Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Factors influencing, and measures to improve, vaccination uptake: rapid evidence summary

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About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children and Youth Affairs, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.
- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.
- **Regulating health services** — Regulating medical exposure to ionising radiation.
- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.
- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.
- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.
- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

List of abbreviations used in this report

CDC	Centers for Disease Control and Prevention
CHD	congestive heart disease
CI	confidence interval
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 2019
EAG	Expert Advisory Group
ECDC	European Centre for Disease Prevention and Control
HCW	Healthcare worker
HIQA	Health Information and Quality Authority
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
HTA	health technology assessment
NICE	The National Institute for Health and Care Excellence
NPHET	National Public Health Emergency Team
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
WHO	World Health Organization

The factors influencing, and measures to improve, vaccination uptake

Key points

- With a number of COVID-19 vaccines currently under consideration by the European Medicines Agency (EMA), it is important to understand the factors that influence and measures that improve vaccination uptake.
- In light of the similarities between influenza and COVID-19 in terms of the populations who may be prioritised for vaccination, influenza vaccination (including seasonal and pandemic influenza) was considered a surrogate for COVID-19 for the purpose of this rapid evidence summary.
- Due to the abundance of studies and existing reviews in the scientific literature, two 'overviews of reviews' were undertaken. An overview of qualitative and mixed methods reviews investigated factors affecting influenza vaccination uptake and an overview of systematic reviews that examined the effectiveness of interventions to improve influenza vaccination uptake internationally.
- In total, 41 reviews were identified, 20 reviews examined factors influencing influenza uptake, 18 reviews examined interventions to increase influenza vaccination uptake and three reviews examined both factors influencing and interventions to increase influenza vaccination uptake.
- Data from nine of the qualitative and mixed methods reviews on the barriers and facilitators to an individual's uptake of vaccination against influenza were synthesised; with the rest deemed to be of critically low quality and unsuitable for informing policy.
- The evidence relating to barriers and facilitators to vaccination uptake can be summarised into ten themes common to both seasonal and pandemic influenza vaccinations. The themes are: 'perceived risks and or benefits of vaccines'; 'access and or contextual factors'; 'psychological and or internal factors'; 'perceived risks and or susceptibility to influenza'; 'perceived responsibility'; 'social influences'; 'past behaviours and or experiences'; 'knowledge'; 'socio-demographic factors' and 'health and health behaviours'. The barriers and facilitators within each theme are listed within the report.
- Overall, these themes were consistent across the different populations groups, that is, those at high risk of severe disease, healthcare workers and pregnant

women. There were some differences in themes identified in the studies of these different groups:

  - In those considered to be at high risk of severe disease, 'perceived responsibility' was not identified as a barrier nor a facilitator.
  - In pregnant women, 'perceived responsibility', 'knowledge' and 'health and health behaviours' were not identified as barriers to vaccination uptake. Pregnant women were more likely to report protection of their baby, knowledge about influenza, vaccination policy and past experiences as reasons for vaccination uptake.
  - In healthcare workers, 'health and health behaviours' were not cited as a barrier to vaccination uptake, and 'psychological and or internal factors' as facilitators were not identified as a theme.

- Of the nine included qualitative reviews six were deemed to be of moderate to high quality and three of low quality, however inherent biases with qualitative literature remain and the transferability of their findings to the current Irish situation needs to be interpreted with caution.
- Twenty-one systematic reviews were identified relating to interventions aimed at increasing influenza vaccine uptake. Of these, seven reviews were considered to be of high methodological quality and the narrative synthesis was based on these high quality reviews. Evidence was retrieved for all populations of interest (older adults, individuals with underlying conditions, pregnant women, healthcare workers and general adult/adolescent/child populations). Significant overlap in terms of included studies was noted between some systematic reviews. The number of primary studies included in systematic reviews ranged from two to 61, published between 1986 and 2018.
- A wide range of heterogeneous interventions were assessed that varied significantly in terms of intensity and resources required for delivery. Studies included both individual-level (e.g. patient letters and phone calls) and system-level (e.g. provider prompts) interventions. None related to national-level interventions aimed at the general public (e.g. mass media campaigns).
- Analysis of systematic reviews of high methodological quality found:
  - moderate-to-high certainty evidence that low- (e.g. postcards), medium- (e.g. personalised phone calls), and high-intensity (e.g. home visits or facilitators in practices) interventions are effective in increasing community demand for, and uptake of, vaccination among older adults. Physician incentives (payments) were also successful.

  - low-to-very low certainty evidence that some interventions, including multicomponent interventions, are effective in increasing uptake among adults and children with underlying conditions and pregnant women. Call and recall methods using more personalised approaches (such as letters, postcards or personal telephone calls) appear to be more effective than simple reminders.

  - low-to-very low certainty evidence that a range of interventions, including multicomponent interventions that combine education, incentives, declination policies (such as written refusal statements along with reasons why), reminders and access are effective in increasing uptake among healthcare workers. Mandatory vaccination is the most effective single intervention (RR 1.71; 95%CI 1.70 to 1.72; six before and after studies, 105,538 participants). However, there are concerns regarding individuals' autonomy when introducing mandatory vaccination. The evidence is less consistent regarding incentives, 'opt-out' and declination policies. In general, concerns exist regarding the acceptability of mandatory vaccination, 'opt-out' and declination policies to healthcare workers, and these policies may negatively affect staff morale.

  - Moderate-certainty evidence that implementing patient reminder and recall systems probably improve influenza vaccine uptake in adult and child populations. Some evidence was also found that educational interventions aimed at parents and provider prompts increased uptake in children.

- This review has a number of limitations. Most reviewed studies focussed on the seasonal influenza vaccine and not the pandemic influenza vaccine. While the target populations for seasonal influenza and COVID-19 vaccination are similar, it is not known how applicable studies on interventions to improve influenza vaccination uptake are to COVID-19. Societal experiences following months of public health measures aimed to contain the COVID-19 pandemic will also likely impact on vaccination uptake preferences and behaviours. Additionally, no review specifically included older individuals in long-term care facilities, a target group of importance for COVID-19 vaccination.

- A number of barriers and facilitators were identified that can negatively or positively affect an individual's uptake of vaccinations, respectively. Interventions (including multicomponent interventions) that can successfully increase the uptake of influenza vaccination across a range of eligible groups, by overcoming the barriers or promoting the facilitators, were identified. These

interventions vary greatly in terms of intensity. Consideration must be given to the resource requirements and the acceptability of the intervention to the target population.

Factors influencing, and measures to improve, vaccination uptake

Background

The Health Information and Quality Authority (HIQA) has developed a series of evidence syntheses to inform advice from HIQA to the National Public Health Emergency Team (NPHET). The advice takes into account expert interpretation of the evidence by HIQA's COVID-19 Expert Advisory Group.

This evidence synthesis was requested by NPHET to address the following policy questions:

1. What are the factors, both demographic and psychological, that are predictors of intention and uptake of vaccination?

2. What is the evidence for interventions and communication strategies to effectively tackle barriers to, and increase informed uptake of, vaccination?

As of 9 December 2020, no vaccine for the prevention of COVID-19 has been authorised by the European Medicines Agency (EMA). While multiple vaccines are in development, published data are limited to results from phase III clinical trials. Therefore, there is an absence of data on effective interventions to increase COVID-19 vaccination. Influenza vaccination (seasonal and or pandemic influenza) was considered a surrogate for COVID-19 vaccination for the purposes of this evidence summary, due to similarities in target populations (older adults, healthcare workers and individuals with underlying conditions), disease outcomes (viral pneumonia) and potential barriers to uptake (e.g., concerns regarding vaccine effectiveness or safety and access to the vaccination programme).

The following two research questions were formulated to inform this policy question:

RQ1: What are the barriers and facilitators to an individual's uptake of vaccination against influenza?

RQ2: What population-based intervention measures increase influenza vaccination uptake rates?

Methods

An initial scoping search of the literature was carried out in preparation for this project and a large body of evidence regarding the uptake of influenza vaccination was identified. This included multiple reviews and systematic reviews of varying quality and scope that evaluated a range of measures aimed at increasing uptake. Based on the volume of literature available and project timelines, an overview of reviews was considered to be the most efficient method to assess the measures and factors that increase vaccination coverage. Additionally, due to the abundance of published systematic reviews, searches were restricted to reviews published post January 2015 (it is noted, however, that high quality systematic reviews will have included earlier primary studies).

The processes outlined in HIQA's protocol for this review (www.hiqa.ie) were followed. The process through which studies were identified had two components:

1. A database search to identify systematic reviews (including qualitative, quantitative or mixed-methods evidence)
2. An additional search of publications from select international public health agencies and institutional websites, including the:
    a. World Health Organization (WHO)
    b. European Centre for Disease Control (ECDC)
    c. UK's National Institute of Clinical Excellence (NICE)
    d. Health Service Executive (HSE)
    e. National Immunisation Advisory Committee (NIAC)
    f. Effective Communication in Outbreak Management: development of an evidence-based tool for Europe (ECOM) website.

Databases were searched on 01 December 2020. The evidence underpinning the review questions was identified from systematic reviews of quantitative, qualitative or mixed-methods evidence that were deemed to be of higher methodological quality. This judgement on quality was based on the application of the seven critical domains of AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews[1]) for quantitative reviews (Table 1), and a modification of AMSTAR-2 for qualitative reviews.

Table 1 AMSTAR-2 critical domains

AMSTAR-2 critical domains	
1.	Protocol registered before commencement of the review
2.	Adequacy of the literature search
3.	Justification for excluding individual studies
4.	Risk of bias from individual studies being included in the review
5.	Appropriateness of meta-analytical me
6.	Consideration of risk of bias when interpreting the results of the review
7.	Assessment of presence and likely impact of publication bias

In line with guidance for applying AMSTAR-2, studies were categorised as low quality if they breached one of these critical domains, and critically low if they breached two or more. Studies that did not breach any were deemed to be high or moderate quality (henceforth referred to as 'high quality'). Where a substantial number of systematic reviews were identified as meeting the inclusion criteria for this evidence summary, the highest quality systematic reviews were prioritised for discussion in the narrative summary. The lower quality systematic reviews were listed in a table. Data extraction was not performed for reviews appraised as being of 'critically low' quality as they should not be used to inform policy, in line with AMSTAR-2 guidance. The analysis of reviews relating to RQ1 had two components. Firstly, qualitative data were extracted and a thematic analysis conducted to identify common themes relating to the barriers and facilitators to influenza vaccination uptake. Secondly, where reported, quantitative data relating to the association of themes with influenza vaccination uptake were extracted.

Results

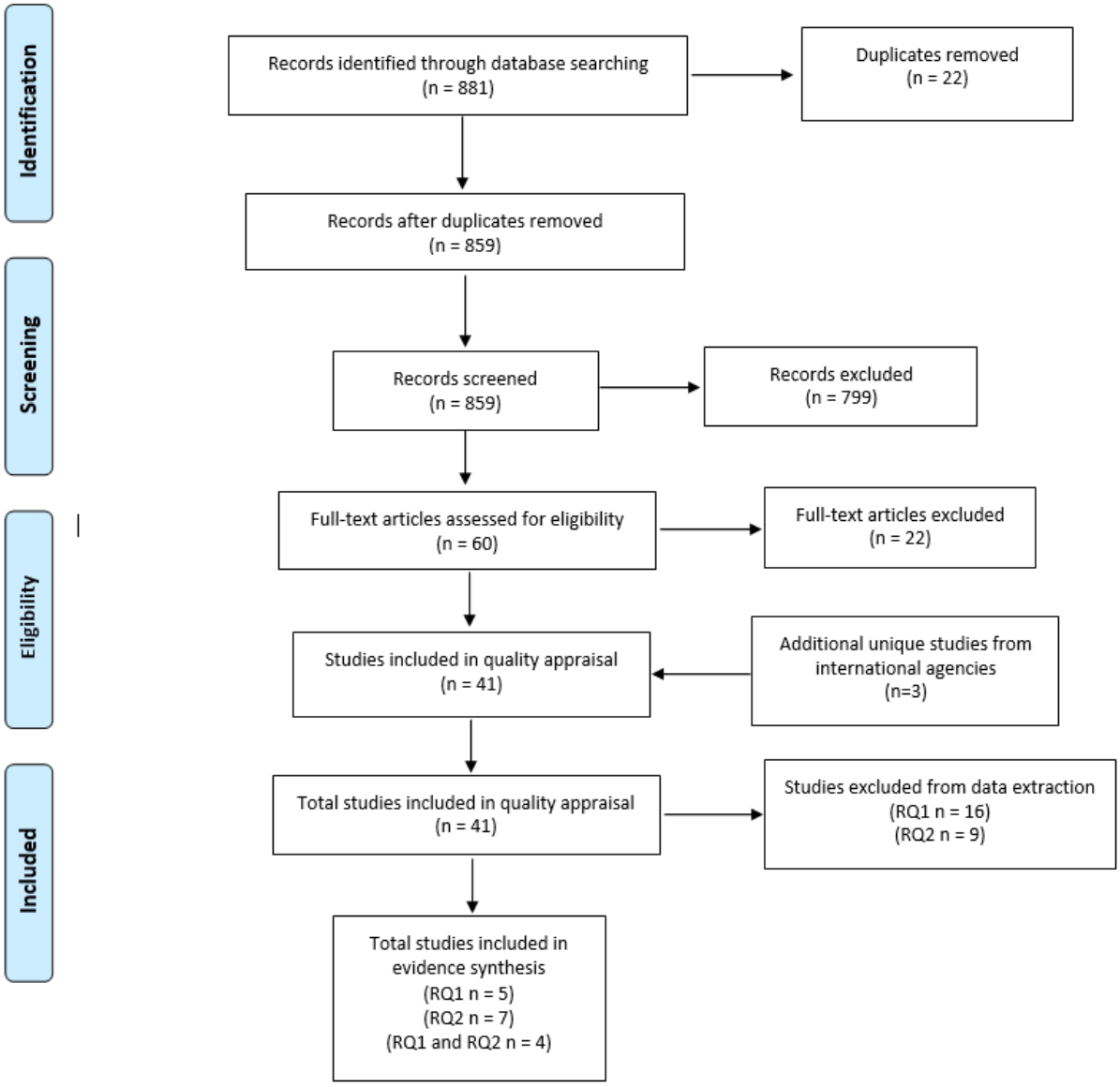
Database research results

The collective search from 1 January 2015 up until 1 December 2020 resulted in 882 citations; following removal of duplicates 860 citations were screened for relevance, with 61 full-texts assessed for eligibility and 22 subsequently excluded (PRISMA diagram is provided in Figure 1). Accordingly, 38 systematic reviews or reviews were included in this evidence summary; 20 related to barriers and facilitators to vaccination uptake, 16 related to interventions to increase vaccination uptake and two related to both aspects, that is, barriers and facilitators to vaccination uptake and interventions to increase vaccination uptake. Of the 38 included reviews, three were published in 2015,[2-4] eight in 2016,[5-12] six in 2017,[13-18] eight in 2018,[10, 19-25] six in 2019[26-31] and eight in 2020.[32-39]

International public health agency search

A search was undertaken for publications from six international public health agencies and institutions listed previously. Of the international agencies searched, three additional (non-duplicate) systematic reviews were identified from the NICE website that met our inclusion criteria.[40, 41]

Figure 1 PRISMA flow diagram of included systematic and rapid reviews



Following quality appraisal, nine reviews were deemed to be of moderate or high quality,[20, 21, 24, 27, 32, 36, 40-42] seven of low quality,[2, 11, 26, 30, 35, 37, 38] and 25 of critically low quality.[3, 5-10, 12-19, 22, 23, 25, 28, 29, 31, 33, 34, 39, 43] Table 2 summarises the quality appraisal for all reviews eligible for inclusion in RQ1 and RQ2 and indicates if data extraction was completed.

Table 2 Quality appraisal of reviews for inclusion in RQ1 and RQ2

First author, year	Relevant RQ	Quality appraisal result	Data extracted (Yes/No)
Abdullahi, 2020[32]	RQ2	Moderate to high	Yes
Aigbogan, 2015[2]	RQ2	Low	Yes
Balzarini, 2020[33]	RQ2	Critically low	No
Bechini, 2020[34]	RQ2	Critically low	No
Bisset, 2018[19]	RQ2	Critically low	No
Borthwick, 2020[35]	RQ1	Low	Yes
Bults, 2015[3]	RQ1	Critically low	No
Carlsen, 2016[5]	RQ1	Critically low	No
Corace, 2016[6]	RQ1	Critically low	No
Dini, 2018[20]	RQ1	Moderate to high	Yes
Gosselin Boucher, 2019[26]	RQ2	Low	Yes
Isenor, 2016[7]	RQ2	Critically low	No
Jacobson Vann, 2018[21]	RQ2	Moderate to high	Yes
Jain, 2017[13]	RQ2	Critically low	No
Jarrett, 2015[4]	RQ2	Critically low	No
Jenkin, 2019[27]	RQ1 and RQ2	Moderate to high	Yes
Kan, 2018[22]	RQ1	Critically low	No
Kang, 2017[14]	RQ1	Critically low	No
Karafillakis, 2017[15]	RQ1	Critically low	No
Kilich, 2020[36]	RQ1	Moderate to high	Yes
Larson, 2018[23]	RQ1	Critically low	No
Lorenc, 2017[16]	RQ2	Critically low	No
Lucyk, 2019[28]	RQ1	Critically low	No
Lytras, 2016[8]	RQ2	Critically low	No
NICE, 2018a[42]	RQ1 and RQ2	Moderate to high	Yes
NICE, 2018b[40]	RQ1 and RQ2	Moderate to high	Yes
NICE, 2018c[41]	RQ1 and RQ2	Moderate to high	Yes
Okoli, 2020a[38]	RQ1	Low	Yes
Okoli, 2020b[37]	RQ1	Low	Yes
Ozisik, 2017[17]	RQ1	Critically low	No
Poliquin, 2019[29]	RQ1	Critically low	No
Rashid, 2016[9]	RQ2	Critically low	No
Sanftenberg, 2019[30]	RQ2	Low	Yes
Schmid, 2017[18]	RQ1 and RQ2	Critically low	No
Sheldenkar, 2019[31]	RQ1	Critically low	No
Smith, 2016[10]	RQ1	Critically low	No
Thomas, 2018[24]	RQ2	Moderate to high	Yes
Vukovic, 2020[39]	RQ1	Critically low	No
Wang, 2018[25]	RQ1	Critically low	No
Wong, 2016[11]	RQ2	Low	Yes
Yeung, 2016[12]	RQ1	Critically low	No

RQ 1: What are the barriers and facilitators to an individual's uptake of vaccination against influenza?

For RQ1, data extraction was completed for nine reviews, of which five[20, 35-38] were specific to RQ1 and four[27, 44-46] covered both RQ1 and RQ2. Six of the nine reviews focused on vaccinations for seasonal influenza[35, 37, 38, 44-46] and three focused on vaccinations for seasonal and or pandemic influenza.[20, 27, 36] However, as themes observed were not always differentiated according to the type of influenza in the primary studies and, where they were differentiated, the same barriers and facilitators were common to both types of influenza, we have not summarised the themes by influenza type in this evidence summary. Table 3 below presents an overview of the themes identified and summarises the barriers and facilitators to influenza vaccination uptake derived from qualitative and mixed methods reviews. See Appendix 1 for the full data extraction of reviews relating to the barriers and facilitators to vaccination uptake.

Table 3 Overview of the barriers and facilitators to vaccination uptake categorised by theme

Themes	Barriers	Facilitators
Perceived risks and or benefits of vaccine	▪ Doubts about vaccine effectiveness. ▪ Being opposed to vaccination in general. ▪ Concerns or uncertainties about side effects.	▪ Higher perceived benefits of vaccine (both clinical and societal). ▪ Beliefs in vaccine safety and effectiveness.
Access and or contextual factors	▪ Access, time, availability, cost and logistics of getting vaccinated. ▪ Living alone.	▪ Lower perceived costs of vaccination.
Psychological and or internal factors	▪ Lack of motivation/procrastination. ▪ Mistrust towards government and pharmaceutical companies. ▪ Forgetfulness. ▪ Lack of perceived behavioural control. ▪ Fear/distrust of being vaccinated. ▪ Perception of rumours/myths related to vaccination. ▪ Perceived poor health.	▪ Actively planning when and where to receive the vaccine. ▪ Belief in one's ability to arrange a time and transportation. ▪ Psychological flexibility. ▪ Fear/regret over not getting vaccinated. ▪ Perceived poor health.
Perceived risks and or susceptibility to influenza	▪ Not caring about influenza. ▪ Believing that influenza is a mild disease. ▪ Low risk perception.	▪ Perceived severity of influenza. ▪ Beliefs about being at heightened risk of influenza if unvaccinated. ▪ Believing that influenza is highly contagious.
Perceived responsibility	▪ Denial of the social benefit of influenza vaccination.	▪ Desire to protect oneself and others.

	▪ Lack of professional or ethical obligation to get vaccinated.	▪ Being willing to prevent influenza transmission. ▪ Believing that influenza prevention is important.
Social influences	▪ Low social pressure (either real or perceived). ▪ Negative influence of family/friends/media.	▪ Receiving recommendation from respected healthcare workers. ▪ Having a family that is usually vaccinated. ▪ Positive influence of family/friends/media and their encouragement to have vaccination.
Past behaviours and or experiences	▪ Not having had influenza in the previous years. ▪ Participants' previous experiences with vaccinations.	▪ Previously had influenza. ▪ Past influenza vaccinations.
Knowledge	▪ Lack of adequate influenza-specific knowledge.	▪ Knowledge that the vaccine is required each year. ▪ Knowing that the vaccine is effective. ▪ Knowledge of influenza in pregnancy. ▪ Knowledge of availability of vaccines.
Socio-demographic factors	▪ Being a nurse. ▪ Being older.* ▪ Not having had a medical check-up in the past year. ▪ Not having health insurance. ▪ Single. ▪ Lower social class. ▪ Not having higher education. ▪ Having a lower household income. ▪ Not having a family doctor.	▪ Being a medical doctor. ▪ Being older.* ▪ Having had a medical check-up in the past year. ▪ Having health insurance. ▪ Married. ▪ Higher social class. ▪ Having higher education. ▪ Having a higher household income. ▪ Having a family doctor.
Health and or health behaviours	▪ Not having a chronic disease. ▪ Being a smoker.	▪ Having a chronic disease. ▪ A non-smoker.

*This was identified as both a barrier and a facilitator by different reviews.

Perceived risks and or benefits of vaccine

Overall, those who were less likely to be vaccinated, or less likely to intend to be vaccinated, had poorer outcome expectancies from the vaccine in terms of effectiveness and side effects. A systematic review by Borthwick et al. included 12 studies published up until August 2018; the population of interest was adults aged 16 years and older with a high-risk physical health condition (for example, chronic respiratory disease, diabetes, kidney transplant patients).[35] They reported that

participants who were not vaccinated were more fearful of side effects; the authors also noted that vaccinated participants had some concerns or uncertainties about side effects.[35] The authors found that five out of seven included quantitative studies reported a significant association between perceived benefits and vaccination behaviour; which seemed to suggest that perceived vaccine benefits play a role in determining vaccine behaviour.[35]

Concerns surrounding vaccination side effects were also evident in a review by Dini et al.. This review included 28 studies published up until April 2017; the population of interest was healthcare workers.[20] The authors reported concerns among healthcare workers regarding the safety of vaccines as well as some opposition to vaccines in general. However, they also reported that higher perceived benefits (both clinical and societal), beliefs in vaccine effectiveness and lack of concern about vaccine safety were associated with willingness and intention to vaccinate oneself.[20] A systematic review by NICE of the evidence for increasing seasonal influenza vaccination uptake in healthcare workers, reported that beliefs about the effectiveness of vaccinations may impact on vaccination uptake in healthcare workers. The authors concluded that education on vaccine effectiveness is important to increase vaccination uptake.[46]

Similarly, this theme was evident in pregnant women. Kilich et al. conducted a systematic review and meta-analysis of the strength of relationships between identified factors and maternal vaccination factors.[36] Perceptions of the vaccine causing harm or being unsafe in pregnancy was a significant indicator of reduced vaccination uptake for pandemic influenza (OR 0.16, 95% CI 0.09-0.29; I^2=89% (six studies – general harm) and OR 0.19, 95% CI 0.10-0.38; I^2=14% (two studies – harm to baby)); similar findings were reported for seasonal influenza vaccine uptake (OR 0.22, 95% CI 0.11-0.44; I^2=84% (seven studies – general harm)).[36]

Perceptions of the vaccine having side effects also resulted in reduced vaccination uptake for pandemic influenza (OR 0.27, 95% CI 0.21-0.34; I^2=0% (two studies – knowledge of side effects) and OR 0.44, 95% CI 0.23-0.81 I^2=0% (two studies – concerns about side effects)). Similar concerns around seasonal influenza vaccines showed decreased uptake as well (OR 0.55, 95% CI 0.27-1.16; I^2=96% (five studies – concerns about side effects) and OR 0.66, 95% CI 0.21-2.14; I^2=57%(two studies – probability of side effects)); although these findings were not statistically significant.[36] Conversely, while perceptions of vaccinations being useful, effective or necessary for the mother or infant were associated with a significant increase in uptake of pandemic influenza vaccine when the benefit to the mother was considered (OR 8.44, 95% CI 2.90-24.61; I^2=0% (two studies – benefit to mother)), no difference in uptake was seen when general benefit was considered (OR 1.02, 95% CI 0.69-1.51; I^2=0% (two studies – general benefit)). However, perceived

benefit of vaccinations was associated with a significant increase in seasonal influenza vaccine uptake (OR 7.22, 95% CI 3.49-14.93; I^2=80% (six studies – general benefit)).[36]

Access and or contextual factors

In a systematic review and meta-analysis of 34 studies on uptake of seasonal influenza vaccination by community dwelling adults aged 65 years or older, Okoli et al. reported that living alone was associated with a decrease in vaccination uptake in Europe (OR 0.70, 95% CI 0.51-0.96; I^2=69(three studies)).[38] In a review of the evidence for increasing seasonal influenza vaccination uptake in children, conducted by NICE in the UK, access was noted as both a barrier and facilitator. It was a barrier in that parents reported being told by their healthcare provider that supply of vaccinations was limited. Moreover, parents reported having to take time off work as a reason why their child was not vaccinated. On the contrary, some parents reported that having multiple or opportunistic access to vaccination clinics would help ensure their child was vaccinated;[45] as would mandatory vaccinations in schools.

Perceived lack of access to vaccination (for pandemic and or seasonal influenza) was cited, by healthcare workers and pregnant women, as a barrier in the reviews by Dini et al.[20] and Kilich et al.,[36] respectively. The latter study, by Kilich et al., also reported that lack of time, vaccine availability, cost and the logistics of getting vaccinated were barriers to vaccination uptake in pregnant women.[36] Similarly a review by NICE in the UK noted that "accessibility is an important factor in improving the likelihood of vaccination uptake and avoidance of missed vaccination opportunities".[10] In another review by NICE, focused on increasing vaccination uptake in healthcare workers, it was noted that mandatory vaccination of healthcare staff would result in feelings of anger, disempowerment and loss of autonomy.[46]

Psychological and or internal factors

The impact of psychological and internal factors on vaccination uptake is both varied and complex. In the review by Borthwick et al., unvaccinated participants (adults aged 16 years and older with a high-risk physical health condition), were more likely to suggest that internal barriers such as lack of motivation may affect their behaviour towards uptake of seasonal influenza vaccination.[35] On the other hand, participants were more likely to intend to receive the vaccine when they had been prompted to actively plan when and where they would receive it. However, this had no significant effect on subsequent behaviour.[35] Borthwick et al., included a study on uptake of influenza vaccination among adults in Thailand who are at high-risk.[47] They reported that higher self-efficacy in one's ability to arrange a time and transport to receive the vaccine increased the likelihood of carrying out the

behaviour (p=0.016); self-efficacy as "an individual's belief in his or her capacity to execute behaviours necessary to produce specific performance attainments".[48]

Another qualitative study, included in the review by Borthwick et al., was a study by Cheung and Mak,[49] that aimed to investigate the relationship between psychological flexibility and health perceptions to predict seasonal influenza vaccination uptake. Psychological flexibility is 'the ability to stay in contact with the present moment regardless of unpleasant thoughts, feelings, and bodily sensations, while choosing one's behaviours based on the situation and personal values'.[50] They found that individuals with chronic respiratory disease who reported higher levels of psychological flexibility were more likely to receive seasonal influenza vaccination.[49] The authors noted that higher psychological flexibility was an independent predictor of vaccination uptake in those with chronic respiratory conditions and may be associated with increased uptake of vaccinations, although there is currently insufficient evidence to support this.[49]

Other psychological and internal factors were related to an individual's mistrust towards government bodies and pharmaceutical companies. Adults with a high-risk chronic condition who were unvaccinated were more likely to hold feelings of mistrust towards these entities;[35] as were parents of children who were eligible for vaccination.[45]

In older community-dwelling adults (aged 65 years or older), poor self-assessed health was associated with increased uptake of seasonal influenza vaccinations, (OR 1.23, 95% CI 1.02–1.40; I^2=78% (nine studies)).[38] Subgroup analysis showed regional variation where poor self-assessed health was associated with a significant increase in seasonal influenza vaccination uptake in Europe (OR 1.32, 95% CI 1.07-1.63; I^2=78% (four studies)), but no association was observed in Asia (OR 1.08, 95% CI 0.66-1.77; I^2=70% (three studies)) or North America (OR 0.63, 95% CI 0.10-3.95; I^2=93% (two studies)).[38]

Psychological and internal factors were also reported in healthcare workers[20] and pregnant women.[36] For example, forgetfulness and lack of perceived behavioural control were barriers to vaccination uptake in healthcare workers.[20] In pregnant women, perceived rumours or myths about vaccination were barriers to vaccination uptake;[36] yet a facilitator to increased vaccination uptake within this same group was feeling fear or regret over not getting vaccinated.[36]

Perceived risks and or susceptibility to influenza

Low risk perception, belief that influenza is a mild disease and apathy towards influenza in general were barriers to vaccination uptake (seasonal or pandemic) in healthcare workers.[20, 27] Conversely, perceived increased susceptibility to, and

severity of influenza in the same population group were associated with increased willingness and intention to vaccinate oneself.[20, 46]

In pregnant women, perceived susceptibility to seasonal influenza and disease severity were reported as barriers to vaccination uptake, although this finding was non-significant.[36] On the contrary, the same factors were significantly associated with an increased uptake of seasonal influenza vaccinations, (OR 1.76, 95% CI 1.26-2.47; I^2=35% (five studies – susceptibility while pregnant) and OR 3.70, 95% CI 1.37-9.94; I^2=78% (three studies – disease harm)). Perceived risk of harm from pandemic influenza was also noted to be associated with a significant increase in vaccine uptake (OR 2.91, 95% CI 2.02-4.18; I^2=0% (2 studies – risk of hospitalisation)).[36] Similar findings were reported in the general population,[10, 35] and in paediatric populations.[45]

Perceived responsibility

While some healthcare professionals reported a sense of responsibility to prevent influenza, a need to protect oneself and others from influenza, and a belief that influenza prevention was important,[46] others reported a lack of professional or ethical obligation to get vaccinated.[27] Similarly, the perceived benefit for the baby was associated with increased uptake of seasonal influenza vaccinations in pregnant women (OR 1.74, 95% CI 1.18-2.57; I^2=44% (seven studies – benefit to baby).[36]

Social influences

Positive and negative influences (socially and professionally) were reported as both barriers and facilitators to vaccination uptake (both seasonal and pandemic). In a systematic review of healthcare workers attitudes towards vaccination, low social pressure (either perceived or real) was a barrier to vaccination uptake. On the contrary, the same systematic review reported that receiving recommendations from respected colleagues to vaccinate was associated with increased vaccination uptake.[20] Another systematic review by Jenkin et al., also in healthcare workers, reported that the success of a vaccination programme may be influenced by the relationships between healthcare workers and the organisation within which they work.[27] Positive influences from health providers increased vaccination uptake in adults with a high-risk physical health condition,[35] in paediatric populations[45] and in pregnant women.[36] In this latter systematic review, uptake of vaccinations for pandemic influenza (OR 6.76, 95% CI 3.12-14.64; I^2=92% (five studies)) and seasonal influenza (OR 12.02, 95% CI 6.80-21.44; I^2=92% (21 studies) by pregnant women was significantly increased if recommended by a healthcare professional.[36] The same study also reported that family, friends and media can have both a positive or negative influence on vaccination uptake.[36]

Past behaviours and or experiences

Both previous experience of seasonal influenza and vaccination for seasonal influenza in the past year were associated with higher ratings of perceived vaccine benefits in adults with a high-risk physical condition;[35] this finding was also reported in healthcare professionals.[20] Additionally, not having had influenza (seasonal or pandemic) or vaccinations for the same previously was a barrier to vaccination uptake in this population group.[20] However, in a review by NICE, focused on healthcare workers, negative experiences of patients who had recently been vaccinated were barriers to seasonal influenza vaccination uptake in healthcare workers.[46] In pregnant women, Kilich et al. reported that participants' previous experiences with vaccinations in pregnancy was significantly associated with increased uptake of pandemic influenza vaccines (OR 9.12, 95% CI 1.99-41.76; I^2=83% (two studies)). Moreover, participants' previous experiences with vaccinations in general was significantly associated with increased uptake of seasonal influenza vaccines (OR 3.78, 95% CI 2.49-5.73; I^2=63% (10 studies)) and pandemic influenza vaccinations (OR 5.49, 95% CI 2.44-12.37; I^2=88% (three studies)).

Knowledge

Borthwick et al. noted that knowledge of the requirement to be vaccinated for seasonal influenza each year was associated with both vaccination uptake in the past and future intentions to be vaccinated. The authors also noted that provision of information is likely to be the most important intervention for individuals who are considering vaccination for the first time.[35] Similarly, in a systematic review of vaccination uptake in clinical risk groups, conducted by NICE, the importance of information provision by healthcare professionals was cited as an important facilitator to vaccination uptake;[44] similar findings were reported in paediatric populations.[45] The authors also highlighted that providers need to understand the risks, benefits and misconceptions about seasonal influenza vaccinations if they are to overcome these barriers. In doing so, they also need to understand the information preferences of patients so that the necessary information is communicated effectively.[44]

In healthcare workers, the possession of influenza specific knowledge was both a barrier and facilitator to uptake of influenza (both seasonal and pandemic) vaccination; it was noted that receipt of information from respected healthcare workers was particularly influential in increasing vaccination uptake.[20] Moreover, education and awareness raising may be an important factor in improving acceptability and uptake of influenza vaccination offers in healthcare workers.[46] In pregnancy, general knowledge of influenza in pregnancy, (including knowledge about the availability of vaccines) was associated with a significant increase in

uptake of pandemic influenza vaccinations (OR 1.50, 95% CI 1.06-2.12; I^2=70% (two studies – general knowledge)) and seasonal influenza vaccinations (OR 2.94, 95% CI 1.01-8.58; I^2=94% (three studies – felt informed) to OR 5.68, 95% CI 1.53-21.33; I^2=84% (four studies – general knowledge)).[36] Additionally, knowledge of policy guidelines or awareness of general recommendations to be vaccinated were associated with a significant increase in seasonal influenza vaccinations (OR 3.68, 95% CI 2.12-6.38; I^2=28% (four studies)).[36]

Socio-demographic factors

Results for socio-demographic factors are mixed. For example, in healthcare professionals, Dini et al. reported that older age was both a barrier and facilitator to influenza vaccination (seasonal and pandemic) uptake depending on the primary study.[20] The same review also reported that being a medical doctor and being male were independent facilitators for vaccination uptake; being a nurse correlated with decreased intentions to vaccinate oneself.[20]

Two systematic reviews and meta-analyses were included from Okoli et al..[37, 38] One included 34 studies conducted in Spain, the US, Hong Kong, Italy, South Korea, the UK, Thailand, Canada, Israel, Taiwan, France, Australia, Japan, Switzerland, Singapore, Serbia, Europe (involving 11 countries) and Ireland (both Ireland and Northern Ireland); published up until 7 January 2020. The population of interest was community-dwelling adults aged 65 years and older.[38]

The review reported that, compared with being white, being non-white was associated with a decrease in seasonal influenza vaccination uptake (OR 0.77, 95% CI 0.67-0.88; I^2=85% (10 studies)). Subgroup analysis indicated that being African American or Hispanic, was associated with a greater reduction in uptake for both (OR 0.69 95% CI 0.51-0.93; I^2=87% and OR 0.69, 95% CI 0.69, 0.53-0.89; I^2=64%, respectively); however, the results should be interpreted with caution given the substantial heterogeneity between the pooled results.[38] In contrast to these findings, the following were all significantly associated with increased seasonal influenza vaccination uptake:

- being older (OR 1.52, 95% CI 1.38–1.67 (21 studies))
- white (OR 1.30, 95% CI 1.14–1.49 (10 studies))
- married (OR 1.23, 95% CI 1.17–1.28 (9 studies))
- of a higher social class (OR 1.20, 95% CI 1.06–1.36 (two studies))
- having a higher education (OR 1.12, 95% CI 1.04–1.21 (14 studies))

- having a higher household income (OR 1.11, 95% CI 1.05–1.18 (eight studies))
- having a family doctor (OR 2.94, 95% CI 1.79– 4.76 (two studies))
- having health insurance (OR 1.58, 95% CI 1.13–2.21 (six studies)).[38]

Being older (OR 1.26, 95% CI 1.11–1.44 (two studies)) was also associated with annual vaccination uptake. Overall, being female was not significantly associated with increased uptake of seasonal influenza vaccination (with evidence of publication bias noted, p=0.027), although there was evidence of regional variation; being female in Asia was associated with a 23% increase in uptake, whereas a 7% decrease in uptake was found in Europe (again with evidence of publication bias, p=0.036), no association was found in North America. Overall, being married was associated with a 23% (17-28%) increase in seasonal influenza vaccination uptake. Again there was evidence of regional variation with being married associated with an increase in uptake in Europe (OR 1.23, 95% CI 1.16-1.30; I^2=15% (five studies – one of which was in Ireland, although the findings were not significant)), but a non-significant increase in Asia (OR 1.59, 95% CI 0.91-2.78; I^2=0% (two studies)) and North America (OR 1.10, 95% CI 0.89-1.37; I^2=0% (two studies)). Higher education was associated with an increase in uptake in North America (OR 1.22 95% CI 1.02-1.47; I^2=83% (four studies), (with high heterogeneity), and a non-significant increase in seasonal influenza vaccination uptake in Asia and Europe.[38]

The second systematic review by Okoli et al. included 10 studies published up until 13 February 2020; the population of interest was cancer patients.[37] This review reported that overall, being older (OR 2.23, 95% CI 1.46-3.38; I^2=92.3% (six studies)), having had a medical check-up in the past year (OR 1.75, 95% CI 1.65-1.86; I^2=0% (two studies)), and having health insurance (OR 1.39, 95% CI 1.13-1.72; I^2=21.8% (three studies)) were associated with increased seasonal influenza vaccination uptake.[37] Compared with being African-American, being white was also associated with increased seasonal influenza vaccination uptake (OR 1.79, 95% CI 1.47-2.13; I^2=10.7% (three studies)). No associations for marital status or income were reported.[37]

Health and or health behaviours

Like other factors identified above, health and health behaviours (for example, smoking, consumption of alcohol) were both barriers and facilitators to influenza vaccination uptake. Pooled analysis of data from community-dwelling adults aged 65 years or older in Europe showed that smoking was generally associated with a non-significant decrease in seasonal influenza vaccination uptake (OR 0.76, 95% CI 0.58-1.00; I^2=86% (three studies)).[38] Conversely, being a non-smoker (OR 1.28, 95%

CI 1.11–1.47 (seven studies)) and having a chronic illness (OR 1.53, 95% CI 1.44–1.63 (16 studies)) were associated with a significant increase in seasonal influenza vaccination uptake. This review also looked at alcohol consumption. In Europe, a non-significant increase in seasonal influenza vaccination uptake was reported for regular compared with irregular or non-alcohol drinkers.[38] In the other review by Okoli et al., there were no associations for alcohol consumption. However, being a non-smoker (OR 1.43, 95% CI 1.32-1.51; I^2=0% (four studies)) and having a chronic illness (OR 1.18, 95% CI 1.07-1.29; I^2=15.7% (five studies)) were associated with increased uptake of seasonal influenza vaccinations.[37]

The presence of chronic conditions was both a barrier and facilitator in healthcare workers;[20] whereas in pregnant women statements about chronic conditions and health status were facilitators for uptake of seasonal or pandemic influenza vaccinations.[36] Cognitive impairment was associated with a non-significant decrease in seasonal influenza vaccine uptake in community-dwelling adults aged 65 years or older.[38] However, when looking at the results for Europe alone, there was a significant decrease in uptake of seasonal influenza vaccinations for those with cognitive impairment in Europe (OR 0.68 95% CI 0.59-0.78; I^2=0% (two studies)).[38]

RQ2: What population-based intervention measures increase influenza vaccination uptake rates?

Database searches, in addition to searches of international public health agencies, retrieved 21 reviews that investigated the effect of interventions to improve Influenza vaccine uptake rates.[2, 7, 11, 13, 18, 19, 33, 40-43, 51-60] Following AMSTAR-2 quality appraisal of seven critical domains,[1] seven reviews were rated as high quality,[40-42, 51, 53, 54, 56] four were rated low quality,[2, 11, 52, 55] and ten were rated critically low quality reviews (the results of which were not included in this assessment).[7, 13, 18, 19, 33, 43, 57-60] Due to the abundance of high quality reviews, the narrative discussion and conclusions of this review were informed by the high quality studies only. Results of the seven high quality reviews are presented below (and Appendix 2). The characteristics and results of studies of low quality are provided in Appendix 2 and the citations of critically low studies are listed in Appendix 3.

Each high quality systematic review investigated the effects of interventions in distinct population groups: older adults (≥60 years),[56] individuals with underlying conditions and pregnant women,[40] healthcare workers,[40, 54] general paediatric and adult populations,[41, 53] and adolescents.[51] Three were undertaken within the Cochrane collaboration,[51, 53, 56] three were undertaken to inform NICE (National Institute for Health and Care Excellence, UK) guidelines[40, 41] and one was undertaken to inform WHO (World Health Organization) guidelines. One review conducted by NICE[40] captured all studies that were included in two reviews that

were deemed "low quality".[2, 11] One study included pandemic and seasonal influenza vaccines,[54] three specifically excluded pandemic vaccines[40, 41] and the remainder did not specify which type of influenza vaccine was included.[51, 53, 56] One study included pandemic and seasonal influenza vaccines,[54] three specifically excluded pandemic vaccines[40, 41] and the remainder did not specify which type of influenza vaccine was included. [51, 53, 56]

Table 4 provides summary characteristics of each study by population.

Table 4 Summary of study characteristics (systematic reviews appraised as high quality, n=7)

Population group	Evidence retrieved	Interventions assessed*
Older adults (≥60 years)	Thomas 2018[56]: 61 primary studies, of which 36 were RCTs and 25 were cluster-randomised trials	1. increasing community demand 2. enhancing access 3. provider or system based interventions 4. societal interventions
Patients with underlying conditions and pregnant women	NICE 2018a[40]: 19 primary studies (13 RCTs and 6 quasi-experimental studies) and 3 systematic reviews of clinical effectiveness. Risk groups included: 1. Patients with underlying disease, aged 6 months to 64 years (chronic respiratory disease, chronic heart disease, chronic kidney disease, chronic liver disease, chronic neurological disease, diabetes, immunosuppression, asplenia or dysfunction of the spleen, morbid obesity) 2. Pregnant women	1. education 2. message framing 3. access 4. reminders (written and call-recall/telephone) 5. SMS messages 6. provider prompts 7. audit and feedback 8. provider incentives 9. multicomponent interventions
Healthcare workers	Jenkin 2019[54]: 52 primary studies, of which 11 RCTs relevant to this review	1. mandatory vaccination 2. provide free and easy access to vaccine 3. behaviour change components (reminders, incentives, education) 4. opt-out programmes 5. multicomponent interventions
	NICE 2018b[40]: 27 primary studies and 4 systematic reviews	1. education 2. national campaigns 3. Planning guides 4. mandatory vaccination policy

		5. declination policy (written refusal statements along with reasons why) 6. access 7. incentives 8. component of interventions 9. multicomponent interventions
General population (adults, adolescents, children)	Jacobson Vann 2018[53]: 75 primary studies, of which 29 relevant to this review: (n=5 on children, n=24 on adults)	Patient reminder (for example letter, postcard text message, auto-diallers, combination approach) or recall interventions
	NICE 2018c[41]: 14 studies in children (RCTs, NRSIs or observational studies)	1. education 2. access 3. SMS messages 4. provider prompts 5. multicomponent interventions
	Abdullahi 2018[51]: 16 studies in adolescents, of which 2 RCTs relevant to this review	Provider prompts (parents as participants in one RCT, health providers as participants in one RCT).

*In each case the main categories of interventions for which evidence was found are presented here. The exhaustive list of interventions for which the review authors searched for can be found in the respective protocols for these individual systematic reviews.
Key: NICE - National Institute for Health and Care Excellence; RCT – randomised controlled trial; NRSI – non-randomised studies of interventions; SMS – Short Message Service.

The following sections present the findings of high quality reviews by population groups: older adults (≥60 years of age), individuals with underlying medical conditions (adults and children), pregnant women, healthcare workers and general adult/adolescent/child populations.

1. Older adults individuals (≥60 years)

One high-quality review investigated interventions to increase influenza vaccination uptake in older adults (≥60 years).[56] This Cochrane review included 61 randomised controlled trials (RCTs), encompassing over one million participants. All included studies enrolled participants living in the community in high-income countries.

Four interventions were assessed: increasing community demand, enhancing access, provider or system-based interventions and societal interventions. The following sections, grouped by intervention, summarise the findings of their assessment.

Increasing community demand (12 strategies, 41 trials, 53 study arms, 767,460 participants)

One effective intervention relating to increasing community demand could be meta-analysed: client reminders or recalls by letter plus leaflet or postcard compared with client reminders only (odds ratio [OR] 1.11, 95% CI 1.07 to 1.15; 3 studies; 64,200 participants). Effective interventions tested by single studies were: patient outreach by retired teachers (OR 3.33, 95% CI 1.79 to 6.22, 193 participants); invitations by clinic receptionists (OR 2.72, 95% CI 1.55 to 4.76, 243 participants); nurses or pharmacists educating and nurses vaccinating patients compared with nurses educating patients (OR 152.95, 95% CI 9.39 to 2490.67, 485 participants); medical students counselling patients (OR 1.62, 95% CI 1.11 to 2.35, 529 participants); and multiple recall questionnaires (OR 1.13, 95% CI 1.03 to 1.24, 13,809 participants).

Many interventions could not be meta-analysed due to significant heterogeneity. Seventeen studies tested simple reminders (11 individual trials reported that the intervention was effective); 16 tested personalised reminders (12 individual trials reported that the intervention was successful); two investigated customised compared to form letters (both trials reported that the intervention was successful); and four studies examined the impact of health risk appraisals (all four trials reported that the intervention was successful).

Enhancing vaccination access (6 strategies, 8 trials, 10 arms, 9,353 participants)

A meta-analysis of the results of two studies of home visits found that the intervention was effective (OR 1.30, 95% CI 1.05 to 1.61). A meta-analysis of the

results of two studies that tested free vaccine compared with patient payment for vaccine found the intervention was successful (OR 2.36, 95% CI 1.98 to 2.82). The results of two studies of home visits by nurses plus a physician care plan could not be meta-analysed, however both were individually effective. The results of two studies of free vaccine compared with no intervention were also not meta-analysed but were individually effective. One study of group visits (visits by groups of participants to a physician or nurse (OR 27.2, 95% CI 1.60 to 463.3) was effective, and one study of home visits compared with safety interventions was not.

Provider- or system-based interventions (11 strategies, 15 trials, 17 arms, 278,524 participants)

Only one intervention that focussed on payments to physicians could be meta-analysed (OR 2.22, 95% CI 1.77 to 2.77). Successful interventions tested by individual studies were: reminding physicians to vaccinate all patients (OR 2.47, 95% CI 1.53 to 3.99); posters in clinics presenting vaccination rates and encouraging competition between doctors (OR 2.03, 95% CI 1.86 to 2.22); and chart reviews and benchmarking to the rates achieved by the top 10% of physicians (OR 3.43, 95% CI 2.37 to 4.97).

Four studies that looked at physician reminders were not meta-analysed, but three of these individual studies reported that the intervention was successful. Three studies of facilitator encouragement of vaccination were also not meta-analysed, but two individual studies reported that the intervention was successful. Interventions that were not effective were: comparing letters on discharge from hospital to letters to general practitioners; posters plus postcards versus posters alone; educational reminders, academic detailing, and peer comparisons compared to mailed educational materials; educational outreach plus feedback to teams versus written feedback; and an intervention to increase staff vaccination rates.

Interventions at the societal level

No studies were retrieved that reported on societal-level interventions or national (for example mass media) campaigns.

Across all interventions, no studies measured if there was a reduction in illness or hospital admissions in this review.

2. Individuals with underlying medical conditions and pregnant women

Only one high-quality systematic review investigated interventions targeted to individuals with underlying conditions and pregnant women. This systematic review, conducted by NICE in 2018,[40] was a comprehensive review that identified 19 primary studies (13 RCTs and six quasi-experimental studies) and three systematic

reviews. In the assessment of adults and children with underlying conditions, participants aged six months to 64 years were included. In the assessment of pregnant women, participants with and without co-morbidities were included. These groups were identified as high clinical risk according to NHS ("green book"[61]) criteria.

Underlying conditions included the following:

- chronic respiratory disease
- chronic heart disease
- chronic kidney disease
- chronic liver disease
- chronic neurological disease
- diabetes
- immunosuppression
- asplenia or dysfunction of the spleen
- morbid obesity.

Within their systematic review, three specific research questions were relevant to our review:

- What interventions to promote information about, and acceptability of, influenza vaccination are the most effective for increasing acceptability and uptake of seasonal influenza vaccination among clinical risk groups?
- What interventions to increase access to seasonal influenza vaccine are the most effective in increasing uptake of seasonal influenza vaccine among clinical risk groups?
- Which provider-based systems and processes for identifying, contacting and inviting clinical risk groups for seasonal influenza vaccination are most effective in increasing uptake of among this population group?

Authors identified a range of interventions, including the following:

- education
- message framing
- access
- reminders (written and call-recall/telephone)
- SMS messages
- provider prompts
- audit and feedback
- provider incentives
- multicomponent interventions.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used by review authors to appraise the quality of the evidence for each outcome.[1] In each case the quality of evidence relates to the certainty of the estimates. The quality of the evidence should be interpreted as follows:

- **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect
- **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
- **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
- **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

The following evidence statements, grouped by intervention, summarise the findings of the NICE assessment.

Education

Underlying conditions:

- **"Low-quality evidence** from 1 RCT of 249 participants with **COPD** found that an evidence-based patient educational manual, which included advice about flu vaccination, did not increase vaccination uptake among participants with lower or higher socioeconomic disadvantage compared to a control COPD pamphlet."
- **"Very low-quality evidence** from 2 before and after studies with a combined total of 23,207 participants showed that educational interventions for providers (with or without electronic record prompts) and for parents (contained in the asthma action plan) increased the uptake of flu vaccination in **children with asthma** (RR 1.90; 95% CI 1.43 to 2.53)."

Pregnant women:

- **"Low-quality evidence** from 1 RCT of 105 participants found that an educational video did not increase flu vaccination uptake among **pregnant women** compared to a communicable disease control hand washing video (RR 1.13; 95% CIs 0.60 to 2.14)."

- **"Very low-quality evidence** from 1 RCT and 1 before and after study with 374 participants showed that educational pamphlets, with or without a verbalised benefit statement, increased the uptake of flu vaccination in **pregnant women** compared to usual antenatal care (RR 1.96; 95% CI 1.32 to 2.91)."

Message framing

Underlying conditions:

- **"Very low-quality evidence** from 1 RCT of 292 participants with **chronic respiratory or cardiac disease**, comparing 'loss' (negatively-framed) to 'gain' (positively-framed) educational messages delivered in an information session, found no difference in flu vaccination uptake rates immediately post-intervention (RR 1.02; 95% CI 0.85 to 1.21) or after three months (RR 0.95; 95% CI 0.81 to 1.11)."

Pregnant women:

- **"Very low-quality evidence** from one RCT of 164 **pregnant women** compared single in-clinic exposure to either a 'gain' (positively-framed) or a 'loss' (negatively-framed) educational message with a control (standard) message. There was no effect of message framing on respondents' intention of getting vaccinated ('Gain' vs. control message: OR 1.25; 95% CI 0.49 to 3.25; 'Loss' vs control message: OR 0.48; 95%0.17 to 1.35)."

- **"Low quality-evidence** from one RCT with 126 participants showed that providing either gain- or loss-framed vaccine information to **pregnant women** did not increase flu vaccination uptake compared with standard vaccine information (RR 0.60; 95% CI 0.35 to 1.03)."

Access

Underlying conditions:

- **"Very low-quality evidence** from one before and after study with an unknown target population size found that providing flu vaccination in community pharmacies did not increase vaccination uptake among **eligible groups** compared with the year before the programme began (pre-intervention uptake: 60.4%. post-intervention uptake 60.5%)."

- **"Very low-quality evidence** from one before and after study with a target population of 247,641 to 269,355 adults aged **18-64 years in clinical risk groups** found that providing flu vaccination in community pharmacies did not increase uptake compared with the year before the programme began (pre-

intervention uptake: 52.8%. post-intervention uptake 51.9%; RR 0.98; 95% CI 0.98 to 0.99)."

- **"Very low-quality evidence** from one before and after study of 264 participants found that providing Saturday clinics in addition to a reminder letter sent to parents did not increase flu vaccination uptake among **children with asthma** compared with a reminder letter alone (RR 1.25; 95% CI 0.78 to 1.99)."

- **"Very low-quality evidence** from one retrospective cohort study with 5,451 participants showed that offering year-round flu vaccination appointments increased uptake among **infants and children with asthma** compared to standard appointment provision limited to flu season only (RR 1.68; 95% CI 1.38 to 2.04)."

Reminders (written and call-recall/telephone)

Underlying conditions:

- **"Moderate-quality evidence** from 2 RCTs with 20,641 participants showed that postcard reminders sent with an additional educational message or an interactive voice reminder (IVR) did not increase uptake of flu vaccination among **people with asthma or COPD** compared with usual postcard-only reminders (RR 1.00; 95% CI 0.97 to 1.03)."

- **"Low-quality evidence** from 1 RCT with 885 participants with **hypertension** found a mail reminder (a letter signed by a pharmacist and physician with additional educational information), sent with or without an additional telephone reminder (a personal call from a doctor) increased flu vaccination uptake compared with standard clinical practice (RR 1.52; 95% CI 1.24, 1.81). The magnitude of effect was greater for the mail + telephone intervention, but not significantly so (mail reminder only: RR 1.37; 95% CI 1.07 to 1.77; mail + telephone reminder: RR 1.68; 95% CI 1.31 to 2.16)."

- **"Moderate-quality evidence** from 4 RCTs and 1 quasi-experimental study with 5,006 participants showed that reminder letters to parents consistently increased uptake of flu vaccination compared to no intervention in **children in clinical risk groups** (RR 1.53; 95% CI 1.25 to 1.89)."

- **"Low-quality evidence** from 2 randomised before and after studies with 490 participants showed that telephone recall (a personal call to parents from a paediatrician) increased flu vaccination uptake among **children in clinical risk groups** compared to usual care (a standard, anonymised mail reminder) (RR 1.62; 95% CI 1.33 to 1.98)."

- **"Low-quality evidence** from 2 before and after studies with 4,491 participants found that mail reminders with or without follow-up telephone calls increased uptake of flu vaccination in **children with asthma** compared to standard practice (RR 4.49; 95% CI 3.34 to 6.04)."

- **"Moderate-quality evidence** from 1 cluster RCT with 183 participants found that personalised postcard reminders increased the uptake of flu vaccination in **people from clinical risk groups** (RR 1.96; 95% CI 1.24 to 3.10)."

- **"Low-quality evidence** from 1 RCT with 525 participants found no increase in uptake of flu vaccination among **adults in clinical risk groups** when comparing mail with telephone reminders (RR 1.05; 95% CI 0.62 to 1.77). Neither form of reminder increased uptake compared with a 'no reminder' control group (Mail vs. control: RR 2.55; 95% CI 1.00 to 6.49; telephone vs. control: RR 2.44; 95% CI 0.95 to 6.24)."

SMS messages

Underlying conditions:

- **"Moderate-quality evidence** from 1 cluster RCT with 102,257 participants showed that there was no important increase in the uptake of flu vaccination among **adult patients in clinical risk groups** who were sent a tailored SMS reminder message compared with patients in control practices that used standard flu campaigns (RR 1.03 95% CI 1.02 to 1.05)."

Pregnant women:

- **"Low-quality evidence** from 1 RCT with 3,905 **pregnant women** showed that, among women who intended to vaccinate at baseline, an SMS message with an interactive component for requesting a reminder was more effective than a 'usual' SMS (with no function to request a reminder) in promoting uptake or maintaining intention to vaccinate, but there is some uncertainty in the importance of the effect (RR 1.08; 95% CI 1.02 to 1.14). Among women who did not intend to vaccinate at baseline, an enhanced educational SMS tailored to the woman's specified reason for not wanting to vaccinate was no more effective than a general educational SMS in promoting uptake or changing their intention to vaccinate (RR 0.94; 95% CI 0.84 to 1.04)."

- **"Very low-quality evidence** from 2 RCTs with 1,357 participants found that SMS messages with educational content about the importance of flu vaccination did not increase the uptake of flu vaccination in **pregnant women** (RR 1.06; 95% CI 0.94 to 1.19)."

Provider prompts

Underlying conditions:

- **"Very low-quality evidence** from 2 before and after studies with 10,113 participants found that provider-directed prompts embedded in the electronic health records of **children from clinical risk groups** increased uptake of flu vaccination compared to pre-intervention rates (RR 1.69; 95% CI 1.26 to 2.26)."
- **"Very low-quality evidence** from 2 RCTs with 1,564 participants found that provider-directed prompts embedded in the electronic health records of **adults from clinical risk groups** did not increase uptake of flu vaccination compared with pre-intervention rates (RR 1.44; 95% CI 0.81 to 2.56). However, very low quality evidence from 2 retrospective cohort studies and 1 before and after study, with 1,487 participants, found that provider-directed prompts in the health records of adults from clinical risk groups did increase uptake of flu vaccination compared with pre-intervention rates (RR 5.70; 95% CI 1.18 to 27.53)."

Pregnant women:

- **"Very low-quality evidence** from a pooled analysis of 1 retrospective cohort study and 1 before and after study with 2624 participants found that provider-directed prompts used in antenatal clinics did not increase flu vaccination uptake in **pregnant women** compared with pre-intervention rates (RR 2.29; 95% CI 0.88 to 5.95)."

Audit and feedback

- **"Very low-quality evidence** from 1 before and after study with 39 participating practices found that practice audits increased flu vaccination uptake in people with **CHD** (mean % difference compared with pre-audit rate: 19.2%; 95% CI 14.4, 24; p<0.001) and **people with diabetes** (mean % difference: 16.9%; 95% CI 10.2 to 23.6; p<0.001). There was no significant increase in flu vaccination uptake among **post-splenectomy patients** (mean difference 6.1%; 95% CI -2.5 to 14.7; p=0.16)."

Provider incentives

Underlying conditions:

- **"Very low-quality evidence** from 1 controlled before and after study with between 8,212 and 8,403 participants (across 4 flu seasons) found that increasing pay-for-performance targets increased practices' mean reported achievement of flu vaccination for eligible **CHD patients** (patients with the

condition and not exception-reported) compared with control conditions **of COPD, diabetes mellitus and stroke**. The mean reported achievement co-efficient increased from 0.94 (95% CI 0.83 to 1.05) to 1.19 (95% CI 1.06 to 1.31) across the four season study."

- **"Very low-quality evidence** from 1 before and after study found that removing pay-for-performance targets for adults with **asthma** did not significantly affect flu vaccination uptake rates. Percentage achievement rates over 8 years remained relatively stable, ranging between 78% and 79%. The practice adjusted mean difference between 2005/06 season (pre-incentive change) and 2011/12 season (post-incentive change) was -0.07% (-1.01 to -0.39)."

Multicomponent (/multifaceted) interventions

Underlying conditions:

- **"Low-quality evidence** from 1 cluster RCT with 26,408 participants found that a multicomponent pharmacy-based intervention did not increase flu vaccination uptake in people with **chronic conditions** compared with unspecified control (RR 0.75; 95% CI 0.74 to 0.77)."

- **"Low-quality evidence** from 1 cluster RCT with 10,703 participants showed that a multi-component intervention for general practice, comprising educational outreach, audit and feedback may increase vaccination uptake across targeted conditions (**people with CHD, diabetes or post-splenectomy**) compared with no intervention (RR 1.06; 95% CI 1.03 to 1.08). Increased uptake was significantly greater for post-splenectomy patients (RR 1.37; 95% CI 1.12 to 1.67) than for people with CHD (RR 1.05; 95% CI 1.02 to 1.08) or diabetes (RR 1.06; 95% CI 1.02 to 1.10)."

- **"Low-quality evidence** from 1 before and after study with 1,128 participants found that a multicomponent intervention incorporating parent and provider education and enhanced clinical informatics increased flu vaccination uptake among **immunocompromised children** compared with pre-intervention rates (RR 1.45; 95% CI 1.30 to 1.63 for 2 vaccinations; RR 1.41 95% CI 1.29 to 1.55 for 1 vaccination). A sub-group analysis found low and very low quality evidence that a clinically important increase in uptake was achieved in children undergoing treatment for **leukaemia/lymphoma** (RR 1.23 95% CI 1.10 to 1.39), **brain tumour** (RR 1.53; 95% CI 1.23 to 1.90) and **solid tumours** (RR 1.56; 95% CI 1.29 to 1.88), but not among children undergoing **stem cell transplant** (RR 1.33; 95% CI 0.97 to 1.89)."

- **"Low-quality evidence** from 1 cluster RCT with 6,460 participants found that a multicomponent educational intervention comprising educational seminars, assistance, action plan review and monthly support may increase flu vaccination uptake among **people with end-stage renal disease** compared with standard practice, but with a low level of certainty in the effect (adjusted mean difference in uptake: 8.86%; 95% CI 0.36% to 17.37%; p=0.04)."

- **"Moderate-quality evidence** from 1 non-randomised control trial with 18,836 participants found that multicomponent interventions, comprising increased access, provider prompts and telephone recall, increased uptake of flu vaccination among **children from clinical risk groups** compared with no intervention (RR 1.36; 95% CI 1.32 to 1.40)."

- **"Moderate-quality evidence** from 1 cluster RCT with 423 participants found that multicomponent interventions that included increasing demand from eligible groups and incorporated provider prompt interventions increased uptake of flu vaccination among **adults in clinical risk groups** compared with provider prompts alone (RR 1.62; 95% CI 1.26 to 2.09)."

- **"Very low-quality evidence** from 1 retrospective cohort and 1 controlled before and after study with 550,254 participants found that multicomponent interventions that included increasing demand from eligible groups and incorporated provider interventions did not increase uptake of flu vaccination among **adults in clinical risk groups** compared with usual care (RR 1.43; 95% CI 0.73 to 2.82)."

- **"Moderate-quality evidence** from 5 RCTs with 27,628 participants found that multicomponent interventions, including improving access and increasing demand from **clinical risk groups** with reminders, education and incentives, increased uptake of flu vaccination compared with usual care (access and reduction of out of pocket expenses alone) among people from clinical risk groups (RR 1.40; 95% CI 1.22 to 1.62)."

- **"Very low-quality evidence** from 1 non-randomised control trial and 1 cluster randomised control trial with 2,291 participants found that multicomponent interventions, including increasing access, improving demand from **eligible groups** and incorporating provider interventions, did not increase uptake of flu vaccination among people from clinical risk groups compared to usual care (RR 1.21; 95% CI 0.80 to 1.82)."

- **"Low-quality evidence** from 1 before and after study with 1,000 participants found that a multicomponent intervention that included increasing access, improving demand from **eligible groups** and incorporated provider

interventions, was significantly less effective at increasing uptake of flu vaccination among people in clinical risk groups 10 years post-intervention compared with 1 year post-intervention (RR 0.75; 95% CI 0.68 to 0.83). However, it remained more effective compared with uptake rates prior to the start of the intervention (RR 1.75; 95% CI 1.52 to 2.01)."

Pregnant women:

- **"Very low-quality evidence** from 1 cluster RCT of 300 participants showed that a multicomponent educational intervention, including recommendation from the obstetrician/gynaecologist, reminder posters, education brochure, flu champion lapel buttons and an iPad-based component did not significantly increase uptake of flu vaccination among **pregnant women** (RR 1.47; 95% CI 0.71 to 3.07). Only recollection of the iPad component was associated with increased vaccination but the level of uncertainty associated with this effect was large (RR 3.17; 95% CI 1.07 to 9.44)."

- **"Low-quality evidence** from 1 retrospective cohort study over 6 years of repeated measures with 12,488 participants (approx. 2,000 per annum) showed that an intervention combining education, standing order for nurse vaccination and feedback to providers increased uptake of flu vaccination in **pregnant women** in year 1 (RR 7.60 [6.50 to 8.88]) which increased further in year 2 (RR 11.29 [9.75 to 13.08]) compared to routine antenatal care delivered before the intervention, this magnitude of change was maintained in subsequent years with no significant change in effect after year 2 (RR14.85 [12.89 to 17.71] in year 6 compared to pre-intervention uptake)."

- **"Very low-quality evidence** from 1 before and after study with 439 participants found that a multicomponent intervention, including improved access, provider and patient education and provider prompts, increased uptake of flu vaccination compared with usual antenatal care in **pregnant women**, but there is some uncertainty in the importance of the effect (RR 1.33; 95% CI 1.02 to 1.77)."

- **"Very low-quality evidence** from 1 retrospective cohort with 602 participants found that a multicomponent intervention, incorporating education, access and nurse standing orders to vaccinate, did not increase uptake of flu vaccination in **pregnant women** compared with usual antenatal care (RR 10.54; 95% CI 0.77 to 143.80)."

- **"Very low-quality evidence** from 1 before and after study with 248 participants found that a multicomponent intervention, incorporating provider and patient education, provider prompts, participant reminders and improved

access, increased flu vaccination uptake in **pregnant women** compared with usual antenatal care (RR 1.63; 1.31 to 2.04)."

3. Healthcare workers

Two high-quality systematic reviews were retrieved that investigated interventions to increase uptake in healthcare workers.[40, 54]

The first systematic review by Jenkin et al. identified a number of high quality RCTs and systematic reviews addressing interventions that increase uptake of influenza vaccination in healthcare workers, the findings of which were used to inform WHO guidelines.[54] Authors found that with the exception of mandatory vaccination, no single intervention component rapidly and substantially raised influenza vaccination rates.[62] However, multicomponent approaches (sustained over time) may increase uptake by over 90%.[63] One overview of reviews identified by Jenkin et al. evaluated seven systematic reviews which together evaluated strategies to increase uptake in over 200,000 healthcare workers.[64] Successful alternatives to mandatory vaccination included 'soft-mandates', such as unvaccinated healthcare workers wearing surgical masks during influenza seasons, declinations statements (e.g. written refusals and providing reasons why) or 'opt-outs', and multicomponent programmes that take into consideration local contexts and include incentives, education, advertising, and easy vaccine access. One meta-regression found that the single most successful strategies after mandatory vaccination were 'soft' mandate strategies and a policy of excluding non-vaccinated healthcare workers from working with highly vulnerable patients.[59]

The second systematic review, conducted by NICE in 2018,[40] also identified a number of high quality studies and systematic reviews, with significant overlap with the review by Jenkin et al. The NICE review was similarly conducted to inform vaccination policy, and GRADE methodology was used by review authors to appraise the evidence. The following evidence statements, grouped by intervention, summarise the findings of their assessment relevant to this review:

Education

- "**Very low-quality evidence** from 1 cluster randomised control trial of 2,345 HCWs found that an information session (including educational slide show, videos and summary leaflet) did not increase flu vaccination uptake compared to a 'no additional information' control (RR 0.86; 95% CIs 0.63 to 1.17)"
- **"Moderate-quality evidence** from 1 randomised control trial of 1,200 HCW (nurses, auxiliary and technical staff) found that a questionnaire (based on QBE), delivered a few months before the study hospitals' annual flu vaccination

campaigns, increased flu vaccination uptake compared with a 'no questionnaire' control, but the importance of the effect is uncertain (RR 1.16; 95% CI 1.00 to 1.33)"

- "**Very low-quality evidence** from 8 before and after studies with 21,543 participants indicates that educational interventions, including educational materials, sessions and reminders increase flu vaccination uptake among HCWs compared with pre-intervention rates (RR 1.15; 95% CI 1.10 to 1.21)"

- "**Low-to-moderate-quality evidence** from 1 RCT with 800 participants found that educational materials alone (RR1.03; 95% CIs 0.80 to 1.31), incentives alone (RR 1.11; 95% CIs 0.87 to 1.41), or both combined (RR 1.17; 95% CIs 0.93 to 1.48) did not increase flu vaccination in HCWs compared with controls who received no intervention but were exposed to usual hospital vaccination publicity"

- "**Moderate-quality evidence** from 2 cluster RCTs and 2 randomised controlled trials, with a total of 6,085 participants, found that educational interventions (including learning and promotional materials, awareness raising by a nurse, letters and personalised phone calls) increased flu vaccination uptake among HCWs compared with no intervention or usual flu campaigns (RR 1.36; 95% CI 1.23 to 1.50)." Additionally, the effect of the intervention varied by setting in subgroup analysis.

Education and incentives

- "**Very low-quality evidence** from 1 controlled before and after study and 1 RCT with a total of 15,628 participants indicates that educational campaigns and incentives including gift cards, entry into a lottery and a party did not increase uptake of flu vaccination among HCWs compared with pre-intervention or control group uptake (RR 1.03; 95% CI 0.98 to 1.09)." A subgroup analysis found very low and low quality evidence that vaccination uptake increased, compared with pre-intervention rates, in HCWs with patient contact.

National campaigns

- "**Very low-quality evidence** from 1 before and after study with 86,765 participants found a national campaign to increase flu vaccination uptake among hospital-based HCWs increased overall uptake by 14.6% compared with baseline (mean pre-intervention rate: 1.7% vs. mean post-intervention uptake: 16.4%)"

Planning guides

- **"Moderate-quality evidence** from 1 cluster randomised control trial with 8,921 participants found that a guide to planning, implementing and evaluating flu vaccination campaigns with support provided (including a facilitated training workshop on how to use the guide) significantly increased flu vaccination uptake among HCWs in hospitals, continuing care and nursing homes compared with no-intervention controls who ran campaigns without the guide or additional support"

Mandatory vaccination policy

- **"Low-quality evidence** from 1 before and after study with 6,957 participants found that mandatory vaccination, with a declination and mask wearing policy and alert system (automated e-mail sent to HCWs not currently compliant) increased year-on-year flu vaccination uptake among HCWs in one medical centre for 4 years following the intervention compared with pre-intervention"

- **"Very low-quality evidence** from 1 before and after study of 271 healthcare facilities indicated that a mandatory vaccination and refusal/declination with mask wearing policy + free vaccine, education and coverage reporting increased flu vaccination uptake among all employees (+17.5%), HCWs in hospitals (+14.6%) and HCWs in care homes (+16.2%) compared with pre-intervention usual care (free access and education but no mandated vaccination or declination / face-mask policy)"

- **"Very low-quality evidence** from 6 before and after studies with 105,538 participants found that mandatory flu vaccinations in healthcare settings increased flu vaccination uptake among HCWs compared with pre-intervention rates (RR 1.71; 95% CI 1.70 to 1.72)"

Declination

- **"Very low-quality evidence** from 1 randomised control trial with 122 participants found that that an opt-out strategy (with pre-booked appointments) delivered by e-mail to HCWs did not increase flu vaccination uptake compared with an opt-in e-mail (requiring an appointment to be booked) (RR 1.70; 95% CI 0.84 to 3.41)"

- **"Low-quality evidence** from 1 before and after study with 20,170 participants indicated that a change from a paper based declination form as part of the declination policy to an internet based form that included an educational intervention, reminder and incentives increased uptake of flu vaccination among HCWs (internet vs. paper-based: RR 1.99; 95% CI 1.92 to 2.07)"

Access

- **"Very low-quality evidence** from 1 before and after study with around 25,000 participants showed that adding flexible worksite delivery of free vaccinations did not increase uptake among HCWs compared with free vaccination alone (RR 0.78; 95% CI 0.76 to 0.79). However very low-quality evidence from another controlled before and after study with 5,946 participants found that flexible worksite delivery of free vaccinations in addition to educational materials and incentives did increase uptake among HCWs compared with free vaccination, education and incentives alone (RR 1.70; 95% CI 1.66 to 1.74)"

Incentives

- "**Very low-quality evidence** from 1 before and after study with 5,151 participants found that adding incentives to an existing intervention that included educational material, reminders and feedback increased uptake of flu vaccination among HCWs with direct patient care compared with uptake rates before the incentives were added, but there is uncertainty in the importance of the effect (RR 1.10; 95% CI 1.01 to 1.20)"

Component of interventions

- **"Very low-quality evidence** from a systematic review of 46 studies, using a component matrix approach, showed that the most effective intervention component for improving uptake of vaccination was hard mandated approaches (RR of remaining unvaccinated = 0.18; 95% CI: 0.08 to 0.45), followed by soft mandates such as declination statements (RR unvaccinated = 0.64; 95% CI: 0.45 to 0.92), increased awareness (RR unvaccinated = 0.83; 95% CI: 0.71 to 0.97) and increased access (RR unvaccinated = 0.88; 95% CI: 0.78 to 1.00). For incentive-based and education-based interventions, there were no significant differences compared with comparator groups in respect of HCWs remaining unvaccinated (incentive-based approaches: RR unvaccinated = 0.89; 95% CI: 0.77 to 1.03; education-based approaches: RR unvaccinated = 0.96, 95% CI: 0.84 to 1.10)

In addition, a number of multicomponent interventions were assessed, that combined two or more interventions (including those listed previously, such as multicomponent interventions incorporating education, incentives, declination, reminders and access). Many multicomponent interventions were found to increase uptake rates by a greater magnitude than single interventions. Multicomponent interventions were highly heterogeneous, and quality was low to very low.

4. General adult, adolescent and child populations

Three high quality systematic reviews were retrieved that investigated interventions targeted at general adult and child populations: one included adults and children,[53] one included children only[41] and one included adolescents.[51]

The first systematic review, conducted by Jacobson Vann et al., focussed on patient reminder and recall interventions.[53] Of 75 included primary studies, 29 were relevant to this review. Five of these assessed the effectiveness in paediatric vaccination and 24 assessed the effectiveness in adults. Relating to adults, the following meta-analyses were carried out:

- For the comparison of 'any' patient reminder or recall intervention (including any type of reminder/recall, such as letters, postcards, SMS messages, auto-dialler, telephone interventions and multicomponent interventions), a meta-analysis of 15 studies found that the intervention was effective, with a RR of 1.29 (95% CI: 1.17 to 1.43, risk difference 9%, n=59,328 participants).

- A meta-analysis of 11 studies of the intervention 'patient letter reminder or recall' was found to be effective, with a RR of 1.35, (95% CI: 1.19 to 1.52; n=44,454 participants)

- A meta-analysis of two studies of the combined intervention 'patient reminder or recall with provider reminder' also found the intervention to be effective, with a RR of 2.91 (95% CI: 2.66 to 3.18, 2 studies). However, meta-analyses of the results of studies that included the following interventions did not achieve statistical significance (likely due to smaller sample sizes): 'patient telephone reminder or recall' (RR 1.53; 95% CI: 0.73 to 3.20; 2 studies, n=1,838 participants), and 'patient postcard reminder or recall' (RR 1.15; 95% CI: 0.95 to 1.39, 3 studies, n=19,265 participants).

Relating to children, only one intervention was suitable for meta-analysis. For the intervention 'patient letter reminder or recall', the intervention was found to be effective, with a RR of 1.51 (95% CI: 1.14 to 1.99, 5 studies, n= 9265 participants).

The authors concluded that, in general, patient reminder or recall interventions probably improve receipt of adult influenza vaccinations (moderate certainty of evidence) and childhood influenza vaccinations (moderate certainty of evidence).

The second systematic review, conducted by NICE in 2018, identified 14 studies relating to increasing vaccine uptake in children and GRADE assessments were undertaken for each outcome. The following evidence statements, grouped by intervention, summarise the findings of their assessment relevant to this review.

Education

- **"Very low-quality evidence** from a pooled analysis of 1 before-and-after study and 1 nonrandomised controlled trial, with a total of 4,970 participants, showed that educational interventions increase uptake of seasonal flu vaccination compared with usual practice (RR 1.73; 95% CI 1.19 to 2.51). However, very low-quality evidence from 1 RCT with 116 participants found an educational intervention that combined risk communication and values clarification did not significantly increase uptake compared with providing standard risk information (RR: 0.86, 95% CI: 0.54 to 1.39)."

- "**Low- and very low-quality evidence** from 2 studies (1 RCT with 407 participants and 1 before and after study with 90 participants) indicates that educational interventions may increase parental intention to vaccinate. The RCT found that combining risk communication and values clarification may increase intention to vaccinate a child compared with either intervention alone, or with standard risk information. However, previous vaccination behaviour or baseline intention moderates the effect of educational interventions. The before and after study found that a computer-based educational intervention (based on 3 learning theories) increased intention to vaccinate children by 2.2%. However the magnitude of effect may have been moderated by high levels of planned vaccination at baseline (89% already planned to get their child vaccinated)"

Access

No studies were identified of interventions for increasing access to improve uptake of seasonal flu vaccination in children.

SMS messages

- "**Moderate-quality evidence** from 3 RCTs with a total of 13,533 participants showed that provider short-message service (SMS) interventions to parents increased uptake of seasonal flu vaccination among children aged 6 months to 17 years compared with usual care, but there is some uncertainty in the importance of the effect (RR 1.12, 95% 95% CI 1.04 to1.19)"

- "**Moderate-quality evidence** from 2 RCTs with a total of 3,981 participants showed that more complex multicomponent SMS interventions to parents were more effective than single component SMS in increasing uptake of seasonal flu vaccination among children aged 6 months to 17 years, but there is some uncertainty in the importance of the effect (RR 1.09, 95% CI 1.02 to 1.17). Similarly, high-quality evidence from 3 RCTs (with a total of 13,313 participants) found that SMS interventions with an educational component were more effective than usual care (a reminder to attend for flu vaccination with information on clinic times and how to book an appointment), again with some uncertainty in

the importance of the effect (RR 1.09, 95% CI 1.03 to 1.19)". Subgroup analysis found similar results when disaggregated by child's age.

Provider prompts

- "**Low-quality evidence** from 2 RCTs with 10,113 participants showed that a provider prompt intervention (using electronic medical records) activated throughout the flu season increased uptake of seasonal flu vaccination among children aged 6 months to 17 years compared with not having the prompt active, but there is some uncertainty in the importance of the effect (RR 1.03; 95% CI 1.01 to 1.06). The timing of provider prompts moderated their effect on vaccination uptake. There were no significant difference in the proportion of children who remained unvaccinated when the provider prompt was on versus off during autumn (Oct-Dec 2011; unvaccinated RR 0.99, 95% CI 0.89 to1.09). However the intervention was effective during the winter compared with no provider prompts (Jan-Feb 2012; unvaccinated RR 0.85; 95% CI 0.76 to 0.95)."

- "**Very low-quality evidence** from 1 controlled before and after study with 788 participants found that practices using a provider prompt intervention (based on academic detailing) significantly increased uptake of flu vaccination in children aged 6 months to 5 years compared with pre-intervention baseline rates (OR 1.40; 95% CI 1.04 to 1.89), while there was no significant increase in control practices (OR 1.30; 95% CI 0.93 to 1.82)."

- **"Moderate quality evidence** from a retrospective cohort study with 43,022 participants found that a hospital based provider prompt associated with the medical record significantly increased in-hospital rates of flu vaccination among inpatients aged 6 months to 17 years from 2.1% pre-intervention to 8% post-intervention (RR 3.81 95% CI 3.45 to 4.21)."

Multicomponent interventions

- **"Low-quality evidence** from 1 cluster randomised controlled trial with 41,500 participants showed that collaborative local programmes with an organisational lead and using provider-based systems significantly increased uptake of seasonal flu vaccination among children compared with usual care (RR 1.09 95% CI 1.06 to1.11). There was a 9.2% change in uptake from baseline (preintervention) in paediatric and family medicine clinics collaborating with a lead public health department, which offered joint community clinics and public health nurses to aid in delivery of flu vaccine, compared with a 3.2 % change in uptake in control group clinics (no public health involvement)."

- **"Very low-quality evidence** from a before and after study in 77 GP practices indicates that interventions to improve access to flu vaccinations by increasing the number and flexible timing of vaccination clinics, either alone or in combination with awareness-raising activities and/or SMS messaging, did not consistently increase uptake of flu vaccination among children (12/35 practices (34%) observed increased uptake; across the 35 practices, change in % uptake ranged from - 35.3% to 48.5%)."

- **"Low-quality evidence** from 1 RCT with 81,599 participants found use of a multicomponent local programme incorporating education, a vaccination champion, improved accessibility and an assigned organisational lead increased uptake of seasonal flu vaccination among children compared with usual care but with uncertainty in the importance of the effect (RR 1.23; 95%CI 1.01 to 1.50). The study found a 7.9% increase in uptake of seasonal flu vaccine in paediatric and family medicine clinics assigned to receive the intervention (a toolkit of evidence-based strategies; provider education and vaccine supply interventions) compared with 4.4 % in control group clinics (operating usual practice). No significant effect was observed in clinics with pre-intervention vaccination rates >58%."

- **"Moderate-quality evidence** from 1 cluster randomised controlled trial with 28,049 participants found that in paediatric and family medicine clinics collaborating with a lead public health department to offer joint community clinics with public health nurses to aid in delivery of flu vaccine, there were significantly fewer missed opportunities to vaccinate children against flu than in control group clinics (with no public health involvement) 2 years post-intervention (RR 0.80; 95%CI 0.78 to 0.82)."

Only one systematic review specifically included adolescents (Abdullahi et al.[51]), although other reviews relating to general paediatric/adult populations also included adolescents.[41, 53] Of 16 included studies, only two RCTs related to interventions aimed at increasing influenza vaccine uptake. Both related to provider prompts, which were found to make little or no difference compared with usual practice; the odds ratio was 0.91 (95% CI 0.61 to 1.34; meta-analysis of 2 studies, 1439 participants; moderate-certainty evidence).

Discussion

This overview of reviews sought to identify the barriers and facilitators associated with influenza vaccination, and interventions that effectively increase uptake in eligible groups. Influenza vaccination was chosen as a surrogate for COVID-19 vaccination, due to similarities in target populations (older adults, healthcare workers and individuals with underlying conditions), disease outcomes (viral pneumonia) and potential barriers to uptake (for example concerns regarding vaccine effectiveness or safety and access to the vaccination programme). Despite these potential similarities, it is not known how applicable studies on interventions to improve influenza vaccination uptake will be to COVID-19.

In 2019/2020 influenza vaccine uptake rates in Ireland, were 58.9% among those aged 65 years and older (HPSC[65]), 45.5% among healthcare workers in long-term care facilities and 58.9% in public hospitals.[66] Additionally, surveys conducted in 2017/2018 indicate that the uptake was 62% in pregnant women and 60.5% in those with underlying conditions aged between 18 and 64 in Ireland.[67]

Barriers/facilitators

This evidence summary considered data from nine studies on the barriers and facilitators to an individual's uptake of vaccination against influenza. There were three systematic reviews and meta-analyses,[36-38] one systematic review,[35] one comprehensive critical appraisal,[20] one rapid evidence appraisal[27] and one evidence review.[10] Overall, the evidence relating to barriers and facilitators to vaccination uptake can be summarised into ten themes common to both seasonal and pandemic influenza vaccinations: perceived risks and or benefits of vaccines; access and or contextual factors; psychological and or internal factors; perceived risks and or susceptibility to influenza; perceived responsibility; social influences; past behaviours and or experiences; knowledge; socio-demographic factors; and health and health behaviours. The factors influencing vaccination uptake, as identified by this review, are reflected in a report from the WHO technical advisory group on the behavioural considerations for acceptance and uptake of COVID-19 vaccines.[68] It concluded that creating an enabling environment, harnessing social influences and increasing motivation were key to increasing vaccination acceptance and uptake.

According to the results of this review, a recommendation to be vaccinated by a respected healthcare professional (that is, social influences), perceived benefits of the vaccine and susceptibility to influenza, as well as having been vaccinated previously (that is, past behaviours and or experiences) were associated with the largest reported effect sizes for increased uptake of vaccination. Perceived risks associated with vaccination, for example side effects, were associated with the largest reported effect size for decreased uptake.

Some differences were noted in terms of the barriers and facilitators identified by different population groups. In those considered to be at high-risk of complications from influenza, perceived responsibility was not found to be either a barrier or a facilitator. In other words, beliefs around protection of oneself and others, willingness to prevent influenza transmission, the importance of influenza prevention were not noted to be factors that would prevent or encourage vaccination uptake in this group. However, the absence of this finding in this evidence summary does not mean it does not exist. Factors grouped under the themes of perceived risks and or susceptibility to influenza, social influences and past behaviours and or experiences were all found to facilitators of vaccine uptake, but were not identified as barriers to uptake.

In pregnant women, socio-demographic factors did not appear to be either a barrier or a facilitator to vaccination uptake. Moreover, factors grouped under the themes of perceived responsibility, knowledge and health and health behaviours were not identified as barriers to vaccination uptake in this group. As such, pregnant women were more likely to report protection of their baby, knowledge about influenza, vaccination policy and past experiences as reasons for vaccination uptake. Under the theme of access and contextual factors, time, availability, cost and logistics of getting vaccinated were all reported to be barriers to vaccination uptake, with no facilitators identified under this theme.

In healthcare workers, factors grouped under the theme of health and health behaviours were not identified as a barrier to vaccination uptake, in fact, those with a chronic disease were more likely to report increased vaccination uptake. 'Psychological and or internal factors' as facilitators were not identified as a theme in healthcare workers. Instead this theme was a barrier in this group, as they were more likely to report that pharmaceutical companies negatively influenced their decision about vaccination uptake, forgetfulness and perceived lack of behavioural control; perceived behavioural control is defined as one's perceived ability to perform a behaviour.[69]

Interventions to increase uptake

Seven high-quality reviews were retrieved that investigated interventions to increase uptake in all populations of interest (older adults, individuals with underlying conditions, pregnant women, healthcare workers, and the general adult or paediatric population). A wide range of interventions were assessed, with significant variation in terms of the intensity of intervention used and the resources required to deliver the intervention. Interventions were delivered by a range of professionals (including nurses, doctors and administrators) and many were technology-driven (for example SMS or telephone reminders, letters and electronic health record prompts). Incentives were also assessed, in addition to mandatory vaccination, 'opt-out' and declination policies in the context of uptake among healthcare workers. Reviews

focussed on interventions were mostly (but not exclusively) delivered in primary care (community) settings. These reviews were undertaken to inform vaccination policy internationally and all were considered applicable to the Irish context.

Little data were retrieved relating to national or societal-level interventions. The review by Thomas et al.[24] did not identify any studies on societal interventions (such administrative frameworks or decisions that differ between societies or regions of societies and that affect vaccination uptake) to increase influenza vaccine uptake in older people. Only one study that used a national campaign to increase uptake in healthcare workers was identified by NICE;[40] in this study from Greece, leaflets on influenza vaccination, educational materials and information on vaccination strategies were sent to hospitals nationwide.[70] The intervention was successful, however review authors raised concerns regarding the methodological quality of this study. No review identified evidence specifically relating to mass media interventions, such as wide-scale population exposure to messages through routine use of existing media (television, radio, newspapers and online). Isolating the effect of national-level or mass media campaigns is particularly challenging, as they are rarely implemented as single interventions, and are typically subject to significant confounding (such as changes in underlying societal trends relating to vaccine awareness and acceptability).

Only one review investigated interventions in older adults, a highly vulnerable group in the context of influenza and COVID-19.[56] All trials enrolled community-dwelling participants; findings are therefore not necessarily applicable to residents of long-term care facilities. A wide variety of interventions were assessed and there was very large heterogeneity in terms of the intensity, cost and resource requirements of interventions. Although authors review found moderate-to-high certainty evidence that low- (e.g. postcards), medium- (e.g. personalised phone calls), and high-intensity (e.g. home visits or facilitators in practices) interventions are effective in increasing community demand for, and uptake of, influenza vaccination, the resource implications associated with the interventions vary. While home visits were found to be highly effective, they are likely to be more resource intensive than other interventions. On the other hand, although reminders are the least intensive intervention, wide-scale roll-out may be more feasible in the short- to medium-term. Public health professionals and policy-makers may wish to assess the local resource implications of each strategy and select those that best meet their capacity and needs. It is notable that their meta-analysis of interventions relating to payments to physicians was successful (OR 2.22, 95% CI 1.77 to 2.77), an intervention that could be investigated in the Irish context. No evidence of the effectiveness of societal-level interventions was identified.

The three systematic reviews conducted by NICE in 2018[40, 41] comprehensively reviewed the evidence across all other populations of interest: adults and children

with underlying conditions (aged 6 months to 64 years), children without underlying conditions, pregnant women (with or without co-morbidities) and healthcare workers. There was evidence that some single interventions and multicomponent interventions were effective in increasing uptake among adults and children with underlying conditions and pregnant women, but effects were inconsistent across different interventions. As a single intervention strategy, there was no evidence that reminders delivered as text messages (with or without an educational element) increased influenza vaccination uptake by a clinically important amount (>5% above control group or baseline uptake levels). However, call and recall methods using more personalised approaches (such as letters, postcards or personal telephone calls) appeared to be more effective. In terms of uptake in children without underlying conditions, there was some evidence to support educational interventions aimed at parents and provider prompts, but effects were inconsistent across studies. In terms of vaccinating healthcare workers, mandatory vaccination (with or without mask-wearing policies for those declining an influenza vaccine) was found to be the most effective intervention. However, such policies may negatively affect staff morale and undermine autonomy.

Across all three NICE reviews, the evidence was of variable quality, mostly low or very low. Downgrading was largely due to risk of bias issues and imprecision of effect estimates, or small sample sizes. In pooled analyses there was evidence of serious or very serious heterogeneity, largely explained by the lack of standardisation of interventions and comparators across studies, and differences between study populations in terms of clinical risk factors in the review on individuals with underlying conditions. Interventions were delivered in a number of health and social care settings, including schools based vaccination in the paediatric population.

Another high quality systematic review also investigated uptake in healthcare workers.[54] Similar to the NICE review, with the exception of mandatory vaccination, no single intervention was found to rapidly and substantially raise influenza vaccination rates among healthcare workers. Mandatory vaccination policies are highly effective at raising vaccine uptake rate, often raising uptake to greater than 95%. However, mandatory interventions have been debated extensively, and a range of sources have argued in favour[71] and against[72] this approach. There are legal and ethical consequences to mandated vaccines. The right to bodily integrity is enshrined in the Irish Constitution[73] and 'there may be implications – different in different cultural, ethical and legal contexts - for government liability in circumstances of adverse events to vaccines.[74]

Other successful interventions aimed at healthcare workers included 'soft-mandates', 'opt-outs' and multicomponent programmes, however it is noted that opt-out policies were not noted to be effective in the NICE review, although declination

policies were (whereby employees to submit a written statement stating that they have refused vaccination and citing their reasons). Opt-out strategies and declination policies may better respects individuals' autonomy than mandatory vaccination, although concerns remain regarding the acceptability of these interventions and the implications for staff morale.

In terms of general adult and paediatric populations (without underlying conditions), the Cochrane review by Jacobson Vann et al. found moderate-to-high certainty evidence that implementing patient reminder and recall systems improve influenza vaccine uptake (RR of 1.29, 95% CI: 1.17 to 1.43, risk difference 9%).[53] In the context of COVID-19, increasing uptake in the general public will likely be of heightened interest once higher risk groups have received vaccination. Across a range of settings, patient reminder and recall systems appear to be effective. The interventions vary greatly in terms of intensity, with likely cost and resource requirements. Therefore, different types of reminder and recall systems should be selected based on local resources and tailored to suit specific provider or practice needs. While person-to-person telephone reminders are most effective, they may also be the most costly, and have not been studied extensively in children. In the absence of a cost-effectiveness analysis, it is difficult to recommend resource-intensive interventions over less costly, yet effective, interventions. Only two studies that specifically enrolled adolescents were identified in the review by Abdullahi et al.[51] Provider prompts were not found to be effective (moderate certainty evidence), although more research is required in this area.

Limitations associated with methodology and approach

There are a number of limitations associated with this review. First, only reviews and systematic reviews were included, along with a limited search of publications from public health agencies internationally. As this evidence summary did not systematically search for primary research studies other than those cited by international organisations or those cited by included reviews, more recent primary research studies that may be of relevance, and were not featured in included reviews, will not have been included. Other limitations include the recent and restricted time period employed and the exclusion of studies that were not published in English. For these reasons, it is likely that some primary studies have been omitted that are relevant to this evidence summary. However, the restricted time period did not prevent earlier studies from being captured, as evidence by the publication dates reported in Appendix 1. Moreover, a large volume of high quality, recent systematic reviews that were retrieved, including a number of Cochrane reviews and other high quality reviews that informed guidance synthesis by the WHO and NICE (UK). Therefore, it was felt that any omission of primary studies is unlikely to change the presented findings.

Among the reviews identified, methodological quality and quality of reporting was found to be of mixed quality. As such, only 14 out of 39 identified reviews were deemed low quality or higher and eligible for data extraction; the remaining 25 reviews were deemed to be of critically low quality and not suitable to inform policy. Regardless of study quality, it is likely that the included reviews are biased both by inherent limitations and the limitation of the studies included within. For example, in the review by Dini et al.,[20] the authors note that the definition of healthcare worker was not consistent across the countries represented by their review. Often, the concept of healthcare worker varies according to jurisdictions' economic prosperity. Moreover, results were typically not disaggregated into different healthcare worker subgroups. Finally, some of the data from RQ1 was qualitative and the synthesis of such data is dependent on the skills of the researcher and more easily influenced by personal biases; for this reason it is more difficult to maintain, assess and demonstrate consistency in qualitative research. Given the time constraints associated with this evidence summary, a detailed content analysis was not possible, instead broad themes were noted and summarised.

The applicability of the evidence to the Irish context is uncertain. Identified reviews included studies from a range of populations that differed in terms of baseline influenza vaccine uptake rates, pre-existing societal knowledge and awareness and willingness to undergo vaccination. Some reviews included studies that were conducted over 30 years ago. The applicability of interventions to improve influenza vaccine uptake to COVID-19 vaccines is unknown. While influenza vaccination was chosen as a surrogate due to similarities in terms of target populations for vaccination, there are many important differences to consider. First, interventions to increase seasonal influenza vaccine uptake (the focus of most included studies) may not be applicable to pandemic viruses. Second, the morbidity and mortality, and perceived risk, associated with both viruses differ substantially. Third, societal experiences following months of public health measures aimed to contain the transmission of COVID-19 will likely impact on vaccination uptake preferences and behaviours. Finally, no pandemic in recent history has had a comparable impact on health, economic activity, travel and societal restrictions internationally.

Conclusions

In conclusion, barriers and facilitators were identified that can negatively or positively affect an individuals' uptake of vaccinations, respectively, and these can be summarised into ten themes. These themes could be further summarised into four overarching themes, namely perceived risks and or benefits, knowledge, social influences and patient-specific factors. Interventions (including multicomponent interventions) that can successfully increase the uptake of influenza vaccination across a range of eligible groups, by overcoming the barriers or promoting the facilitators, were identified. While effect sizes for many interventions were modest,

they may have a large impact at a population level. These interventions vary greatly in terms of intensity. Consideration must be given to the resource requirements and the acceptability of the intervention to the target population.

References

1. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.
2. Aigbogun NW, Hawker JI, Stewart A. Interventions to increase influenza vaccination rates in children with high-risk conditions--a systematic review. Vaccine. 2015;33(6):759-70.
3. Bults M, Beaujean DJ, Richardus JH, Voeten HA. Perceptions and behavioral responses of the general public during the 2009 influenza A (H1N1) pandemic: a systematic review. Disaster Med Public Health Prep. 2015;9(2):207-19.
4. Jarrett C, Wilson R, O'Leary M, Eckersberger E, Larson HJ, Hesitancy SWGoV. Strategies for addressing vaccine hesitancy - A systematic review. Vaccine. 2015;33(34):4180-90.
5. Carlsen B, Glenton C. The swine flu vaccine, public attitudes, and researcher interpretations: a systematic review of qualitative research. BMC Health Serv Res. 2016;16:203.
6. Corace KM, Srigley JA, Hargadon DP, Yu D, MacDonald TK, Fabrigar LR, et al. Using behavior change frameworks to improve healthcare worker influenza vaccination rates: A systematic review. Vaccine. 2016;34(28):3235-42.
7. Isenor JE, Edwards NT, Alia TA, Slayter KL, MacDougall DM, McNeil SA, et al. Impact of pharmacists as immunizers on vaccination rates: A systematic review and meta-analysis. Vaccine. 2016;34(47):5708-23.
8. Lytras T, Kopsachilis F, Mouratidou E, Papamichail D, Bonovas S. Interventions to increase seasonal influenza vaccine coverage in healthcare workers: A systematic review and meta-regression analysis. Human vaccines & immunotherapeutics. 2016;12(3):671-81.
9. Rashid H, Yin JK, Ward K, King C, Seale H, Booy R. Assessing Interventions To Improve Influenza Vaccine Uptake Among Health Care Workers. Health Aff (Millwood). 2016;35(2):284-92.
10. Smith S, Sim J, Halcomb E. Nurses' knowledge, attitudes and practices regarding influenza vaccination: an integrative review. J Clin Nurs. 2016;25(19-20):2730-44.
11. Wong VW, Lok KY, Tarrant M. Interventions to increase the uptake of seasonal influenza vaccination among pregnant women: A systematic review. Vaccine. 2016;34(1):20-32.
12. Yeung MP, Lam FL, Coker R. Factors associated with the uptake of seasonal influenza vaccination in adults: a systematic review. J Public Health (Oxf). 2016;38(4):746-53.
13. Jain A, van Hoek AJ, Boccia D, Thomas SL. Lower vaccine uptake amongst older individuals living alone: A systematic review and meta-analysis of social determinants of vaccine uptake. Vaccine. 2017;35(18):2315-28.
14. Kang GJ, Culp RK, Abbas KM. Facilitators and barriers of parental attitudes and beliefs toward school-located influenza vaccination in the United States: Systematic review. Vaccine. 2017;35(16):1987-95.

15. Karafillakis E, Larson HJ, consortium A. The benefit of the doubt or doubts over benefits? A systematic literature review of perceived risks of vaccines in European populations. Vaccine. 2017;35(37):4840-50.
16. Lorenc T, Marshall D, Wright K, Sutcliffe K, Sowden A. Seasonal influenza vaccination of healthcare workers: systematic review of qualitative evidence. BMC Health Services Research. 2017;17(1).
17. Ozisik L, Tanriover MD, Altinel S, Unal S. Vaccinating healthcare workers: Level of implementation, barriers and proposal for evidence-based policies in Turkey. Human vaccines & immunotherapeutics. 2017;13(5):1198-206.
18. Schmid P, Rauber D, Betsch C, Lidolt G, Denker ML. Barriers of Influenza Vaccination Intention and Behavior - A Systematic Review of Influenza Vaccine Hesitancy, 2005 - 2016. PloS one. 2017;12(1):e0170550.
19. Bisset KA, Paterson P. Strategies for increasing uptake of vaccination in pregnancy in high-income countries: A systematic review. Vaccine. 2018;36(20):2751-9.
20. Dini G, Toletone A, Sticchi L, Orsi A, Bragazzi NL, Durando P. Influenza vaccination in healthcare workers: A comprehensive critical appraisal of the literature. Human vaccines & immunotherapeutics. 2018;14(3):772-89.
21. Jacobson Vann JC, Jacobson RM, Coyne-Beasley T, Asafu-Adjei JK, Szilagyi PG. Patient reminder and recall interventions to improve immunization rates. Cochrane Database Syst Rev. 2018;1:CD003941.
22. Kan T, Zhang J. Factors influencing seasonal influenza vaccination behaviour among elderly people: a systematic review. Public health. 2018;156:67-78.
23. Larson HJ, Clarke RM, Jarrett C, Eckersberger E, Levine Z, Schulz WS, et al. Measuring trust in vaccination: A systematic review. Human vaccines & immunotherapeutics. 2018;14(7):1599-609.
24. Thomas RE, Lorenzetti DL. Interventions to increase influenza vaccination rates of those 60 years and older in the community. Cochrane Database Syst Rev. 2018;5:CD005188.
25. Wang Q, Yue N, Zheng M, Wang D, Duan C, Yu X, et al. Influenza vaccination coverage of population and the factors influencing influenza vaccination in mainland China: A meta-analysis. Vaccine. 2018;36(48):7262-9.
26. Gosselin Boucher V, Colmegna I, Gemme C, Labbe S, Pelaez S, Lavoie KL. Interventions to improve vaccine acceptance among rheumatoid arthritis patients: a systematic review. Clin Rheumatol. 2019;38(6):1537-44.
27. Jenkin DC, Mahgoub H, Morales KF, Lambach P, Nguyen-Van-Tam JS. A rapid evidence appraisal of influenza vaccination in health workers: An important policy in an area of imperfect evidence. Vaccine X. 2019;2:100036.
28. Lucyk K, Simmonds KA, Lorenzetti DL, Drews SJ, Svenson LW, Russell ML. The association between influenza vaccination and socioeconomic status in high income countries varies by the measure used: a systematic review. BMC Med Res Methodol. 2019;19(1):153.
29. Poliquin V, Greyson D, Castillo E. A Systematic Review of Barriers to Vaccination During Pregnancy in the Canadian Context. J Obstet Gynaecol Can. 2019;41(9):1344-55.
30. Sanftenberg L, Brombacher F, Schelling J, Klug SJ, Gensichen J. Increasing Influenza Vaccination Rates in People With Chronic Illness. Dtsch Arztebl Int. 2019;116(39):645-52.

31. Sheldenkar A, Lim F, Yung CF, Lwin MO. Acceptance and uptake of influenza vaccines in Asia: A systematic review. Vaccine. 2019;37(35):4896-905.
32. Abdullahi LH, Kagina BM, Ndze VN, Hussey GD, Wiysonge CS. Improving vaccination uptake among adolescents. Cochrane Database Syst Rev. 2020;1:CD011895.
33. Balzarini F, Frascella B, Oradini-Alacreu A, Gaetti G, Lopalco PL, Edelstein M, et al. Does the use of personal electronic health records increase vaccine uptake? A systematic review. Vaccine. 2020;38(38):5966-78.
34. Bechini A, Lorini C, Zanobini P, Mando Tacconi F, Boccalini S, Grazzini M, et al. Utility of Healthcare System-Based Interventions in Improving the Uptake of Influenza Vaccination in Healthcare Workers at Long-Term Care Facilities: A Systematic Review. Vaccines (Basel). 2020;8(2).
35. Borthwick C, O'Connor R, Kennedy L. Psychological predictors of seasonal influenza vaccination uptake among adults with a high-risk physical health condition: a systematic review. Psychol Health. 2020:1-22.
36. Kilich E, Dada S, Francis MR, Tazare J, Chico RM, Paterson P, et al. Factors that influence vaccination decision-making among pregnant women: A systematic review and meta-analysis. PloS one. 2020;15(7):e0234827.
37. Okoli GN, Lam OLT, Abdulwahed T, Neilson CJ, Mahmud SM, Abou-Setta AM. Seasonal influenza vaccination among cancer patients: A systematic review and meta-analysis of the determinants. Curr Probl Cancer. 2020:100646.
38. Okoli GN, Lam OLT, Racovitan F, Reddy VK, Righolt CH, Neilson C, et al. Seasonal influenza vaccination in older people: A systematic review and meta-analysis of the determining factors. PloS one. 2020;15(6):e0234702.
39. Vukovic V, Lillini R, Lupi S, Fortunato F, Cicconi M, Matteo G, et al. Identifying people at risk for influenza with low vaccine uptake based on deprivation status: a systematic review. Eur J Public Health. 2020;30(1):132-41.
40. NICE. Flu vaccination: increasing uptake. NICE guideline NG103. Evidence reviews for increasing uptake in health

and social care staff. 2018.
41. NICE. Flu vaccination: increasing uptake. NICE guideline NG103. Evidence reviews for increasing uptake in children. 2018.
42. NICE. Flu vaccination: increasing uptake NICE guideline [NG103]. Evidence reviews for increasing uptake in clinical risk groups. 2018.
43. Jarrett C, Wilson R, O'Leary M, Eckersberger E, Larson HJ. Strategies for addressing vaccine hesitancy - A systematic review. Vaccine. 2015;33(34):4180-90.
44. NICE. Flu vaccination: increasing uptake. 2018.
45. NICE. Flu vaccination: increasing uptake

Evidence reviews for increasing uptake in children. 2018.
46. NICE. Flu vaccination: increasing uptake

Evidence reviews for increasing uptake in health and social care staff. 2018.
47. Payaprom Y, Bennett P, Alabaster E, Tantipong H. Using the Health Action Process Approach and implementation intentions to increase flu vaccine uptake in high risk Thai individuals: a controlled before-after trial. Health Psychol. 2011;30(4):492-500.

48. Bandura A, Adams NE, Beyer J. Cognitive Processes Mediating Behavioral Change. The Journal of Personality and Social Psychology. 1977;35.
49. Cheung KW, Mak YW. Association between Psychological Flexibility and Health Beliefs in the Uptake of Influenza Vaccination among People with Chronic Respiratory Diseases in Hong Kong. Int J Environ Res Public Health. 2016;13(2):155.
50. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. Behav Res Ther. 2006;44(1):1-25.
51. Abdullahi LH, Kagina BM, Ndze VN, Hussey GD, Wiysonge CS. Improving vaccination uptake among adolescents. The Cochrane database of systematic reviews. 2020;1(1):Cd011895.
52. Gosselin Boucher V, Colmegna I, Gemme C, Labbe S, Pelaez S, Lavoie KL. Interventions to improve vaccine acceptance among rheumatoid arthritis patients: a systematic review. Clinical rheumatology. 2019;38(6):1537-44.
53. Jacobson Vann JC, Jacobson RM, Coyne-Beasley T, Asafu-Adjei JK, Szilagyi PG. Patient reminder and recall interventions to improve immunization rates. The Cochrane database of systematic reviews. 2018;1(1):Cd003941.
54. Jenkin DC, Mahgoub H, Morales KF, Lambach P, Nguyen-Van-Tam JS. A rapid evidence appraisal of influenza vaccination in health workers: An important policy in an area of imperfect evidence. Vaccine: X. 2019;2.
55. Sanftenberg L, Brombacher F, Schelling J, Klug SJ, Gensichen J. Increasing Influenza Vaccination Rates in People With Chronic Illness. Deutsches Arzteblatt international. 2019;116(39):645-52.
56. Thomas RE, Lorenzetti DL. Interventions to increase influenza vaccination rates of those 60 years and older in the community. The Cochrane database of systematic reviews. 2018;5(5):Cd005188.
57. Bechini A, Lorini C, Zanobini P, Mandò Tacconi F, Boccalini S, Grazzini M, et al. Utility of Healthcare System-Based Interventions in Improving the Uptake of Influenza Vaccination in Healthcare Workers at Long-Term Care Facilities: A Systematic Review. Vaccines. 2020;8(2).
58. Lorenc T, Marshall D, Wright K, Sutcliffe K, Sowden A. Seasonal influenza vaccination of healthcare workers: systematic review of qualitative evidence. BMC health services research. 2017;17(1):732.
59. Lytras T, Kopsachilis F, Mouratidou E, Papamichail D, Bonovas S. Interventions to increase seasonal influenza vaccine coverage in healthcare workers: A systematic review and meta-regression analysis. Human vaccines & immunotherapeutics. 2016;12(3):671-81.
60. Rashid H, Yin JK, Ward K, King C, Seale H, Booy R. Assessing Interventions To Improve Influenza Vaccine Uptake Among Health Care Workers. Health affairs (Project Hope). 2016;35(2):284-92.
61. Public Health England. Influenza: the green book, chapter 19. Influenza immunisation information including updates for public health professionals. Published 20 March 2013, last updated 29 October 2020. Available at: https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19. 2013.

62. Pitts SI, Maruthur NM, Millar KR, Perl TM, Segal J. A systematic review of mandatory influenza vaccination in healthcare personnel. American journal of preventive medicine. 2014;47(3):330-40.
63. Salgado CD, Giannetta ET, Hayden FG, Farr BM. Preventing nosocomial influenza by improving the vaccine acceptance rate of clinicians. Infection control and hospital epidemiology. 2004;25(11):923-8.
64. Dini G, Toletone A, Sticchi L, Orsi A, Bragazzi NL, Durando P. Influenza vaccination in healthcare workers: A comprehensive critical appraisal of the literature. Human Vaccines & Immunotherapeutics. 2018;14(3):772-89.
65. HPSC. Seasonal influenza vaccine uptake (provisional) in older people in Ireland, September 2019-May 2020. Available at: https://www.hpsc.ie/a-z/respiratory/influenza/seasonalinfluenza/influenzaandadults65yearsandolder/Seasonal%20Flu%20Vacc%20Uptake_65%20report_Sep%202019%20May%202020%20provisional%20for%20website.pdf.
66. HPSC. Uptake of the Seasonal Influenza Vaccine in Acute Hospitals and Long Term/Residential Care Facilities in Ireland in 2019-2020. Available at: https://www.hpsc.ie/a-z/respiratory/influenza/seasonalinfluenza/influenzaandhealthcareworkers/hcwinfluenzavaccineuptakereports/Summary%20Findings-Seasonal%20Influenza%20Vaccine%20Uptake-2019-2020-v2.0.pdf Accessed 7/12/2020.
67. ECDC. Seasonal influenza vaccination and antiviral use in EU/EEA Member States. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/seasonal-influenza-antiviral-use-2018.pdf Accessed 7/12/2020. 2018.
68. WHO. Who Technical Advisory Group on Behavioural Insights and Sciences for Health: Behavioural Considerations for Acceptance and Uptake Of Covid-19 Vaccines. Meeting Report 15 October 2020. Available at: https://apps.who.int/iris/bitstream/handle/10665/337335/9789240016927-eng.pdf?sequence=1&isAllowed=y. Accessed: 14.12.2020.
69. Ajzen I. The Theory of Planned Behavior Organizational Behavioural and Human Decision Processes. 1991;50:179-211.
70. Maltezou HC, Maragos A, Halharapi T, Karagiannis I, Karageorgou K, Remoudaki H, et al. Factors influencing influenza vaccination rates among healthcare workers in Greek hospitals. Journal of Hospital Infection. 2007;66(2):156-9.
71. Frederick J, Brown AC, Cummings DA, Gaydos CA, Gibert CL, Gorse GJ, et al. Protecting Healthcare Personnel in Outpatient Settings: The Influence of Mandatory Versus Nonmandatory Influenza Vaccination Policies on Workplace Absenteeism During Multiple Respiratory Virus Seasons. Infection control and hospital epidemiology. 2018;39(4):452-61.
72. De Serres G, Skowronski DM, Ward BJ, Gardam M, Lemieux C, Yassi A, et al. Influenza Vaccination of Healthcare Workers: Critical Analysis of the Evidence for Patient Benefit Underpinning Policies of Enforcement. PLoS One. 2017;12(1):e0163586.
73. Government of Ireland. Constitution of Ireland 1937 [Available from: http://www.irishstatutebook.ie/eli/cons/en/html.

74. Fine P, Eames K, Heymann DL. "Herd immunity": a rough guide. Clin Infect Dis. 2011;52(7):911-6.

Appendix 1 Data extraction template for barriers to vaccination uptake

Study descriptors	Main findings
First author: Borthwick[35] **DOI:** 10.1080/08870446.2020.1772971 **Search date:** August 2018 **Included studies:** n=12 studies published from 2007-2018 **Study population:** Adults (16 and older) with a high-risk physical health condition **Influenza type:** Seasonal influenza	**Barriers:** ▪ Expecting a less favourable outcome following vaccination was associated with reduced vaccination intentions. ▪ Unvaccinated participants were more fearful of side effects. Authors noted that vaccinated participants also had some concerns or uncertainties about side effects. ▪ Unvaccinated participants were more likely to suggest that internal motivational or practical barriers such as lack of time or procrastination could affect their behaviour. ▪ Mistrust towards government and pharmaceutical companies. Unvaccinated individuals seemed to harbour mistrust which may have affected their decisions about uptake. **Facilitators:** ▪ Out of eight studies testing perceived severity, three (37.5%) reported a significant association with vaccination behaviour. Perceived severity of influenza was a significant predictor of lifetime vaccination behaviour, vaccination in last year and future vaccination. ▪ Out of seven quantitative studies, five (71.4%) reported a significant association between perceived benefits and vaccination behaviour. Overall, the evidence seemed to suggest that perceived vaccine benefits play a role in determining vaccine behaviour. ▪ Lower perceived barriers to vaccination was linked with increased vaccination behaviour. ▪ Having influenza in the past year, being vaccinated in the previous year and beliefs about being at heightened risk of influenza if unvaccinated were associated with higher ratings of perceived vaccine benefits. ▪ Some evidence to suggest that cues to action in the form of health provider recommendation was associated with increased vaccination behaviour.

Study descriptors	Main findings
	▪ Participants were more likely to intend to receive the vaccine when they had been prompted to actively plan when and where they would receive the vaccine; however, there was no significant effect on subsequent behaviour. ▪ Higher self-efficacy in one's ability to arrange a time and transportation to receive the vaccine was predictive of increased vaccination intentions and likelihood of carrying out the behaviour. ▪ Knowledge that the vaccine is required each year was associated with both past vaccination uptake and future intentions. ▪ Provision of information is likely to be most helpful for individuals who are considering the vaccination for the first time, as those who have previous experience of being offered the vaccine have likely formed more entrenched beliefs about the personal risks and rewards associated with uptake. ▪ Psychological flexibility (ability to accept rather than avoid negative thoughts and emotions about a particular experience). Individuals with chronic respiratory disease with higher reported levels of psychological flexibility were more likely to receive the seasonal influenza vaccination. Vaccinated participants scored significantly higher than unvaccinated individuals on this construct indicating greater levels of acceptance towards their high-risk condition. There is insufficient evidence available at this stage to conclude that psychological flexibility is associated with vaccination behaviour.
First author: Dini[20] **DOI:** 10.1080/21645515.2017.1348442 **Search date:** 18 April 2017 **Included studies:** n=28 studies published from 2006-2017	**Barriers (pandemic):** ▪ Being a nurse correlated with negative intention towards vaccination uptake. **Barriers (seasonal):** ▪ Idea that pharmaceutical companies could influence decision about vaccination programs was negatively associated with vaccination uptake. ▪ Not caring about influenza. ▪ Doubts about vaccine effectiveness. ▪ Fear of adverse effects. ▪ Being opposed to vaccination in general. ▪ Forgetfulness. ▪ Believing that vaccines do not have a protective effect.

Study descriptors	Main findings
Study population: Healthcare workers **Influenza type:** Seasonal and pandemic influenza	▪ Believing that influenza is a mild disease. **Barriers (pandemic and seasonal):** ▪ Low risk perception. ▪ Denial of the social benefit of influenza vaccination. ▪ Low social pressure (either real or perceived). ▪ Lack of perceived behavioural control. ▪ Negative attitude towards vaccination in general. ▪ Not having been vaccinated in the previous influenza vaccination campaigns. ▪ Not having had influenza in the previous years. ▪ Lack of adequate influenza-specific knowledge. ▪ Lack of access to vaccination facilities. ▪ Socio-demographic variables (including age, gender, additional risk factors such as unhealthy life-style factors). **Facilitators (pandemic):** ▪ Willingness and intention to vaccinate oneself were associated with: o Higher perceived susceptibility to H1N1 influenza virus. o Higher perceived severity of the disease. o Higher perceived benefits (both clinical and societal). o Lower perceived costs of vaccination. ▪ Those more likely to vaccinate themselves were typically older age and male. ▪ Protect oneself and others. ▪ Beliefs in vaccine safety and effectiveness. ▪ Previously had influenza. ▪ Past influenza vaccinations. ▪ Receiving adequate knowledge and information delivered from official sources played a major role. ▪ Receiving recommendation from respected healthcare workers. **Facilitators (seasonal):** ▪ Being a medical doctor. ▪ Not having concern about vaccine safety. ▪ Perception of an increased risk of developing influenza.

Study descriptors	Main findings
	▪ Older age. ▪ Having a chronic disease. ▪ Knowing the vaccine is effective. ▪ Being willing to prevent influenza transmission. ▪ Believing that influenza is highly contagious. ▪ Believing that influenza prevention is important. ▪ Having a family that is usually vaccinated. ▪ Desire of self-protection as well as protection of family, patients and of other people.
First author: Jenkin[27] **DOI:** 10.1016/j.jvacx.2019.100036 **Search date:** 2006 to 2018 **Included studies:** n=3 studies published from 2017-2018 **Study population:** Healthcare workers **Influenza type:** Seasonal and pandemic influenza	**Barriers:** ▪ Strongest barriers to uptake were lack of confidence about disease severity or vaccine effectiveness. ▪ Lack of professional or ethical obligation to get vaccinated. ▪ Success of a vaccination program may be influenced by the complex relationship between healthcare workers and the organization and management of the health care system within which they work. **Facilitators:** ▪ Strongest reason to vaccinate was to protect oneself and not patients. ▪ Need to expand discussion on the importance of top-down support for vaccine programs in healthcare workers to develop a culture of vaccination.
First author: Kilich[36] **DOI:** 10.1371/journal.pone.0234827	**Barriers:** ▪ Access, time, availability, cost and logistics of getting vaccinated. ▪ Negative influence of family/friends/media and their discouragement of vaccination. ▪ Fear/distrust of being vaccinated.

Study descriptors	Main findings
Search date: 22 November 2018 **Included studies:** n=120 studies published from 1997-2019 **Study population:** Pregnant women **Influenza type:** H1N1 influenza and seasonal influenza	▪ Perceived susceptibility to infection associated with decreased vaccination uptake (not significant) (OR 0.83, 95% CI 0.25-2.70; I^2=0% [2 studies – seasonal influenza]). ▪ Perceived susceptibility to disease harm and severity of disease for mother and infant associated with decreased vaccination uptake (not significant) (OR 0.57, 95% CI 0.22-1.45 I^2=0% [2 studies – seasonal influenza]). ▪ Perception of rumours/myths related to vaccination. ▪ Perception of the vaccine causing harm or being unsafe in pregnancy was an indicator of reduced vaccination uptake for pandemic influenza (OR 0.16, 95% CI 0.09-0.29; I^2=89% [6 studies – general harm] and OR 0.19, 95% CI 0.09-0.40; I^2=14% [2 studies – harm to baby]). ▪ Similar findings were reported for seasonal influenza (OR 0.22, 95% CI 0.11-0.44; I^2=84% [7 studies – general harm]). ▪ Perception of the vaccine having side effects also indicated reduced vaccination uptake for pandemic influenza (OR 0.27, 95% CI 0.21-0.34; I^2=0% [2 studies – knowledge of side effects] and OR 0.44, 95% CI 0.23-0.81 I^2=0% [2 studies – concerns about side effects]). ▪ Concerns about side effects was also associated with decreased vaccination uptake for seasonal influenza (OR 0.55, 95% CI 0.27-1.16; I^2=96% [5 studies – concerns about side effects] and OR 0.66, 95% CI 0.21-2.14; I^2=57% [2 studies – probability of side effects]); although these findings were not significant. **Facilitators:** ▪ Participants' previous experiences with vaccinations, in pregnancy was associated with increase vaccination uptake in seasonal influenza (OR 1.51, 95% CI 0.71-3.24; I^2=76% [3 studies – seasonal influenza]) and (OR 9.12, 95% CI 1.99-41.76; I^2=83% [2 studies – pandemic influenza]); although not significant for seasonal. ▪ Participants' previous experiences with vaccinations in general was associated with a significant increase in vaccination uptake (OR 3.78, 95% CI 2.49-5.73; I^2=63% [10 studies – seasonal influenza]) and (OR 5.49, 95% CI 2.44-12.37;

Study descriptors	Main findings
	I^2=88% [3 studies – pandemic influenza]). ▪ Healthcare professionals recommendations were associated with a significant increase in vaccination uptake (OR 6.76, 95% CI 3.12-14.64; I^2=92% [5 studies – pandemic influenza]) and (OR 12.02, 95% CI 6.80-21.44; I^2=92% [21 studies – seasonal influenza]). ▪ Statements regarding chronic conditions or other health status influencing vaccination decisions. ▪ Positive influence of family/friends/media and their encouragement to have vaccination. ▪ Knowledge of influenza in pregnancy and availability of vaccines was significantly associated with increased uptake of pandemic influenza vaccinations (OR 1.50, 95% CI 1.06-2.12; I^2=70% [2 studies – general knowledge]) and seasonal influenza vaccinations (OR 2.94, 95% CI 1.01-8.58; I^2=94% [3 studies – felt informed] to OR 5.68, 95% CI 1.53-21.33; I^2=84% [4 studies – general knowledge]). ▪ Knowledge of policy guidelines or awareness of general recommendations to be vaccinated were associated with a significant increase in seasonal influenza vaccinations (OR 3.68, 95% CI 2.12-6.38; I^2=28% [4 studies]). ▪ Fear/regret over not getting vaccinated. ▪ Perceived susceptibility to disease harm and severity of disease for mother and infant were significantly associated with an increased uptake of seasonal influenza vaccinations (OR 1.76, 95% CI 1.26-2.47; I^2=35% [5 studies – susceptibility whilst pregnant] and OR 3.70, 95% CI 1.37-9.94; I^2=78% [3 studies – disease harm]). This was also noted for pandemic influenza vaccinations (OR 2.91, 95% CI 2.02-4.18; I^2=0% [2 studies – risk of hospitalisation]). ▪ Pregnant women reported perceived benefit of seasonal influenza vaccinations to the baby (OR 1.74, 95% CI 1.18-2.57; I^2=44% [7 studies – benefit to baby]). ▪ Perceptions of vaccinations being useful, effective or necessary for the mother or infant was associated with increased vaccination uptake in pandemic

Study descriptors	Main findings
	influenza (OR 1.02, 95% CI 0.69-1.51; I^2=0% [2 studies – general benefit] and OR 8.44, 95% CI 2.90-24.61; I^2=0% [2 studies – benefit to mother]); the findings were not significant for general benefit in pandemic influenza. ▪ However, perceived benefit of vaccinations in general were observed and significant for seasonal influenza (OR 7.22, 95% CI 3.49-14.93; I^2=80% [6 studies – general benefit]).
Organisation: NICE (2018a)[10] (NICE guideline NG103, Evidence reviews, August 2018) **URL:** https://www.nice.org.uk/guidance/ng103/evidence/3-increasing-flu-vaccination-uptake-in-clinical-risk-groups-pdf-6532083616 **Search date:** 1996-April 2016 **Included studies:** n=9 studies published from 2008-2016 **Study population*:** Clinical risk groups aged 6 months to 64 years: ▪ chronic respiratory disease ▪ chronic heart disease ▪ chronic kidney disease ▪ chronic liver disease ▪ chronic neurological disease ▪ diabetes ▪ immunosuppression ▪ asplenia or dysfunction of the spleen ▪ pregnant women	**Qualitative evidence statements:** ▪ Perception of the severity of flu may impact on decision to accept vaccination offers (recipients) or to make vaccination offers (providers). ▪ Understanding risk, benefits and overcoming misconceptions is important in ensuring providers offer the vaccination and in improving acceptability of flu vaccination offers by parents of or people with chronic conditions. ▪ Accessibility is an important factor in improving likelihood of vaccination uptake or not missing vaccination opportunities. ▪ Importance of information provision/advice and offer by a healthcare professional. ▪ Provider concerns in pregnant women limiting their capacity for recommendations was affected by provider knowledge. ▪ Information access preferences and communication preferences are important factors in delivering messages to pregnant women.

Study descriptors	Main findings
▪ morbid obesity. *None of the qualitative studies on barriers and facilitators included children; one study included parents of children aged 2-16 years who were eligible for vaccination. **Influenza type:** Seasonal Influenza	
Organisation (year): NICE (2018b)[45] (NICE guideline NG103, Evidence reviews for increasing uptake in children, August 2018) **URL:** https://www.nice.org.uk/guidance/ng103/evidence/evidence-review-2-increasing-flu-vaccination-uptake-in-children-pdf-6532083615 **Search date:** 1996-April 2016 **Included studies:** n=10 studies published from 2010-2016 **Study population:** Children **Influenza type:** Seasonal influenza	**Qualitative evidence statements:** ▪ Knowledge, information and over-coming misconceptions. ▪ Perception of the severity of flu may impact on decision to accept vaccination offers. ▪ Trust in government, practitioner and pharmaceutical company information may affect uptake decisions. ▪ Accessibility including evening and weekend clinics may support uptake. ▪ Vaccine supply limited planning and access to vaccinations. ▪ Belief in accuracy of records and prompts. ▪ Mandatory vaccination in schools is a factor that may affect uptake decisions. ▪ Vaccination Delivery Mode may affect uptake. ▪ Who endorses flu vaccination may be important in decision making.
Organisation (year): NICE (2018c)[46] (NICE guideline NG103, Evidence reviews for increasing uptake in health and social care staff, August 2018)	**Qualitative evidence statements:** ▪ Perception of personal risk of flu may impact on decision to accept vaccination offers in healthcare workers, this may be important for information and education approaches.

Study descriptors	Main findings
URL: https://www.nice.org.uk/guidance/ng103/evidence/4-increasing-flu-vaccination-uptake-in-health-and-social-care-staff-pdf-6532083617 **Search date:** 1996-April 2016 **Included studies:** n=8 studies published from 2006-2015 **Study population:** Healthcare workers **Influenza type:** Seasonal influenza	▪ Protecting patients may be an important factor in accepting vaccination offers in healthcare workers, this may be important for information and education approaches. ▪ Efficacy beliefs may impact on acceptability of flu vaccination offers in healthcare workers, this may be important for information and education approaches. ▪ Overcoming misconceptions may be important in improving acceptability of flu vaccination offers by healthcare workers, this may be important for information and education approaches. ▪ Education and awareness raising may be an important factor in improving acceptability and uptake of flu vaccination offers in healthcare workers. ▪ Accessibility is an important factor in improving likelihood of vaccination uptake. ▪ Incentives may be a factor in accepting offer of a flu vaccination in healthcare workers. ▪ Perceptions of mandatory and/or declination policies are different in policy makers or implementers than in healthcare workers. ▪ Reducing absenteeism, is considered a factor in flu vaccination acceptance. ▪ Negative personal experiences may be important in deciding whether to accept flu vaccination offers in healthcare workers.
First author: Okoli (2020a)[38] **DOI:** 10.1371/journal.pone.0234702 **Search date:** 7 January 2020 **Included studies:** n=34 studies published from 2004-2019	**Barriers:** ▪ Compared with being white, being non-white was associated with a 23% decrease in seasonal influenza vaccination uptake. The associated decrease in seasonal influenza vaccination uptake was higher for being an African American or Hispanic (both by 31%); however, with substantial heterogeneity between the pooled results. ▪ Compared with not living alone, living alone was associated with a 30% decrease in seasonal influenza vaccination uptake in Europe (OR 0.70, 95% CI 0.51-0.96; [3 studies]). A non-significant decreased seasonal influenza vaccination uptake was found in Asia (OR 0.96, 95% CI (0.69-1.35; [3 studies]).

Study descriptors	Main findings
Study population: Community-dwelling older individuals (≥65years old) **Influenza type:** Seasonal influenza	▪ Overall, a non-significant decrease in seasonal influenza vaccination uptake was found for having a cognitive impairment, and the same observation was found in Asia. However, an associated 32% decrease was found in Europe (OR 0.68, 95% CI 0.59–0.78). ▪ Seven studies examined the influence of smoking status. Generally, smoking was associated with a decreased seasonal influenza vaccination uptake by 22% (10-32%), and a 36% decrease in seasonal influenza vaccination uptake in Asia (with substantial heterogeneity). A non-significant decreased seasonal influenza vaccination uptake was found in Europe. **Facilitators:** ▪ The following were associated with increased seasonal influenza vaccination uptake: being older (OR 1.52, 95% CI 1.38–1.67 [21 studies]), white (OR 1.30, 95% CI 1.14–1.49 [10 studies]), married (OR 1.23, 95% CI 1.17–1.28 [9 studies]), non-smoker (OR 1.28, 95% CI 1.11–1.47 [7 studies]), of a higher social class (OR 1.20, 95% CI 1.06–1.36 [2 studies]), having a higher education (OR 1.12, 95% CI 1.04–1.21 [14 studies]), having a higher household income (OR 1.11, 95% CI 1.05–1.18 [8 studies]), having a chronic illness (OR 1.53, 95% CI 1.44–1.63 [16 studies]), having poor self-assessed health (OR 1.23, 95% CI 1.02–1.40 [9 studies]), having a family doctor (OR 2.94, 95% CI 1.79– 4.76 [2 studies]), and having health insurance (OR 1.58, 95% CI 1.13–2.21 [6 studies]). ▪ Being older (OR 1.26, 95% CI 1.11–1.44 [2 studies]) was also associated with increased vaccination adherence. Age-associated increased seasonal influenza vaccination uptake was found in Asia (by 42%), Europe (by 60%) and North America (by 49%). ▪ Overall, being female was not significantly associated with increased seasonal influenza vaccination uptake but there was evidence of publication bias (p=0.027). However, being female in Asia was associated with a 23% increased seasonal influenza vaccination uptake, whereas a 7% decreased seasonal influenza vaccination uptake was found in Europe (with evidence of publication bias; p=0.036). A non-significant increased association was found

Study descriptors	Main findings
	in North America. ▪ Overall, being married was associated with an increased seasonal influenza vaccination uptake by 23% (17-28%); a 23% increase in Europe, and a non-significant increase in Asia and North America. ▪ Education – a 22% increase in North America (with high heterogeneity), and a non-significant increased seasonal influenza vaccination uptake in Asia and Europe. ▪ Chronic disease – Overall, having a chronic disease(s) was associated with increased seasonal influenza vaccination uptake by 53% (44-63%). A similar association was found in Asia (by 65%), Europe (by 49%), and North America (by 50%). ▪ Alcohol – There was one study each from Asia and Europe for alcohol consumption, and these reported a non-significant decrease and increase in seasonal influenza vaccination uptake, respectively, for regular compared with irregular or non-alcohol drinkers. ▪ Self-assessed health – Overall, poor self-assessed health was associated with an increased seasonal influenza vaccination uptake by 23% (2-47%), (OR 1.23, 95% CI 1.02–1.40; [9 studies]). This varied by region. Poor self-assessed health was associated with a significant increase in seasonal influenza vaccination uptake in Europe (OR 1.32, 95% CI 1.07-1.63; [4 studies]), a non-significant increase in Asia (OR 1.08, 95% CI 0.66-1.77; [3 studies]) and non-significant decrease in North America (OR 0.63, 95% CI 0.10-3.95; [2 studies]).
First author: Okoli (2020b)[37] **DOI:** 10.1016/j.currproblcancer.2020.100646 **Search date:** 13 February 2020	**Facilitators:** ▪ Overall, being older (OR 2.23, 95% CI 1.46-3.38; I^2=92.3% [6 studies]), a non-smoker (OR 1.43, 95% CI 1.32-1.51; I^2=0% [4 studies]), having a chronic illness (OR 1.18, 95% CI 1.07-1.29; I^2=15.7% [5 studies]), having had a medical check-up in the past year (OR 1.75, 95% CI 1.65-1.86; I^2=0% [2 studies]), and having health insurance (OR 1.39, 95% CI 1.13-1.72; I^2=21.8% [3 studies]) were associated with increased seasonal influenza vaccination uptake.

Study descriptors	Main findings
Included studies: n=10 studies published from 2013-2020 **Study population:** Cancer patients (no country restriction, but ended up with 4 USA, 3 South Korea, 1 Israel, Germany, Spain) **Influenza type:** Seasonal influenza	▪ No associations for alcohol consumption, being an ethnic minority/Hispanic (see exception below), sex, education, area of residence, marital status, or income (except for rural males in South Korea – increase in odds of uptake; and higher education in USA). ▪ Compared with being African-American, being Caucasian was also associated with increased seasonal influenza vaccination uptake (OR 1.79, 95% CI 1.47-2.13; I^2=10.7% [3 studies]).

Appendix 2. Tables of study characteristics and primary outcomes: (measures/ interventions to increase uptake)

Study descriptors	Study quality and main findings
Abdullahi 2020 **DOI:** 10.1002/14651858.CD011895.pub2 **Date of literature search:** 31 October 2018 **Included studies:** Two studies, RCTs (published as a single paper) **Date of publication for included studies** 2015 **Population(s) assessed:** Adolescents, (health providers as participants – one study) **Intervention(s) assessed:** provider prompts **Vaccine(s) assessed:** Seasonal influenza vaccine **Outcome(s) assessed:** Uptake of vaccine. Reported ORs and adjusted ORs (2 RCTs)	**Quality of systematic review (GRADE):** High **Intervention:** *Use of provider prompts to increase uptake (based on 2 RCTs)* **Relative change in uptake:** In the national network of paediatric clinics (USA), Adjusted OR 0.89, 95% CI: 0.69 to 1.16, 878 participants) Uptake at baseline: intervention 479 (49%), control 410 (43%) Uptake end of study period: intervention 457 (48%), control 421 (44%) In the local network of primary care practices (USA), adjusted OR 0.93, 95% CI:0.69 to 1.25, 561 participants) Uptake at baseline: intervention 252 (32%), control 243 (30%) Uptake end of study period: intervention 279 (35%), control 282 (35%) Pooling from both networks, adjusted OR 0.91, 95% CI: 0.61 to 1.34, 1439 participants) **Authors' conclusions:** Provider prompts probably make little or no difference compared to usual practice on completion of vaccination schedules.
Aigbogun 2015 **DOI:** 10.1016/j.vaccine.2014.12.013 **Date of literature search:** 18 December 2014. **Included studies:** n=18 studies, including one systematic review, seven RCTs, six before-and-after	**Quality of systematic review (GRADE):** Low All included studies are contained in the later 2018 NICE review; therefore, detailed results are only presented for NICE 2018 review. **Authors' conclusions:** There is good evidence that reminder letters will improve influenza vaccination uptake in children with HRCs, but the evidence that telephone recall or a combination

studies, one non-randomized controlled trial, one retrospective cohort study, one quasi-experimental post-test study and one letter to editor. **Date of publication for included studies** 1992, 1993, 1997, 2001, 2004, 2006 (5), 2007, 2008, 2009 (2), 2010, 2011, 2012 (2), **Population(s) assessed:** Children with high risk conditions (e.g. asthma) **Intervention(s) assessed:** Any intervention **Vaccine(s) assessed:** Influenza vaccination **Outcome(s) assessed:** Uptake of vaccination against influenza, primary measure of effect: OR's	of letter reminder and telephone recall will improve uptake is weak. It is not known if multiple reminder letters are more effective than single letters or if multi-component strategies are more effective than single or dual component strategies.
Boucher 2019 **DOI:** 10.1007/s10067-019-04430-7 **Date of literature search:** 25 July 2018 **Included studies:** 5 studies (5 quasi-experimental), but only 3 had outcomes for influenza vaccination. **Date of publication for included studies** 2009, 2016, 2018 **Population(s) assessed:** Patients with rheumatoid arthritis **Intervention(s) assessed:** Behavioural interventions targeting providers and/or patients to	**Quality of systematic review (GRADE):** Critically low **Findings:** Post-intervention (12-month follow-up) vaccination rates increased by a mean of 8.4 ± 13.6% for influenza" across all 3 studies [relating to influenza] **Interventions targeting providers (n=1 for influenza)** *Electronic health record, best practice alert (n=1)* ▪ Pre-intervention, 47% vaccination rate ▪ Post-intervention, 65% vaccination rate ▪ Relative change in uptake, not reported ▪ Relative change per subgroup: N/A. **Interventions targeting providers and patients (n=2 for influenza)** *Reminders to prescribe vaccination, performance feedback to physicians and letters*

enhance vaccination uptake among RA patients. **Vaccine(s) assessed:** Any vaccine **Outcome(s) assessed:** Vaccination uptake	*to patients (n=1)* ▪ Pre-intervention, 90.2% ever received, 79.4% received in previous season ▪ Post-intervention, 86.1% ever received, 78.2% received in previous season ▪ Relative change in uptake, not reported ▪ Relative change per subgroup: N/A. **Multimodal intervention using education session, EMR-based alerts and personalised e-mail reminders for patient (n=1)** ▪ Pre-intervention, 47% missed an influenza vaccine ▪ Post-intervention, 23% missed an influenza vaccine ▪ Relative change in missing rate, not reported, but p<0.001 ▪ Relative change per subgroup: N/A.
Jacobson Vann 2018 (Cochrane review) **DOI:** 10.1002/14651858.CD003941.pub3 **Date of literature search:** February 2013 to 31 January 2017 **Included studies:** 29 studies relevant to review (5 on children, 24 on adults) **Date of publication for included studies** 1982, 1985, 1986 (2), 1987 (3), 1988, 1989, 1991 (3), 1992 (3), 1993, 1997 (2), 1998 (3), 2002(2), 2004, 2005, 2011, 2012 (2), 2013 **Population(s) assessed:** Children needing influenza vaccination, adults needing influenza vaccination**.**	**Quality of systematic review (GRADE):** High Five studies on childhood influenza immunisations were included, all 5 were included in meta-analysis. Twenty four studies on adult influenza immunisations were included, 15 were included in meta-analysis. Six studies were excluded from meta-analysis as randomised households, families, clinicians or practices. The median OR for these studies was 3.08. One before-after study was also excluded from meta-analysis. **<u>Results of Meta-analysis</u>** **Intervention**: *Any patient reminder or recall intervention* ▪ **Uptake rate without intervention:** *Childhood influenza immunisations:* Assumed risk without intervention: 431 per 1000

Intervention(s) assessed: Patient reminder or recall interventions for receipt of immunisations **Vaccine(s) assessed:** Influenza vaccine in children and adults **Outcome(s) assessed:** Receipt of immunisation. Results were presented as relative rates using risk ratios, and risk differences for randomized trials, and as absolute changes in percentage points for controlled before-after studies.	*Adult influenza immunisations:* Assumed risk without intervention: 292 per 1000 ▪ **Uptake rate with intervention**: *Childhood influenza immunisations:* Corresponding risk with intervention: 651 per 1000 (491 to 857) *Adult influenza immunisations:* Corresponding risk with intervention: 376 per 1000 (342 to 418) ▪ **Relative change in uptake:** *Childhood influenza immunisations:* RR 1.51 (95% CI: 1.14 to 1.99); risk difference of 22% (5 studies n=9265 particpants) *Adult influenza immunisations:* RR 1.29 (95% CI: 1.17 to 1.43), risk difference of 9% (15 studies n=59,328 participants) ▪ **Relative change per subgroup**: *e.g. peds/adult/older adults, underlying conditions, pregnancy* **Intervention:** ***Patient telephone reminder or recall*** **Uptake rate without intervention:** *Adult influenza immunisations:* Without intervention:298/920, 32.4% ▪ **Uptake rate with intervention**: *Adult influenza immunisations:* With intervention: 352/918, 38.3% ▪ **Relative change in uptake:**

	Adult influenza immunisations: RR 1.53 (95% CI: 0.73 to 3.20), (2 studies, n=1838 participants) **Intervention:** ***Patient letter reminder or recall*** ▪ **Uptake rate without intervention:** *Childhood influenza immunisations:* Without intervention:1997/4637, 43.1% *Adult influenza immunisations:* Without intervention:5134/18066, 28.4% ▪ **Uptake rate with intervention**: *Childhood influenza immunisations:* Without intervention:2354/4628, 50.9% *Adult influenza immunisations:* With intervention: 8418/26388, 31.9% ▪ **Relative change in uptake:** *Childhood influenza immunisations:* RR 1.51 (95% CI: 1.14 to 1.99), (5 studies, n= 9265 participants) *Adult influenza immunisations:* RR 1.35 (95% CI: 1.19 to 1.52), (11 studies, n= 44,454 participants) **Intervention**: ***Patient postcard reminder or recall*** ▪ **Uptake rate without intervention:** *Adult influenza immunisations:* Without intervention:2627/6449, 40.7%

	▪ **Uptake rate with intervention**: *Adult influenza immunisations:* With intervention: 5666/12816, 44.2% ▪ **Relative change in uptake:** *Adult influenza immunisations:* RR 1.15 (95% CI: 0.95 to 1.39), (3 studies, n= 19,265 participants) **Intervention**: *Combination patient reminder or recall with provider reminder* ▪ **Relative change in uptake:** *Adult influenza immunisations:* RR 2.91 (95% CI: 2.66 to 3.18), (2 studies, n= 3856) **Authors' conclusions:** Patient reminder or recall interventions probably improve receipt of childhood influenza vaccinations with moderate certainty of evidence (GRADE). Patient reminder or recall interventions probably improve receipt of adult influenza vaccinations based on moderate certainty evidence (GRADE).
Jenkin 2019 **DOI:** 10.1016/j.jvacx.2019.100036 **Date of literature search:** 2006 to 2018 **Included studies:** 14 studies, **11 studies on interventions** and 3 studies on barriers to influenza uptake	**Quality of systematic review (GRADE):** High **Summary of main findings:** Mandatory Vaccination to be able to work remains the most successful intervention to increase uptake. Other successful interventions are: ▪ multi-faceted including many elements together (the more the better) ▪ sustained over time ▪ provide free and easy access to vaccine

Date of publication for included studies 2010, 2012 (2), 2013 (4), 2015 (3), 2018 **Population(s) assessed:** Healthcare workers **Intervention(s) assessed:** Successful practical interventions to increase healthcare workers vaccine uptake of influenza vaccine **Vaccine(s) assessed:** Influenza vaccination **Outcome(s) assessed**: *e.g. uptake rate pre- and post-intervention, any measure of relative change such as OR's* Increased uptake of influenza vaccination	▪ use behaviour change components (reminders, incentives, education) ▪ develop targeted multi-faceted interventions using baseline data collection to identify barriers in that population ▪ vaccine promotion from highest levels ▪ having a vaccine organizer from inside ▪ opt-out programs (declination statements, required mask use, flu-safe zones) ▪ appears that intervention success is linked in some respects to the number of interventions **Details:** Consensus that no single intervention component rapidly and substantially raised influenza vaccination rates in healthcare workers, aside from mandatory vaccination. Several systematic reviews and tool kits highlighted that multifaceted approaches which sustain over time can produce increases >90%. One review included 7 systematic reviews (> 200,000 subjects, Dini et al) and found successful alternatives to mandatory vaccination included "soft-mandates", such as masks, "opt-out", or declinations statements, and multi-faceted programmes which take into consideration the local context, include incentives, education, advertising, and easy vaccine access as efforts to enhance behaviour change. Other systematic reviews also reported the most successful strategies after mandatory vaccination were "soft" mandate strategies and a policy excluding non-vaccinated healthcare workers from working with highly vulnerable patient groups. Another found that successful interventions included: free and easy access to vaccine; educational activities; reminders and incentives; management/organizational approaches including personnel charged with implementing the programme; and a long-term strategy. In addition a study (n= 121 publications) concluded that all interventions increased uptake to some extent with the most successful being those which required vaccination as a condition of being allowed to work. .
NICE 2018a *(NICE guideline NG103, Evidence reviews, August 2018)*	**Effectiveness evidence statements** *(taken directly from review)* **Education** ▪ **"Low-quality evidence** from 1 RCT of 105 participants found that an educational video did

Available at:
https://www.nice.org.uk/guidance/ng103/evidence/3-increasing-flu-vaccination-uptake-in-clinical-risk-groups-pdf-6532083616

Review question(s):

RQ 1: What interventions to promote information about, and acceptability of, flu vaccination are the most effective for increasing acceptability and uptake of seasonal flu vaccination among clinical risk groups?

RQ 2: What interventions to increase access to seasonal flu vaccine are the most effective in increasing uptake of seasonal flu vaccine among clinical risk groups?

RQ 3: Which provider-based systems and processes for identifying, contacting and inviting clinical risk groups for seasonal flu vaccination are most effective in increasing uptake of among this population group?

Date of literature search:

April-May 2016

Included studies:

19 primary studies (13 RCTs and 6 quasi-experimental studies) and 3 systematic reviews of clinical effectiveness.

not increase flu vaccination uptake among **pregnant women** compared to a communicable disease control handwashing video (RR 1.13; 95% CIs 0.60 to 2.14)." Influenza vaccination rates were 28% (15/53) in the intervention group and 25% (13/52) in the control group (p=0.70).

- **"Low-quality evidence** from 1 RCT of 249 participants with **COPD** found that an evidence-based patient educational manual, which included advice about flu vaccination, did not increase vaccination uptake among participants with lower or higher socioeconomic disadvantage compared to a control COPD pamphlet (lower disadvantage: intervention vs. control: +2% vs. 0%, p = 0.44; higher disadvantage: intervention vs. control: +4% vs. 0% p = 0.13)." Baseline measures & current flu vaccination: intervention (88/125, 70.4%), control (87/124, 65.3%).

- **"Very low-quality evidence** from 2 before and after studies with a combined total of 23,207 participants showed that educational interventions for providers (with or without electronic record prompts) and for parents (contained in the asthma action plan) increased the uptake of flu vaccination in **children with asthma** (RR 1.90; 95% CI 1.43 to 2.53)." Vaccine rate: Intervention group (2,291/12,268, 18.7%), Control group (1,464/10,939, 13.4%).

- **"Very low-quality evidence** from 1 RCT and 1 before and after study with 374 participants showed that educational pamphlets, with or without a verbalised benefit statement, increased the uptake of flu vaccination in **pregnant women** compared to usual antenatal care (RR 1.96; 95% CI 1.32 to 2.91)." Vaccine rate: Intervention group (169/266, 63.5%), Control group (35/108, 32.4%).

Message framing

- **"Very low-quality evidence** from 1 RCT of 292 participants with **chronic respiratory or cardiac disease**, comparing 'loss' (negatively-framed) to 'gain' (positively-framed) educational messages delivered in an information session, found no difference in flu vaccination uptake rates immediately post-intervention (RR 1.02; 95% CI 0.85 to 1.21) or after 3 months (RR 0.95; 95% CI 0.81 to 1.11)." Vaccine rate post intervention: Intervention group (91/144, 63.2%), Control group (92/148, 62.2%). Vaccine rate 3 months post intervention: Intervention group (94/144, 65.3%), Control group (102/148, 68.9%).

- **"Very low-quality evidence** from 1 RCT of 164 **pregnant women** compared single in-clinic

9 primary qualitative studies.

Date of publication for included studies

Primary studies: 1996, 2002, 2004, 2006, 2008 2010, 2011, 2012, 2014 (3), 2015 (5), 2016

Systematic reviews:2005, 2015,2016

Qualitative studies: 2008, 2011, 2012, 2013, 2014 (2), 2015 (2), 2016

Population(s) assessed:

Clinical risk groups aged 6 months to 64 years:

- chronic respiratory disease
- chronic heart disease
- chronic kidney disease
- chronic liver disease
- chronic neurological disease
- diabetes
- immunosuppression
- asplenia or dysfunction of the spleen
- pregnant women
- morbid obesity.

Intervention(s) assessed:

RQ1: Information campaigns, Education, Tailored information and advice, Flu vaccination 'champion', Recommendations from a respected person.

RQ2: Vaccination clinics in community settings, Dedicated flu vaccination clinics, Mass vaccination clinics in community or other settings ,Walk in or open access immunisation clinics, Extended hours clinics,

exposure to either a 'gain' (positively-framed) or a 'loss' (negatively-framed) educational message with a control (standard) message. There was no effect of message framing on respondents' intention of getting vaccinated ('Gain' vs. control message: OR 1.25; 95% CI 0.49 to 3.25; 'Loss' vs control message: OR 0.48; 95%0.17 to 1.35)."

- **"Low-quality evidence** from 1 randomised control trial with 126 participants showed that providing either gain- or loss-framed vaccine information to **pregnant women** did not increase flu vaccination uptake compared with standard vaccine information (RR 0.60; 95% CI 0.35 to 1.03)." Vaccine rate 'gain framed': Intervention group (11/45, 24.4%), Control group (8/20, 40%). Vaccine rate 'loss framed': Intervention group (10/42, 23.8%), Control group (8/20, 40%).

Access

- **"Very low-quality evidence** from 1 before and after study with an unknown target population size found that providing flu vaccination in community pharmacies did not increase vaccination uptake among **eligible groups** compared with the year before the programme began (pre-intervention uptake: 60.4%. post-intervention uptake 60.5%)."
- **"Very low-quality evidence** from 1 before and after study with a target population of 247,641 to 269,355 adults aged **18-64 years in clinical risk groups** found that providing flu vaccination in community pharmacies did not increase uptake compared with the year before the programme began (pre-intervention uptake: 52.8%. post-intervention uptake 51.9%; RR 0.98; 95% CI 0.98 to 0.99)."
- **"Very low-quality evidence** from 1 before and after study of 264 participants found that providing Saturday clinics in addition to a reminder letter sent to parents did not increase flu vaccination uptake among **children with asthma** compared with a reminder letter alone (RR 1.25; 95% CI 0.78 to 1.99)." Vaccination rate: Intervention group (35/264, 13.3%), Control group (28/264, 10.6%).
- **"Very low-quality evidence** from 1 retrospective cohort study with 5,451 participants showed that offering year-round flu vaccination appointments increased uptake among **infants and children with asthma** compared to standard appointment provision limited to flu season

Outreach or mobile services, Parallel clinics, Opportunistic vaccination, Flu vaccination vouchers. RQ3: Local programme, Programmes to modify standard searches of patients databases to identify eligible patients, Reminder and recall systems (for providers), Personal invitation, Booking systems, Payment systems, Reminders (to eligible groups), Approaches to follow-up, Personal health records, Shared health records for providers, Audit and feedback on uptake rates, Incentives (for eligible groups), Incentives (for providers) **Vaccine(s) assessed:** Seasonal Influenza **Outcome(s) assessed:** *Primary outcome:* Changes in uptake rate among target groups **Secondary outcomes:** Changes in: ▪ knowledge ▪ attitudes ▪ beliefs ▪ acceptance ▪ intentions ▪ any adverse outcome.	only (RR 1.68; 95% CI 1.38 to 2.04)." Vaccine rate total sample: Intervention group (1,462/2,754, 53.1%), Control group (861/2,697, 31.9%). **Reminders (written and call-recall/telephone)** ▪ **"Moderate-quality evidence** from 2 RCTs with 20,641 participants showed that postcard reminders sent with an additional educational message or an interactive voice reminder (IVR) did not increase uptake of flu vaccination among **people with asthma or COPD** compared with usual postcard-only reminders (RR 1.00; 95% CI 0.97 to 1.03)." Vaccine rate: Intervention group (10,405/16,784, 62%), Control group (8,586/12,769, 67.2%). ▪ **"Low-quality evidence** from 1 RCT with 885 participants with **hypertension** found a mail reminder (a letter signed by a pharmacist and physician with additional educational information), sent with or without an additional telephone reminder (a personal call from a doctor) increased flu vaccination uptake compared with standard clinical practice (RR 1.52; 95% CI 1.24, 1.81). The magnitude of effect was greater for the mail + telephone intervention, but not significantly so (mail reminder only: RR 1.37; 95% CI 1.07 to 1.77; mail + telephone reminder: RR 1.68; 95% CI 1.31 to 2.16)." Vaccine rate total sample: Intervention group (285/571, 49.9%), Control group (104/314, 33.1%). ▪ **"Moderate-quality evidence** from 4 RCTs and 1 quasi-experimental study with 5,006 participants showed that reminder letters to parents consistently increased uptake of flu vaccination compared to no intervention in **children in clinical risk groups** (RR 1.53; 95% CI 1.25 to 1.89)." Vaccine rate: Intervention group (806/2,147, 37.5%), Control group (853/2,859, 29.8%). ▪ **"Low-quality evidence** from 2 randomised before and after studies with 490 participants showed that telephone recall (a personal call to parents from a paediatrician) increased flu vaccination uptake among **children in clinical risk groups** compared to usual care (a standard, anonymised mail reminder) (RR 1.62; 95% CI 1.33 to 1.98)." Vaccine rate: Intervention group (244/490, 49.8%), Control group (150/490, 30.6%). ▪ **"Low-quality evidence** from 2 before and after studies with 4,491 participants found that mail reminders with or without follow-up telephone calls increased uptake of flu vaccination in

	children with asthma compared to standard practice (RR 4.49; 95% CI 3.34 to 6.04)." Vaccine rate: Intervention group (1,110/2,494, 44.5%), Control group (190/1,997, 9.5%). ▪ **"Moderate-quality evidence** from 1 cluster RCT with 183 participants found that personalised postcard reminders increased the uptake of flu vaccination in **people from clinical risk groups** (RR 1.96; 95% CI 1.24 to 3.10)." Vaccine rate: Intervention group (79/199, 39.7%), Control group (17/84, 20.2%). ▪ **"Low-quality evidence** from 1 RCT with 525 participants found no increase in uptake of flu vaccination among **adults in clinical risk groups** when comparing mail with telephone reminders (RR 1.05; 95% CI 0.62 to 1.77). Neither form of reminder increased uptake compared with a 'no reminder' control group (Mail vs. control: RR 2.55; 95% CI 1.00 to 6.49; telephone vs. control: RR 2.44; 95% CI 0.95 to 6.24)." Vaccine rate: Intervention group (26/267, 9.7%), Control group (24/258, 9.3%). **SMS messages** ▪ **"Low-quality evidence** from 1 RCT with 3,905 **pregnant women** showed that, among women who intended to vaccinate at baseline, an SMS message with an interactive component for requesting a reminder was more effective than a 'usual' SMS (with no function to request a reminder) in promoting uptake or maintaining intention to vaccinate, but there is some uncertainty in the importance of the effect (RR 1.08; 95% CI 1.02 to 1.14). Among women who did not intend to vaccinate at baseline, an enhanced educational SMS tailored to the woman's specified reason for not wanting to vaccinate was no more effective than a general educational SMS in promoting uptake or changing their intention to vaccinate (RR 0.94; 95% CI 0.84 to 1.04)." Vaccine rate: **'**Intention to vaccinate' Intervention group (251/292, 86%), Control group (1,082/1,360, 79.6%). **'**No **i**ntention to vaccinate' Intervention group (367/1,025, 35.8%), Control group (470/1,228, 38.3%). ▪ **"Moderate-quality evidence** from 1 cluster RCT with 102,257 participants showed that there was no important increase in the uptake of flu vaccination among **adult patients in clinical risk groups** who were sent a tailored SMS reminder message compared with patients in control practices that used standard flu campaigns (RR 1.03 95% CI 1.02 to 1.05)." Vaccine rate: Intervention group (26,804/51,121, 52.4%), Control group (25,939/51,136, 50.7%).

	▪ **"Very low-quality evidence** from 2 RCTs with 1,357 participants found that SMS messages with educational content about the importance of flu vaccination did not increase the uptake of flu vaccination in **pregnant women** (RR 1.06; 95% CI 0.94 to 1.19)." Vaccine rate: Intervention group (318/680, 46.8%), Control group (300/677, 44.3%). **Provider prompts** ▪ **"Very low-quality evidence** from 2 before and after studies with 10,113 participants found that provider-directed prompts embedded in the electronic health records of **children from clinical risk groups** increased uptake of flu vaccination compared to pre-intervention rates (RR 1.69; 95% CI 1.26 to 2.26)." Vaccine rate: Intervention group (1,275/7,024, 18.2%), Control group (461/3,684, 12.5%). ▪ **"Very low-quality evidence** from 2 RCTs with 1,564 participants found that provider-directed prompts embedded in the electronic health records of **adults from clinical risk groups** did not increase uptake of flu vaccination compared with pre-intervention rates (RR 1.44; 95% CI 0.81 to 2.56). However, very low quality evidence from 2 retrospective cohort studies and 1 before and after study, with 1,487 participants, found that provider-directed prompts in the health records of adults from clinical risk groups did increase uptake of flu vaccination compared with pre-intervention rates (RR 5.70; 95% CI 1.18 to 27.53)." Vaccine rate RCTs: Intervention group (209/782, 26.7%), Control group (126/782, 16.1%). Vaccine rate observational studies: Intervention group (508/851, 59.7%), Control group (54/636, 8.5%). ▪ **"Very low-quality evidence** from a pooled analysis of 1 retrospective cohort study and 1 before and after study with 2624 participants found that provider-directed prompts used in antenatal clinics did not increase flu vaccination uptake in **pregnant women** compared with pre-intervention rates (RR 2.29; 95% CI 0.88 to 5.95)." Vaccine rate: Intervention group (838/1,481, 56.6%), Control group (341/1,143, 29.8%). **Audit and feedback** ▪ **"Very low-quality evidence** from 1 before and after study with 39 participating practices found that practice audits increased flu vaccination uptake in people with **CHD** (mean %

difference compared with pre-audit rate: 19.2%; 95% CI 14.4, 24; p<0.001) and **people with diabetes** (mean % difference: 16.9%; 95% CI 10.2 to 23.6; p<0.001). There was no significant increase in flu vaccination uptake among **post-splenectomy patients** (mean difference 6.1%; 95% CI -2.5 to 14.7; p=0.16)."

Provider Incentives (UK general practice Quality and Outcomes Framework)

- **"Very low-quality evidence** from 1 controlled before and after study with between 8,212 and 8,403 participants (across 4 flu seasons) found that increasing pay-for-performance targets increased practices' mean reported achievement of flu vaccination for eligible **CHD patients** (patients with the condition and not exception-reported) compared with control conditions **of COPD, diabetes mellitus and stroke**. The mean reported achievement co-efficient increased from 0.94 (95% CI 0.83 to 1.05) to 1.19 (95% CI 1.06 to 1.31) across the four season study."

- **"Very low-quality evidence** from 1 before and after study found that removing pay-for-performance targets for adults with **asthma** did not significantly affect flu vaccination uptake rates. Percentage achievement rates over 8 years remained relatively stable, ranging between 78% and 79%. The practice adjusted mean difference between 2005/06 season (pre-incentive change) and 2011/12 season (post-incentive change) was -0.07% (-1.01 to -0.39)."

Multicomponent

- **"Low-quality evidence** from 1 cluster RCT with 26,408 participants found that a multicomponent pharmacy-based intervention did not increase flu vaccination uptake in people with **chronic conditions** compared with unspecified control (RR 0.75; 95% CI 0.74 to 0.77)." Vaccine rate: Intervention group (6,763/12,716, 53.2%), Control group (9,659/13,692, 70.5%).

- **"Low-quality evidence** from 1 cluster RCT with 10,703 participants showed that a multi-component intervention for general practice, comprising educational outreach, audit and feedback may increase vaccination uptake across targeted conditions (**people with CHD, diabetes or post-splenectomy**) compared with no intervention (RR 1.06; 95% CI 1.03 to 1.08). Increased uptake was significantly greater for post-splenectomy patients (RR 1.37; 95% CI 1.12 to 1.67) than for people with CHD (RR 1.05; 95% CI 1.02 to 1.08) or diabetes (RR 1.06; 95% CI 1.02 to 1.10)." Vaccine rate all target groups: Intervention group (3,884/5,146,

	75.5%), Control group (3,962/5,557, 71.3%). ▪ **"Low-quality evidence** from 1 before and after study with 1,128 participants found that a multicomponent intervention incorporating parent and provider education and enhanced clinical informatics increased flu vaccination uptake among **immunocompromised children** compared with pre-intervention rates (RR 1.45; 95% CI 1.30 to 1.63 for 2 vaccinations; RR 1.41 95% CI 1.29 to 1.55 for 1 vaccination). A sub-group analysis found low and very low quality evidence that a clinically important increase in uptake was achieved in children undergoing treatment for **leukaemia/lymphoma** (RR 1.23 95% CI 1.10 to 1.39), **brain tumour** (RR 1.53; 95% CI 1.23 to 1.90) and **solid tumours** (RR 1.56; 95% CI 1.29 to 1.88), but not among children undergoing **stem cell transplant** (RR 1.33; 95% CI 0.97 to 1.89)." Vaccine rate all conditions: **2 vaccines** Intervention group (418/648, 64.5%), Control group (213/480, 44.4%). Vaccine rate all conditions: **1 vaccine** Intervention group (502/648, 77.5%), Control group (263/480, 54.8%). ▪ **"Very low-quality evidence** from 1 cluster RCT of 300 participants showed that a multicomponent educational intervention, including recommendation from the obstetrician/gynaecologist, reminder posters, education brochure, flu champion lapel buttons and an iPad-based component did not significantly increase uptake of flu vaccination among **pregnant women** (RR 1.47; 95% CI 0.71 to 3.07). Only recollection of the iPad component was associated with increased vaccination but the level of uncertainty associated with this effect was large (RR 3.17; 95% CI 1.07 to 9.44)." Vaccine rate: Intervention (16/149, 10.7%), Control (11/151, 7.3%). ▪ **"Low-quality evidence** from 1 cluster RCT with 6,460 participants found that a multicomponent educational intervention comprising educational seminars, assistance, action plan review and monthly support may increase flu vaccination uptake among **people with end-stage renal disease** compared with standard practice, but with a low level of certainty in the effect (adjusted mean difference in uptake: 8.86%; 95% CI 0.36% to 17.37%; p=0.04)." Mean Baseline Vaccine rate: Standard Intervention (mean 45.58% SD 12.91%), Intensive Intervention (mean 43.19%, SD 13.09%). ▪ **"Moderate-quality evidence** from 1 non-randomised control trial with 18,836 participants

found that multicomponent interventions, comprising increased access, provider prompts and telephone recall, increased uptake of flu vaccination among **children from clinical risk groups** compared with no intervention (RR 1.36; 95% CI 1.32 to 1.40)." Vaccine rate: Intervention (4,813/8,117, 59.3%). Control (4,684/10,719, 43.7%).

- **"Moderate-quality evidence** from 1 cluster RCT with 423 participants found that multicomponent interventions that included increasing demand from eligible groups and incorporated provider prompt interventions increased uptake of flu vaccination among **adults in clinical risk groups** compared with provider prompts alone (RR 1.62; 95% CI 1.26 to 2.09)." Vaccine rate: Intervention (83/177, 46.9%). Control (71/246, 28.9%).
- **"Very low-quality evidence** from 1 retrospective cohort and 1 controlled before and after study with 550,254 participants found that multicomponent interventions that included increasing demand from eligible groups and incorporated provider interventions did not increase uptake of flu vaccination among **adults in clinical risk groups** compared with usual care (RR 1.43; 95% CI 0.73 to 2.82)." Vaccine rate: Intervention (23,330/250,143, 9.3%). Control (27,030/300,111, 9%).
- **"Moderate quality evidence** from 5 RCTs with 27,628 participants found that multicomponent interventions, including improving access and increasing demand from **eligible groups** with reminders, education and incentives, increased uptake of flu vaccination compared with usual care (access and reduction of out of pocket expenses alone) among people from clinical risk groups (RR 1.40; 95% CI 1.22 to 1.62)." Vaccine rate: Intervention (8,631/20,324, 42.5%). Control (2,611/7,304, 35.7%).
- **"Very low-quality evidence** from 1 non-randomised control trial and 1 cluster randomised control trial with 2,291 participants found that multicomponent interventions, including increasing access, improving demand from **eligible groups** and incorporating provider interventions, did not increase uptake of flu vaccination among people from clinical risk groups compared to usual care (RR 1.21; 95% CI 0.80 to 1.82)." Vaccine rate: Intervention (493/1,178, 41.9%). Control (324/1,113, 29.1%).
- **"Low-quality evidence** from 1 before and after study with 1,000 participants found that a multicomponent intervention that included increasing access, improving demand from **eligible**

	groups and incorporated provider interventions, was significantly less effective at increasing uptake of flu vaccination among people in clinical risk groups 10 years post-intervention compared with 1 year post-intervention (RR 0.75; 95% CI 0.68 to 0.83). However, it remained more effective compared with uptake rates prior to the start of the intervention (RR 1.75; 95% CI 1.52 to 2.01)." Vaccine rate: Intervention (261/500, 52.2%). Control (347/500, 69.4%). ▪ **"Low-quality evidence** from 1 retrospective cohort study over 6 years of repeated measures with 12,488 participants (approx. 2,000 per annum) showed that an intervention combining education, standing order for nurse vaccination and feedback to providers increased uptake of flu vaccination in **pregnant women** in year 1 (RR 7.60 [6.50 to 8.88]) which increased further in year 2 (RR 11.29 [9.75 to 13.08]) compared to routine antenatal care delivered before the intervention, this magnitude of change was maintained in subsequent years with no significant change in effect after year 2 (RR14.85 [12.89 to 17.71] in year 6 compared to pre-intervention uptake)." Vaccine rate **Year 6**: Intervention (760/2,032, 37.4%). Control (222/8,813, 2.5%). ▪ **"Very low-quality evidence** from 1 before and after study with 439 participants found that a multicomponent intervention, including improved access, provider and patient education and provider prompts, increased uptake of flu vaccination compared with usual antenatal care in **pregnant women**, but there is some uncertainty in the importance of the effect (RR 1.33; 95% CI 1.02 to 1.77)." Vaccine rate: Intervention (96/240, 40%), Control (60/199, 30.1%). ▪ **"Very low-quality evidence** from 1 retrospective cohort with 602 participants found that a multicomponent intervention, incorporating education, access and nurse standing orders to vaccinate, did not increase uptake of flu vaccination in **pregnant women** compared with usual antenatal care (RR 10.54; 95% CI 0.77 to 143.80)." Vaccine rate: Intervention (78/412, 18.9%), Control (2/190, 1.1%). ▪ **"Very low-quality evidence** from 1 before and after study with 248 participants found that a multicomponent intervention, incorporating provider and patient education, provider prompts, participant reminders and improved access, increased flu vaccination uptake in **pregnant women** compared with usual antenatal care (RR 1.63; 1.31 to 2.04)." Vaccine rate: Intervention (149/480, 31%). Control (99/520, 19%).
NICE 2018b *(NICE guideline NG103, Evidence*	**Effectiveness evidence statements** *(taken directly from review)*

reviews for increasing uptake in children, August 2018) **Available at:** https://www.nice.org.uk/guidance/ng103/evidence/evidence-review-2-increasing-flu-vaccination-uptake-in-children-pdf-6532083615 **Review question(s):** RQ 1: What interventions to promote information about, and acceptability of, flu vaccination are the most effective for increasing acceptability and uptake of seasonal flu vaccination among children? RQ 2: What interventions to increase access to seasonal flu vaccine are the most effective in increasing uptake of seasonal flu vaccine among children? RQ 3: Which provider-based systems and processes for identifying, contacting and inviting clinical risk groups for seasonal flu vaccination are most effective in increasing uptake of among this population group? **Included studies:** 14 primary studies **Date of publication for included studies** 2009, 2011, 2012, 2013, 2014 (3), 2015 (6), 2016 **Population(s) assessed:** Children **Intervention(s) assessed:**	**Education** "Very low-quality evidence from a pooled analysis of 1 before-and-after study and 1 nonrandomised controlled trial, with a total of 4,970 participants, showed that educational interventions increase uptake of seasonal flu vaccination compared with usual practice (RR 1.73; 95%CI 1.19 to 2.51). However, very low quality evidence from 1 RCT with 116 participants found an educational intervention that combined risk communication and values clarification did not significantly increase uptake compared with providing standard risk information (RR: 0.86, 95%CI: 0.54 to 1.39, 15/35, 42.9% uptake in usual care group, 30/81, 37.0% uptake in education group) "Low and very low quality evidence from 2 studies (1 RCT with 407 participants and 1 before and after study with 90 participants) indicates that educational interventions may increase parental intention to vaccinate. The RCT found that combining risk communication and values clarification may increase intention to vaccinate a child compared with either intervention alone, or with standard risk information. However, previous vaccination behaviour or baseline intention moderates the effect of educational interventions. The before and after study found that a computer-based educational intervention (based on 3 learning theories) increased intention to vaccinate children by 2.2%. However the magnitude of effect may have been moderated by high levels of planned vaccination at baseline (89% already planned to get their child vaccinated). **Access** No studies were identified of interventions for increasing access to improve uptake of seasonal flu vaccination in children. **SMS messages** "Moderate-quality evidence from 3 RCTs with a total of 13,533 participants showed that provider short-message service (SMS) interventions to parents increased uptake of seasonal flu vaccination among children aged 6 months to 17 years compared with usual care, but there is some uncertainty in the importance of the effect (RR 1.12, 95% 95%CI 1.04 to 1.19, 2245/5766, 38.9% uptake in control group, 3274/7762, 42.2% uptake in intervention group).

RQ1: Information campaigns, Education, Tailored information and advice, Flu vaccination 'champion', Recommendations from a respected person. RQ2: Vaccination clinics in community settings, Dedicated flu vaccination clinics, Mass vaccination clinics in community or other settings ,Walk in or open access immunisation clinics, Extended hours clinics, Outreach or mobile services, Parallel clinics, Opportunistic vaccination, Flu vaccination vouchers. RQ3: Local programme, Programmes to modify standard searches of patients databases to identify eligible patients, Reminder and recall systems (for providers), Personal invitation, Booking systems, Payment systems, Reminders (to eligible groups), Approaches to follow-up, Personal health records, Shared health records for providers, Audit and feedback on uptake rates, Incentives (for eligible groups), Incentives (for providers) **Vaccine(s) assessed:** Seasonal Influenza **Outcome(s) assessed:** ***Primary outcome:*** Changes in uptake rate among target groups **Secondary outcomes:** Changes in: ▪ knowledge ▪ attitudes ▪ beliefs ▪ acceptance ▪ intentions	"Moderate-quality evidence from 2 RCTs with a total of 3,981 participants showed that more complex multicomponent SMS interventions to parents were more effective than single component SMS in increasing uptake of seasonal flu vaccination among children aged 6 months to 17 years, but there is some uncertainty in the importance of the effect (RR 1.09, 95%CI 1.02 to 1.17, 771/1985, 38.8% uptake in control group, 843/1996, 42.2% uptake in intervention group). Similarly, high quality evidence from 3 RCTs (with a total of 13,313 participants) found that SMS interventions with an educational component were more effective than usual care (a reminder to attend for flu vaccination with information on clinic times and how to book an appointment), again with some uncertainty in the importance of the effect (RR 1.09, 95%CI 1.03 to 1.19, 2246/5767, 38.9% uptake in control group, 3117/7546, 41.3% uptake in intervention group) A subgroup analysis of moderate quality evidence from 2 RCTs (with a total of 4,875 participants aged 23-59 months and 5,146 participants aged 5-17 years) found that provider SMS interventions targeting parents were more effective than usual care in increasing uptake of seasonal flu vaccination among children in both age groups, but with some uncertainty in the importance of these effects (age: 23-59 months: RR 1.08; 95%CI 1.01 to 1.16; 869/2113, 41.1% uptake in control group, 1213/2762, 43.9% uptake in intervention group; age 5-17 years: RR 1.10; 95%CI 1.00-1.20, 567/2105, 26.9% uptake in control group, 919/3041, 30.2% uptake in intervention group)." **Provider Prompts** "Low-quality evidence from 2 RCTs with 10,113 participants showed that a provider prompt intervention (using electronic medical records) activated throughout the flu season increased uptake of seasonal flu vaccination among children aged 6 months to 17 years compared with not having the prompt active, but there is some uncertainty in the importance of the effect (RR 1.03; 95%CI 1.01 to 1.06, 3172/4959, 64.0% uptake in control group, 3207/5154, 62.2% uptake in intervention group). The timing of provider prompts moderated their effect on vaccination uptake. There were no significant difference in the proportion of children who remained unvaccinated when the provider prompt was on versus off during autumn (Oct-Dec 2011; unvaccinated RR 0.99, 95%CI 0.89 to 1.09, 1975/2582, 76.5% uptake in control group, 1895/2469, 76.8% uptake in intervention group). However the intervention was effective during the winter compared with no provider prompts (Jan-Feb 2012; unvaccinated RR 0.85; 95%CI 0.76 to 0.95, 720/1158, 62.2% uptake in control group, 735/1082, 67.9% uptake in intervention group). Very low quality evidence

▪ any adverse outcome.	from 1 controlled before and after study with 788 participants found that practices using a provider prompt intervention (based on academic detailing) significantly increased uptake of flu vaccination in children aged 6 months to 5 years compared with preintervention baseline rates (OR 1.40; 95% CI 1.04 to 1.89, 55.4% uptake at baseline in intervention group, 63.1% uptake at follow-up in intervention group), while there was no significant increase in control practices (OR 1.30; 95% CI 0.93 to 1.82, 73.0% uptake at baseline in control group, 77.4% uptake at follow-up in control group). Moderate quality evidence from a retrospective cohort study with 43,022 participants found that a hospital based provider prompt associated with the medical record significantly increased inhospital rates of flu vaccination among inpatients aged 6 months to 17 years from 2.1% preintervention to 8% post-intervention (RR 3.81 95%CI 3.45 to 4.21)." In addition, a number of multicomponent interventions were assessed.
NICE 2018c *(NICE guideline NG103, Evidence reviews for increasing uptake in health and social care staff, August 2018)* **Available at:** https://www.nice.org.uk/guidance/ng103/evidence/4-increasing-flu-vaccination-uptake-in-health-and-social-care-staff-pdf-6532083617 **Review question(s):** Do education and programme leadership activities increase acceptability and uptake of seasonal flu vaccination among health and social care staff? Do opportunities to increase access to seasonal flu vaccination increase uptake among health and social care staff? **Included studies:** 14 primary studies **Date of publication for included studies**	**Effectiveness evidence statements** *(taken directly from review)* **Intervention 1:** Education "Very low-quality evidence from 1 cluster randomised control trial of 2,345 HCWs found that an information session (including educational slide show, videos and summary leaflet) did not increase flu vaccination uptake compared to a 'no additional information' control (RR 0.86; 95%CIs 0.63 to 1.17, 80/1144, 7.0% uptake in control group, 72/1201, 6.0% uptake in intervention group)." "Very low-quality evidence from 1 before and after study with 124 1st year medical students found that a 2 hour educational session (including interactive activities and discussions with infectious disease physicians) significantly changed Likert-scale responses to 7 out of 8 statements about the importance and acceptability of flu vaccination for HCWs. The most significant changes in pre- to post-intervention agreement were with the following statements: 'It is important to be vaccinated against influenza' (mean difference, MD: 0.68; 95%CI 0.43 to 0.93), 'I would recommend the influenza vaccine to family/friends' (MD: 0.48 (95%CI 0.26 to 0.70), 'HCWs should receive influenza vaccine' (MD: 0.36; 95%CI 0.17 to 0.55), and in disagreement with the statement: 'Influenza vaccine may cause influenza' (MD: -0.63; 95%CI -0.89 to -0.37)." "Moderate-quality evidence from 1 randomised control trial of 1,200 HCW (nurses, auxiliary and technical staff) found that a questionnaire (based on QBE), delivered a few months before the

Primary studies: 2003, 2004 (2), 2007 (4), 2008 (2), 2009, 2010, 2011 (3), 2012(3), 2013 (2), 2014 (2), 2015 (5), 2016 Systematic reviews: 2010, 2012, 2014, 2016 **Population(s) assessed:** Children **Intervention(s) assessed:** ▪ Assigned organisational lead to promote annual flu programme to peers. ▪ Targeted and settings-based information campaigns. ▪ Education, for example, multidisciplinary, peer education, educational outreach, educational DVDs, myth busting and e-learning packages. ▪ Flu vaccination 'champions'. ▪ Recommendations from a respected person, for example, a peer. ▪ Reminders and follow-up approaches (such as verbal reminders, text messages, emails, postcards and posters). ▪ Feedback on uptake rates. ▪ Incentive schemes, including targets for providers. ▪ Policies on conditions of employment (including the use of surgical masks, where applicable) and opt-out for health and social care staff. ▪ Signed statements from staff who decline a vaccine. ▪ Shared health record for providers of flu vaccination.	study hospitals' annual flu vaccination campaigns, increased flu vaccination uptake compared with a 'no questionnaire' control, but the importance of the effect is uncertain (RR 1.16; 95%CI 1.00 to 1.33, 218/600, 36.3% uptake in control group, 252/600, 42.0% uptake in intervention group)." "Very low-quality evidence from 8 before and after studies with 21,543 participants indicates that educational interventions, including educational materials, sessions and reminders increase flu vaccination uptake among HCWs compared with pre-intervention rates (RR 1.15; 95%CI 1.10 to 1.21, 2440/21012, 11.6% uptake in control group, 2920/21543, 13.6% uptake in intervention group)." "Low-to-moderate-quality evidence from 1 RCT with 800 participants found that educational materials alone (RR1.03; 95%CIs 0.80 to 1.31), incentives alone (RR 1.11; 95%CIs 0.87 to 1.41), or both combined (RR 1.17; 95%CIs 0.93 to 1.48, 76/200, 38.0% uptake in control group, 89/200, 44.5% uptake in intervention group) did not increase flu vaccination in HCWs compared with controls who received no intervention but were exposed to usual hospital vaccination publicity." "Moderate-quality evidence from 2 cluster RCTs and 2 randomised controlled trials, with a total of 6,085 participants, found that educational interventions (including learning and promotional materials, awareness raising by a nurse, letters and personalised phone calls) increased flu vaccination uptake among HCWs compared with no intervention or usual flu campaigns (RR 1.36; 95%CI 1.23 to 1.50, 657/3589, 18.3% uptake in control group, 607/2496, 24.3% uptake in intervention group). A subgroup analysis of one of the cluster RCTs, with 2,984 participants, found low to moderate quality evidence that, compared with no intervention, educational interventions increased vaccination uptake among HCWs in nursing homes (RR 1.80; 95% CI 1.33 to 2.43, 77/1364, 5.6% uptake in control group, 78/768, 10.2% uptake in intervention group) but not in primary care settings (RR 1.04 95%CI 0.80 to 1.35, 83/395, 21.0% uptake in control group, 100/457, 21.9% uptake in intervention group). A subgroup analysis of one of the RCTs with 496 participants found low to moderate quality evidence that, compared with no intervention, an educational intervention along with a letter from the chief of infectious diseases increased flu vaccination uptake among HCWs (RR 2.71; 95%CI 1.53 to 4.81, 14/175, 8.0% uptake in control group, 39/180, 21.7% uptake in intervention group), but there was no effect if the letter was substituted with a personalised phone call (RR 1.77; 95%CI 0.79 to 3.96, 8/71, 11.3% uptake in control group, 14/70, 20.0% uptake in intervention group)."

Vaccine(s) assessed: Seasonal Influenza **Outcome(s) assessed:** *Primary outcome:* Changes in uptake rate among target groups **Secondary outcomes:** Changes in: ▪ knowledge ▪ attitudes ▪ beliefs ▪ acceptance ▪ intentions ▪ any adverse outcome.	**Intervention 2:** Education and Incentives "Very low-quality evidence from 1 controlled before and after study and 1 RCT with a total of 15,628 participants indicates that educational campaigns and incentives including gift cards, entry into a lottery and a party did not increase uptake of flu vaccination among HCWs compared with pre-intervention or control group uptake (RR 1.03; 95%CI 0.98 to 1.09, 1091/2828, 38.6% uptake in control group, 5090/12800, 39.8% uptake in intervention group). A subgroup analysis of data from the controlled before and after study found very low and low quality evidence that vaccination uptake increased, compared with pre-intervention rates, in HCWs with indirect patient contact (RR 1.29; 95%CI 1.12 to 1.50, 138/412, 33.5% uptake in control group, 640/1478, 43.3% uptake in intervention group) and in those with direct contact, although there is some uncertainty in the importance of this effect (RR 1.11; 95% CI 1.02 to 1.21, 430/1247, 34.5% uptake in control group, 1499/3907, 38.4% uptake in intervention group). However, there was low quality evidence that vaccination uptake declined among business and administration staff following the intervention (RR 0.86; 95%CI 0.80 to 0.92, 447/969, 46.1% uptake in control group, 2778/7015, 39.6% uptake in intervention group)." **Intervention 3:** National campaigns "Very low-quality evidence from 1 before and after study with 86,765 participants found a national campaign to increase flu vaccination uptake among hospital-based HCWs increased overall uptake by 14.6% compared with baseline (mean pre-intervention rate: 1.7% vs. mean post-intervention uptake: 16.4%)." **Intervention 4:** Planning guides "Moderate quality-evidence from 1 cluster randomised control trial with 8,921 participants found that a guide to planning, implementing and evaluating flu vaccination campaigns with support provided (including a facilitated training workshop on how to use the guide) significantly increased flu vaccination uptake among HCWs in hospitals, continuing care and nursing homes compared with no-intervention controls who ran campaigns without the guide or additional support (median % change in vaccination rate from baseline to year 2: intervention: +7.1% (median rate at baseline 43% to year 2 51%) vs control: -5.8% (median rate at baseline 62% to year 2 55%); p=0.0001)."

	Intervention 5: Mandatory vaccination policy "Low-quality evidence from 1 before and after study with 6,957 participants found that mandatory vaccination, with a declination and mask wearing policy and alert system (automated e-mail sent to HCWs not currently compliant) increased year-on-year flu vaccination uptake among HCWs in one medical centre for 4 years following the intervention compared with pre-intervention uptake (Yr 1: RR 1.48; 95%CI 1.45 to 1.52; Year 2: RR 1.59; 95%CI 1.55 to 1.62; Year 3: RR 1.66; 95%CI 1.62 to 1.69; Year 4: RR 1.66 95% CI 1.62 to 1.69. Pre-intervention uptake 58%, this increased to 96% within 3 years)." "Very low-quality evidence from 1 before and after study of 271 healthcare facilities indicated that a mandatory vaccination and refusal/declination with mask wearing policy + free vaccine, education and coverage reporting increased flu vaccination uptake among all employees (+17.5%, 69.7% at baseline to 87.2% after intervention), HCWs in hospitals (+14.6%, 74% baseline to 88.6% after intervention) and HCWs in care homes (+16.2%, 55% baseline to 71.2% after intervention) compared with pre-intervention usual care (free access and education but no mandated vaccination or declination / face-mask policy)." "Very low-quality evidence from 6 before and after studies with 105,538 participants found that mandatory flu vaccinations in healthcare settings increased flu vaccination uptake among HCWs compared with pre-intervention rates (RR 1.71; 95%CI 1.70 to 1.72, 60726/105538, 57.5% uptake in control group, 103705/105538, 98.3% uptake in intervention group) **Intervention 6:** Declination "Very low-quality evidence from 1 randomised control trial with 122 participants found that that an opt-out strategy (with pre-booked appointments) delivered by e-mail to HCWs did not increase flu vaccination uptake compared with an opt-in e-mail (requiring an appointment to be booked) (RR 1.70; 95%CI 0.84 to 3.41, 10/61 16.4% uptake in control group, 17/61, 27.9% uptake in intervention group)." "Low-quality evidence from 1 before and after study with 20,170 participants indicated that a change from a paper based declination form as part of the declination policy to an internet based form that included an educational intervention, reminder and incentives increased uptake of flu vaccination among HCWs (internet vs. paper-based: RR 1.99; 95%CI 1.92 to 2.07)."

	Intervention 7: Access "Very low-quality evidence from 1 before and after study with around 25,000 participants showed that adding flexible worksite delivery of free vaccinations did not increase uptake among HCWs compared with free vaccination alone (RR 0.78; 95%CI 0.76 to 0.79, 13500/25000, 54% uptake in control group and 10500/25000, 42% uptake in intervention group). However very low quality evidence from another controlled before and after study with 5,946 participants found that flexible worksite delivery of free vaccinations in addition to educational materials and incentives did increase uptake among HCWs compared with free vaccination, education and incentives alone (RR 1.70; 95%CI 1.66 to 1.74, 3389/5946, 57.0% uptake in control group, 5768/5946, 97% uptake in intervention group)." **Intervention 8:** Incentives "Very low-quality evidence from 1 before and after study with 5,151 participants found that adding incentives to an existing intervention that included educational material, reminders and feedback increased uptake of flu vaccination among HCWs with direct patient care compared with uptake rates before the incentives were added, but there is uncertainty in the importance of the effect (RR 1.10; 95%CI 1.01 to 1.20, 430/1247, 34.5% uptake in control group, 1484/3904, 38.0% uptake in intervention group)." **Intervention 9:** Component of interventions "Very low-quality evidence from a systematic review of 46 studies (2 RCT, 9 cRCT, 3cB&A, 32 B&A), using a component matrix approach, showed that the most effective intervention component for improving uptake of vaccination was hard mandated approaches (RR of remaining unvaccinated = 0.18; 95%CI: 0.08 to 0.45), followed by soft mandates such as declination statements (RRunvacc = 0.64; 95%CI: 0.45 to 0.92), increased awareness (RRunvacc = 0.83; 95%CI: 0.71 to 0.97) and increased access (RRunvacc = 0.88; 95%CI: 0.78 to 1.00). For incentive-based and education-based interventions, there were no significant differences compared with comparator groups in respect of HCWs remaining unvaccinated (incentive-based approaches: RRunvacc = 0.89; 95%CI: 0.77 to 1.03; education-based approaches: RRunvacc = 0.96, 95% CI: 0.84 to 1.10)." In addition, a number of multicomponent interventions were assessed, that combined two or more interventions (including those listed previously).

Sanftenberg 2019 **DOI:** 10.3238/arztebl.2019.0645 **Date of literature search:** October 2018 **Included studies:** 15 RCTs **Date of publication for included studies** 1987, 1991(2), 1992, 1996, 1997, 1998, 2002 (2), 2004, 2005, 2016 (2), 2017, 2018, **Population(s) assessed:** Patients with physical or mental chronic diseases; patients who have endured a chronic illness for three months or more, or who were recently diagnosed with a condition that is expected to last more than three months. **Intervention(s) assessed:** Provider- or system-based interventions in primary care. **Vaccine(s) assessed:** Influenza **Outcome(s) assessed:** Change in influenza vaccination coverage Vacccination rates in control group ranged from 49.1% to 72.5% depending on subgroup – highest was in coronary heart disease subgroup	**Quality of systematic review (GRADE):** Low **Interventions targeting medical professionals (n=7)** "Altogether, simple interventions achieved greater effects and were more likely to produce significant results than complex interventions" *Training programs for office teams (n = 3)* ▪ Effectiveness of intervention; RR 1.35 (95% CI 1.14; 1.59), RR 1.29 (95% CI, 1.03; 1.62) in two studies. ▪ Absolute differences in vaccination rate between control and intervention arms, +22% and +14.1% in these two studies. ▪ Effectiveness per sub-groups in third study; CHD, RR 1.02 (95% CI, 1.00-1.04), Diabetes, RR 1.02 (95% CI, 1.00-1.04), splenectomy, RR 1.08 (95% CI 0.90-1.25) ▪ Uptake rates in control group 61.6%, 49.1% per sub-groups in third study; CHD, 72.5%, Diabetes, 70.2%, splenectomy, 58.0% ▪ Absolute differences in vaccination rate between control and intervention arms per subgroup, +3.6% (CHD), +4.2% (diabetes) and +22.6% (splenectomy) in this study *Reminder systems for physicians (n = 2)* ▪ Effectiveness of intervention; RR 1.86, (p=0.001) and RR 0.95, (95% CI0.67-1.35), in two studies ▪ Absolute differences in vaccination rate between control and intervention arms, -2.2% in one study where this is reported. ▪ Uptake rates in control group 21.3% ▪ Effectiveness per subgroup: N/A *Extending competence of medical professionals (n = 2)* ▪ Effectiveness of intervention, RR 1.27 (95% CI, 1.11-1.46) and RR 0.89 (95% CI, 0.70-1.12) in two studies ▪ Absolute differences in vaccination rate between control and intervention arms, -7.4% in one study and +17% in the other. ▪ Uptake rate in control groups 64.0% and 64.5% ▪ Effectiveness per subgroup: N/A

Interventions targeting patients (n=8)

Text message (n = 2)

- Effectiveness of intervention, RR 1.05 (95% CI, 1.00-1.11) and RR 1.41 (95% CI, 1.22-1.63) in two studies
- Absolute differences in vaccination rate between control and intervention arms, +1.7% and +3.8% in two studies.
- Uptake in control groups 50.7%, 9.1%
- Effectiveness per subgroup: N/A

Reminder Postcard (n = 2)

- Effectiveness of intervention, RR 2.77 (95% CI, 2.05-3.75) in one study
- Absolute differences in vaccination rate between control and intervention arms, +16.1% in one study
- Uptake in control group 9.1%
- Effectiveness per subgroup: In both subgroups (older and younger than 65 years), "a personalized postcard achieved a significant result, with generally greater effect sizes (RR 1.09 and 1.11; p <0.05) than for a non-personalized postcard (RR 1.05 and 1.07; p >0.05)." Control group vaccination rate was 35.8% for patients under 65 years and 50.7% for those over 65 years.

Reminder Letter (n = 3)

- Effectiveness of intervention, RR 0.99 (95% CI, 0.60-1.63 and RR 1.29 (95% CI, 1.15-1.45) in 2 studies.
- Absolute differences in vaccination rate between control and intervention arms, -0.4% in one study and +8.8% in the other.
- Uptake in control group 30.9%, 30.1%
- Effectiveness per subgroup: "Only in their younger subpopulation (<65 years) did Baker et al. achieve a significant effect (RR 1.09; p <0.05) by sending a reminder letter."
- Two studies (1 of which already included above) "compared sending two reminders to each patient with sending only one reminder. In one study, the vaccination rate fell by

	5.8% in 18- to 49-year-olds and rose by 4.6% in 50- to 64-year-olds (RR 0.94 (95% CI, 0.84-1.05) and RR 1.08 (95% CI, 1.00; 1.15), respectively. In the other study, the rate went down by 6.1%, RR 0.80 (95% CI 0.46; 1.38)." *Educational brochure (n = 1)* ▪ The combination of brochure and financial incentive (RR 2.78 [1.13; 6.87]) was superior to the brochure alone (RR 2.53 [1.04; 6.15]), but not to the financial incentive alone (RR 2.79 [1.18; 6.62]) ▪ Absolute differences in vaccination rate between control and intervention arms, +14.3% and +16.7% for these 2 interventions. ▪ Uptake in control group 9.4% ▪ Effectiveness per subgroup: N/A *Financial incentive (n = 1)* ▪ Effectiveness of intervention, RR 2.79 (95% CI, 1.18-6.62) in 1 study. ▪ Absolute differences in vaccination rate between control and intervention arms, +16.8% ▪ Uptake in control group 9.4% ▪ Effectiveness per subgroup: N/A
Thomas 2018 [Cochrane Review] **DOI:** 10.1002/14651858.CD005188.pub4 **Date of literature search:** 7 December 2017 This is a Cochrane review that updated prior versions published in 2010 and 2014. **Included studies:** 61 studies: 36 were RCTs and 25 were cluster-randomised trials **Date of publication for included studies** 1986, 1987(2), 1989 (2), 1991(4), 1992, 1993, 1994 (2), 1995(5), 1996, 1997(2), 1998 (4), 1999 (6), 2000 (3), 2001 (3), 2002 (9), 2003 (2), 2004, 2006, 2007,	**Quality of systematic review (GRADE):** High **Intervention 1:** Increasing community demand for vaccination (12 strategies, 41 trials, 767,460 participants) Effective interventions: reminders/recalls using letters and leaflets, and nurses or pharmacists educating and nurses vaccinating patients. Individual effective studies consisted of client outreach by retired teachers, receptionists, nurses, and medical students. One successful intervention that could be meta-analysed was client reminders or recalls by letter plus leaflet or postcard compared to reminder: Odds ratio (OR) 1.11, 95% confidence interval (CI) 1.07 to 1.15; 3 studies; 64,200 participants, anticipated absolute effects: 208 per 1000 in comparator group and 225 per 1000 in intervention group.

2008 (2),2010, 2011 (3), 2012(2), 2015, 2017 (2), **Population(s) assessed:** People aged 60 years or older in the community **Intervention(s) assessed:** Increasing community demand, enhancing access, provider or system based interventions, societal interventions **Vaccine(s) assessed:** influenza vaccination **Outcome(s) assessed:** Uptake of vaccination against influenza in those aged 60 years or older, primary measure of effect: OR's	Successful interventions tested by single studies were: patient outreach by retired teachers (OR 3.33, 95% CI 1.79 to 6.22, anticipated absolute effects: 231 per 1000 in comparator group and 500 per 1000 in intervention group); invitations by clinic receptionists (OR 2.72, 95% CI 1.55 to 4.76, anticipated absolute effects:220 per 1000 in comparator group and 433 per 1000 in intervention group); nurses or pharmacists educating and nurses vaccinating patients (OR 152.95, 95% CI 9.39 to 2490.67); medical students counselling patients (OR 1.62, 95% CI 1.11 to 2.35, anticipated absolute effects: 254 per 1000 in comparator group and 355 per 1000 in intervention); and multiple recall questionnaires (OR 1.13, 95% CI 1.03 to 1.24, anticipated absolute effects: 750 per 1000 in comparator group and 773 per 1000 in intervention group). **Intervention 2:** Improving vaccination access (6 strategies, 8 trials, 9353 participants) Effective interventions: home visits, client group clinic visits, and free vaccine offers. Meta-analysis results from 2 studies of home visits: OR 1.30, 95% CI 1.05 to 1.61 (anticipated absolute effects:213 per 1000 in comparator group and 260 per 1000 in intervention); 2 studies that tested free vaccine compared to patient payment for vaccine: OR 2.36, 95% CI 1.98 to 2.82 anticipated absolute effects:304 per 1000 in comparator group and 507 per 1000 in intervention). **Intervention 3:** Improving provision by providers or the healthcare system (11 strategies, 15 trials, 278,524 participants) Effective interventions: physician payment, physician reminders, clinic posters encouraging physician competition, and chart reviews plus benchmarking to rates of the top 10% of physicians. One successful intervention that could be meta-analysed focused on payments to physicians (OR 2.22, 95% CI 1.77 to 2.77, anticipated absolute effects: 100 per 1000 in comparator group and 198 per 1000 in intervention). Successful interventions tested by individual studies were: reminding physicians to vaccinate all patients (OR 2.47, 95% CI 1.53 to 3.99, anticipated absolute effects: 314 per 1000 in comparator group and 530 per 1000 in intervention); posters in clinics presenting vaccination rates and encouraging competition between doctors (OR 2.03, 95% CI 1.86 to 2.22, anticipated absolute effects: 504 per 1000 in comparator group and 673 per 1000 in intervention); and chart reviews and benchmarking to the rates achieved by the top 10% of physicians (OR 3.43, 95% CI 2.37 to 4.97, anticipated absolute effects: 60 per 1000 in comparator group and 180 per

	1000 in intervention). **Individual studies <u>not</u> effective**: posters plus postcards versus posters alone, educational reminders to physicians compared with mailed educational materials, educational outreach plus feedback to teams versus written feedback, and increasing staff vaccination rates. ***Note:*** *no evidence for societal interventions retrieved*
Wong 2016 **DOI:** 10.1016/j.vaccine.2015.11.020 **Date of literature search:** August 2014 **Included studies:** 11 studies (4 RCTS, 7 observational studies). **Date of publication for included studies** 2007, 2010 (2), 2011, 2012 (3), 2013 (3), 2014 **Population(s) assessed:** Pregnant women **Intervention(s) assessed:** Any intervention to increase influenza vaccine uptake during pregnancy. **Vaccine(s) assessed:** Seasonal influenza **Outcome(s) assessed:** Vaccination uptake	**Quality of systematic review (GRADE):** Low All 11 studies in this systematic review are encompassed in the NICE 2018 evidence summary, hence a very high-level overview only is presented here: **Provider-focused interventions (n=3 studies), Pregnant woman-focused interventions (n=5 studies), Interventions with bundled components (n=3 studies)** ▪ One moderate quality RCT, targeting pregnant women, showed that an influenza pamphlet, with or without a verbalised benefit statement, improved the vaccination rate (RD = 0.26 and RD = 0.39 respectively). ▪ The 3 other reviewed RCTs, which targeted pregnant women, showed discordant results, with RDs ranging from −0.15 to 0.03. ▪ Although all 7 observational studies (3 provider-focussed, 1 pregnant women-focussed and 3 bundled interventions) significantly improved vaccination rates (RDs ranged from 0.03 to 0.44), the quality of the evidence varied.

Appendix 3. Citations for reviews of interventions of 'critically low' quality

First Author	Year Published	DOI	Reference
Balzarini	2020	10.1016/j.vaccine.2020.05.083	Balzarini, F., et al. (2020). "Does the use of personal electronic health records increase vaccine uptake? A systematic review." Vaccine 38(38): 5966-5978.
Bechini	2020	10.3390/vaccines8020165	Bechini, A., et al. (2020). "Utility of Healthcare System-Based Interventions in Improving the Uptake of Influenza Vaccination in Healthcare Workers at Long-Term Care Facilities: A Systematic Review." Vaccines 8(2).
Bisset	2018	10.1016/j.vaccine.2018.04.013	Bisset, K. A. and P. Paterson (2018). "Strategies for increasing uptake of vaccination in pregnancy in high-income countries: A systematic review." Vaccine 36(20): 2751-2759.
Isenor	2016	10.1016/j.vaccine.2016.08.085	Isenor, J. E., et al. (2016). "Impact of pharmacists as immunizers on vaccination rates: A systematic review and meta-analysis." Vaccine 34(47): 5708-5723.
Jain	2017	10.1016/j.vaccine.2017.03.013	Jain, A., et al. (2017). "Lower vaccine uptake amongst older individuals living alone: A systematic review and meta-analysis of social determinants of vaccine uptake." Vaccine 35(18): 2315-2328.
Jarrett	2015	https://www.sciencedirect.com/science/article/pii/S0264410X15005046	Jarrett, C., et al. (2015). "Strategies for addressing vaccine hesitancy - A systematic review." Vaccine 33(34): 4180-4190.
Lorenc	2017	10.1186/s12913-017-2703-4	Lorenc, T., et al. (2017). "Seasonal influenza vaccination of healthcare workers: systematic review of qualitative evidence." BMC health services research 17(1): 732.
Lytras	2016	10.1080/21645515.2015.110665	Lytras, T., et al. (2016). "Interventions to increase

		6	seasonal influenza vaccine coverage in healthcare workers: A systematic review and meta-regression analysis." Human Vaccines & Immunotherapeutics 12(3): 671-681.
Rashid	2016	10.1377/hlthaff.2015.1087	Rashid, H., et al. (2016). "Assessing Interventions To Improve Influenza Vaccine Uptake Among Health Care Workers." Health affairs (Project Hope) 35(2): 284-292.
Schmid	2017	10.1371/journal.pone.0170550	Schmid, P., et al. (2017). "Barriers of Influenza Vaccination Intention and Behavior - A Systematic Review of Influenza Vaccine Hesitancy, 2005 - 2016." PloS one 12(1): e0170550.

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