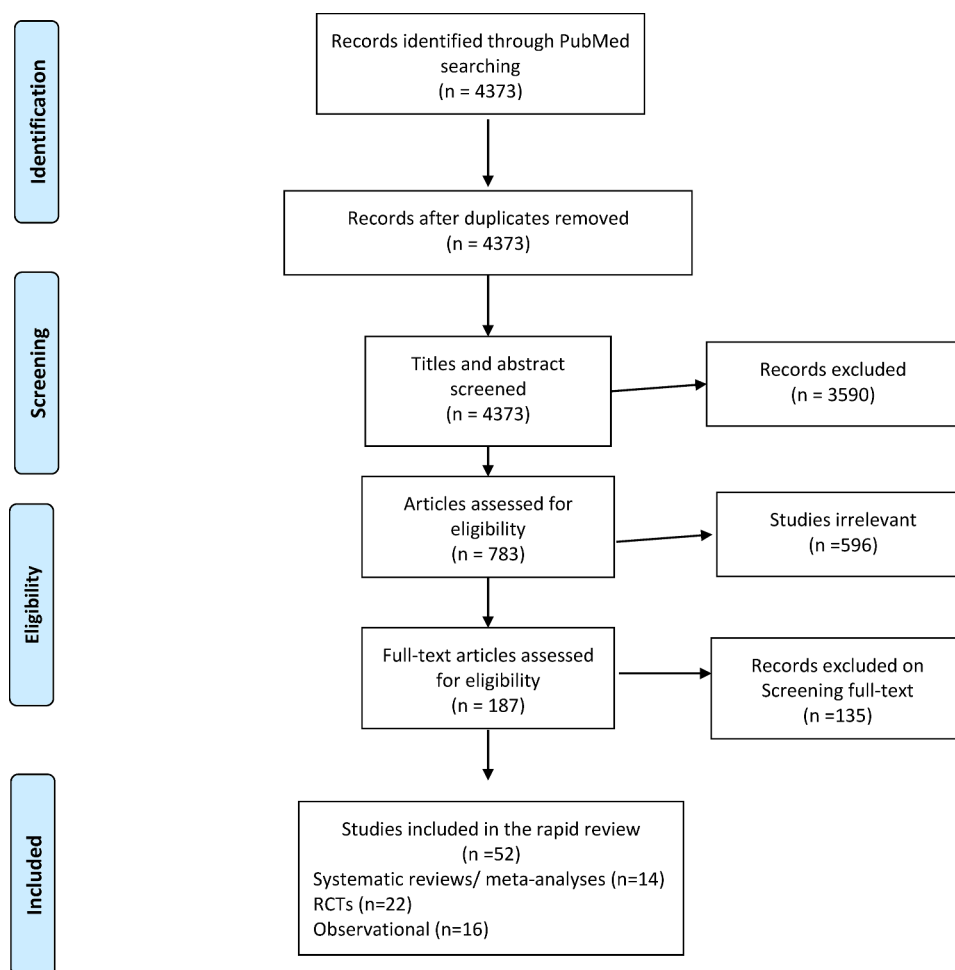


Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) summary of the paper-screening process.

NHMRC level I and II: systematic reviews

The included systematic reviews covered in this rapid review incorporated i) a broad range of settings and intervention types for influenza vaccination programs targeting a variety of high risk/vulnerable groups, ii) influenza vaccine program or interventions for a particular high-risk group (e.g. pregnant women) or a particular setting (e.g. antenatal clinics or hospital providing services to pregnant women) and iii) an aspect of influenza vaccine programs/intervention within the articles reviewed, although the systematic review may not have been solely focused on influenza immunization programs (Table 3). For systematic reviews identified in this rapid review, the available evidence on the effectiveness of interventions are discussed among the high-risk groups i) people with medical conditions ii) elderly iii) pregnant women and iv) interventions targeted to the general population.

(i) People with medical conditions

The systematic review by Sanftenberg et al.⁷ (2019) included 15 RCTs that focused on primary care physicians and evaluated interventions to improve the uptake of influenza vaccination among people with chronic disease. The high-quality review

(NHMRC level I)⁷ demonstrated that training programs for medical practice teams that focused on particular chronic diseases improved influenza vaccination uptake by as much as 22% and may be more effective than vaccination-centered approaches. The review⁷ also found that reminder systems for healthcare providers in primary care setting is another effective strategy with a maximum 3.8% absolute increase in vaccination rates among people with chronic illness (Table 3). Another systematic review of 11 studies (five RCTs and six quasi experimental)¹⁵ (NHMRC level II) also demonstrated that implementation of reminder/recall systems improve influenza vaccination rates in children with asthma (Table 3).

Normal et al.⁸ (2021) and Aigbogun et al.⁹ (2014) conducted a systematic review of 35 studies (five RCTs and 29 non-RCTs) and 18 studies (seven RCTs & 12 non-RCTs) respectively assessing interventions aimed at increasing influenza vaccination rates in children with high-risk conditions. Normal et al.⁸ (2021) identified a further 17 studies not captured by Aigbogun et al.⁹ (2014) and pooled effect estimates for each intervention type in the included RCTs and other study methods (NHMRC level I). Both systematic reviews^{8,9} found sufficient evidence that reminder letters to parents can improve influenza vaccination uptake in children with high-risk conditions (Table 3).

(ii) Elderly adults

Thomas et al.⁵ (2018) conducted a systematic review of 61 RCTs focused on improving influenza vaccination rates in people aged 60 years and older in the community. Although heterogeneity limited some meta-analyses, the review⁵ (NHMRC level I) identified strategies that demonstrated significant moderate effects of low (client reminders by post-cards), medium (personalized phone calls), and high (home visits, facilitators) intensity interventions to increase community demand for vaccination, enhance access and provider or system response (Table 3).

(iii) Pregnant women

Two systematic reviews^{16,18} collected the available evidence on the effectiveness of interventions used to improve influenza vaccination uptake in pregnant women. Reminders about influenza immunization on antenatal healthcare records, midwives providing vaccination, and education and information provision for healthcare providers (HCPs) and patients were found to be effective strategies in improving maternal influenza vaccination rates.^{16,18}

(iv) The general population

A meta-analysis that pooled data from 8 RCTs (NHMRC level I) showed that educational interventions in general were not effective in improving influenza vaccination rates (OR = 1.16, 95% CI: 0.95–1.41) among different population groups.⁶ However, a sub-group analysis demonstrated educational interventions delivered via text messages and personalized letters were effective in increasing influenza vaccination rates (OR = 1.30, 95% CI: 1.05–1.61), whilst educational interventions delivered via poster/pamphlet (OR = 1.00, 95% CI: 0.92–1.08), or face-to-face (OR = 1.16, 95% CI: 0.69–1.94) were ineffective.⁶ Another systematic review of eight studies¹⁰ assessed the effect of providing patients with access to their Personal Electronic Health Records (PEHR) in improving vaccination uptake (four RCTs focused on influenza vaccine). Findings from an RCT included in this review found study participants with access to PEHR were 6.7% (intervention vs control: 11.6% vs 4.9%; $p = .008$) more likely to receive an influenza vaccine than those with no access to PEHR. A similar positive effect of PEHR on influenza vaccination uptake was observed in one of the other RCT, although improvements were not statistically significant (intervention vs control: 24% vs 19%; $p = .50$).¹⁰ Moreover, two RCTs included in the review have demonstrated patients with access to PEHR in combination with messages promoting influenza vaccines (adjusted OR = 1.20, 95% CI: 1.06–1.35) or active vaccine reminders via electronic messages (intervention vs control: 22.0% vs 14.0%; $p = .018$) were effective in improving influenza vaccination uptake.¹⁰

A review¹¹ of four RCTs that evaluated the use of multiple mail-order reminders suggested that more than one reminder sent by mail improves adherence to influenza vaccination in older adults. In contrast to these findings, multiple mail-order

reminders to parents make little or no difference in adherence to influenza vaccination in children under 6 years of age. However, another systematic review¹³ demonstrated reminders improve vaccinations for childhood influenza (RR 1.51, 95% CI 1.14 to 1.99; risk difference of 22%; five studies; 9265 participants) and adult influenza (RR 1.29, 95% CI 1.17 to 1.43; risk difference of 9%; 15 studies; 59,328 participants).

Okoli et al.¹² (2021) conducted a systematic review and meta-analysis of the effectiveness of interventions (included seven RCTs and 32 observational studies) on HCPs to improve seasonal influenza vaccination rates among patients. Pooled data from two RCTs (20.1%, 95% CI: 7.5–32.7%) and two observational studies (13.4%, 95% CI: 8.6–18.1%) showed that team-based training /education of physicians significantly increased influenza vaccination rates in adult patients as well as in pediatric patients (7%, 95% CI: 0.1–14%; two observational studies).¹² One-off provision of guidelines to physicians, and to both physicians and nurses, significantly improved influenza vaccination rates by an average 24% in adult patients (23.8%, 95% CI: 15.7–31.8%; three observational studies) and pediatric patients (24%, 95% CI: 8.1–39.9%; two observational studies).¹²

A systematic review¹⁷ (included 31 studies) of hospital-based strategies in acute care settings aimed at improving influenza vaccination rates for adult inpatients showed that standing order protocols were significantly more effective than other individual interventions, but multi-component interventions (which included standing order protocols) were more effective than standing order protocols alone. Isenor et al.¹⁴ (2016) conducted a high-quality systematic review and meta-analysis assessing the impact of pharmacists as educators, facilitators, and administrators of vaccines on immunization rates. Pharmacist participation in these three roles improved vaccination rates compared to vaccine provision by traditional providers without pharmacist involvement (Table 3).¹⁴

NHMRC level II, III and IV: summary of primary research findings by setting and intervention and targeted population groups

For other individual studies included in this rapid review, influenza vaccine interventions or programs are discussed in five different settings i) hospital/tertiary-care settings ii) primary-care settings iii) venue-based iv) large-scale programs and v) targeted delivery.

(i) Hospital/tertiary-care settings

Hospital-and tertiary-care-based programs for improving influenza vaccination rates generally focused on the provider and included standing orders and reminders to hospital staff. The evidence around influenza vaccination programs in hospital settings is both limited and generally of lower quality (mostly Levels III). One observational study evaluated the impact of an active choice intervention in the electronic health record (EHR) in improving influenza vaccination rates.¹⁹ Rather than the standard approach of depending on HCPs to recognize the need for vaccination, the EHR confirmed patient eligibility during the hospital visit and used an alert to ask the HCP which resulted in

a significant relative increase in influenza vaccination rates by 37.3% compared to the pre-intervention period.¹⁹ Similarly, an observational study evaluated clinical decision support in the EHR and found it to improve influenza vaccination rate by 20 times higher a year after the program's implementation.²⁰ One pre-post study assessed the effectiveness of a multifaceted intervention to improve influenza vaccination rates among children in a large pediatric hospital in the USA.²¹ The interventions targeted medical and nursing providers and included web-based education modules, reminders in EHR and financial incentives (an end-of-year financial bonus) for resident doctors.²¹ The intervention was associated with 1.23 (95% CI 1.11–1.35) times higher odds of a child receiving influenza vaccination at discharge.²¹ Another four-year before-and-after observational study (n = 3734) evaluated a vaccination campaign of an Emergency Department (EDVC) at Bichat hospital in Paris with 80,000 visits per year.²² The intervention during the fourth year incorporated standing orders to enable nurses to administer vaccines to patients admitted through the emergency department (ED) without an individually prescribed medication from doctors. The vaccination uptake of patients in ED setting was shown to effectively double during the post intervention period (33% to 66%) (Supplementary table 2).²²

(ii) Primary-care settings

Primary care was the most common setting for studies of influenza vaccination multicomponent programs for high-risk populations, and interventions were directed at the patient, provider, and/or organization levels. The evidence around influenza vaccination programs in a primary setting were generally higher quality (14 RCTs-level II & five level III studies) and the majority of the interventions incorporated in these studies were patient centered. Patient reminders were among the most frequent patient-level program components (portal & interactive voice response (IVR) calls^{23,24} and letters or text messaging influenza vaccine reminders.^{6,21,25–30} Three RCTs^{28–30} evaluated the effectiveness of text reminder to patients in combination with other promotional messages. Overall, these studies^{28–30} provided modest evidence that patient reminder systems to improve influenza vaccination rates in high-risk groups can be effective (Supplementary table 2).

Other patient-level interventions in primary care settings included advertising campaigns for influenza vaccination using posters and pamphlets in general practice sites for different at-risk populations.^{31–33} Whilst an RCT³¹ evaluating clinic-based advertising to the elderly did not show improvement in influenza vaccine delivery, two other RCTs demonstrated significant increases in influenza vaccination rates in the elderly and children respectively.^{32,33} Additionally, one of the RCTs³⁴ demonstrated that websites with vaccine information and interactive social media components sent to pregnant women, positively influence maternal influenza vaccine uptake. Two longitudinal studies^{35,36} evaluated provider focused intervention in primary care settings. The two studies assessed the effectiveness of implementation of a “best practice alert (BPA)” within the electronic medical record in an integrated pediatric health care delivery system³⁵ and quality improvement initiative with continuing vaccine education for

primary care physicians, respectively.³⁶ Whilst the BPA did not demonstrate a significant improvement in the uptake of influenza vaccination among pediatric subpopulation,³⁵ the 3-stage longitudinal educational intervention on physicians did significantly improve influenza vaccination rates by 3.4% in elderly patients >65 years of age and by 2.1% in high-risk groups ($P < .001$)³⁶ (Supplementary table 2).

(iii) Venue-based influenza vaccination delivery

An effective strategy for immunizing individuals at high risk of influenza is to target venues frequented by high-risk groups. Venues frequented by high-risk groups included nursing homes, which are specialized tertiary-care facilities. Evidence obtained from the systematic review (level I)⁵ discussed above, demonstrated enhancing vaccine access in long-term care facilities can improve influenza vaccination uptake among the elderly. Giles et al.³⁷ (2018) assessed the feasibility of an outreach mobile influenza vaccination program led by a large hospital network targeting high-risk and vulnerable populations in residential aged care facilities, sites attended by homeless people, and refugee centers in Melbourne, Australia. The pilot study has demonstrated the value and feasibility of a mobile outreach influenza immunization program focusing on hard-to-reach and vulnerable populations.³⁷ School-based influenza clinics are an alternative venue-based influenza vaccination delivery targeting school aged children. One of the RCTs³⁸ evaluated text message reminders sent to parents from the school nurse which did not improve children's influenza vaccination rates. In contrast, the RCT by Humiston et al.³⁹ (2014) showed that school aged children are more likely to be vaccinated in school-located vaccination versus standard care control schools (Supplementary table 2).

(iv) Large-scale regional programs

Nine studies have evaluated large-scale vaccination interventions in different populations using a variety of approaches alone or in combination. Three RCTs^{40–42} and one observational study⁴³ examined the effect of centralized reminder/recall (autodialer, postcard, text reminders),⁴⁰ a state-wide immunization information system (IIS) for seasonal influenza vaccine reminders from local health departments,⁴¹ large-scale messaging using mobile applications⁴² and a free national text service providing influenza vaccination education and reminders.⁴³ The interventions in all these studies reported a modest impact on improving influenza vaccination coverage across large high-risk populations.^{40–43} In contrast to the systematic review findings by Isenor et al.¹⁴ recent studies of level III quality^{44–48} produced inconsistent results in the effectiveness of a large-scale pharmacy-based vaccine distribution in increasing influenza vaccination rates (Supplementary table 2). Two recent studies^{44,45} that reported no association of improved influenza vaccine rates following pharmacist administered vaccination encounters were identified as having a high risk of bias, primarily due to non-randomized design and use of historical control data to compare changes in influenza vaccination rates.

(v) *Influenza Immunization programs involving active community engagement*

Community-wide programs are less commonly reported. Borg et al.⁴⁹ (2018) evaluated a communication-based program that sent personalized letter or pamphlets to parents of Victorian children (aged 6 months to <5 years) who identified as Aboriginal or Torres Strait Islander aimed at increasing influenza vaccination coverage among Aboriginal children in Victoria, Australia. The communication program involved designs that align with recommendations for designing health information resources for Aboriginal communities (i.e. pamphlets including Aboriginal artwork, pictures of Aboriginal families). Sending pamphlets directly to parents/guardians did not improve vaccination rates but a personalized letter was found to be an effective strategy for improving influenza vaccination by 34% among Aboriginal children.⁴⁹ The authors suggested the lack of effectiveness of the pamphlet in improving vaccine uptake may be due to the lack of personalization and the authority related with the letter.⁴⁹ Esteban-Vasallo et al.⁵⁰ (2019) evaluated the effectiveness of influenza vaccination campaign in the Autonomous Community of Madrid improving the uptake of influenza vaccination in patients with rare diseases. The intervention including SMS text messaging and a reminder was modestly effective by an average 30% in improving influenza vaccination uptake in patients with rare diseases (Supplementary table 2).⁵⁰

Discussion

This rapid review was conducted to identify interventions that were effective in improving uptake of influenza vaccination in high-income countries to inform recommendations for influenza vaccination programs in Australia. Although the review identified 40 studies evaluating interventions aimed at increasing influenza vaccination rates, there was substantial heterogeneity in study designs, intervention types, target groups, settings and vaccination status ascertainment methods. Furthermore, several of the studies used multiple component interventions in their study population making it difficult to identify effectiveness by individual strategies.

Overall, recall/reminders for patients and HCP reminders had the highest level of evidence and were the most effective interventions in improving influenza vaccination rates in all high-risk groups and in all types of setting including from primary and tertiary hospitals to large-scale community interventions in the real-world settings.^{5-9,15,18,21,25-30,39-41,43,50,51} Most reminders identified in this review incorporated educational information to either patients or HCPs. Although, the evidence on whether patient focused educational interventions in improving influenza vaccination uptake is mixed and varies with different target populations, they have shown a positive impact in improving vaccination uptake when administered through different outlets.^{5,7,8,14,18,33} Additionally, specific educational training programs for HCPs that sought to improve

influenza vaccination rates in people at high risk for developing influenza-related complications³⁶ including people with chronic illness⁷ was successful. Another important provider-centered approach is standing orders which have been applied in various settings, such as in clinics, hospitals,¹⁸ emergency rooms,²² and community pharmacies.¹⁴ Standing orders allowing community pharmacists,¹⁴ nurses,²² and midwives^{16,18} to administer vaccination without medical prescription has improved influenza vaccination rates in different high risk groups.

The present rapid review revealed that pharmacist participation in vaccination as educators, facilitators, or administrators of vaccines has improved influenza vaccination rates.¹⁴ Across Australia there has been progressive implementation of pharmacist-administered vaccination programs and Western Australia was the first state to comprehensively evaluate the program.⁵² The evaluation report suggested a high proportion of pharmacist administered vaccinations in regional areas with 12% to 17% of consumers receiving the vaccine in pharmacies despite their eligibility to receive free influenza vaccinations under NIP.⁵² Victoria is the only state in Australia that allow pharmacists to administer both government-funded (NIP) and privately purchased vaccines in either a community or hospital-based pharmacy.⁵³ Although pharmacist vaccination account for a small percentage of vaccinations in Australia (2.7% in 2019),⁵⁴ a recent report indicated that COVID-19 pandemic has affected the capability of pharmacists in Australia to offer vaccination services.⁵⁵ Community pharmacists are well positioned to improve influenza vaccination rates, considering that influenza vaccine programs being rolled out in 2021 alongside the COVID-19 vaccines is creating logistical challenges.^{54,55}

Strengths and limitations

This was a rapid systematic review, conducted under time constraints in order to be relevant and apply findings from current evidence to the context of COVID-19. This review was originally conducted as part of an independent evaluation to determine the best process for distribution and increase uptake of publically funded influenza vaccine in South Australia. The review was expanded to identify strategies that were effective in improving uptake of influenza vaccination in high-income countries to inform recommendations for influenza vaccination programs in Australia. Therefore there was no published a priori protocol for the present rapid review. Although rapid review methods enable a timely review of publications, they do involve trade-offs compared with the methodological rigor of an in-depth systematic review.⁵⁶ Other limitations of this rapid review are the small number of studies particularly in the Australian context and the poor methodological quality of most observational studies. Meta-analysis was not possible in this review due to the heterogeneity of study designs and outcome measures used in the included studies.

Recommendations and public health and policy implications

The authors suggest that the evidence found in this review supports the following recommendations:

(i) Patient level

- Deliver community wide education and information regarding influenza vaccination to a target high-risk groups through different outlets including posters, leaflets, booklet, brochure and educational-text message or letter reminders.
- Set up patient reminder/recall systems. Send alerts that influenza vaccinations are due (reminders) or late (recall) to high-risk groups; delivery techniques can include telephone calls, postcards, letters or mail tailored to patient's needs.
- The evidence, while limited, suggest delivery of culturally appropriate interventions for Aboriginal or Torres Strait Islanders within Aboriginal health services might improve influenza vaccination rates.

i. Provider or system level

- Standing orders: empower and authorize nurses/midwives, community pharmacists to deliver seasonal influenza vaccinations without a medical order.
- Pharmacist-administered vaccination programs may have an important role in improving influenza vaccination coverage in Australia particularly in regional and rural areas where there may be difficulty in accessing other primary healthcare services.
- Encourage computer-based clinical decision support systems for vaccine providers in a variety of settings including clinics, hospitals, and residential aged care facilities.
- Provider reminders/recall system: Notify those who administer influenza immunization that individual patients are due (reminder) or overdue (recall) for vaccination.
- Deliver information to immunization providers to increase their knowledge; techniques include vaccine education and training programs and computer-based learning programs.
- Assess the feasibility of improving access to influenza vaccine for vulnerable populations for example a mobile service that attends relevant sites attended by homeless people.

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ORCID

Hassen Mohammed  <http://orcid.org/0000-0003-0189-3739>
 Mark McMillan  <http://orcid.org/0000-0002-6490-7707>
 Prabha H. Andraweera  <http://orcid.org/0000-0003-2434-8370>
 Helen S. Marshall  <http://orcid.org/0000-0003-2521-5166>

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