National Institute for Health and Care Excellence

Final

Flu vaccination: increasing uptake

Evidence reviews for increasing uptake in clinical risk groups

NICE guideline NG103

Evidence reviews

August, 2018

Final

These evidence reviews were developed by Public Health – Internal Guideline Development team

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ISBN: 978-1-4731-2864-4

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Introduction

Each winter hundreds of thousands of people see their GP and tens of thousands are hospitalised because of flu.

Deaths attributable to flu range from around 4,000 to 14,000 per year, with an average of around 8,000 per year (Public Health England). Rates of morbidity and mortality from flu-related illness are higher among people with certain underlying health conditions and pregnant women. Flu during pregnancy may also be associated with perinatal mortality, prematurity, smaller neonatal size and lower birth weight. The Green Book estimates that in England during 2010/11, the mortality rate per 100,000 population for those aged 6 months to 64 years with one of the following health conditions was:

- immunosuppression – 20 per 100,000
- chronic liver disease – 15.8 per 100,000
- chronic neurological disease (excluding stroke and transient ischaemic attacks) – 14.7 per 100,000
- chronic renal disease – 4.8 per 100,000
- chronic heart disease – 3.7 per 100,000
- chronic respiratory disease – 2.4 per 100,000
- diabetes – 2.2 per 100,000.

Vaccine uptake among clinical risk groups is generally low. In 2017/18 in England it was 49% overall, and 47% for pregnant women. This compared with 73% for people aged 65 years or over.

NHS England is responsible for commissioning the seasonal flu vaccination programme for at risk people in the community (see section 7A of the NHS public health functions agreement 2017-18, Department of Health).

The aim of this review was to examine interventions that can be delivered in the community to increase the uptake of influenza vaccination in clinical risk groups.

The review focused on identifying studies that fulfilled the criteria specified in Table 1. For full details of the review protocol see Appendix A.

PICO table

Table 1: PICO inclusion criteria for the review questions on increasing uptake in clinical risk groups

Population	Clinical risk groups eligible for free vaccination according to the Green Book[a]
Interventions RQ1	Information campaigns: ○ targeted ○ community based, including local radio campaigns ○ settings based ○ online campaigns, including social media and apps Education: ○ educational tools ○ peer education (carried out by a community member who shares similar life experiences to the community they are working with) ○ lay education (carried out by community members working in a non-professional capacity) Tailored information and advice delivered: ○ during home visits ○ during consultation with health and social care workers ○ at support group meetings for patients and other people who use services Flu vaccination 'champion' : ○ practitioner ○ peer Recommendations from a respected person: ○ health or social care worker ○ carer ○ peer ○ volunteer ○ family member
Interventions RQ2	Vaccination clinics in community settings: ○ community pharmacies ○ antenatal clinics ○ specialist clinics e.g. drug and alcohol services, mental health services ○ community venues e.g. libraries, children's centres Dedicated flu vaccination clinics Mass vaccination clinics in community or other settings Walk in or open access immunisation clinics Extended hours clinics: ○ weekends

[a] https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19

	○ evenings (after 6 pm) ○ early mornings (before 8 am) ○ 24 hour access Outreach or mobile services: ○ home or domiciliary or day centre visits ○ support group meeting visits ○ residential or care home visits ○ special schools visits ○ inpatient visits ○ custodial visits ○ immigration settings ○ mobile clinics e.g. in community Parallel clinics: ○ offer flu vaccination in parallel with regular appointments e.g. with midwives, clinicians, inpatient and outpatient clinics, long stay wards, etc. ○ coordinated timing of other programmes e.g. retinal screening for diabetic patients within flu season Opportunistic vaccination e.g. visits to GP, practice nurse or consultant for other medical conditions Flu vaccination vouchers to enable eligible groups to receive flu vaccination from community providers
Interventions RQ3	Local programme ○ assigned lead for an annual flu programme ○ local approach ○ systems and processes in working with the community ○ practice approach Programmes to modify standard searches of patient databases to identify eligible patients. Reminder and recall systems (for providers) ○ clinical alerts and prompts Personal invitation ○ GP ○ community pharmacist ○ health or social care worker ○ from several professionals Booking systems ○ dedicated flu lines or online systems Payment systems (fiscal arrangements) ○ outside primary care Reminders (to eligible groups) ○ text messages ○ emails ○ postcards ○ posters ○ telephone call Approaches to follow-up ○ phoning patients Personal health record (so eligible people can see if their vaccination is due) Shared health records for providers. ○ Integration of primary and secondary care health records ○ Centralised uptake record Audit and feedback on uptake rates

	○ weekly statistics ○ content and delivery of feedback ○ practical relevance (e.g. how many more people need to be vaccinated to achieve target number) ○ comparison data e.g. between GP practices Incentives (for eligible groups) ○ voucher schemes Incentive schemes (for providers) ○ targets ○ quality and outcomes framework ○ voucher schemes
Comparators RQ1-3	• Other intervention • Status quo/do nothing/control • Time (before and after)
Outcomes RQ1-3	• Uptake (Critical) • Acceptability (Critical) • Knowledge (Important) • Attitudes (Important) • Beliefs (Important) • Intentions (Important) • Adverse outcomes [any] (Important)
Economic Outcomes RQ1-3	• Economic evaluations • Cost-utility (cost per QALY) • Cost benefit (i.e. Net benefit) • Cost-effectiveness (Cost per unit of effect) • Cost minimisation • Cost-consequence

Public Health evidence

Included studies

Studies were included if they met the PICO and were:

- Randomised controlled trials (RCT) including cluster randomised controlled trials (cRCT), non-randomised controlled trials (nRCT), randomised pragmatic trials (RPT), controlled before and after studies, before and after studies.
- Observational studies were included only if they provided evidence on approaches where there was no experimental study design and they included a comparison group (i.e. comparative case control and cohort studies).
- Systematic reviews of effectiveness studies that directly answered the questions and reported critical or important outcomes were included. If they did not directly answer the questions they were citation chased for relevant studies.
- Qualitative studies (interviews and focus groups) that assessed the views and opinions of people in the relevant clinical risk groups (or their carers) on any of the interventions listed in table 1.
- Economic studies which included costs and benefits of any (or a combination) of the interventions listed in table 1.

See table 2 (effectiveness and observational studies), and table 3 (qualitative studies) for a summary of included studies.

Excluded studies

Studies were excluded if they were:

- Narrative reviews, case studies/reports, case series, non-comparative studies (unless they were qualitative studies meeting the inclusion criteria).
- Cross-sectional surveys, epidemiological studies, correlation studies and studies to assess coverage rates.
- Economic studies that included only costs, burden of disease and cost of illness.
- Cost-effectiveness studies of the flu vaccination itself.
- Animal studies.
- Not published in the English language.

For the list of studies that were excluded after full-text review, with reasons for their exclusion, see Appendix L.

Evidence Review

In total, 6017 references were found for these review questions, and full-text versions of 227 citations that seemed potentially relevant to this topic were retrieved. In total 19 primary studies and 3 systematic reviews are included in the effectiveness section of the review, 9 studies are included in the qualitative review section and 2 cost effectiveness studies are included (see PRISMA diagram in Appendix M).

Summary of studies included in the effectiveness evidence review

Table 2a Included effectiveness primary studies for each review question (RQ1-3)

RQ1: Information, education, tailoring, flu champions and recommendation by a respected person					
First author, year	**Design**	**Country**	**Setting**	**Population**	**Intervention**
Frew (2014)	RCT	USA	Variety of consenting venues (Clinics)	Pregnant women	Message framing (gain and loss – safety, risks and protection to mother and baby)
Goodman (2015)	RCT	USA	Obstetrician /Gynaecologist providers from suburban clinics	Pregnant women	Education video (CDC educational video 'Protect yourself, protect your baby' (3 ½ minutes))
Harris (2006)	RCT	Australia	3 hospital COPD clinics	People with Chronic Obstructive Pulmonary Disease (COPD)	A patient manual, 'Talking to your doctor about COPD'
O'Connor (1996)	RCT	Canada	Patient respiratory and cardiac clinics	Unimmunized patients with chronic respiratory or cardiac disease	Message framing (positive and negative - % who remain flu free or not & side effects of vaccine
RQ2: Flexible, walk-in/open access, outreach and parallel clinics or other opportunistic approach					
Atkins (2016)	Before and After	UK	Community pharmacies	Pregnant women or people with a Green-book specified chronic disease: • Kidney disease • Immunosuppression	Enabling NHS reimbursed pharmacies to provide seasonal flu vaccination to all eligible individuals registered with a London borough primary care trust

				• Respiratory disease • Neurological disease • Liver disease	
Rai & Wood (2017)	Before and After	UK	Community pharmacies	Adults (18-64) in a clinical risk group as specified in Green Book	Flu vaccination service commissioned by NHSE regional team for Birmingham, Solihull and Black Country for 2014/15 flu season. Scheme enabled pharmacists to provide the seasonal flu vaccine to eligible adults.
RQ3: Local leadership, reminder-recall, provider prompts, incentives, audit and feedback					
Herrett (2016)	cRCT	UK	GP practices	People in 'at risk' groups: • CHD • Diabetes • Respiratory • Liver disease • Kidney disease • Neurological • Immunosuppressio n	Text message reminders in addition to usual flu campaign activities
Jordan (2015)	RCT	USA	US wide mobile text messaging service	Pregnant women	Enhanced message plus the opportunity to set up a general or specific reminder
Kontopantelis 2012	cB&A	UK	Primary care	Asthma patients 16+	Increasing pay for performance targets for CHD patients (QOF)
Kontopantelis 2014	B&A	UK	Primary care	CHD patients	Removing financial incentive for immunising asthma patients (QOF)
Minor (2010)	RCT	USA	Hypertension clinic	Patients with hypertension	Mail and telephone reminders
Shoup (2015)	RCT	USA	Managed care organization	Adults (19-64yrs) with asthma or chronic obstructive pulmonary disease (COPD)	Reminder strategies: postcard reminder only (usual care) Interactive Voice Reminder (IVR) only, postcard plus IVR reminder
Siriwardena, 2004	Before and After (subgroup analysis of 2002 study)	UK	General Practices,	People aged 65yrs+ and patients with CHD, diabetes or a previous splenectomy	Multi-practice audit and feedback directed at improving influenza vaccination rates in high risk groups
Walter 2008	RCT (with 2 embedded before and after studies)	USA	Primary care practices	Asthma	Postcard reminders including an additional education message (Postcard Plus) and a practice improvement intervention

RQ1-3: Multi-component interventions crossing over review questions					
Information/Education (RQ1) and Audit and Feedback (RQ3)					
Bond 2011	cRCT	USA	Outpatient dialysis centres	People with end stage renal disease	Audit and feedback report; educational materials and seminars. Plus, monthly support and monitoring of plan implementation
Siriwardena 2002	Cluster RCT	UK	General Practices	People aged 65yrs+ and patients with CHD, diabetes or a previous splenectomy	An educational visit to primary healthcare teams, in addition to audit and feedback directed at improving influenza vaccination rates
Patient/family and provider education (RQ1), outpatient clinic, inpatient intervention (RQ2), leadership and enhanced office systems (RQ3)					
Freedman 2015	Before and after	USA	Oncology inpatients unit and 3 outpatient clinic sites at a Children's Hospital	Immunocompromised (undergoing chemotherapy or stem cell transplant (SCT))	5 interventions delivered concomitantly: Parent/family education, clinical informatics, outpatient clinic interventions, inpatient intervention, provider education intervention
Information and education (RQ1), personalised invitation (RQ3)					
Marra (2014)	Cluster RCT	Canada	pharmacy based immunisation services	2-64 year olds with a chronic condition.	Multicomponent intervention: standardised training on providing injections, the use and safety monitoring of influenza vaccination, personalised invitation letters to the eligible clients; advertisements in the media and posters
Vaccine champion, promotion and education (RQ1), peer to peer vaccination, location maps and vaccination in community settings (RQ2)					
Chamberlain 2015	Cluster RCT	USA	Obstetric clinics	Pregnant women	Multi component practice, provider and patient level interventions including: vaccine champions, Lapel buttons, posters, brochures, provider-to-patient talking points, peer to peer vaccination promotion education, i-pad interactive tutorial; local vaccination provider maps.

Table 2b: Included effectiveness systematic reviews with included studies noted where relevant to each review question (RQ1-3)

First author, year	Design	Country	Setting	Population	Intervention
Aigbogun 2015	Systematic Review	Various	Various	Children with Chronic Conditions	Education (RQ1) Access (RQ2)

					Reminder, recall, prompts (RQ3) plus Multi -component interventions
Ndiaye 2005	Systematic Review	Various	Various	Adults with Chronic Conditions	Reminder, recall, prompts (RQ3) plus Multi -component interventions
Wong 2016	Systematic Review	Various	Various	Pregnant Women	Provider prompts (RQ3) plus Multi -component interventions

For full evidence tables detailing studies included in this review see Appendix G:.

Synthesis and quality assessment of effectiveness evidence

Included studies were a mix of experimental and observational study designs. Studies with a control group were assessed for risk of bias using the Cochrane Effective Practice and Organisation of Care (EPOC) checklist as referenced in Appendix H of the NICE methods manual. The Effective Public Health Practice Project (EPHPP) QA Checklist was applied to assess risk of bias in uncontrolled before-and-after studies.

Data analyses were undertaken in Review Manager (version 5.3). Where data from more than one study were pooled in a meta-analysis, a random effects model was used to account for the different effects anticipated across different study populations and types of intervention. A fixed effects model was used only where it was clear that an intervention with identical content and mode of delivery was examined in different studies undertaken in the same population subgroup (for example, children with asthma).

A general approach was taken to pool data from RCTs with data from observational studies where the same outcome was being investigated under conditions that were considered to be sufficiently similar. This is because although observational studies may introduce more bias than RCTs, it has been suggested that this issue might be outweighed by the potential benefits of including data from observational studies to improve inferences from RCT trials, particularly where RCT evidence is limited, as the increased sample size may provide additional evidence to choose a correct intervention for a condition (Shrier et al 2007)[b]. A sensitivity analysis was conducted in all instances where RCTs and observational studies were pooled to assess the impact of the pooling. Appendix K details instances where sensitivity analyses resulted in a decision not to pool different study types.

GRADE methodology was used to appraise the evidence across five potential sources of uncertainty: risk of bias, indirectness, inconsistency, imprecision and other issues. Overall ratings start at 'High' where the evidence comes from RCTs, and 'Low' for evidence derived from observational studies. Where RCT and observational studies remained pooled in analyses, a decision was made to start GRADE from 'Low'. Details of how the evidence for each outcome was appraised across each of the quality domains is given below.

[b] Shrier, I., Boivin, J., Steele, R. J. et al. 2007. Should Meta-Analyses of Interventions Include Observational Studies in Addition to Randomized Controlled Trials? A Critical Examination of Underlying Principles. *American Journal of Epidemiology,* 166 (10); 1203-1209.

Quality domain	Description
Risk of bias	Limitations in study design and implementation may bias the estimates of the treatment effect. Major limitations in studies decrease the confidence in the estimate of the effect. Examples of such limitations are selection bias (often due to poor allocation concealment), performance and detection bias (often due to a lack of blinding of the patient, healthcare professional or assessor) and attrition bias (due to missing data causing systematic bias in the analysis). Where there are no study limitations, evidence is assessed as having 'no serious' risk of bias. Alternatively, evidence may be downgraded one level ('serious' risk of bias) or two levels ('very serious' risk of bias).
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question. Where the evidence is directly applicable to the PICO, it is assessed as having 'no serious' risk of indirectness. Alternatively, evidence may be downgraded one level ('serious' risk of indirectness) or two levels ('very serious' risk of indirectness).
Inconsistency	Inconsistency refers to an unexplained heterogeneity of effect estimates between studies pooled in the same meta-analysis. The I^2 statistic describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance). For the purposes of this review, the committee agreed that a large amount of clinical and methodological diversity would be expected from pooled analyses of studies in this area. Heterogeneity could be explained by differences in study design, content of interventions and comparators, or differences in clinical risk factors between study populations. A decision was therefore made to downgrade pooled analyses by 1 level (indicating 'serious' inconsistency) only when the I^2 statistic was ≥75%. If the I^2 statistic for a pooled analysis was less than 75%, the evidence was not downgraded for inconsistency.
Imprecision	Results are imprecise when studies include relatively few patients and few events (or highly variable measures) and thus have wide confidence intervals around the estimate of the effect relative to clinically important thresholds. 95% confidence intervals denote the possible range of locations of the true population effect at a 95% probability, and so wide confidence intervals may denote a result that is consistent with conflicting interpretations (for example a result may be consistent with both public health benefit AND public health harm) and thus be imprecise. For the purpose of this review, the committee agreed that a relative increase in vaccination uptake of 5% would be clinically important for all target populations. Imprecision was therefore assessed with reference to minimally important difference (MID) thresholds of RR 0.95 and RR 1.05. It was decided that the point measure would be used to decide whether or not the result was clinically important, and that the 95% confidence intervals would indicate certainty of this importance. Uncertainty is introduced where confidence intervals crossed the MID threshold. If the confidence interval crosses either the lower (RR 0.95) or upper MID threshold (RR 1.05), this indicates 'serious' risk of imprecision. Crossing both MID thresholds indicates 'very serious' risk of imprecision in the effect estimate. Where the 95%CI does not cross either MID threshold, the evidence is assessed as having 'no serious' risk of imprecision unless the effect estimate is derived on the basis of few events and a small study sample (that is, less than 300 'vaccination events' across both intervention and comparator

Quality domain	Description
	groups). In that case the results were downgraded one level for 'serious' imprecision to reflect uncertainty in the effect estimate.
Other issues	Publication bias is a systematic underestimate or overestimate of the underlying beneficial or harmful effect due to the selective publication of studies. A closely related phenomenon is where some papers fail to report an outcome that is inconclusive, thus leading to an overestimate of the effectiveness of that outcome. Sometimes randomisation may not adequately lead to group equivalence of confounders, and if so this may lead to bias, which should be taken into account. Potential conflicts of interest, often caused by excessive pharmaceutical company involvement in the publication of a study, should also be noted. A decision to upgrade was made where there was evidence of a dose-response relationship, or evidence from 2 or more observational studies consistently indicated a large effect size (RR of 2 or more).

Overall GRADE rating	Description
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

See Appendix I: for full GRADE tables by outcome.

The GRADE tables and forest plots (Appendix K) are used to generate the overall evidence quality rating and, where applicable, the pooled results that are summarised in the evidence statements below. Each GRADE table and forest plot (where applicable) includes a cross reference to the associated evidence statement.

Effectiveness evidence statements

Each evidence statement is associated with the relevant review question, for example ES 1.1 corresponds to evidence statement 1 for review question 1. ES123.1 relates to a study that is multicomponent and crosses review questions where the data cannot be disaggregated for separate review questions. SR-ES indicates this evidence statement is associated with a systematic review.

Education

ES 1.1 Low quality evidence from 1 randomised control trial of 105 participants found that an educational video did 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). [GRADE profile 1]

ES 1.2 Low quality evidence from 1 randomised control trial 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). [GRADE profile 1]

SR-ES 1.1 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). [GRADE profile 5]

SR-ES 1.2 Very low quality evidence from 1 randomised control trial 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) [GRADE profile 7].

Message Framing

ES 1.3 Very low quality evidence from 1 randomised control trial 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). [GRADE profile 1]

ES 1.4 Very low quality evidence from 1 randomised control trial 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). [GRADE profile2]

SR-ES 1.3 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) [GRADE profile 7].

Access

ES 2.1 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%) [GRADE profile 1].

ES 2.2 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) [GRADE profile 1].

SR-ES 2.1 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) [GRADE profile 5].

SR-ES 2.2 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 only (RR 1.68; 95%CI 1.38 to 2.04) [GRADE profile 5] .

Reminders (written and call-recall/telephone)

ES 3.1 Moderate quality evidence from 2 randomised control trials 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) [GRADE profile 3].

ES 3.2 Low quality evidence from 1 randomised controlled trial 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) [GRADE profile 3].

SR-ES 3.1 Moderate quality evidence from 4 randomised control trials 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) [GRADE profile 5]

SR-ES 3.2 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) [GRADE profile 5]

SR-ES 3.3 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) [GRADE profile 5]

SR-ES 3.5 Moderate quality evidence from 1 cluster randomised control trial 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) [GRADE profile 6].

SR-ES 3.6 Low quality evidence from 1 randomised control trial 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) [GRADE profile 6]

SMS messages

ES 3.3 Low quality evidence from 1 randomised control trial 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) [GRADE profile 3].

ES 3.4a Moderate quality evidence from 1 cluster randomised controlled trial 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) [GRADE profile 3]

SR-ES 3.8 Very low quality evidence from 2 randomised controlled trials 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) [GRADE profile 7]

Provider Prompts

SR-ES 3.4 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) [GRADE profile 5].

SR-ES 3.7 Very low quality evidence from 2 randomised controlled trials 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). [GRADE profile 6].

SR-ES 3.9 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) [GRADE profile 7]

Audit and Feedback

ES 3.4b 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) [GRADE profile 3]

Provider Incentives (UK general practice Quality and Outcomes Framework)

ES 3.5 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 [GRADE profile 8].

ES 3.6 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) [GRADE profile 8].

Multicomponent

As noted above the following section includes studies that are multicomponent where the data cannot be disaggregated for separate review questions or interventions

ES 123.1 Low quality evidence from 1 cluster randomised control trial with 26,408 participants found that a multicomponent pharmacy-based intervention did not increase flu vaccination uptake in people with chronic conditions compared with control (RR 0.75; 95%CI 0.74 to 0.77). Details of the control were not outlined, except that the intervention was not available to control pharmacies [GRADE profile 4].

ES 123.2 Low quality evidence from 1 cluster randomised control trial 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). [GRADE profile 4].

ES 123.3 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) [GRADE profile 4].

ES 123.4 Very low quality evidence from 1 cluster randomised control trial 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) [GRADE profile 4]

ES 123.5 Low quality evidence from 1 cluster randomised control trial 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) [GRADE profile 4]

SR-ES 123.1 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) [GRADE profile 5].

SR-ES 123.2 Moderate quality evidence from 1 cluster randomised control trial 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). [GRADE profile 6]

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). [GRADE profile 6]

SR-ES 123.3 Moderate quality evidence from 5 randomised control trials 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) [GRADE profile 6].

SR-ES 123.4 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) [GRADE profile 6]

SR-ES 123.5 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) [GRADE profile 6].

SR-ES 123.6 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) [GRADE profile 7]

SR-ES 123.7 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) [GRADE profile 7]

SR-ES 123.8 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) [GRADE profile 7]

SR-ES 123.9 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) [GRADE profile 7].

Qualitative evidence review

To consider acceptability of flu vaccination and interventions to increase uptake, the views and experiences of parents of children or adults with an eligible clinical condition, and of providers, were assessed from the qualitative literature. The quality of included studies was appraised based on a checklist adapted from the Quality in qualitative evaluation framework (see Appendix H of the NICE methods manual). A summary of included studies and their final quality rating is included in Table 3 below. The quality ratings used were:

++ All or most of the checklist criteria have been fulfilled, and where they have not been fulfilled the conclusions are very unlikely to alter.

+ Some of the checklist criteria have been fulfilled, and where they have not been fulfilled, or are not adequately described, the conclusions are unlikely to alter.

– Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

Included qualitative studies

See Appendix G for full evidence tables for the included qualitative studies.

Table 3: Included qualitative studies for each review question (RQ1-3) in clinical risk groups

First author, year	Design & analysis	Country	Setting	Population	Subject	Quality rating
Colley 2008	Interviews and Thematic analysis	UK	Home or GP practice	Chronic conditions (18+)	Views about flu and factors that influence accept or reject offer	++
Evans 2016	Interviews and Thematic analysis	UK	Pharmacies	Pregnant women or people with a Green-book specified chronic disease: • Kidney disease • Immunosuppression • Respiratory disease • Neurological disease • Liver disease	Views about barriers and facilitators to delivering NHS flu vaccination in community pharmacies for 'at risk' groups	+

Maher 2014	Interviews and Thematic analysis	AUS	GP practice	Pregnant women (Provider)	Knowledge attitudes, beliefs and practices of GPs in relation to flu and its vaccination in pregnant women	+
Marsh 2014	Interviews and Thematic analysis	USA	ObGyn clinic	Pregnant women	Message framing of messages to target pregnant women	-
Meharry 2013	Interviews and Thematic analysis	USA	Post-partum clinics (hospital)	Pregnant women	Understand reasons women reject or accept flu vaccination offer	+
O'Grady 2015	Focus Groups and Thematic analysis	AUS	Various (yarning circles) acceptable to aboriginal populations	Pregnant women	Determinants of vaccination uptake	++
Sampson 2011	Interviews and Thematic analysis	UK	GP practices, Inverness	Chronic conditions (2-16 yrs)	Explore parental reasons for non-uptake in young at risk groups	-
Schindler 2012	Interviews and Thematic analysis	Switzerland	Maternity unit	Pregnant women	Explore risks associated with seasonal flu and its vaccination	-
Wiley 2015	Interviews and Thematic analysis	AUS	Antenatal clinics in hospitals	Pregnant women	Understanding of risk perception of flu and vaccination against it	+

Summary of included qualitative evidence

Colley (2008 [++]) completed 12 semi-structured interviews (Male = 4, Female = 8, Age 33-62 with a chronic condition) to explore their views on flu and its vaccination for them. Key themes identified include perception of personal risk from flu, misconceptions, information provision by healthcare professionals.

Evans (2016 [+]) completed 16 interviews with pharmacists in Wales offering NHS flu vaccination to eligible; 'at risk' groups to identify key facilitators and barriers. Three key themes influencing vaccination uptake were identified: accessibility, information provision by healthcare professionals

Maher (2014 [+]) undertook 17 semi-structured interviews with GPs to explore the Knowledge attitudes, beliefs and practices of GPs in relation to flu and its vaccination in pregnant women. Key themes identified include risk of flu for pregnant women, safety of the vaccine, adverse events and litigation.

Marsh (2014 [-]) undertook 21 semi-structured interviews with pregnant women to explore their message framing preferences. Key themes include perception of risk of the vaccine to baby, information provision by healthcare professionals, preferred communication approaches and framing.

Meharry (2013 [+]) undertook 60 semi-structured interviews with pregnant women in 3rd trimester or mothers on a post-partum unit (18+) to explore why they do or do not accept the offer of flu vaccination. Key themes identified include information provision by healthcare professionals, accessibility or logistics/appointments, understanding of risk and benefits.

O'Grady (2015 [++]) completed an informal focus group with 7 pregnant women or recent mothers (< 16 weeks post-partum) to explore Determinants of vaccination uptake. Key themes include perception of risk/safety of the vaccine to self and foetus, information provision by healthcare professionals, understanding of risk and benefits, and accessibility or logistics/appointments.

Sampson (2011 [-]) undertook semi structured questionnaire that could be completed in writing, via a telephone interview or a face to face interview with parents of children aged 2-16 years with a chronic condition, to explore parental reasons for rejecting offer of vaccination for their child. Key themes include perception of risk of flu for their child, accessibility, information provision by healthcare professionals, understanding of risk and benefits and misconceptions, and logistics/appointments.

Schindler (2012 [-]) completed 29 semi-structured interviews with post-partum women (3-5 days after giving birth) to evaluate risks associated with seasonal flu and its vaccination. Key themes include perception of risk of flu to self, understanding of risk and benefits, information provision by healthcare professionals.

Wiley (2015 [+]) completed 20 (11 via telephone and 9 face to face) semi-structured interviews pregnant women to explore risk perception of influenza and vaccination against influenza, through the eyes of pregnant women. Key themes include perception of risk of flu to foetus and severity of flu, accessibility or logistics/appointments, information provision by healthcare professionals and, preferences for accessing information online.

The studies are not grouped together under question or condition as many themes cross populations so results are grouped under themes for this secondary thematic analysis to devise themed evidence statements.

Qualitative evidence statements

Q-ES 2.1 *Perception of the severity of flu may impact on decision to accept vaccination offers (recipients) or to make them (providers).*

2 UK (++[1]; -[3]) 2 AUS (+[2,5]) and 1 Swiss (-[4]) study examining the views and experiences of parents of children in clinical risk groups, people who are at higher risk due to having a chronic condition or being pregnant indicated that risk perception of the severity of flu (for themselves, their child or the unborn baby) may affect the uptake of flu vaccination offers. The acceptance of vaccination offers appeared to be based on a number of assumptions including the underlying health of the child who is eligible for vaccination, beliefs about health behaviours such as having a good lifestyle and the potential impact of the flu on the

individual offered vaccination. This may be relevant to information and educational approaches

"At the moment I don't really need it"[1]; '[Child's] asthma had seemed to be "dormant" for several years so we didn't think a flu jab was necessary. Also, we thought as her asthma is quite mild she wasn't high risk"[3]. ''We hear that pregnant women are at risk, but I think that pregnant women who have no health problems won't have anything serious because of the flu"[4].

Flu was considered a mild disease by some pregnant women with most framing their response in relation to their foetus's health, whilst flu was perceived as a disease of the mother with no direct effect on the foetus[5]. One AUS study[2] highlighted that providers' perception of risk may be a factor in them recommending vaccination with many not having direct experience of a pregnant patient contracting flu and having serious consequences and this in turn decreased their perception of the risk[2].

1. Colley 2008 [++]
2. Maher 2014 [+]
3. Sampson 2011 [-]
4. Schindler 2012 [-]
5. Wiley 2015 [+]

Q-ES 2.2 *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*

2 UK(++[1];-[6]), 2 AUS (+[2]; ++[5]), 1 Swiss (-[7]) and 2 US (-[3];+[4]) studies covering views and experiences from parents, adult or parents of children with chronic conditions, pregnant or recent post-partum women and providers suggested that information on the risk and benefits of flu vaccination was desirable and may alter acceptability of flu vaccination offers. The decision maker needed enough information to make an informed decision, the contents of which could include the risk and benefits of the vaccination, as well as addressing a number of areas where there appeared to be concerns with or misconceptions including the vaccination causing illness, the seriousness of flu particularly around complications for children. "The focus is more on older… it's difficult to imagine a child getting the flu and being very ill"[6], that the flu is not a broad name for a number of common cold like illnesses, along with the alternatives that may be less associated with pain such as the nasal spray.

For pregnant women the need to understand that the vaccination confers a "two for one" benefit to mother and child, something that was considered pivotal[4]. as well as it not being a risk to the foetus was important for example in one study participants were interested in the safety of the vaccine, what products were used to make the vaccine and wanted to understand the risks of vaccination to self and the foetus[5]. This this was also important to providers as GPs indicated they were less concerned with the risk of flu during pregnancy, but more concerned with the safety of the vaccination or adverse effects during pregnancy "With the small amount of risk involved [with influenza] I don't see that the benefits [of the vaccination] outweigh the risks"[2] and potential issues of litigation "I just think if they had the flu injection, then whether it was a day, a month, or at any stage after getting the vaccine, that if anything went wrong like foetal death or early labour, I know that they would look at pointing the finger at the flu vaccine as the cause. Whether it is or not. So it is safer as a doctor not to do that"[2].

1. Colley 2008 [++]
2. Maher 2014 [+]
3. Marsh 2014 [-]
4. Meharry 2013 [+]

5. O'Grady 2015 [++]
6. Sampson 2011 [-]
7. Schindler 2012 [-]

Q-ES 2.3 *Accessibility is an important factor in improving likelihood of vaccination uptake or not missing vaccination opportunities.*

2UK (-[3]; +[5]), 2 AUS (++[2]; +[4]), and 1 US (+[1]) study indicated that parents of children with chronic conditions, pregnant women and pharmacists considered that accessibility may be a barrier or facilitator in improving uptake. Some parents suggested difficulties gaining an appointment and the challenges of inter-current illnesses compounding appointment difficulties were barriers "the clinic was busy and it was well into November before I could get an appointment. By the time she was unwell with chest infections, or if not had temperatures. [Child] did actually get her flu jab last winter but it was actually February before she was well enough to have it"[3]. Pregnant women also expressed issues around access, appointments or making the most of opportunities to vaccinate were an issue affecting acceptance of vaccination offer,[1] suggested that conveniently located venues for vaccination reduces barriers to uptake, their study indicated the majority of women seeking vaccination did eventually locate one, but suggested wasting time and energy locating a vaccine is a major barrier with several eventually becoming fed-up. Some women indicated that opportunistic vaccination would be better and that providers should give the vaccine at the time the person was there as the steps required to get vaccinated (i.e. go to pharmacy, come back to clinic etc.) were difficult to complete given competing priorities, "When you go in there they have to give you all these descriptions and all that but they don't do nothing about it… they should just say if you wanted to get the needle, they should just pull out the needle"[2]. There was a reliance on the system providing them with the vaccination in some way through clinics, hospital or GPs[4]. Pharmacists indicated that factors such as staffing levels and workload may affect the ability of pharmacists to offer vaccinations: "We've got two pharmacists here so it means that dispensing continues without disrupting the normal day-to-day activities".

1. Meharry 2013 [+]
2. O'Grady 2015 [++]
3. Sampson 2011 [-]
4. Wiley 2015 [+]
5. Evans 2016 [+]

Q-ES 2.4 *Importance of information provision/advice and offer by a healthcare professional*

All studies in recipients 3 UK (++[1];-[5]; +[8]); 2 Aus (++[4];+[7]); 1 Swiss (-[6]) and 2 US (-[2];++[3]) indicated that information provision by a respected other in their case a healthcare professional is likely to have a positive influence on vaccination uptake. In adults with chronic conditions a vaccinated group offer by a professional was important "I assume that if I go to the doctor or nurse it's a professional view of the people they have so I accept that they're going to be right"; whilst an unvaccinated group indicated they had not received information or advice to have the vaccination "If someone suggested it would be a good idea, I would do it"[1]. Pharmacists indicated that availability of promotional material could affect vaccination rates, and that promotional activity may be driven by perceptions of accountability: "we could have more proactively promoted it (the service) but didn't particularly want to step on the GPs toes". Pregnant women indicated that if providers explain the threat of influenza and recommend maternal vaccination, most women accept the vaccine "For me, I trust my doctor. If you don't trust your doctor, you may as well not go to them. So, you know, he told me I should get it and I listened to him."[3]. In particular making the offer with conviction was considered important with pregnant women perceiving an indifferent provider as a barrier to

vaccination "The doctor just asked if you wanted the vaccine and when you said no, she didn't follow-up with any information"[3]; furthermore doubt arose when the message is not delivered with conviction "She didn't suggest [vaccination] while I was doing the exam. Then all of a sudden, when I was walking down the hallway to leave, she tells me: "I don't know if you would be interested…" and she talks to me a little bit about [vaccination] in the hallway. I thought, if it had really been serious maybe she would have talked about it right away"[6].

1. Colley 2008 [++]
2. Marsh 2014 [-]
3. Meharry 2013 [+]
4. O'Grady 2015 [++]
5. Sampson 2011 [-]
6. Schindler 2012 [-]
7. Wiley 2015 [+]
8. Evans 2016 [+]

Q-ES 2.5 *Provider concerns in pregnant women limiting their capacity for recommendations was affected by provider knowledge*

1 AUS [+] study in GPs indicated that there were concerns about offering the vaccination in pregnant women with over half having significant concerns about the safety of the vaccine during pregnancy suggesting it is relatively new and many need a longer period of time where this was practiced without adverse outcomes before they could be confident that the vaccine was completely safe for pregnant women[1]. Those confident that the vaccine is safe were either more informed about the evidence regarding safety or were more willing to trust that the vaccine is safe, based on the fact that it is recommended under the national immunisation guidelines.[1]

1. Maher 2014 [+]

Q-ES 2.6 *Information access preferences and communication preferences are important factors in delivering messages to pregnant women*

1 US (-[1]) study suggested that positive framing (benefits) of vaccination rather than negative framing (risk of not getting vaccinated) messages was preferred "…your emotions are already all over the place and last thing you want to hear is…not getting this could cause serious complications, might kill you, might kill the baby… "with the majority of women suggesting that if the benefits to the infant were clearly communicated, they were more likely to accept the offer[1]. 1 AUS (+[2]) study highlighted that they also sought out information via other routes than a healthcare professional with the majority of pregnant women seeking additional information via Google to search for influenza information. Even without direct information from a healthcare professional they did seek information from credible sources with a preference for information arising from the system (such as government websites), compared to other sources such as social media. "Only if it's like a specific website . . . recommended by the government or something . . . not like a dodgy website . . . because I believe that they would, like, source the right information, and they would look into it a little bit more and tell me what's right and what's wrong."[2]. Although other women's experiences shared online remained important.

1. Marsh 2014 [-]
2. Wiley 2015 [+]

Economic evidence

To consider cost effectiveness of interventions to increase uptake of flu vaccination economic literature was assessed. Included studies (n=2) were rated individually to indicate their quality, based on assessment using the checklist detailed in Appendix H of the NICE methods manual. A summary of the included studies and their final quality rating is included in Table 4 below. The quality ratings used were:

++ All or most of the checklist criteria have been fulfilled, and where they have not been fulfilled the conclusions are very unlikely to alter.

+ Some of the checklist criteria have been fulfilled, and where they have not been fulfilled, or are not adequately described, the conclusions are unlikely to alter.

– Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

Table 4 Included studies assessing cost-effectiveness of interventions to increase uptake of flu vaccination

First author, year	Design	Country	Setting	Population	Intervention	Quality rating
RQ2: Flexible, walk-in/open access, outreach and parallel clinics or other opportunistic approach						
Skedgel (2011)	CUA	Canada	Family practitioner visit	Pregnant women	Opportunistic vaccination (targeted and universal approaches) at a routine family practitioner visit compared to a no vaccination strategy.	-
Teufell (2015)	CEA	US	Paediatric hospital department	Hospitalised children with Asthma	Opportunistic assessment and vaccination during a period of hospitalisation.	-

Health economic evidence statements

CE-ES 2.1 *Incorporating a targeted vaccination offer programme for pregnant women into routine family practice visits is cost effective and may be cost saving.*

Low quality evidence from 1 cost utility analysis of a cohort of 10,000 modelled participants indicates that, relative to a no vaccination strategy, a targeted strategy (offer of vaccination to pregnant women with at least 1 co-morbidity) was cost saving (dominant). A universal offer to all pregnant women during routine appointments cost $39,942 per QALY relative to the targeted strategy. If vaccination required an additional practice visit the targeted strategy would lose dominance and cost $62,796 per QALY with the universal offer exceeding $150,000.

CE-ES 2.2 *Incorporating an opportunistic screening and flu vaccination offer programme among children in a clinical risk group (asthma) in a paediatric hospital setting may be cost saving.*

Low quality evidence from a cost effectiveness analysis of a hypothetical cohort of hospitalised children aged 1-14 years with asthma shows that assessing vaccination status and offering vaccine dependent on need during the period of hospitalisation was cost saving for both the assessment ($5.45/child assessed) and vaccination ($9.19/child vaccinated). Sensitivity analysis demonstrated the results to be robust and generalizable.

Economic model

Please see the separate economic modelling report produced by the Economic Modelling Unit (EMU) for de novo modelling for this guideline

Appendix A: Review protocols

Review protocols for 'Flu vaccination: increasing uptake in clinical risk groups' (Review questions 1-3)

A number of elements within the protocols are common across each question namely:

- searches
- methods for selecting evidence (data screening);
- data extraction and quality assessment;
- strategy for data synthesis
- exclusion criteria
- strategy to manage low numbers of references

To reduce repetition these details are provided here:

Searches	The identification of evidence will conform to the methods set out in chapter 5 of the "Developing NICE Guidelines Manual" (October 2014). Relevant databases and websites will be searched systematically to identify relevant qualitative, quantitative and cost effectiveness evidence. The search will use a traditional systematic approach, using PICO to formulate the search strategy. Effectiveness	

	Two searches will be carried out on effectiveness. One will cover interventions for effectiveness for the clinical risk groups, carers and children age 2-17 years and the other will cover the health and social care worker population. These will be carried out separately because the interventions vary between these groups. Study filters will be applied for Systematic review, RCT, Observational study and Qualitative study types. Results will then be split between those with and without study filters for sifting so that, if necessary, studies that have been excluded by the study filters can be identified. Cost-effectiveness These searches will comprise: the effectiveness searches for Medline and Embase without study type filter but with an economics filter; effectiveness searches of the other databases with no filters applied (economics studies to be identified by sifting); additional searches of Econlit and NHS-EED using the main body of the effectiveness search strategy without study type filters. Limits: Sources will be searched from 1996-2016. Language: English language. A separate search will also be carried out about theories and models of behaviour change to address sub questions within question 1a and 4a. Sources to be searched: see Appendix 1. See Appendix 2 for details of the search strategy.	
Selecting evidence (data screening)	Stage 1. Title abstract screening All references from the database searches will be downloaded, de-duplicated and screened on title and abstract against the criteria above. A randomly selected initial sample of 10% of records will be screened by two reviewers independently. The rate of agreement for this sample will be recorded, and if it is over 90% then	As noted elsewhere, if large numbers of papers are identified and included at full text, the following may be implemented:

	remaining references will screened by one reviewer only. Disagreement will be resolved through discussion. Where abstracts meet all the criteria, or if it is unclear from the study abstract whether it does, the full text will be retrieved. <u>Stage 2. Full text screening</u> Full-text screening will be carried out by two reviewers independently on a 10% sample and any differences resolved by discussion. The rate of agreement for this sample will be recorded, and if it is over 90% then remaining references will screened by one reviewer only. Disagreement will be resolved through discussion. Reasons for exclusion at full paper will be recorded. Inter-rater agreement will be recorded.	Prioritising evidence with critical or highly important outcomes Prioritising evidence of higher quality in terms of study type Prioritising evidence with larger participant numbers (> 100)or number of sites it applies to Consideration of a date cut off (on advice of topic experts)
Data extraction and quality assessment	Data extraction of included studies will be conducted using approaches described in Developing NICE guidelines: the manual. Each included study will be data extracted by 1 reviewer and the data extraction sheet will be confirmed by a second reviewer. Any differences will be resolved by discussion or recourse to a third reviewer. Quality assessment for all included studies will be conducted using the tools in Developing NICE guidelines: the manual. Each included study will be quality assessed by 1 reviewer and checked by another. Any differences in quality grading will be resolved by discussion or recourse to a third reviewer.	
Strategy for data synthesis	Data will be grouped and synthesised into concise evidence statements in line with Developing NICE guidelines: the manual. We will routinely use narrative synthesis for the effectiveness	

	reviews and may pilot GRADE on one review question. See individual protocols for potential a priori groupings. If sufficiently homogeneous and high-quality data are located, meta-analysis will be conducted, including any unintended consequences of an intervention.	
Exclusion criteria	<u>Exclusion criteria:</u> ○ The epidemiology of influenza ○ Uptake of pandemic influenza vaccines ○ Not English Language ○ Not EU/OECD countries ○ Dissertation and theses ○ Opinion pieces (e.g. letters, editorials, commentaries) ○ Conference abstracts ○ Poster presentations	
Strategy to manage low number of references	Extrapolation to other groups (e.g. older people to other eligible groups) Call for Evidence Expert Testimony	

1

2 **PICO RQ 1-3 (Clinical risk groups)**

	Details			Additional comments
Study design	**(A)** Comparator studies (effectiveness): ○ Systematic reviews ○ Randomised or non-randomised controlled trials ○ Before and after studies *Observational studies will be included to fill gaps where effectiveness evidence is not available*[c]: ○ Cohort studies ○ Case-control studies	**(B)** Qualitative primary studies: • Interviews • Focus groups • Case studies	**(C)**Economic studies with both costs and benefits: • Economic evaluations • Cost-utility (cost per QALY) • Cost benefit (i.e. Net benefit) • Cost-effectiveness (Cost per unit of effect) • Cost minimisation • Cost-consequence	**Exclusions** (study design): Non-comparative studies. **Exclusions** (Quantitative): •Cross-sectional surveys, epidemiological studies, correlation studies and studies to assess coverage rates are excluded. **Exclusions** (Qualitative): •Cross-sectional surveys/epidemiological studies/ correlations studies/studies to assess coverage rates which contain information related to knowledge/attitudes/beliefs/ perception/intentions/acceptance about vaccination are excluded. **Exclusions** (study design): Systematic reviews will only be included if the review question matches the reviews questions in

[c] Available was defined as having any evidence. After screening, anything that would be an 'included study' but used an observational study design was coded separately. This group was assessed once the included studies list was complete based on the studies noted above, i.e. SR, RCT nRCT and B&A. Where gaps were present in RCT data in particular, this was supplemented with observational study data. Both might be included if overall there was a lower level of evidence or if observational studies were from systematic reviews that were included.

	Details			Additional comments
				our reviews or as a source for citation searching if primary searches do not yield a substantial amount of evidence. **Exclusions** (econ): Theory papers, cost only studies, 'burden of disease' studies and 'cost of illness' studies, which do not report data to inform a model will be excluded. Cost-effectiveness of flu vaccine studies will be excluded.
Setting	**Settings:** o Primary and secondary healthcare settings o Community settings Included countries (Quantitative): Europe and OECD: Australia, Austria, Belgium, Canada, Chile, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Korea, Luxembourg, Mexico, Netherlands, New Zealand, Norway, Poland, Portugal, Spain, Sweden, Switzerland, Turkey, UK, USA. Included countries (qualitative): Europe, North America, Canada, Australia, New Zealand only			**Excluded settings** : Occupational health settings **Excluded countries (quantitative)**: Non-OECD. If too many studies are identified those OECD countries where there are significant cultural differences – Japan, Korea, South and Central America, and Eastern Europe will be excluded. **Excluded countries** (qualitative): Non-OECD, Japan, Korea, South and Central America. If too many studies are identified those European countries where

	Details				Additional comments
					there are significant cultural differences – Eastern Europe will be excluded and priority will be given to UK studies.
Population	Clinical risk groups aged 6 months to 64 years				
Intervention group	**Information about, and acceptability of, flu vaccination (RQ1)**	**Access to flu vaccination (RQ2)**	**Provider based systems: (RQ3)**	**Behaviour change models, techniques and theories**	
Intervention	Information campaigns: ○ targeted ○ community based, including local radio campaigns ○ settings based ○ online campaigns., including social media and apps Education: ○ educational tools ○ peer education (carried out by a community	Vaccination clinics in community settings : ○ community pharmacies ○ antenatal clinics ○ specialist clinics e.g. drug and alcohol services, mental health services ○ community venues e.g. libraries, children's centres	Local programme assigned lead for an annual flu programme local approach systems and processes in working with the community practice approach Programmes to modify standard searches of patient databases to identify eligible patients.	Behaviour change models, techniques and theories, including: Motivational interviewing • Trans-theoretical model (stages of change) • Theory of planned behaviour Theory of reasoned action Health Protection Theory	**Exclusions:** Interventions related to uptake of pandemic flu vaccines during pandemic outbreaks. Note: papers related to interventions to increase uptake of H1N1 vaccination (swine flu vaccine) where results are also relevant to uptake of seasonal flu vaccine (i.e. the intervention is not delivered during a pandemic outbreak) will be included. Interventions related to haemophilus influenza type B vaccine are excluded as this vaccine is not a flu vaccine. It is given to prevent against meningitis.

	Details				Additional comments
	member who shares similar life experiences to the community they are working with) ○ lay education (carried out by community members working in a non-professional capacity) Tailored information and advice delivered: ○ during home visits ○ during consultation with health and social care workers ○ at support group meetings for patients and other people who use services.	Dedicated flu vaccination clinics Mass vaccination clinics in community or other settings Walk in or open access immunisation clinics Extended hours clinics ○ weekends ○ evenings (after 6 pm) ○ early mornings (before 8 am) ○ 24 hour access. Outreach or mobile services: ○ home or domiciliary or day centre visits ○ support group meeting visits ○ residential or care home visits ○ special schools visits ○ inpatient visits	Reminder and recall systems (for providers) clinical alerts and prompts Personal invitation GP community pharmacist health or social care worker from several professionals Booking systems dedicated flu lines or online systems Payment systems (fiscal arrangements) outside primary care Reminders (to eligible groups) text messages emails postcards posters telephone call Approaches to follow-up phoning patients	Protection motivation Theory Social cognitive theory Perceptions of risk	

	Details				Additional comments
	Flu vaccination 'champion' : ○ practitioner ○ peer Recommendations from a respected person: ○ health or social care worker ○ carer ○ peer ○ volunteer ○ family member	○ custodial visits ○ immigration settings ○ mobile clinics e.g. in community Parallel clinics: ○ Offer flu vaccination in parallel with regular appointments e.g. with midwives, clinicians, inpatient and outpatient clinics, long stay wards etc. ○ coordinated timing of other programmes e.g. retinal screening for diabetic patients within flu season Opportunistic vaccination e.g. visits	Personal health record (so eligible people can see if their vaccination is due) Shared health records for providers. Integration of primary and secondary care health records Centralised uptake record Audit and feedback on uptake rates weekly statistics content and delivery of feedback practical relevance (e.g. how many more people need to be vaccinated to achieve target number)		

	Details				Additional comments
		to GP ,practice nurse or consultant for other medical conditions Flu vaccination vouchers to enable eligible groups to receive flu vaccination from community providers	comparison data e.g. between GP practices Incentives (for eligible groups) voucher schemes Incentive schemes (for providers) targets quality and outcomes framework voucher schemes		
Comparator	Comparators that will be considered are: • Other intervention • Status quo • Time (before and after) or area (i.e. matched city a vs b) comparisons				
Outcomes	Primary outcome: • Changes in uptake rate among target groups Secondary outcomes: • Changes in: o knowledge o attitudes o beliefs o acceptance o intentions • Unintended consequences of an activity, including o increase uptake of other vaccines				

	Details	Additional comments
	o increase in inequalities o increase in issues of concern if vaccinated outside health and social care settings e.g. about resuscitation facilities, aseptic techniques, needle contamination o increase in distress caused by having the vaccine within specific groups e.g. people with learning disabilities o Vaccinations not captured by other providers o Risk of being vaccinated twice o Vaccine wastage • Cost effectiveness and economic outcomes: o Cost per quality-adjusted life year o Cost per unit of effect	

1

Appendix B: Health economic analysis

See separate modelling report

Appendix C: Research recommendations

See full guideline for prioritised research recommendations

Appendix D: Included evidence study selection

Aigbogun N W, Hawker J I, and Stewart A. (2015). Interventions to increase influenza vaccination rates in children with high-risk conditions--a systematic review. Vaccine 33: 759-70.

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Sampson R, Wong L, and MacVicar R. (2011). Parental reasons for non-uptake of influenza vaccination in young at-risk groups: a qualitative study. British Journal of General Practice, pp.444-445.

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Appendix E: Economic evidence study selection

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Appendix F:Literature search strategies

Search Strategy 1 – Main search strategy (carers, clinical risk groups, children)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
1 exp Influenza, Human/ (40799)
2 Influenza A virus/ (17642)
3 Influenza B virus/ (3359)
4 Influenzavirus C/ (309)
5 (influenza* or flu or grippe).tw. (93602)
6 or/1-5 (99916)
7 exp Vaccination/ (70018)
8 Vaccines/ (18041)
9 Immunization/ (46296)
10 (vaccin* or immuni*).tw. (387373)
11 or/7-10 (416475)
12 6 and 11 (30641)
13 exp Influenza Vaccines/ (18322)
14 12 or 13 (33248)
15 Disabled Persons/ (35102)
16 clinical risk group*.tw. (97)
17 ((underlying or exist* or chronic or long term) adj3 (condition* or illness* or disease*)).tw. (242566)
18 co-morbid*.tw. (15582)
19 Lung Diseases/ (63247)
20 chronic respiratory disease*.tw. (2113)
21 Asthma/ (109906)
22 asthma*.tw. (120671)
23 Pulmonary Disease, Chronic Obstructive/ (26787)
24 chronic obstructive pulmonary disease*.tw. (29526)
25 copd.tw. (27023)
26 Bronchitis/ or Bronchitis, Chronic/ (20924)
27 bronchitis.tw. (18234)
28 Emphysema/ (6551)
29 emphysema.tw. (18387)
30 Bronchiectasis/ (7053)
31 bronchiectasis.tw. (6474)
32 Cystic Fibrosis/ (30266)
33 cystic fibrosis.tw. (33453)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
34 Lung Diseases, Interstitial/ (6875)
35 Idiopathic Pulmonary Fibrosis/ (1703)
36 ((interstitial lung or idiopathic pulmonary) adj2 (fibrosis* or disease*)).tw. (9318)
37 Pneumoconiosis/ (6426)
38 pneumoconiosis.tw. (3617)
39 Bronchopulmonary Dysplasia/ (3494)
40 ((bronchopulmonary or lung) adj2 dysplasia).tw. (4486)
41 Respiratory Tract Diseases/ (20044)
42 respiratory tract disease*.tw. (2303)
43 Heart diseases/ (62496)
44 Coronary Artery Disease/ (45659)
45 coronary artery disease*.tw. (61377)
46 Heart Defects, Congenital/ (45915)
47 Myocardial Ischemia/ (34302)
48 ((congenital or isch?emic or chronic) adj3 (heart disease* or heart defect* or myocardial or malform*)).tw. (76447)
49 Hypertension/ (207757)
50 Heart Failure/ (93857)
51 (hypertension or hypertensive or heart failure).tw. (418293)
52 Renal Insufficiency, Chronic/ (10210)
53 Kidney Failure, Chronic/ (82195)
54 ((kidney or renal) adj3 (disease* or failure*)).tw. (157262)
55 renal insufficienc*.tw. (18844)
56 Nephrotic Syndrome/ (14539)
57 Kidney Transplantation/ (83636)
58 (nephrotic syndrome or kidney transplant*).tw. (42243)
59 (transplant* adj2 recipient*).tw. (41251)
60 Liver Diseases/ or Liver Cirrhosis/ (119266)
61 Biliary Atresia/ (2502)
62 Hepatitis, Chronic/ (5491)
63 (chronic adj3 (liver disease* or hepatitis)).tw. (52503)
64 (((biliary or bile duct) adj2 atresia) or cirrhosis).tw. (69797)
65 Multiple Sclerosis/ or Nervous System Diseases/ (80798)
66 ((nervous system or neurological or motor neurone or parkinson*) adj3 disease*).tw. 67 (81953)
67 (multiple sclerosis or ms).tw. (236121)
68 Cardiovascular Diseases/ (115708)
69 cardiovascular disease*.tw. (103272)
70 Stroke/ or Ischemic Attack, Transient/ (85925)
71 (stroke* or transient isch?emic attack* or TIA or cerebrovascular accident*).tw. 73 (163996)
72 Postpoliomyelitis Syndrome/ (739)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
73 (postpolio* or polio*).tw. (25647)
74 Cerebral Palsy/ (17020)
75 cerebral palsy.tw. (15143)
76 Learning Disorders/ (13091)
77 (learning adj3 (disabilit* or disorder*)).tw. (7401)
78 Diabetes Mellitus, Type 1/ or Diabetes Mellitus, Type 2/ or Diabetes Mellitus/ (243804)
79 diabet*.tw. (423612)
80 Immunosuppression/ or Immune System Diseases/ (40379)
81 (immun* adj3 (disease* or disorder)).tw. (36680)
82 immunosuppress*.tw. (107268)
83 Bone Marrow Transplantation/ (43235)
84 bone marrow transplant*.tw. (29053)
85 exp HIV Infections/ (243267)
86 (AIDS or HIV*).tw. (298104)
87 Multiple Myeloma/ (33980)
88 myeloma.tw. (38052)
89 Interleukin-1 Receptor-Associated Kinases/ (998)
90 Immunologic Deficiency Syndromes/ (13400)
91 Complement System Proteins/ (25518)
92 (interleukin-1 receptor-associated kinase* or interleukin 1 receptor associated kinase* or IRAK or NEMO or Nuclear factor-kappa B essential modulator* or Nuclear factor kappa B essential modulator*).tw. (1836)
93 (complement* adj3 (deficienc* or disorder* or system*)).tw. (10292)
94 aspleni*.tw. (1388)
95 ((splenic or spleen) adj3 dysfunction*).tw. (123)
96 Anemia, Sickle Cell/ (17969)
97 sickle cell.tw. (17893)
98 Celiac Disease/ (17410)
99 c?eliac.tw. (20524)
100 Pregnant Women/ (5605)
101 Pregnancy Trimester, Third/ or Pregnancy/ or Pregnancy Trimester, First/ or Pregnancy Trimester, Second/ (769116)
102 Pregnancy Trimesters/ (1477)
103 (pregnant or pregnancy or gestation*).tw. (430574)
104 Obesity, Morbid/ (13223)
105 (obes* adj2 morbid*).tw. (10134)
106 or/15-105 (3930956)
107 Child/ or Parents/ or Adolescent/ or Child, Preschool/ (2588133)
108 (child* or boy* or girl* or toddler* or kid or kids or adolescent* or youngster* or young person* or young people or schoolchild* or minor or minors or teen* or juvenile* or student* or pupil or pupils or

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
pre-school* or preschool* or under 18* or under eighteen* or underage* or over 1* or over one* or parent*).tw. (1802780)
109 107 or 108 (3342672)
110 Caregivers/ (24586)
111 (carer* or careworker* or care worker* or care giver* or caregiver*).tw. (52544)
112 110 or 111 (60206)
113 Health Promotion/ (58861)
114 ((increas* or improv* or rais* or higher) adj4 (uptake or rate* or immuni* or vaccin* or complian*)).tw. (395235)
115 ((information or advice or advised or recommend*) adj3 (campaign* or consult* or doctor* or GP or physician* or clinician* or nurse* or support group* or patient* or peer* or forum* or social media or online or apps or social care or socialcare or health care or healthcare or carer or volunteer* or famil* or parent* or son* or daughter* or child* or brother* or sister* or sibling*)).tw. (925543)
116 Health Education/ or Patient Education as Topic/ or Leadership/ (160477)
117 ((education* or learn*) adj3 (tool* or resource* or peer* or lay)).tw. (9381)
118 ((flu or influenza) adj3 (lead* or champion*)).tw. (213)
119 or/113-118 (688201)
120 Health Services Accessibility/ or House Calls/ or Mass Vaccination/ (61774)
121 ((vaccin* or immuni*) adj3 (access or communit* or pharmac* or clinic* or mass or service or GP or doctor* or physician* or clinician* or nurse practitioner* or midwife or midwives or walk-in or walk in or outreach or mobile or residential home* or care home* or residential care or nursing home* or home visit* or house call* or support group* or on-site or on site or weekend* or evening* or 24-hour* or 24 hour* or extended-hour* or extended hour* or opportunistic or opportunit* or open access or parallel* or voucher*)).tw. (11917)
122 or/120-121 (72786)
123 Health Policy/ or Reminder Systems/ or Motivation/ or Physician Incentive Plans/ or Reimbursement, Incentive/ or Medical Audit/ or Clinical Audit/ or Feedback/ or Registries/ or Immunization Programs/ or Information Systems/ or Medical Records Systems, Computerized/ or Electronic Health Records/ (268368)
124 ((local or vaccin* or immuni*) adj3 (policy or policies or program* or provider* or approach* or computer* or information system*)).tw. (23009)
125 ((system* or process* or search* or program*) adj3 (identif* or contact* or invit* or find* or locat*)).tw. (76839)
126 (remind* or track* or alert* or postcard* or mail* or email* or text* or sms or recall* or telephon* or registry or registries or letter* or appointment* or schedul* or invite* or invitation* or prompt* or poster*).tw. (856532)
127 "Appointments and Schedules"/ (7615)
128 ((book* or on-line or online or data or record*) adj3 system*).tw. (37248)
129 ((system* or process*) adj3 (re-book or re book or follow-up or follow up)).tw. (2517)
130 ((system* or process*) adj3 (audit* or feedback or statistic* or response*)).tw. (55445)
131 ((vaccin* or immuni*) adj3 (pay* or financ* or fiscal)).tw. (185)
132 ((incentive* or reward*) adj3 (scheme* or program* or target* or voucher*)).tw. (1701)
133 "quality and outcomes framework".tw. (282)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
134 ((share* or personal or integrat* or centrali*) adj3 (health record* or healthcare record* or health care record* or social care record* or data interchange or data record*)).tw. (875)
135 or/123-134 (1240108)
136 or/119,122,135 (1886974)
137 or/106,109,112 (6567492)
138 and/14,136-137 (6166)
139 Randomized Controlled Trial.pt. (410079)
140 Controlled Clinical Trial.pt. (90300)
141 Clinical Trial.pt. (497803)
142 exp Clinical Trials as Topic/ (289214)
143 Placebos/ (33136)
144 Random Allocation/ (85966)
145 Double-Blind Method/ (133970)
146 Single-Blind Method/ (21522)
147 Cross-Over Studies/ (37571)
148 ((random$ or control$ or clinical$) adj3 (trial$ or stud$)).tw. (806804)
149 (random$ adj3 allocat$).tw. (22641)
150 placebo$.tw. (161447)
151 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw. (131082)
152 (crossover$ or (cross adj over$)).tw. (60235)
153 or/139-152 (1479689)
154 Observational Studies as Topic/ (1266)
155 Observational Study/ (19166)
156 Epidemiologic Studies/ (7023)
157 exp Case-Control Studies/ (764103)
158 exp Cohort Studies/ (1509575)
159 Cross-Sectional Studies/ (209746)
160 Controlled Before-After Studies/ (111)
161 Historically Controlled Study/ (45)
162 Interrupted Time Series Analysis/ (124)
163 Comparative Study.pt. (1729351)
164 case control$.tw. (83680)
165 case series.tw. (38633)
166 (cohort adj (study or studies)).tw. (97500)
167 cohort analy$.tw. (4089)
168 (follow up adj (study or studies)).tw. (38237)
169 (observational adj (study or studies)).tw. (49507)
170 longitudinal.tw. (145584)
171 prospective.tw. (369555)
172 retrospective.tw. (295058)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
173 cross sectional.tw. (180405)
174 or/154-173 (3535459)
175 Meta-Analysis.pt. (62777)
176 Meta-Analysis as Topic/ (14637)
177 Review.pt. (2023681)
178 exp Review Literature as Topic/ (8461)
179 (metaanaly$ or metanaly$ or (meta adj3 analy$)).tw. (74269)
180 (review$ or overview$).ti. (298311)
181 (systematic$ adj5 (review$ or overview$)).tw. (69561)
182 ((quantitative$ or qualitative$) adj5 (review$ or overview$)).tw. (5049)
183 ((studies or trial$) adj2 (review$ or overview$)).tw. (28640)
184 (integrat$ adj3 (research or review$ or literature)).tw. (6241)
185 (pool$ adj2 (analy$ or data)).tw. (16315)
186 (handsearch$ or (hand adj3 search$)).tw. 95896)
187 (manual$ adj3 search$).tw. (3527)
188 or/175-187 (2198774)
189 Qualitative Research/ (26004)
190 Nursing Methodology Research/ (15827)
191 Interview.pt. (25945)
192 exp Interviews as Topic/ (46155)
193 Questionnaires/ (337357)
194 Narration/ (5872)
195 Health Care Surveys/ (26736)
196 (qualitative$ or interview$ or focus group$ or questionnaire$ or narrative$ or 197 narration$ or survey$).tw. (941983)
197 (ethno$ or emic or etic or phenomenolog$ or grounded theory or constant compar$ or (thematic$ adj4 analys$) or theoretical sampl$ or purposive sampl$).tw. (45654)
198 (hermeneutic$ or heidegger$ or husser$ or colaizzi$ or van kaam$ or van manen$ or giorgi$ or glaser$ or strauss$ or ricoeur$ or spiegelberg$ or merleau$).tw. (7533)
199 (metasynthes$ or meta-synthes$ or metasummar$ or meta-summar$ or metastud$ or meta-stud$ or metathem$ or meta-them$).tw. (517)
200 or/189-199 (1098914)
201 or/139-200 (6824454)
202 and/14,106,136 (2929)
203 and/14,106,136,201 (2116)
204 and/14,109,136 (4474)
205 and/14,109,136,201 (3016)
206 and/14,112,136 (419)
207 and/14,112,136,201 (294)
208 animals/ not humans/ (4175932)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
209 News/ (165247)
210 Editorial/ (373604)
211 or/208-210 (4693453)
212 202 not 211 (2819)
213 limit 212 to (english language and yr="1996 - 2016") (2316)
214 203 not 211 (2091)
215 limit 214 to (english language and yr="1996 - 2016") (1762)
216 204 not 211 (4346)
217 limit 216 to (english language and yr="1996 - 2016") (3477)
218 205 not 211 (2995)
219 limit 218 to (english language and yr="1996 - 2016") (2481)
220 206 not 211 (412)
221 limit 220 to (english language and yr="1996 - 2016") (369)
222 207 not 211 (294)
223 limit 222 to (english language and yr="1996 - 2016") (260)

Search Strategy 2 – Additional search strategy on behaviour change (carers, healthcare workers, children, clinical risk groups) to supplement primary searches (targeted search in psychinfo database).

Database: Ovid PsycINFO <1996 to May Week 3 2016>
1 exp Immunization/ (3441)
2 (vaccin* or immuni*).tw. (9248)
3 1 or 2 (9301)
4 INFLUENZA/ (1089)
5 (influenza* or flu or grippe).tw. (2599)
6 4 or 5 (2602)
7 3 and 6 (1014)
8 exp Health Behavior/ or exp Health Attitudes/ or exp Behavior Change/ or exp Health Knowledge/ or exp Risk Management/ or exp At Risk Populations/ or exp Risk Perception/ or exp MOTIVATION/ or exp Planned Behavior/ or exp Behavioral Intention/ or exp Reasoned Action/ or exp Social Cognition/ or exp Behavior Modification/ (163753)
9 ((behavio?r* or cognitive or attitude* or knowledge* or lifestyle* or life-style*) adj3 (chang* or adapt* or alter* or intent* or influenc* or modification or modify or modifying or belie* or control* or adopt*)).tw. (140294)
10 ((increas* or improv* or rais* or high* or more or better or best or low* or less or worse or worst or fewer) adj3 (motivat* or confiden* or opportunit* or feasib* or plan*)).tw. (35163)
11 ((vaccin* or immuni*) adj3 (barrier* or facilitat* or hinder* or block* or obstacle* or restrict* or restrain* or obstruct* or inhibit* or impede* or delay* or constrain* or hindrance or uptake or take up or

Database: Ovid PsycINFO <1996 to May Week 3 2016>
increas* or impact* or effect* or improve* or enhance* or encourag* or support* or promot* or optimiz* or optimis* or adher* or access* or motivat* or accept* or satisfaction or compliance or comply or complie* or refus* or availabl* or provision or provid* or offer or incentive* or start or attend* or adopt* or persuad* or persuation or attitude* or intend* or intention or counsel*)).tw. (2535)
12 or/8-11 (306151)
13 exp Psychological Theories/ or exp Motivational Interviewing/ (19480)
14 ("Trans?theoretical model*" or "stage* of change" or "theor* adj3 planned behavio?r" or "theor* adj3 reasoned action" or "health protection adj3 theor*" or "protection motivation adj3 theor*" or "social cogniti* adj3 theor*").tw. (3417)
15 ((theor* or trans?theor* or belie*) adj3 (framework* or model*)).tw. (52686)
16 (health belie* adj3 (model* or theor*)).tw. (1508)
17 ((theor* or model* or program* or therap* or treatment* or intervention*) adj3 (plan* or behavio?r or reason* or action* or protect* or motivat* or confiden* or opportunit* or feasib* or persua* or cognit*)).tw. (140448)
18 (motivation* adj3 (interview* or question* or model* or theor* or program*)).tw. (9878)
19 or/13-18 (202987)
20 12 or 19 (459291)
21 7 and 20 (600)
22 limit 21 to (english language and yr="1996 - 2016") (575)

Appendix G: Evidence tables

G.1 Effectiveness – primary studies

G.1.1 Bond 2011

<table>
<tr><th colspan="4">Bond 2011</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Bond TC, Patel PR et al (2011)

Quality score
+
Study type
Cluster RCT

Aim of the study
To evaluate a multicomponent intervention to increase influenza vaccination rates in poorly performing dialysis centres.</td>
<td>Clinical risk group
People with end stage renal disease.

Number of participants
77 eligible centres were on the final list for randomisation
To account for year-to-year variability in vaccination rates in the selected centres, centres were stratified into 3 groups:
no 2005- 2006 rate reported
2005-2006 rate within 1 SD (standard deviation) of the 2006-2007 rate (+/-18%)
2005-2006 rate more than 1 SD different from the 2006-2007 rate.</td>
<td>Intervention / Comparison
Standard Intervention
Standard intervention: baseline influenza vaccination practice of selected 3 networks including: feedback report and educational materials developed for past influenza vaccination campaigns. All centres also have access to network staff and can request additional assistance.
All treatment centres received a centre-specific quality-of-care feedback report that summarised findings from the 2006-2007 immunisation survey.
All centres were provided with educational materials previously developed for staff and patients by the STIC coalition, along with videos,</td>
<td>Primary outcomes

<table>
<tr><th>Centres selected</th><th>Centres that submitted data</th></tr>
<tr><td>77</td><td>68</td></tr>
</table>

<table>
<tr><th></th><th>Standard intervention data submitted</th><th>Intensive interventions data submitted</th></tr>
<tr><td></td><td>33/39</td><td>35/38</td></tr>
<tr><td>Mean. Baseline vaccination</td><td>45.58% (+/- 12.91%)</td><td>43.19% (+/- 13.09%)</td></tr>
</table>
</td>
</tr>
</table>

Bond 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Location and setting Outpatient dialysis centres in 14 different US states. Length of study 7 months Source of funding Contract HHSM-500-2006-NW006C sponsored by the Centers for Medicare & Medicaid Services (CMS), Department of Health and Human Services (DHHS).	Within these rate strata, centres were stratified further by size (at the median or higher vs less than the median for the network as a whole) to ensure balanced selection. Thus, 18 strata were defined: 3 networks x 3 variability groups x 2 size categories. Centres were randomly assigned in a 1:1 ratio to intensive or standard intervention within networks and within blocks for each network. Centres were identified only by network, identification number, size, and vaccination rates, and assignment was performed centrally. The intensive intervention group included 38 centres, with 39 in the standard intervention group. Participant characteristics Not reported Inclusion criteria	booklets, and brochures related to established guidelines and the importance of immunisation. Intensive Intervention Standard intervention + multifaceted intervention that included: - educational seminars - assistance with and review of centre-specific action plans for improving immunisation coverage - monthly calls between the networks and centres to monitor plan implementation and proportion of patients vaccinated. No additional centre staff were used for the program, and the centres reported to the director of QI for their network. Educational Seminars three 30-to-45-minute internet educational seminars using online meeting software. Printed materials were sent to the medical director, centre	<table><tr><td>rate (2006/07)</td><td></td><td></td></tr><tr><td>Mean number of participants</td><td>95 (+/- 62.4)</td><td>90.2 (+/- 46.3)</td></tr><tr><td>Mean change rate (2006/07)</td><td>67.6%</td><td>73.6%</td></tr><tr><td>Crude difference (%)</td><td colspan="2">8.38% (95%CI -2.98% to 17.05%); p=0.04</td></tr><tr><td>Adjusted difference in change (%)</td><td colspan="2">8.86% (95% CI 0.36 to 17.37); p=0.04</td></tr></table> There were no significant differences between standard- and intensive-intervention centres with regard to mean baseline (2006-2007) influenza immunisation rate, size, percentage of black patients, profit status, mean age of patients, and sex distribution. Breakdown by network showed that this difference varied from1.6%-18.1% across the 3 networks.

Bond 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
	Centres were eligible for selection if they met the following criteria: (1) responded to the 2006-2007survey of influenza immunisations (2) had 30 patients or more on their treatment roster (3) either reported an influenza immunisation rate <75% in2005-2006 or failed to report a rate for 2005-2006. Exclusion criteria Not outlined	administrator, and director of nursing. The seminars covered: - influenza immunisation basics (influenza, its health burden in the ESRD population, the efficacy and safety of immunisation, and CDC guidelines for ESRD) - how QI methods could be used to identify, design, and implement a centre-specific plan to overcome barriers to immunisation - overcoming barriers (potential barriers to immunisation, information about successful programs, and details from the 2006 survey regarding concerns vs experiences with standing-order policies). Centres selected for the intensive intervention were called by network staff to confirm that staff had attended the seminar and/or reviewed the materials. Quality Improvement (QI) Assistance and Review Assistance with and review of centre-specific action plans were provided by each network's staff including an	Secondary outcomes – QI plans as part of the 'Intensive intervention' The mean change in vaccination rates from 2006-07 to 2007-08 did not differ significantly by inclusion of any specific topic

Bond 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
		immunisation goal for the 2007-2008 influenza season, problem statements defining each problem or underlying cause that had prevented this goal from being met in the past, and action plan steps for addressing each problem or underlying cause. The QI plan was submitted by the centre and reviewed by network staff in consultation with its own medical review board; approved or returned with feedback and then resubmitted until approved by the network. Monthly Monitoring Conducted by its network's QI coordinator between October 2007 and May 2008. If necessary, network staff or a designated member of the network's medical review board provided telephone consultation to treatment centres that had difficulty implementing their action plan or showing improvement in immunisation coverage.	
Limitations identified by author The increases seen here are from a pre-intervention year (2006-2007) for which only overall centre figures were collected to a post-intervention year (2007-2008). Patient-specific data were collected (except for standard-intervention centres in 1 network). These 2 contexts may produce different reported immunisation			

Bond 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
rates. Patients with missing data may be more likely to be erroneously excluded altogether from an overall centre tally (as in 2006-2007), producing an artificially higher rate. Possible missed data - Centres were not eligible for inclusion in the study if they did not report a rate for 2006-2007. Otherwise eligible centres also were missed (Network 15 - improved by a mean of 48.8%, from 28.8% to 77.6 %.) No data were collected for strategies in the standard-intervention centres. These factors and the differing sizes of the networks make a precise comprehensive definition of the target facilities difficult. Intervention took place in the context of a larger multiyear program to increase vaccination rates. Centres in both groups were not blinded to the evaluation process, Frequent communication occurs among centres Standard intervention group may have known of the intervention and may have affected their behaviour. Cross-talk, which potentially spurs additional action, complicates the interpretation of this study <u>Limitations identified by review team</u> <u>Other comments</u>			

G.1.2 Chamberlain 2015

Chamberlain 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year	Clinical risk group	Intervention components	Primary outcomes

<table>
<tr><th colspan="4">Chamberlain 2015</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Chamberlain AT, Seib K et al (2015)

Quality score
+

Study type
Cluster RCT

Aim of the study
To test the effectiveness of a practice-, provider-, and patient-focused influenza and Tdap (Tetanus, diphtheria and pertussis) vaccine promotion package on improving antenatal influenza and Tdap vaccination in the obstetric setting.</td>
<td>Pregnant women

Number of participants
325 women were enrolled in the study from 11 obstetric practices

Participant characteristics*
<table>
<tr><td>Characteristic
Study group;</td><td colspan="3">no. (%) of patients</td></tr>
<tr><td></td><td>Intervention (n = 161)</td><td>Control (n = 164)</td><td>Total (n = 325)</td></tr>
<tr><td>Maternal age at enrolment</td><td>26.9 (5.2)</td><td>27.5 (6.0)</td><td>27.2 (5.6)</td></tr>
<tr><td colspan="4">Race</td></tr>
<tr><td>Caucasian/White</td><td>78 (48)</td><td>76 (46)</td><td>154 (47)</td></tr>
<tr><td>African American/Black</td><td>64 (40)</td><td>69 (42)</td><td>133 (41)</td></tr>
<tr><td>Asian</td><td>2 (1)</td><td>5 (3)</td><td>7 (2)</td></tr>
<tr><td>Other or missing</td><td>17 (11)</td><td>14 (9)</td><td>31 (10)</td></tr>
</table>
</td>
<td>Practice level:
Vaccine champion - A staff member identified by the practice to be the primary resource for vaccine-related information for all practice staff.
Lapel buttons promoting antenatal vaccination
Posters promoting vaccination
Brochures - providing education on the importance of antenatal vaccination, composition of influenza and Tdap vaccines, safety of the vaccines, timing of vaccination and protection of an infant through vaccinating close contacts.
Provider level
Provider-to-patient talking points – talking points for promoting</td>
<td>Data on antenatal influenza were obtained for 300 (92.3%). Two-hundred seventy-seven (85.2%) women responded to the post-partum follow-up survey and were included in analyses of secondary outcomes.

Uptake: Participants receiving flu vaccination*
<table>
<tr><td>Intervention</td><td>Control</td></tr>
<tr><td>16/149 (10.7%)</td><td>11/151 (7.3%)</td></tr>
</table>
<table>
<tr><td></td><td>Risk diff. (95%CI)</td><td>Relative risk (95%CI)</td><td>p</td></tr>
<tr><td>Unadjusted for study design†</td><td>3.5% (−3.0, 9.9)</td><td>1.47 (0.71, 3.07)</td><td>0.3</td></tr>
<tr><td>Adjusted for clustered study design</td><td>3.6% (−4.0, 11.2)</td><td>1.47 (0.57, 3.81)</td><td>0.38</td></tr>
<tr><td>Adjusted for study design and intention to receive the vaccine</td><td>0.4% (−2.2, 3.2)</td><td>1.12 (0.49, 2.56)</td><td>0.77</td></tr>
</table>
</td>
</tr>
</table>

Chamberlain 2015

<table>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Location and setting
Obstetric clinics in Georgia, US.

Length of study
Unreported. Pregnant women were recruited between December 2012 – April 2013 and were followed up at 3 months post-partum.

Source of funding
Centers for Disease Control and Prevention (CDC),grant no. 5P01TP000300</td>
<td>
<table>
<tr><td>Ethnicity</td><td></td><td></td><td></td></tr>
<tr><td>Hispanic</td><td>12 (7)</td><td>8 (5)</td><td>20 (6)</td></tr>
<tr><td>Non-Hispanic or missing</td><td>149 (93)</td><td>156 (95)</td><td>305 (94)</td></tr>
<tr><td>Parity (number of current children)</td><td>1.0 (1.1)</td><td>1.1 (1.2)</td><td>1.1 (1.1)</td></tr>
<tr><td>Education</td><td></td><td></td><td></td></tr>
<tr><td><High school graduate/GED</td><td>9 (6)</td><td>16 (10)</td><td>25 (8)</td></tr>
<tr><td>High school graduate or GED test</td><td>69 (43)</td><td>58 (36)</td><td>127 (39)</td></tr>
<tr><td>Technical/vocational/Associates</td><td>32 (20)</td><td>41 (25)</td><td>73 (23)</td></tr>
<tr><td>Bachelor’s degree or higher</td><td>51 (32)</td><td>47 (29)</td><td>98 (30)</td></tr>
<tr><td>Health insurance</td><td></td><td></td><td></td></tr>
<tr><td>Health insurance</td><td>19 (12)</td><td>25 (15)</td><td>44 (14)</td></tr>
<tr><td>Any private insurance</td><td>68 (42)</td><td>73 (45)</td><td>141 (43)</td></tr>
<tr><td>Medicaid or no insurance</td><td>73 (45)</td><td>65 (40)</td><td>138 (43)</td></tr>
</table>
</td>
<td>antenatal influenza and Tdap vaccination were provided on coloured paper to vaccine champions.
Peer-to-peer vaccine promotion education - Provided over one lunch session by a nurse or physician, the 1-hour session covered the importance of antenatal vaccination, tips for starting an in-house vaccination program, and financial aspects of managing vaccines in the obstetric setting.
Patient level
iPad based interactive tutorial - text and audio/video content covering the importance of vaccination during pregnancy, dangers of influenza and pertussis to infants, safety of antenatal vaccination,</td>
<td>
<table>
<tr><td>before delivery</td><td></td><td></td><td></td></tr>
<tr><td>Adjusted for study design, intention to receive the vaccine before delivery and stocking vaccine in-house</td><td>0.5% (−1.8, 2.8)</td><td>1.16 (0.49, 2.78)</td><td>0.69</td></tr>
</table>

*the numbers in these tables differs from those outlined in the ‘participants characteristics’ table as it focuses on flu vaccination only and data received was analysed (per protocol)

The majority of women who received either vaccine were white, not Hispanic, had health insurance, were enrolled from practices that offered the vaccines, and had received a seasonal influenza vaccine at least one time in the past five years.

Intention:</td>
</tr>
</table>

Chamberlain 2015

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results

<table>
<tr><td>Missing</td><td>1 (1)</td><td>1 (0)
2</td><td>(0)</td></tr>
<tr><td colspan="4">Number of times treated by healthcare provider in the past year</td></tr>
<tr><td>0 times</td><td>67 (42)</td><td>73 (45)</td><td>140 (43)</td></tr>
<tr><td>1–4 times</td><td>84 (52)</td><td>76 (46)</td><td>160 (49)</td></tr>
<tr><td>5+ times</td><td>7 (4)</td><td>13 (8)</td><td>20 (6)</td></tr>
<tr><td>Don’t know</td><td>2 (1)</td><td>2 (1)</td><td>4 (2)</td></tr>
<tr><td colspan="4">Previous receipt of seasonal influenza vaccine in past 5 years</td></tr>
<tr><td>0 times</td><td>91 (57)</td><td>93 (57)</td><td>184 (57)</td></tr>
<tr><td>1 time</td><td>27 (17)</td><td>33 (20)</td><td>60 (19)</td></tr>
<tr><td>2–4 times</td><td>28 (17)</td><td>24 (15)</td><td>52 (16)</td></tr>
<tr><td>5 times</td><td>6 (4)</td><td>5 (3)</td><td>11 (3)</td></tr>
<tr><td>Don’t know</td><td>9 (6)</td><td>9 (5)</td><td>18 (6)</td></tr>
</table>

timing of antenatal vaccination and an introduction to childhood vaccination. Videos included obstetric physicians talking about antenatal vaccination as well as two testimonials from mothers whose infants contracted influenza and pertussis.

Maps to local pharmacies/health departments that provide vaccines – Provided only to practices that did not offer one or both vaccines, these handouts included a list and map of health departments and retail outlets within 5 –10 miles of a practice.

Control components

Control group practices did not receive any package materials for the duration of the study.

Antenatal influenza vaccine was significantly associated with receipt (Mean intention-to-receive scores: intervention group: 5.6, s.e. 3.5 vs. control group: 2.5, s.e. 3.0; ($p < 0.0001$).

Associations between individual intervention package components and vaccine uptake

Recollection	Un-adjust (yes/no)	% uptake flu vac (yes /no)	Adjust. RR (95%CI)/p
OB/GYN or midwife recs.	89/48	16.9%/ 0%	No estimates
Poster	93/43	14%/ 4.7%	3.28 (0.77, 17.07)/0.11
Educational brochure	60/77	16.7%/ 6.5%	2.57 (0.92, 7.18)/0.07
Lapel buttons	23/114	21.7%/ 8.8%	2.49 (0.93, 6.67)/0.07

<table>
<tr><th colspan="4">Chamberlain 2015</th></tr>
<tr><th>Study detail</th><th colspan="2">Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td></td>
<td colspan="2">
<table>
<tr><td>Enrolled from a practice stocking influenza vaccine</td><td>81 (50)</td><td>98 (60)</td><td>179 (60)</td></tr>
<tr><td>Likelihood of receiving an influenza vaccine prior to delivery</td><td>3.2 (3.4)</td><td>2.6 (2.9) 2.9 (3.2)</td><td></td></tr>
</table>
*this table has participants for flu and Tdap vaccination
Inclusion criteria
Unvaccinated in 2012/2013 pregnant women ages 18–50 years, able to read and write English

Exclusion criteria
Not outlined
</td>
<td>They were requested to maintain their standard of care regarding influenza.</td>
<td>
<table>
<tr><td>i-pad base education</td><td>10/127</td><td>30%/ 9.5%</td><td>3.17 (1.06, 9.53)/0.04</td></tr>
</table>
</td>
</tr>
<tr><td colspan="4">Limitations identified by author
It was a small cluster randomised trial, powered to find a larger absolute difference between study groups than what was observed.
Sample included practices that both stocked and did not stock vaccine

Limitations identified by review team
Potential bias associated with cluster randomisation, especially with such a small number of participants and rate of vaccine uptake.

Other comments
This US study was conducted in clinics where women’s decisions to be vaccinated was influenced by cost of vaccines and health insurance status. These would be irrelevant in the UK and this limits the usefulness of this study.</td></tr>
</table>

Chamberlain 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Received a $10 gift card and a second $25 gift card upon completion of a follow-up survey 2–3 months post-partum			

G.1.3 Freedman 2015

<table>
<tr><th colspan="4">Freedman 2015</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention/Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Freedman 2015

Quality score
-
Study type
Before and after

Aim of the study
To increase the influenza immunisation rate of oncology</td>
<td>Clinical risk group
Immunocompromised (undergoing chemotherapy or stem cell transplant (SCT))

Number of participants
1128:
480 in baseline year
648 in intervention year

Participant characteristics
<table>
<tr><th></th><th>2011-12</th><th>2012-13</th><th>P</th></tr>
<tr><td>Age, mean</td><td>10.5</td><td>10.5</td><td>0.94</td></tr>
<tr><td>Gender, n (%)</td><td></td><td></td><td></td></tr>
</table>
</td>
<td>Intervention / Comparison

5 interventions were instituted concomitantly:

Parent/family education:
Posters reminding families about the importance of vaccination; more detailed educational materials in English and Spanish available in waiting rooms and via the patient family nurse educator

Posters titled ‘Influenza: What you should know’</td>
<td>Primary outcomes

Overall vaccination uptake:
<table>
<tr><th></th><th>Baseline yr</th><th>Intervention yr</th><th>% change</th><th>p</th></tr>
<tr><td>% Unvaccinated (n)</td><td>45.2 (217)</td><td>22.5 (145.8)</td><td>-22.7</td><td><0.001</td></tr>
<tr><td>% partial vaccination* (n)</td><td>10.4 (50)</td><td>12.96 (84)</td><td>2.56</td><td>0.19</td></tr>
</table>
</td>
</tr>
</table>

Freedman 2015

Study detail	Inclusion/Exclusion and Patient population	Intervention/Comparators	Results

Study detail

patients receiving chemotherapy, through a multifaceted quality improvement initiative

Location and setting

Oncology inpatients unit and 3 outpatient clinic sites at the Children's Hospital of Philadelphia (USA)

Length of study

7 months (Sept 1 2012 – March 31 2013)

Inclusion/Exclusion and Patient population

Female	218 (45.4)	284 (43.8)	0.59
Male	262 (54.6)	364 (56.2)	0.59
Patient number (%)			
Leukaemia/lymphoma	142 (29.5)	258 (39.8)	<0.001
Solid tumours	165 (34.4)	187 (28.9)	0.048
Brain tumours	121 (25.2)	164 (25.3)	0.97
SCT	52 (10.8)	39 (6.1)	0.003

Inclusion criteria

>6 months of age, had a cancer or SCT diagnosis and had received chemotherapy in the 365 days before their scheduled visit to the hospital

Exclusion criteria

<6 months old

Allergy to vaccination

Intervention/Comparators

Containing statistics on deaths and hospitalisations from influenza; recommendations from the Centers for Disease Control and Prevention; information about influenza and it's transmission, influenza symptoms; who should get the vaccine; how the vaccine is made; how the vaccine works; when you should get the vaccine; answers why the vaccine is safe; the difference between seasonal vaccine and a pandemic; information on eligibility for pregnant women; information on protection without vaccine

Clinical informatics:

Appointments for the day in oncology clinics were retrieved daily, analysed for inclusion criteria, immunisation status and any contraindications cross referenced. A report was given to the clinic team. This daily report was emailed to the clinic triage team and clinic nursing

Results

% complete vaccination (n)	44.4 (213)	64.5 (418)	20.1	<0.001

*partial vaccination = patients under 9 who have never been immunised against influenza, receiving only 1 dose of vaccine (should be receiving 2) – numbers calculated by review team

% >/= 1 vaccination (n)	Baseline yr	Intervention yr	% change	p
Leukaemia/lymphoma	70.4 (100)*	86.8 (224)*	16.4	<0.001
Solid tumour	46.7 (77)*	72.7 9136)*	26	<0.001
Brain tumour	46.5 (56)*	70.7 (116)*	24.2	<0.001
SCT	50.0 (26)*	66.7 (26)*	16.7	0.11

Freedman 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
Source of funding No external funding	Medical contraindication (determined by the primary treating team) Being too close to SCT (<100 days)	leadership, reviewed in pre-clinic conferences Outpatient clinic interventions: An improvement in training of clinic support associates (responsible for triaging patients) was undertaken. Education focused on the provider team to identify patients needing vaccines through standardised questions having referred to the list of patients due for a vaccine. If lack of vaccination was confirmed, a bright yellow wrist band was put on the patient, cueing providers to order the vaccine. Inpatient intervention: Orders for influenza vaccination were built into admission order sets to trigger vaccination at discharge. Clinicians reviewed ordering prompts and the patient's immunisation history to confirm the need for vaccination.	<table><tr><td>Overall</td><td>54.8 (263) *</td><td>77.7 (502)*</td><td>22.9</td><td><0.001</td></tr></table> *Numbers calculated by review team Secondary outcomes Vaccines were refused or deferred in 1.8% of patients in baseline year and 2.9% of patients in intervention year. Parent refusal was the most common reason for non-vaccination accounting for 70% of refusals during baseline and 85% during the intervention. Providers deferring vaccination was rare and due to clinically sound reasoning.

Freedman 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
		Provider educational intervention: Tutorials and information about the quality improvement initiative were presented to staff at appropriate opportunities (meetings; conferences etc.) and delivered via email. Information described the process of patient screening, correct ordering and dosing of vaccines, contraindications precluding vaccination. Influenza vaccination rates were reported monthly to maintain momentum and awareness The proportion of all patients meeting high-risk criteria at their last clinic visit and receiving none, some or all recommended doses of influenza vaccine were compared to the previous year.	
Limitations identified by author Instituting several process changes at once makes it difficult to identify specific changes with greatest impact Limitations identified by review team			

Freedman 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
None Other comments None			

G.1.4 Frew 2014

Frew 2014			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
Author/year Frew PM, Owens LE et al (2014) Quality score + Study type RCT Aim of the study	Clinical risk group Pregnant women Number of participants 251 pregnant women were randomised to one of three conditions: single exposure to gain-framed, loss-framed, or control messages. Participant characteristics Characteristic / Total (n=251) / Control (n=79) / Gain (n=85) / Loss (n=87) Number (%) / Number (%) / Number (%) / Number (%)	Intervention / Comparison Message framing: Intervention messages delivered in 'clinics' (no indications as to who and how it was delivered) Women who met the eligibility criteria and agreed to participate (n = 251) were randomised to one of three conditions: single exposure to gain-framed, loss-framed, or control messages.	Primary outcomes The likelihood of obtaining flu vaccination by message framing type vs. control intervention / vs.control Gain-frame group: / OR 1.25 (95%CI: 0.49, 3.25) Loss-frame group: / OR 0.48 (95%CI: 0.17, 1.35)

Frew 2014

Study detail	Inclusion/Exclusion and Patient population	Intervention/Comparators	Results
To examine pregnant women's intention to obtain the seasonal influenza vaccine Location and setting Atlanta, Georgia, US. In "a variety of consenting venues across metropolitan Atlanta." Length of study 8 months – Sept 2011 – May 2012 Source of funding	<table><tr><td colspan="5">Age (missing=3)</td></tr><tr><td>18–25</td><td>136 (54.8%)</td><td>40 (51.9%)</td><td>45 (53.6%)</td><td>51 (58.6%)</td></tr><tr><td>26–35</td><td>93 (37.5%)</td><td>33 (42.9%)</td><td>33 (39.3%)</td><td>27 (31.0)</td></tr><tr><td>36–45</td><td>19 (7.7%)</td><td>4 (5.2%)</td><td>6 (7.1%)</td><td>9 (10.3%)</td></tr><tr><td colspan="5">Racial/Ethnic Background (missing=2)</td></tr><tr><td>African American/Black</td><td>221 (88.8%)</td><td>70 (89.7%)</td><td>77 (91.7%)</td><td>74 (85.1%)</td></tr><tr><td>Hispanic/Latino/Chicano</td><td>17 (6.8%)</td><td>4 (5.1%)</td><td>6 (7.1%)</td><td>7 (8.0%)</td></tr><tr><td>Multiracial/Other</td><td>11 (4.4%)</td><td>4 (5.1%)</td><td>1 (1.2%)</td><td>6 (6.9%)</td></tr><tr><td colspan="5">Employment Status (missing=2)</td></tr><tr><td>Employed</td><td>95 (38.2%)</td><td>28 (36.4%)</td><td>34 (40.0%)</td><td>33 (37.9%)</td></tr><tr><td>Unemployed</td><td>139 (55.8%)</td><td>44 (57.1%)</td><td>46 (54.1%)</td><td>49 (66.3%)</td></tr><tr><td>Other</td><td>15 (6.0%)</td><td>5 (6.5%)</td><td>5 (5.7%)</td><td>5 (6.0%)</td></tr><tr><td colspan="5">Health Insurance</td></tr><tr><td>Yes</td><td>182 (72.5%)</td><td>58 (73.4%)</td><td>59 (69.4%)</td><td>65 (74.7%)</td></tr></table>	Study materials were developed in English and Spanish. Survey had a Flesch-Kincaid reading score of 7.4, in either language, which met the acceptable criteria of 6–8th grade reading level for the target population.	The analysis suggests there was no significant difference in the likelihood of obtaining flu vaccination vs usual care from either form of message framing Logistic regression: factors associated with likelihood of obtaining flu vaccination by messages type Model 1: gain vs. loss <table><tr><td>intervention</td><td>vs. loss</td><td></td></tr><tr><td>Gain-frame group:</td><td>OR 2.01 (95%CI: 0.79, 5.11)</td><td></td></tr><tr><td colspan="3">Additional factors</td></tr><tr><td>Normative support from family, friends, health care providers and community</td><td>OR 2.87 (1.10, 7.53)</td><td></td></tr></table>No significant difference between gain vs loss framing for likelihood of flu vac uptake; significant difference for gain frame + normative support vs. loss framing

Frew 2014

Study detail	Inclusion/Exclusion and Patient population	Intervention/Comparators	Results

partially supported by a Kaiserr Permanente Georgia community benefits grant and a grant from the Centers for Disease Control and Prevention (CDC) grant 5P01TP000300

No	63 (25.1%)	21 (26.6%)	23 (27.1%)	19 (21.8%)
Don't Know	6 (2.4%)	0 (0.0%)	3 (3.5%)	3 (3.4%)
Likelihood of Obtaining Influenza Immunisation During Pregnancy				
Likely	65 (25.9%)	17 (21.5%)	29 (34.1%)	19 (21.8%)
Unlikely	186 (74.1%)	62 (78.5%)	56 (65.9%)	68 (78.2%)

Inclusion criteria

Eligible individuals were women aged 18–50 who self-identified as Black/African American

or Hispanic, had not already received an influenza or T-dap vaccine during the 2011–2012 influenza season, and were able to provide written informed consent.

Exclusion criteria

Not outlined

Model 2: gain vs. control

intervention	vs. control	
Gain-frame group:	OR 1.25 (95%CI 0.49, 3.25)	
Additional factors		
Normative support from family, friends, health care providers and community	OR 2.98 (95% CI 1.12, 7.93)	

No significant difference between gain vs control for likelihood of flu vac uptake; significant difference for gain framing + normative support vs. control

Model 3: Loss vs control

intervention	vs. control	
Loss-frame group:	OR 0.48 (95%CI 0.17, 1.35)	
Additional factors		

<table>
<tr><th colspan="4">Frew 2014</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention/Comparators</th><th>Results</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>Normative support from family, friends, health care providers and community</td><td>OR 4.22 (95% 1.48, 12.01)</td><td></td></tr>
</table>
No significant difference between loss framing vs control for likelihood of flu vac uptake; significant difference for loss framing normative support vs. loss framing</td></tr>
<tr><td colspan="4">Limitations identified by author
Convenience sampling - not representative of other cities in the United States.
Larger proportion study cohort were younger (18–25 y) and not entirely representative of the actual population of pregnant Hispanic or African American women.
Participatory bias as women who agreed to participate in the study may hold stronger views on immunisation and health behaviours compared with those who did not participate.

Limitations identified by review team
No detailed methodological information available about randomisation, message content, mechanism of delivery etc.
Survey instrument measuring intent to immunise may not reflect actual immunisations. Big potential demand response.
US healthcare system relies on payment or health insurance. Behaviour may be substantially different in the UK where vaccination is free for risk groups.

Other comments</td></tr>
</table>

Frew 2014			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
Participants compensated $20 for time			

G.1.5 Goodman 2015

<table>
<tr><th colspan="4">Goodman 2015</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention/Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Goodman MD, Mossad SB et al (2015)

Quality score
++

Study type
RCT

Aim of the study
To evaluate the impact of pre-visit video education on patients vaccination</td>
<td>Clinical risk group
Pregnant women

Number of participants
105 women were randomised into two groups 53 intervention and 52 control. 100 patients completed both pre and post questionnaires (51 intervention, 49 control)

Participant characteristics
<table>
<tr><th>Characteristic</th><th>Control (n=52)</th><th>Intervention (n=53)</th></tr>
<tr><td>Age (mean, years)</td><td>32.23</td><td>31.23</td></tr>
<tr><td colspan="3">Race, %</td></tr>
<tr><td>Black</td><td>23.1</td><td>20.8</td></tr>
<tr><td>Asian</td><td>1.9</td><td>0</td></tr>
</table>
</td>
<td>Intervention / Comparison
Consenting participants were randomised by a study co-ordinator into control or intervention groups. Physicians were blinded to patient allocation and were not given instructions regarding any change in their routine.
Participants were requested to:
Complete a pre-visit questionnaire
Watch an intervention or control video
Attend the prenatal visit as usual
Complete a post-visit survey before leaving.
The intervention consisted of a CDC educational video ‘Protect yourself, protect your baby’ (3 ½ minutes).</td>
<td>Primary outcomes

Impact of video intervention on health belief scores Influenza vaccination rates during the office visit were 28% (15/53) in the intervention group and 25% (13/52) in the control group (p=0.70).
<table>
<tr><td></td><td colspan="2">Educational video</td><td colspan="2">Control video</td></tr>
<tr><td rowspan="2">Vaccine offered during visit</td><td>Uptake/Event</td><td>Total</td><td>Uptake/Event</td><td>Total</td></tr>
<tr><td>15</td><td>53</td><td>13</td><td>52</td></tr>
</table>

Secondary outcomes</td>
</tr>
</table>

<table>
<tr><th colspan="4">Goodman 2015</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention/Comparators</th><th>Results</th></tr>
<tr>
<td>health beliefs and vaccination rate.
Location and setting
11 OB/GYN providers from suburban clinics in Cleveland, US

Length of study
Three months – November 2013 to January 2014

Source of funding
Cleveland Clinic Research Programme</td>
<td>
<table>
<tr><td>White</td><td>71.2</td><td>73.6</td></tr>
<tr><td>Hispanic</td><td>1.9</td><td>1.9</td></tr>
<tr><td>Multiracial</td><td>1.9</td><td>0</td></tr>
<tr><td>Refused</td><td>0</td><td>1.9</td></tr>
<tr><td>Other</td><td>0</td><td>1.9</td></tr>
<tr><td colspan="3">Insurance, %</td></tr>
<tr><td>Private</td><td>86.5</td><td>92.5</td></tr>
<tr><td colspan="3">Previous flu vaccine (2012-13)</td></tr>
<tr><td>Yes</td><td>30</td><td>30</td></tr>
</table>
Inclusion criteria
Women with no documented influenza vaccination in the 2013 – 2104 influenza season who were scheduled for a routine prenatal visit.

Exclusion criteria
Employees of the clinic
Cared for by a co-investigator
Had egg or vaccine allergy
Had high risk pregnancies
Did not speak English as a primary language.
</td>
<td>The control group watched a CDC video called ‘Put your hands together’, a similar length video addressing handwashing hygiene.</td>
<td>Of 97 participants who reported whether the provider recommended vaccination, 45 (46%) indicated a shot was recommended.

Patients recalling a provider recommendation were more likely to be vaccinated than those who did not (47% [21/45] if recommended vs. 12% [6/52] otherwise, p<0.001).</td>
</tr>
</table>

Goodman 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
Limitations identified by author Limited to English language Limited to those scheduled for care. Lack of effect of video could relate to video content rather than mode of delivery. Limitations identified by review team Mostly subjective measurements from survey.			

G.1.6 Harris 2006

Harris 2006			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year Harris M, Smith BJ et al (2006) **Quality score** + **Study type** nRCT	**Clinical risk group** People with Chronic Obstructive Pulmonary Disease (COPD) **Number of participants** 249 participants were allocated to intervention (125) or control (124) based on the hospital clinic they attended. **Participant characteristics**	**Intervention** A patient manual, 'Talking to your doctor about COPD': 80 pages, A5 size manual containing 22 summaries of evidence, organized into tagged sections on treatments for COPD, using best practice methods for presenting evidence to consumers.	Primary outcomes Outcome Change scores at 3m by socioeconomic disadvantage median | | Intervention | Control | Sig. level | | --- | --- | --- | --- | | SE disadvantage levels | Higher /Lower | Higher/ Lower | Higher/ Lower |

Harris 2006

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results

Aim of study

To assess the effectiveness of an evidence based patient manual designed to improve implementation of evidence by the patient's doctors in treating COPD.

Location and setting

3 hospital COPD clinics in Adelaide, Australia.

Length of study

3 months

Source of funding

Characteristic	Intervention	Control	Significance
Demographics			
% Male	55	52	0.66
% On oxygen at baseline	34	25	0.12 2
% Smoker at baseline	18	23	0.38
Mean years of formal education	10	10	0.18
Mean age	73.6	73.1	0.64
Mean index of socioeconomic disadvantage for postcode	1002.41	938.85	<0.001
Baseline measures			
% Current flu vaccination	88	87	0.83

Inclusion criteria

- moderate or severe COPD

Manual based on reviews of evidence from the Cochrane Collaboration and also included topics identified by two patient and carer focus groups and a support group.

Each summary was accompanied by a tip or suggested question to prompt doctor-patient consideration and implementation of the evidence. Designed to be a stand-alone intervention which could be easily read by patients and used in consultations without training.

Comparison

Participants were provided with an existing COPD education pamphlet produced by the Australian Lung Foundation.

Change in Flu vac. Rate (%)	+4%/+2%	0/0	0.13/ 0.44

No significant difference in uptake rate of flu vaccination in the lower or higher socioeconomic group compared to control.

Harris 2006			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
The Australian Commonwealth Department of Health and Ageing.	• recently discharged from one of three Adelaide hospitals with primary diagnosis of COPD, or attending respiratory clinic for management of COPD • well enough to be invited to participate and able to give informed consent • patient or agreed carer reads English at basic level • not participants in another trial **Exclusion criteria** Not outlined	Treatment allocation based on geographic location (patients living in northern and western areas of Adelaide were allocated to the control group and patients living in southern areas of Adelaide were allocated to the intervention group).	
Limitations identified by author The large number of patients invited to join the study that declined or did not respond is a threat to generalisability (462 out of 711). Non-randomised allocation Need to adjust for socioeconomic difference reduced power of study. High baseline rate of flu vaccine No blinding. Short (3 month) timescale. Limitations identified by review team Little intervention detail. No detail of content of manual, nor of distribution, whether doctors were asked to cue patients about it. Other comments Intervention not really designed to increase influenza vaccination.			

G.1.7 Herrett 2016

Herrett 2016

Study details	Methods	Intervention/Comparator	Study Population	Results
Full citation Herrett 2016 **Quality score** + Study type Cluster RCT **Aim of study** To assess effectiveness of text messaging flu vaccine reminders in increasing uptake in patients with chronic conditions **Length of follow-up**	**Recruitment** Patient records accessed from three settings: 1) Clinical Practice Research Datalink (CPRD) dataset covering 8% of UK population, 2) TPP SystmOne software users, 3) iPLATO text messaging users in London **Site recruitment:** July 2013- Oct 2013 **Inclusion criteria:** GP practices already using text messaging but not to contact patients about flu vac in 2012/13 season.	**Intervention** In addition to standard care flu campaign practices asked to send text message flu reminder to patients in at-risk groups aged 18-64 years. This required two steps: 1) identify eligible patients using software algorithm, 2) send tailored text message to these patients using software embedded in the electronic health record. **Control** Standard care which comprised of usual flu vaccination campaign, typically using measures such as posters in the practice and letters to patients	**Participation rate:** 156/300 (52%) eligible sites 156 practices (77 Intervention group, 79 Control group) [1 intervention site lost to follow-up) [see table below]	Flu vaccination rate: Practice and Patient level effectiveness summary [see table below] *Minimum variance weighted t test found absolute 2.62% (95% CI -0.09% to 5.33%), p=0.058 increase in practice-level vaccine uptake in intervention group relative to control. This corresponds to a relative increase of 5.17%. NNT to achieve one additional flu vaccination is 38.2 (95% CI -1.01 to 77.4).

	Control	Intervention
Clusters	79	76
Clinical software or iPLATO user		
CPRD	1	2
TPP	61	59
iPLATO	10	10
Patients at risk	51,136	51,121
Median (min, max) per cluster	583 (125, 1678)	637 (79,3022)
Risk groups, n(%)[ǂ]		
CHD	8,419(17)	8,291 (16)
Diabetes	12,999(25)	13,370 (26)
Respiratory	24,244(47)	24,393 (48)
Liver	1,728 (3)	1,605 (3)
Kidney	3,190 (6)	3,045 (6)
Neurological	5,949 (12)	5,853 (11)
Immunosuppression	3,341 (7)	3,766 (7)

[ǂ] Groups not exclusive

	Mean % (SD) vaccine uptake across practices	Patient level vaccination rate (%)
Intervention	54.3% (8.4)	26,804 / 51,121 (52.4%)
Control	51.7% (8.8)	25,939 / 51,136 (50.7%)

Herrett 2016				
Study details	**Methods**	**Intervention/Comparator**	**Study Population**	**Results**
Sep – Dec 2013 **Location and setting** London UK, GP practices **Source of funding:** Wellcome Trust and Public Health England	**Eligible patients:** • aged 18-64yrs • in risk groups as set out by the Chief Medical Officer at the start of flu season. **Exclusion criteria:** • Pregnant women and carers; • Patients who transferred out of the practice or died before the end of data collection **Randomisation, allocation and blinding** 1:1 allocation to standard care or intervention			Secondary outcomes: Acceptability 100/825 (12%) of invited patients completed sub-study. 75/100 recalled receiving message. Of these 4 (5.3%) objected to message (no reason given) but 48 (64%) reported being encouraged by text message to make an appointment for their vaccine. Post hoc non-randomised analysis found sending messages in the morning resulted in lower odds of being vaccinated relative to other times of the day. 3 (4.2%) practices reported difficulties in sending text message; 5 (6.9%) practices report complaints from patients about message (though total number of complaints were not recorded). Cost <£1 per person targeted.

Herrett 2016				
Study details	**Methods**	**Intervention/Comparator**	**Study Population**	**Results**
	Randomisation stratified by region and borough Block randomisation using block sizes of 2,4,6. Allocation sequence generated by independent blinded statistician. Coordinators enrolling and allocating practices was blinded until complete block randomised Not possible to blind practices but data management and analysis performed blind to allocation. **Sample size:** 100 practices for 90% power with 5% significance assuming ICC of 0.024 to identify a			

Herrett 2016				
Study details	**Methods**	**Intervention/Comparator**	**Study Population**	**Results**
	7.5% relative increase in vaccine uptake from 54% to 58%. Target of 150 to account for differences in number of eligible patients Analysis ITT analysis			
Limitations identified by author: Contamination between trial arms occurred: a third of control practices sent text messages and 10% of intervention practices failed to send a message. Pool of eligible patients that could receive intervention was smaller than expected because not all patients have a mobile phone and many don't give their numbers to their GP practice. Unable to control adherence to intervention as practice staff members identified at-risk patients and sent message using in-practice software. Some practice modified the suggested wording of the text message to suit vaccination clinic times. Practices taking part in the trial tended to have slightly larger at-risk populations than those not taking part (mean practice at-risk population in trial 705 vs. 574 not in trial, p=0.02) Limitations identified by review team: No further				

G.1.8 Jordan 2015

Jordan 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year Jordan ET, Bushar JA et al (2015) Quality score + Study type RCT Aim of the study Examine whether a text-based reminder or tailored education improved self-reported influenza vaccination or intent to	Clinical risk group Pregnant women and new mothers Number of participants Intending to get vaccination: Pregnant: 5024; Not intending to get vaccination: Pregnant: 5292; Participant characteristics Not reported Inclusion criteria Enrolees on the Text4baby programme. Self-reported as either 'pregnant' or 'mother of child <1 year' Exclusion criteria None reported	Intervention / Comparison Current Enrolees received a baseline survey via text on October 16 or 17, 2012 that asked, 'Are you planning to get a flu shot this year?' There were three response options: 'Yes', 'No', and 'I already got it'. Enrolees responding Yes or No were eligible to participate in the evaluation. Participants responding to the baseline survey that they were planning to be vaccinated ("planners") were randomly assigned to two groups (simple randomization scheme using the sum of the digits of their phone number [even/odd]). The "usual message" group received one encouragement message advising them to put a reminder on their calendar. The "enhanced messages" group received one encouragement message plus the opportunity to set up a general reminder (sent 2 weeks after receiving	Primary outcomes: Among women who received enhanced messages, there were no notable differences between those who were eligible to receive the follow-up survey and those who were not or between those who responded to the follow-up survey and those who did not. Nearly one third (28,609/89,792) of Text4baby enrolees responded to the baseline survey. Among respondents, 36% (n=10,423) reported they received the influenza vaccination, 32% (n=9,119) reported they were planning to receive it, and 32% (n=9,067) reported they were not planning to receive it. Respondents were slightly more likely to be earlier in their pregnancy and most recently enrolled for a shorter period of time. Loss to follow-up could occur during the delivery of the enhanced messages or at follow-up and for two reasons (failure to respond to surveys or cancellation of the service). Vaccination status at follow-up

<table>
<tr><th colspan="4">Jordan 2015</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>be vaccinated later in the influenza season among Text4baby participants.

Location and setting
US wide mobile text messaging service.

Length of study
N/A

Source of funding
No specific funding.</td>
<td></td>
<td>their response) or a specific reminder (sent 1 day before their chosen date).
Participants responding at baseline that they were not planning to be vaccinated (“non-planners”) were randomly assigned using the same process.
The “usual message group” received a general message stressing the importance of influenza vaccination.
The “enhanced messages” group was asked why they were not planning to be vaccinated with five options:
I think it may give me flu,
Cost,
Don’t think it’s safe,
Don’t need it
Other.
An educational message tailored to the identified concern was sent to each participant who responded.
Planners who received specific reminders were sent the follow- up survey 1 week after receiving their reminder. All other participants were sent the follow-up survey in late November. The survey asked if</td>
<td>Reminders: Pregnant Women planning at baseline to get vaccinated
<table>
<tr><th></th><th>Total</th><th>No vac</th><th>Yes vac</th><th>Intention to vac</th></tr>
<tr><td>Usual message</td><td>1360</td><td>278</td><td>821</td><td>261</td></tr>
<tr><td>Reminder</td><td>292</td><td>41</td><td>171</td><td>80</td></tr>
<tr><td>- General</td><td>211</td><td>31</td><td>125</td><td>55</td></tr>
<tr><td>- Specific</td><td>81</td><td>10</td><td>46</td><td>25</td></tr>
</table>
Education: pregnant women who reported not planning to get vaccinated
<table>
<tr><th></th><th>Total</th><th>No vac</th><th>Yes vac</th><th>Intention to vac</th></tr>
<tr><td>Usual message</td><td>1,228</td><td>758</td><td>267</td><td>203</td></tr>
<tr><td>Tailored education (Any)</td><td>1,025</td><td>658</td><td>219</td><td>148</td></tr>
</table>
</td>
</tr>
</table>

Jordan 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
		participants received the vaccine, with three response options: 'Yes', 'No', and 'No, but planning to'.	
Limitations identified by author Large non-response rate Lack of demographic detail. Self-reported data Limitations identified by review team US study where vaccines must be paid for. Other comments Jordan et al (2015) reported data on 'mothers' but has not been reported as they are not a clinical risk group and are outside the scope of this guideline			

G.1.9 Kontopantelis 2012

Kontopantelis 2012			
Study detail	**Inclusion / exclusion and patient population**	**Intervention / comparators**	**Results**
Author name and year Kontopantelis, 2012	Clinical risk group Coronary heart disease Number of participants	Intervention / Comparison Increasing upper thresholds of pay-for-performance schemes: The upper threshold for immunisation of CHD patients was increased from 85 to	Primary outcomes CHD reported achievement increased significantly, relative to other indicators when the upper CHD upper threshold increased. Model 1 assumes that the increase is the same

<table>
<tr><th colspan="4">Kontopantelis 2012</th></tr>
<tr><th>Study detail</th><th>Inclusion / exclusion and patient population</th><th>Intervention / comparators</th><th>Results</th></tr>
<tr>
<td>Quality score
-

Study type
Controlled before and after

Aim of the study
To analyse the effect of setting higher targets in a primary care pay-for-performance scheme, on rates of influenza immunisation and exception reporting

Location and setting</td>
<td>8212-8403 (depending on the year)

Participant characteristics
N/A

Inclusion criteria
All patients eligible for influenza vaccination within the clinic risk groups: CHD, COPD, diabetes mellitus or stroke patient

Exclusion criteria
None</td>
<td>90%. This means the number of patients needed to be immunised in order to achieve the same financial reward was greater.

Points awarded (which translate into financial incentives) are determined by:

Max points x [(immunisation rate – lower threshold) / (upper threshold – lower threshold)]

<table>
<tr><th></th><th>Pre-intervention</th><th>Post-intervention</th></tr>
<tr><td>Lower threshold</td><td>25%</td><td>40%</td></tr>
<tr><td>Upper threshold</td><td>85%</td><td>90%</td></tr>
<tr><td>Max points</td><td>7</td><td>7</td></tr>
</table>

Therefore, an immunisation rate of 70%, for example, would achieve fewer points post intervention than pre-intervention:</td>
<td>in all post-intervention years. Model 2 is similar to Model 1 but allows the association between the CHD upper threshold increase and CHD outcomes to vary across the years following the increase in the upper threshold.

<table>
<tr><th></th><th colspan="2">Before</th><th colspan="4">After</th></tr>
<tr><td>Mean reported achievement % (SD)</td><td>04/05</td><td>05/06</td><td>06/07</td><td>07/08</td><td>08/09</td><td>09/10</td></tr>
<tr><td>CHD</td><td>86.7 (10.0)</td><td>90.5 (7.0)</td><td>92.5 (6.3)</td><td>92.4 (5.7)</td><td>92.4 (5.6)</td><td>92.3 (6.0)</td></tr>
<tr><td>COPD</td><td>88.3 (1.1)</td><td>91.7 (7.4)</td><td>92.7 (6.4)</td><td>92.4 (6.2)</td><td>92.3 (6.0)</td><td>93.4 (5.9)</td></tr>
<tr><td>Diabetes mellitus</td><td>85.2 (11.2)</td><td>89.7 (7.5)</td><td>90.9 (6.9)</td><td>90.8 (6.2)</td><td>90.6 (6.0)</td><td>90.9 (6.0)</td></tr>
<tr><td>Stroke</td><td>83.8 (12.9)</td><td>88.3 (9.4)</td><td>89.8 (8.3)</td><td>90.9 (7.8)</td><td>89.8 (7.4)</td><td>89.7 (7.7)</td></tr>
</table>

Mean reported achievement = number of patients immunised/ number with condition and not exception reported

CHD = intervention group
COPD, diabetes mellitus and stroke = control groups
Before intervention = 04/05 and 05/06</td>
</tr>
</table>

<table>
<tr><th colspan="4">Kontopantelis 2012</th></tr>
<tr><th>Study detail</th><th>Inclusion / exclusion and patient population</th><th>Intervention / comparators</th><th>Results</th></tr>
<tr>
<td>UK family practices

Source of funding
In part by the Department of Health via its core funding to the National Primary care Research and Development Centre.</td>
<td></td>
<td>Before intervention:

7 x [(0.7 – 0.25) / (0.85 – 0.25)]
= 5.25

After intervention:

7 x [(0.7 – 0.4) / (0.9 – 0.4)]
= 4.2

This intervention therefore gave an incentive to practitioners to immunise more patients with CHD. The increase in the upper threshold means that in order to achieve the maximum number of points, 90% of patients need to be immunised as compared to 85% previously

Comparator:

Financial years 2004/05-2005/06 are pre-intervention years, as explained in the table above.</td>
<td>Post-intervention = 06/07 – 09/10

<table>
<tr><th>Year</th><th>Reported achievement coefficient % (95% CI)</th><th>p</th></tr>
<tr><td>06/07</td><td>1.17 (1.09, 1.26)</td><td><0.001</td></tr>
<tr><td>07/08</td><td>1.06 (0.97, 1.16)</td><td><0.001</td></tr>
<tr><td>08/09</td><td>0.94 (0.83, 1.05)</td><td><0.001</td></tr>
<tr><td>09/10</td><td>1.19 (1.06, 1.31)</td><td><0.001</td></tr>
</table>
Year compared with 05/06</td>
</tr>
</table>

Kontopantelis 2012			
Study detail	**Inclusion / exclusion and patient population**	**Intervention / comparators**	**Results**
		Control groups are 3 other clinical risk groups for which the upper thresholds for influenza immunisation was not altered over the study period – chronic obstructive pulmonary disease; diabetes mellitus and stroke	
Notes Limitations identified by author The variability in achievement of immunisation rates is to be expected, as CHD, COPD, diabetes and stroke patients are likely to differ in terms of disease severity, age and co-morbidities. There was not much room for improvement from baseline to intervention years as the immunisation rate was already high. Limitations identified by review team While the 3 CRGs acting as a control didn't have an upper threshold alteration, they did have an increase in the lower threshold, which increased from 25% to 40% in all 3 risk groups over the same period as the intervention. While this may not act to increase the rate of vaccination over 85% to 90%, the heightened lower threshold means that a lower financial reward is given if the immunisation rate is below 85% post-intervention. For example, an immunisation rate in these 'control' groups of 80% during pre-intervention would have resulted in 6.4 points/ 7, whereas the same rate post-intervention would have resulted in 6.22 points/ 7. This alone may incentivise a higher rate of immunisation			

G.1.10 Kontopantelis 2014

<table>
<tr><th colspan="4">Kontopantelis 2014</th></tr>
<tr><th>Study detail</th><th>Inclusion / exclusion and patient population</th><th>Intervention / comparators</th><th>Results</th></tr>
<tr>
<td>Author name and year
Kontopantelis, 2014
Quality score
+

Study type
Observational before and after

Aim of the study
To investigate the effect of withdrawing incentives on recorded quality of care, in the context of the UK Quality and Outcomes</td>
<td>Clinical risk group
Asthma

Number of participants
Unknown (all patients of practices receiving QOF)

Participant characteristics
Asthmatic patients aged 16 or over

Inclusion criteria
Asthmatic;
Aged over 16

Exclusion criteria
None</td>
<td>Intervention / Comparison

Intervention:
Financial incentives were removed for influenza immunisation of over 15yr old asthmatic patients who received an influenza immunisation between 1st September to 31st March

The denominator was the number of patients with asthma in the relevant financial year and the numerator was the number of those patients who were immunised between September to March

Comparator:
Rates of influenza immunisation during 2004/05 and 2005/06</td>
<td>Primary outcomes

Observed mean (SD) practice indicator scores (percentage achievement rates over time, by group):
<table>
<tr><th>2004/05</th><th>2005/06</th><th>2006/07</th><th>2007/08</th><th>2008/09</th><th>2009/10</th><th>2010/11</th><th>2011/12</th></tr>
<tr><td>78.0 (7.0)</td><td>78.2 (6.8)</td><td>78.0 (6.9)</td><td>78.2 (6.9)</td><td>78.0 (6.9)</td><td>78.2 (6.6)</td><td>79.0 (6.6)</td><td>78.8 (6.5)</td></tr>
</table>
2004/05-2005/06 were years where incentives were still in place
From 2006/07 onwards, incentives were removed

Mean performance remained relatively stable across the incentivisation (2004/05 to 2005/06) and post-intervention (2006/07 to 2011/12) periods ranging from 78.0% to 79.0%

The adjusted (controlled for practices' characteristics) back transformed mean difference between 2005/06 and 2011/12 levels was -0.70% (95% CI: -1.01 to -0.39%)

Results were broadly similar in all sensitivity analyses</td>
</tr>
</table>

Kontopantelis 2014			
Study detail	**Inclusion / exclusion and patient population**	**Intervention / comparators**	**Results**
Framework pay for performance scheme Location and setting English GP practices, broadly representative in terms of areas of deprivation Source of funding National Institute for Health Research School for Primary Care Research, under the title "An investigation of the Quality			

Kontopantelis 2014			
Study detail	**Inclusion / exclusion and patient population**	**Intervention / comparators**	**Results**
and Outcomes Framework using the general practice research database"			
Limitations identified by author Indirect incentivisation of withdrawn indicators exists for certain subpopulations of patients (for example, for 2011/12, 18.8% of asthma patients aged 16 or over had at least one of the four comorbidities for which the influenza immunisation incentive was not withdrawn) UK practices are also incentivised through a different scheme to immunise patients aged 65 or over against influenza further partially incentivising the asthma influenza indicator for approximately 25.2% of our patients in 2011/12 Clinical Practice Research Datalink practices tend to be larger than the average English practice and use a single clinical computing system. Choice of clinical system is a predicator of QOF performance so the generalisability of our findings might be limited Exceptions were not modelled, and for some patients, the care represented by an indicator will be inappropriate Limitations identified by review team No others			

G.1.11 Marra 2014

<table>
<tr><th colspan="4">Marra 2014</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Marra F, Kaczorowski J et al (2014)

Quality score
+

Study type
Cluster RCT

Aim of the study
To promote pharmacy based immunisation services by looking for innovative ways to extend</td>
<td>Clinical risk group
2-64 year olds with a chronic condition.

Number of participants
Based on post hoc analysis of the data by the review team: 20,455

Participant data outlined in the study was based on those that submitted questionnaire responses (per protocol: 880) – actually participant numbers were provided in the study and have been utilised by the review team – see results column

Participant characteristics

The study did not disaggregate its demographics by the population of interest

Inclusion criteria
Communities
The 2006 Canadian Census was used to identify</td>
<td>Intervention
All pharmacies in the intervention communities were approached and invited to participate. The strategies provided by pharmacies allocated to the intervention arm included the standardised training of pharmacists on providing injections and the use and safety monitoring of influenza vaccination. All the pharmacists who provided immunizations as part of this study had received training through the accredited “Administration of Injections” course provided by the BC Pharmacy Association.
The pharmacists generated personalised invitation letters to the eligible clients (based on age or filled prescription for 1 or more medications for a chronic medical condition), which were directed to their clients (target population), inviting them to be vaccinated at the pharmacy clinics.
Public promotion of the pharmacy-based clinics through advertisements in the media, such as local papers, radio</td>
<td>Primary outcomes

Impact of pharmacy based strategies of flu vaccination uptake in 2 to 64 year olds with chronic conditions
<table>
<tr><td></td><td colspan="2">Intervention</td><td colspan="2">Control</td></tr>
<tr><td>Vaccination rate</td><td>Uptake</td><td>Total*</td><td>Uptake</td><td>Total*</td></tr>
<tr><td>2010 season</td><td>6763</td><td>12716</td><td>9659</td><td>13692</td></tr>
</table>
*analysis undertaken by review team. ‘Total’ numbers are based on Marra et al assumption that 30% of the population in the communities are immunised

In 2010, there was a significant difference in influenza immunisation rates in the 14 intervention communities compared with the 15 control communities for those between 2 and 64 years of age in the intervention (54.0% [SD 22.9]) compared with control communities (70.8% [SD 19.2]), p = 0.04 (difference of 16.8%, 95% CI –14.36% to -0.655%).</td>
</tr>
</table>

Marra 2014			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
service provision. Location and setting Small communities in British Columbia, Canada Length of study 2 years Source of funding Funded by the Partners in Health Grant through the Canadian Institutes of Health Research (CIHR), Michael	29 communities with at least 1 pharmacy that did not meet any of the exclusion criteria. All pharmacies in each community were identified and invited to participate. Communities were stratified by size and randomly assigned to the intervention or control arm using a computer-generated randomization sequence. Participants Those 65 years and older and those between the ages of 2 and 64 years with at least 1 chronic condition, such as cardiac or pulmonary disorders immunosuppression due to underlying disease or therapy chronic kidney disease, chronic liver disease, anaemia and haemoglobinopathy, and conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration Exclusion criteria: Townships, first nations reserves, amalgamated townships and counties were excluded. Population size <2000 or >6000.	and cable TV, and in pharmacy-based posters. In addition, posters within the pharmacies advertised the influenza vaccination clinics, which included the hours of service and eligibility criteria. Participating pharmacies were encouraged to hold 1 or 2 clinics per week during the influenza vaccination period (October 15 to December 31) and had a dedicated nurse or pharmacist to educate patients on the benefits of vaccination, to vaccinate patients, monitor for potential adverse events and provide education on influenza prevention (e.g., handwashing, lack of effect of antibiotics for influenza). Comparison The strategies described above were not made available to pharmacies in the control communities during the 2 years of the study.	Secondary outcomes Most participants had received an influenza vaccination the year prior to the influenza season, with the majority of the participants receiving their vaccination at a public health clinic. A high association between the respondents having the influenza vaccination in previous years with those coming in for influenza vaccination the current year. Approximately one-third of the participants heard of the influenza vaccination clinic at the pharmacy from the local newspaper, and just over 20% came to the pharmacy because of a personalized letter from their pharmacist. The most common reason provided by the participants for coming to the influenza clinic was because of the expanded hours associated with pharmacies.

Marra 2014			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Smith Foundation for Health Research (MSFHR), Pharmaceutical Services Division within the Ministry of Health and Safety.			
Limitations identified by author The first year coincided with the H1N1 pandemic. As a result, seasonal vaccine was only indicated for those 65 years and older in that year, which meant that conclusions could not be drawn from those 2 to 64 years Lack of accurate denominator data. Participant honesty, memory and motivation to complete the survey are all variables that could have skewed the results. Limitations identified by review team No further Other comments Due to the limitation above for 2009 season, only data for 2010 has been extracted to ensure directness to PICO for GRADE.			

G.1.12 Minor 2010

<table>
<tr><th colspan="4">Minor 2010</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Minor DS, Eubanks JT et al (2010)

Quality score
+

Study type
RCT

Aim of the study
To identify strategies that would increase vaccination rates above baseline in the clinic.</td>
<td>Clinical risk group
Hypertension*
*The author highlights hypertension itself is not a specific qualifying disease according to recommendation guidelines, most of the patients have other chronic conditions including cardiovascular, metabolic diseases, or renal dysfunction. Others qualify based on age recommendations or because they live with or care for persons at high risk for influenza-related complications.)

Number of participants
An initial review identified 1712 patients with at least one clinic visit within the previous 15 months. Those whose record documented recent flu vaccination were excluded (n=341).

The remaining 1371 patients, who had attended the clinic in the past 15 months, were randomised in mid-November to intervention groups or control group.</td>
<td>Intervention / Comparison
Mail and telephone reminder strategies to improve existing clinic flu vaccination rates among those not seeking early seasonal vaccination. The project was timed to begin after mid-November to exclude those who actively seek vaccination early in the season and potentially include those less likely to received vaccination.
Intervention group 1: a mail reminder (letter addressed from the clinic and signed by the clinic pharmacist and physician medical director plus the Centers for Disease Control [CDC] Influenza Vaccine Information Statement). The letter contained information regarding the influenza vaccination, including explanations of the importance of receiving the vaccination and indications. Vaccination was encouraged, although not specifically at this site. The clinic charge for vaccination was provided at all encounters and the mention of possible</td>
<td>Primary outcomes

Change in Vaccination (%) vs. control:

<table>
<tr><th></th><th>% flu vac rate</th><th>OR/ 95% CI/p</th></tr>
<tr><td>Mail</td><td>46%</td><td>OR 1.8, 95% [CI], 1.3-2.5; P=.001</td></tr>
<tr><td>Phone reminder</td><td>56%</td><td>OR, 2.8; 95% CI, 1.9-4.0;P<.0001</td></tr>
<tr><td>Usual care</td><td>33%</td><td>reference</td></tr>
</table>

Both phone and mail reminders were more effective than control, but phone reminders resulted in higher vaccination rates with a better response in all age/sex groups

Change in Vaccination uptake: mail vs usual care

<table>
<tr><td>Mail reminder</td><td>Usual care: standard clinical practice</td></tr>
</table>
</td>
</tr>
</table>

<table>
<tr><th colspan="4">Minor 2010</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Location and setting
Hypertension clinic, USA.

Length of study
Mid-November to following spring

Source of funding
None.</td>
<td>At follow up, the following spring, those who could not be contacted or who were found to already have received the vaccination prior to the intervention, were then excluded from analysis (n=487).

The remainder (n=884) were included in the analysis :
Mail reminder group = 325
Phone reminder group = 246
Control group = 313

Participant characteristics:
Final analysis included 627 patients (257 patients were >65 and not considered in the further analysis)

<table>
<tr><td colspan="3">Age</td></tr>
<tr><td><50</td><td>(n=248-30%)</td><td></td></tr>
<tr><td>50-65</td><td>(n=379 – 43%)</td><td></td></tr>
</table>

Inclusion criteria
Records for all included patients were initially screened for documentation of influenza vaccination. Those without documentation</td>
<td>less expensive options (i.e. state public health clinics).

Intervention group 2: phone reminder - personal phone call from a doctor of pharmacy resident within the clinic. Phone calls were made between the hours of 8:00 AM and 8:00 PM. A minimum of 5 call attempts were made on different days and times. (same information as above but via a personal phone call)

Control group: standard clinic practice</td>
<td>
<table>
<tr><td>numbers vaccinated</td><td>Total</td><td>numbers vaccinated</td><td>total</td></tr>
<tr><td>148</td><td>325</td><td>52</td><td>157</td></tr>
</table>

Change in Vaccination uptake: telephone reminder vs. usual care
<table>
<tr><td colspan="2">Telephone reminder</td><td colspan="2">Usual care: standard clinical practice</td></tr>
<tr><td>Number vaccinated</td><td>Total</td><td>Numbers vaccinated</td><td>total</td></tr>
<tr><td>137</td><td>246</td><td>52</td><td>157</td></tr>
</table>

Observed Vaccination Rates (%) by Study Group, Age Group, and Sex:

<table>
<tr><td></td><td></td><td colspan="3">Study group</td></tr>
<tr><td>Age group</td><td>Sex</td><td>Control</td><td>Mail</td><td>Phone</td></tr>
<tr><td><50, n=248 (30)</td><td>F</td><td>13.5</td><td>24.1</td><td>34.1</td></tr>
<tr><td></td><td>M</td><td>29.0</td><td>36.7</td><td>61.5</td></tr>
<tr><td>50-65, n=379 (43)</td><td>F</td><td>29.8</td><td>47.5</td><td>57.7</td></tr>
<tr><td></td><td>M</td><td>24.5</td><td>46.7</td><td>63.0</td></tr>
</table>

Vaccination rates increase with age:
30% in those <50years</td>
</tr>
</table>

Minor 2010			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
	received a phone call from the same pharmacy resident inquiring about vaccination status and approximate date, if received at another site. Exclusion criteria Persons who reported over the phone that they had received vaccination prior to the intervention period (at another site, not documented in our clinic medical record), and those who could not be contacted after a minimum of 5 attempts, were excluded.		43% in those 50-65yrs Both interventions increased vaccination rates in all age/sex groups Vaccination rates were approximately 8% higher in men than women (49% vs 41%).
Limitations identified by author: No data on race, education, socioeconomic status, insurance coverage, or chronic medical conditions were collected. Each study group included many patients who had previously been vaccinated in other settings. There were more patients in the phone group that were identified and excluded initially. All phone calls were also made by a female pharmacy resident Clinic visits corresponding with our intervention period were not looked at. Patients in the control group and those in the intervention groups, may or may not have come into the clinic during the study period. Relied on self-report of vaccination for all those who were not actually vaccinated in our clinic. Patients were lost to follow-up. Results are specific for our clinic and represent patients that are seen in a referral setting. Limitations identified by review team US study where vaccines must be paid for. 29% of the study population were over 65			

G.1.13 Shoup 2015

Shoup 2015

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results
Author/year Shoup JA, Madrid C, Koehler C et al (2015) Quality score + Study type RCT Aim of the study To assess the effectiveness and cost of interactive voice response (IVR)	Clinical risk group Adults (19-64yrs) with asthma or chronic obstructive pulmonary disease (COPD). Number of participants n= 12,285: postcard-only group n= 4095 IVR-only n= 4095 postcard plus-IVR group n=4095 (The above numbers apply to the allocation, follow-up and the analysis stage; this is despite the IVR reminders not reaching all participants in the 'IVR-only' group (656 did not receive IVR) and the 'postcard plus-IVR' group (657 did not receive IVR). Participant characteristics Characteristic | Postcard | IVR | Postcard +IVR Sex | | |	Intervention / Comparison A 3-arm, randomized control trial was conducted of different reminder strategies for annual influenza vaccination. Subjects were aware of what type of reminder they received; however, the study aims were not described in the reminders. Randomization was performed by simple random allocation with no restrictions. Participants were randomized to receive 1 of the following vaccination reminders: 1) postcard reminder only (usual care [UC] at this clinic) 2) Interactive Voice Reminder [IVR] only, 3) postcard plus IVR reminder.	Primary outcomes The primary outcome was influenza vaccination by October 31, 2012, December 31 2012, March 31 2013: Influenza vaccination rates by October 31 IVR | | UC | | IVR +UC | | Vac uptake | total | Vac uptake | total | Vac uptake | total 1208 (31.1%) | 4095 | 1274 (29.5%) | 4095 | 1253 (30.6%) | 4095 For subjects receiving an IVR, 57% received a message on their answering machine; 27% answered the call; and 16% were not reached. % point difference in vaccination (95%CI) between different study arms as at Oct 31 2012: IVR only vs postcard only | 1.6% (–0.4 to 3.6) Postcard plus IVR vs postcard only | 1.1 % (–0.9 to 3.1)

Shoup 2015

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results

reminders for influenza vaccination compared with postcards, among adults with asthma or chronic obstructive pulmonary disease (COPD).

Location and setting
USA, managed care organization

Length of study
6.5 months

Male	1417 (34.6)	1427 (34.9)	1486 (36.3)
Female	2678 (65.4)	2668 (65.2)	2609 (63.7)
Age in yrs (%)			
19-29	898 (21.9)	875 (21.4)	874 (21.3)
30-39	1088 (26.6)	1136 (27.7)	1065 (26.0)
40-49	967 (23.6)	972 (23.7)	1024 (25.0)
50-59	826 (20.2)	789 (19.3)	819 (20.0)
60-64	316 (7.7)	323 (7.9)	313 (7.6)
Race (%)			
Black	154 (3.8)	140 (3.4)	132 (3.2)
White	2759 (67.4)	2797 (68.3)	2820 (68.9)
Native American/ Alaskan Native/Asian Pacific Islander	118 (2.9)	148 (3.6)	117 (2.9)
Missing	1064 (26.0)	1010 (24.7)	1026 (25.1)

The content of the postcard and IVR reminders was similar:
subjects were encouraged to receive influenza vaccination;
groups at increased risk from influenza were highlighted;
subjects were informed that no appointment was needed for vaccination;
and subjects were told that vaccination was provided at no cost.

Subjects receiving IVR reminders could access additional information during the IVR call.
An existing IVR system was used to contact subjects by telephone. The caller identification displayed “Kaiser Permanente” on the subject’s phone. The IVR reminders were designed to be interactive; using the numbers on a touch-tone telephone, subjects could listen to general information about influenza vaccination and hear a message from an asthma/COPD specialist at KPCO, with the option to listen to additional information about

IVR only vs postcard plus IVR	0.5% (–1.5 to 2.5)

Unadjusted and Adjusted Relative Risk of Receipt of Influenza Vaccine by October 31, 2012 (n = 12,285)

Characteristic Intervention arm	Unadjusted Relative Risk (95% CI)	Adjusted Relative Risk (95% CI)
Postcard only	1.00 (Ref)	1.00 (Ref)
IVR only	1.05 (0.99-1.13)	1.05 (0.99-1.11)
Postcard plus IVR	1.04 (0.97-1.11)	1.05 (0.99-1.11)

Influenza vaccination rates by Dec 31 2012

IVR		UC		IVR +UC	
Vac uptake	total	Vac uptake	total	Vac uptake	total

Shoup 2015

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results

Source of funding

Internal pilot grant from Kaiser Permanente Colorado's Institute for Health Research

Hispanic[a]	490 (12.0)	457 (11.2)	473 (11.6)
Qualifying condition (%)			
Asthma only	3829 (93.5)	3847 (93.9)	3834 (93.6)
COPD only	206 (5.0)	198 (4.8)	192 (4.7)
Asthma and COPD	60 (1.5)	50 (1.2)	67 (1.6)
Proportion of prior 4 influenza seasons vaccinated (%)			
0%	1791 (43.7)	1809 (44.2)	1823 (44.5)
25-33%	619 (15.1)	607 (14.8)	626 (15.3)
50-75%	810 (19.8)	841 (20.5)	798 (19.5)
100%	745 (18.2)	713 (17.4)	711 (17.4)
Newly enrolled	130 (3.2)	125 (3.1)	137 (3.4)

[a] Data on Hispanic ethnicity missing for n = 1614 (13%) of subjects.

influenza infections if desired. A maximum of 2 telephone calls were made per subject. If the IVR system reached an answering machine, a message was left encouraging influenza vaccination. Calls were made to the primary listed telephone number in the EHR, and the IVR system requested the responder to verify their identity. The IVR system tracks when the call ends, providing specific information on how much call content each subject received.

Subjects in the postcard-plus-IVR reminder group may have received their IVR call before or after their postcard.

1675 (40.9%)	4095	1766 (43.1%)	4095	1674 (40.9%)	4095

% point difference in vaccination (95%CI) between different study arms as at Dec 31 2012:

IVR only vs postcard only	2.2% (0.1-4.4)
Postcard plus IVR vs postcard only	0.0% (–2.1 to 2.2
IVR only vs postcard plus IVR	2.3% (0.1-4.4)

Influenza vaccination rates by Mar 31 2013

IVR		UC		IVR +UC	
Vac uptake	total	Vac uptake	total	Vac uptake	total
1941 (47.4%)	4095	1866 (45.6%)	4095	1844 (45.0%)	4095

% point difference in vaccination (95%CI) between different study arms as at Mar 31 2013:

IVR only vs postcard only	1.8% (–0.3 to 4.0)
Postcard plus IVR vs postcard only	-0.6% (–2.7 to 1.6)

Shoup 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
	Inclusion criteria All adults aged 19 to 64 years at KPCO with a diagnosis of asthma or COPD Subjects with asthma were included if they had an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code of asthma (493.x) in the prior 3 years. Subjects with COPD were included if they had an ICD-9-CM diagnosis code of COPD (491.x, 492.x, 493.2, and 496.x) at any time in the past. Exclusion criteria Children and the elderly were not included in the trial, because they were already receiving vaccination reminders based upon their age. From the population with asthma, subjects were excluded if they had no dispensing of an asthma-related medication in the prior 2 years. From the population with asthma or COPD, subjects were excluded if they lived in a household with other individuals in high-risk categories for influenza morbidity because these households were already scheduled to receive postcard		IVR only vs postcard plus IVR: 2.4% (0.2-4.5) Cost effectiveness: The costs of each of the 3 interventions were examined; costs were calculated for the study population and were also extrapolated to the entire population at KPCO that typically receives influenza vaccination reminders (approximately 100,000 individuals): Program costs were $0.78, $1.23, and $1.93 per subject for postcard-only, IVR-only, and postcard-plus-IVR reminders, respectively. Extrapolating costs to the entire population at the study site that typically receives influenza vaccination reminders (approximately 100,000 individuals), reminder costs would have been $0.55, $0.05, and $0.60 per subject for postcard-only, IVR-only, and postcard-plus-IVR reminders, respectively. The authors conclude that IVR reminders are not more effective at promoting influenza vaccination than postcard reminders, but IVR reminders may be less expensive for large patient populations.

Shoup 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
	reminders for influenza vaccination as usual care		

Limitations identified by author

The study did not include a control group that received no reminders - vaccination reminders are a recommended standard of care nationally, and KPCO, having a “no reminder” study arm was not appropriate on ethical grounds.

Reminders were left on answering machines, but it is not known whether these messages were ultimately heard by the intended recipients.

Some subjects may have received influenza vaccination outside of KPCO, this information would not routinely be captured within the EHR.

While standard cost-capture methods were used, it is possible that not all reminder costs were measured.

IVR systems can be expensive, (>$50,000). The IVR purchase or start-up costs were not included in our IVR reminder cost estimates it is unlikely that a healthcare entity would purchase an IVR system solely for influenza vaccination reminders - thus limiting the generalizability of our cost findings to organizations with existing IVR systems or those willing to purchase one

Limitations identified by review team

None reported

Other comments

None reported

G.1.14 O'Connor 1996

O'Connor 1996

<table>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
O'Connor, A. M., Pennie, R. A., Dales, R. E. (1996)

Quality score
+

Study type

RCT

Aim of the study
To examine the effects of using positive or negative frames to describe</td>
<td>Clinical risk group:
unimmunized patients with chronic respiratory or cardiac disease

Number of participants: 292

Participant characteristics
<table>
<tr><th>Variable</th><th>Positive frame (n=148)</th><th>Negative frame (n=144)</th><th>Test statistic</th><th>p</th></tr>
<tr><td>Mean age (SD)</td><td>53 (14)</td><td>52 (14)</td><td>t = 0.10</td><td>0.92</td></tr>
<tr><td>% Cardiac</td><td>69%</td><td>65%</td><td>x2 = 0.56</td><td>0.91</td></tr>
<tr><td>% Males</td><td>66%</td><td>61%</td><td>x2 = 0.82</td><td>0.82</td></tr>
<tr><td>% Previously aware of</td><td>93%</td><td>90%</td><td>x2 = 0. 46</td><td>0.50</td></tr>
</table>
</td>
<td>Intervention / Comparison

Randomly assigned to receive benefit/risk information that was framed:

(1) Positively as the percentage who remain free of influenza and have no vaccine side effects Positive frame described the % of individuals who remain flu-free and free of vaccine side effects with and without immunization

(2) Negatively as the percentage who acquire influenza and have vaccine side effects. Negative frame used % who acquire flu and vaccine side effects with and without immunisation

All information presented via oral flip charts and decision aid posters, large lettering, 8th grade reading level, illustrative graphics

Participants then completed a self-administered questionnaire eliciting their</td>
<td>Primary outcomes: t-test/chi-square; self-reported data

Immunisation behaviour (blind independent review of patient records) – the effect of positive or negative framed messages on vaccination uptake
<table>
<tr><td></td><td colspan="2">-ve framed</td><td colspan="2">+ve framed</td></tr>
<tr><td>Immediately vaccination</td><td>91</td><td>144</td><td>92</td><td>148</td></tr>
<tr><td>Vaccination By Dec</td><td>94</td><td>144</td><td>102</td><td>148</td></tr>
<tr><td colspan="5">Test statistic</td></tr>
<tr><td colspan="3">Immediately</td><td>X^2= 0.42</td><td>0.93</td></tr>
<tr><td colspan="3">By Dec</td><td>X^2= 0.69</td><td>0.40</td></tr>
</table>

Decisional conflict - likelihood of taking up vaccination (O'Connor decisional conflict scale).</td>
</tr>
</table>

O'Connor 1996

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results
influenza vaccine benefits and side effects on patients' expectations, decisions, decisional conflict, and reported side effects. Location and setting: Patient respiratory and cardiac clinics at two teaching hospitals and, one private group respiratory practice during normally scheduled	flu vaccine Mean contact time with research nurse minutes (SD): 19 (5) vs 18 (4), t = 1.10, 0.27 Location Resp clinic A: 16% vs 16%, x2 = 0.00, 0.96 Private respirol: 16% vs 19%, x2 = 0.33, 0.56 Cardiac clinic A: 5% vs 5%, x2 = 0.00, 0.96 Cardiac clinic B: 64% vs 60%, x2 = 0.62, 0.43 Baseline outcome measures: Estimated baseline infection rate for non-immunized to inform 'information frames' persons was set at 30%d,	expectations of vaccine risks and benefits, decision to be immunized, and decisional conflict. Those in agreement were immunized immediately and telephoned 3 days later about vaccine side effects they experienced. The unimmunized group was contacted in 3 months later (September to December) to ascertain whether they remained unimmunized. Patients informed they would receive information in 1 of 2 formats but not told what; physicians and nurses blinded to group assignment; The research nurses who presented the information were not blind but did not collect or influence data collection Co-intervention: recommendations of the 20 attending physicians in the study.	Frame / Variable / Positive (n=148) / Negative (n=144) / Test statistic / p Mean decisional conflict: 16 (5) / 16 (5) / t= 0.90 / 0.37 * a score can be between 9 (no conflict and more likely to take up vaccination) and 45 (high conflict less likely to take up vaccination) There were no statistical effect on decisional conflict scores by the framing of the message received Mean expectations of vaccine side effects or benefit by framing group (21-point probability scales); Outcome / Standard / Mean expectation (SD) Frame

[d] derived from previous research

<table>
<tr><th colspan="4">O'Connor 1996</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr><td>follow-up or referral visits; Ottawa, Canada.

Length of study

3 months

Source of funding
Ontario Ministry of Health Grant No. 04151 and the Canadian Lung Association. Influenza vaccine was donated by Connaught</td><td>Estimated baseline infection rate in immunized persons was estimated to be 10%1

The estimated intermediate rate of local side effects (e.g. a sore arm) set at 40%1

The estimated 'systemic effects' such as fever, chills, myalgia, and fatigue were set at 5%1

Most patients had heard of the influenza vaccine before (positive frame = 93%; negative frame = 90%).

Inclusion criteria:
Patients 65 and over, or under 65 with chronic pulmonary or cardiac disorders severe enough to require regular medical follow-up or hospital care; 18 years and over, and speak and read English or French.

Exclusion criteria:
(1) were allergic to eggs; (2) had current or past neurological problems; (3) were pregnant; (4) had a current acute infection or fever; (5) had received influenza vaccines previously; or</td><td></td><td>
<table>
<tr><td></td><td>prob. in poster</td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td>Positive (n=148)</td><td>Negative (n=144)</td><td>t</td><td>p</td></tr>
<tr><td>Acq*. flu</td><td>10%</td><td>19% (21)</td><td>16.9 % (19)</td><td>0.9</td><td>0.39</td></tr>
<tr><td>Acq*. side effects</td><td>5%</td><td>26.5 % (26)</td><td>30.6 % (30)</td><td>1.2</td><td>0.22</td></tr>
<tr><td>Acq*. local side effects</td><td>40%</td><td>35.6 % (31)</td><td>46.6 % (30)</td><td>3.0</td><td>.003</td></tr>
<tr><td>Rem*. Flu free</td><td>90%</td><td>81.2 % (19)</td><td>75.4 % (25)</td><td>2.2</td><td>.03</td></tr>
<tr><td>Rem*. Free side</td><td>95%</td><td>69.4 % (29)</td><td>62% (34)</td><td>2.0</td><td>.05</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th colspan="4">O’Connor 1996</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr><td>Laboratories .</td><td>(6) were considered unsuitable for immunization by the attending physician.</td><td></td><td>
<table>
<tr><td>effects</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Rem *. Free local side effects</td><td>60%</td><td>60.2 % (32)</td><td>49.6 % (31)</td><td>2.9</td><td>.005</td></tr>
</table>

*(Acq = expecting to acquire a negative outcome from vaccination – e.g. they will get a side effect from vaccination; Rem = expecting to remain free of negative outcome from vaccination – e.g will not give them flu)

Secondary outcomes:
Work absenteeism (structured checklist by Scheifel et al).
Positive frame group reported a lower incidence of work absenteeism: (x’ = 4.3, p = 0.04).

Vaccine side effects (structured checklist by Scheifel et al).</td></tr>
</table>

O'Connor 1996			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
			Positive frame group reported lower incidence of chills (x' = 8.9, p = 0.003); myalgia (x' = 6.2, 1, = 0.01),
Limitations identified by author Positive framing limited impact on patients due to other factors overwhelming choice 1) perceived risk of flu and 2) physicians advice Differences in point of reference between health care workers (to stop spreading flu to CRG) and patients (higher risk of immunisation complications e.g. pneumonia and death) Difference in perspectives from work-based physicians and personal physicians regarding the value of vaccination Limitations identified by review team Use of Self-report			

G.1.15 Siriwardena 2002

Siriwardena 2002			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
Author/year Siriwardena, AN, Rashid,	Clinical risk group People aged 65yrs+ and patients with CHD, diabetes or a previous splenectomy.	Intervention / Comparison At baseline, practices recorded for patients aged 65 years and over and in	Primary outcomes Vaccination rates, by practices in patients with coronary heart disease (CHD), diabetes and a

<table>
<tr><th colspan="4">Siriwardena 2002</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention/Comparators</th><th>Results</th></tr>
<tr>
<td>A, Johnson, MRD & Dewey ME. (2002)

Quality score
++

Study type
Cluster RCT

Aim of the study
To investigate the effect of an educational outreach visit
to primary healthcare teams on influenza and</td>
<td>Number of participants
30 General Practices, randomised:
15 to intervention
15 to the control group

Participant characteristics
Characteristics of participating compared with non-participating practices:
<table>
<tr><th></th><th>Participating practices (n = 30)</th><th>Non-participating practices (n = 62)</th><th>X2</th></tr>
<tr><td>Practice
TFCRNa
WLPCTb</td><td>
10
20</td><td>
42
20</td><td>P = 0.002</td></tr>
<tr><td>No. of partners:
1
2–3
4–6
7+</td><td>
6
14
7
3</td><td>
10
22
26
4</td><td>P = 0.38</td></tr>
</table>
</td>
<td>each disease group, if patients had received influenza vaccination in the previous year.

Fifteen practices were randomised to intervention and 15 to the control group, after stratifying for baseline vaccination rate. Baseline influenza vaccination rate was chosen for diabetes as the stratifying variable (all the rates were correlated). Within strata, practices were randomly allocated to intervention or control.

Intervention practices:
Received an educational outreach visit to primary healthcare teams, in addition to audit and feedback directed at improving influenza and pneumococcal vaccination rates in high risk groups.

The educational outreach visit was based on the principles of academic detailing. The visit took place at the practice, lasted no longer than one hour, and often took place during a primary health care team meeting, at which at</td>
<td>history of splenectomy, six months after the educational outreach visit.

The authors note that improvements for influenza vaccination were usually greater in intervention practices but did not reach statistical significance.

The groups were treated separately for the analysis although they were overlapping:

Improvement in vaccination uptake of intervention and control practices
<table>
<tr><th></th><th colspan="2">Educational outreach</th><th colspan="2">Feedback (control)</th></tr>
<tr><td>Patient</td><td>% Vac uptake</td><td>Total</td><td>Vac uptake</td><td>total</td></tr>
<tr><td>CHD</td><td>2302</td><td>3025</td><td>2307</td><td>3182</td></tr>
<tr><td>Diabetes</td><td>1532</td><td>2059</td><td>1592</td><td>2268</td></tr>
<tr><td>Splenectomy</td><td>50</td><td>62</td><td>62</td><td>107</td></tr>
</table>
*calculated by review team</td>
</tr>
</table>

Siriwardena 2002

Study detail	Inclusion/Exclusion and Patient population	Intervention/Comparators	Results
pneumococcal vaccination uptake in high-risk patients Location and setting General Practices, Trent region, UK Length of study 8 months (from baseline data collection to measurement of primary outcomes. Source of funding	<table><tr><td>List size <3000 3000–5999 6000–8999 ≥9000</td><td> 7 (23.2) 11 (36.7) 8 (26.7) 4 (13.3)</td><td> 8 (12.9) 18 (29.0) 23 (37.1) 13 (21.0)</td><td> P = 0.39</td></tr><tr><td>Dispensing</td><td>13 (43.3)</td><td>16 (25.8)</td><td>P = 0.46</td></tr><tr><td>Location Rural or semi-rural Suburban or city</td><td> 12 (40.0) 18 (60.0)</td><td> 16 (25.8) 46 (74.2)</td><td> P = 0.17</td></tr></table> aTrent Focus Collaborative Research Network; bWest Lincolnshire Primary Care Trust. Practices in both study groups were also similar in their stated strategies for improving vaccination uptake at baseline. This was	least one GP, practice nurse, and practice manager (but often the majority of the primary care team). The visit was delivered by one of the research team — a GP — who provided evidence-based information, presenting both sides of controversial issues, encouraging active learning, using simple overheads and graphs and emphasising the essential messages. The educational element of this method was a dialogue around perceived barriers to vaccination within the organisation. Feedback of practice vaccination rates in relation to other practices in the study and national targets was then provided. Following this there was a discussion about current practice policy and techniques employed to improve adult vaccination rates, with a summary of the evidence of effective interventions emphasising patient reminders and recall, professional recommendation, reminder systems, audit and feedback, and a team approach.	The mean increases (%) for influenza vaccination in intervention versus control practices <table><tr><td></td><td colspan="2">Mean Improvement (%)</td><td rowspan="2">OR/ CI(95%)/ p</td></tr><tr><td></td><td>Intervention</td><td>Control</td></tr><tr><td>CHD</td><td>18.1</td><td>13.1</td><td>OR = 1.06, 95% CI = 0.99 to 1.12 p=0.09</td></tr><tr><td>Diabetes</td><td>15.5</td><td>12</td><td>OR = 1.07, 95% CI = 0.99 to 1.16 p=0.08</td></tr><tr><td>Splenectomy</td><td>16.1</td><td>2.9</td><td>OR = 1.22, 95% CI = 0.78 to</td></tr></table>

Siriwardena 2002			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention/Comparators**	**Results**
No specific funding.	assessed by means of a postal questionnaire to each practice. Inclusion criteria All practices in West Lincolnshire Primary Care Trust (n = 39) and Trent Focus Collaborative Research Network (n = 50) were invited to participate in the study in June 2000. Twenty practices from the PCT and ten practices from the research network agreed to participate and all subsequently undertook the study. Exclusion criteria Not specified	Control practices: Undertook baseline data collection and received audit and written feedback alone. Follow up: Both intervention and control practices undertook a follow-up data collection six months after the educational intervention, which took place at the start of the annual influenza vaccination campaign. All practices measured influenza and pneumococcal vaccination rates in high-risk groups.	<table><tr><td></td><td></td><td></td><td>1.93 p= 0.38</td></tr></table> Secondary outcomes
<u>Limitations identified by author</u> Possible confounding increase in vaccination rates in both the intervention and control groups due to ongoing national and local campaigns for influenza vaccination linked to financial incentives for GPs <u>Limitations identified by review team</u> No further			

G.1.16 Siriwardena 2004

<table>
<tr><th colspan="4">Siriwardena 2004</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Siriwardena AN, Wilburn T, Hazelwood L (2004)

Quality score
-

Study type
before and after study

Aim of the study
To investigate the ability of practices in</td>
<td>Clinical risk group
Patients with CHD, diabetes, splenectomy and patients aged 65yrs+

Number of participants
39 practices participated

Participation in influenza vaccination audit (1999/2000):
<table>
<tr><td></td><td colspan="3">No of participating practice n=39</td></tr>
<tr><td>Risk group</td><td>1st cycle</td><td>2nd cycle</td><td>Both cycles</td></tr>
<tr><td>CHD</td><td>20</td><td>32</td><td>20</td></tr>
<tr><td>Diabetes</td><td>21</td><td>32</td><td>21</td></tr>
<tr><td>Splenectomy</td><td>18</td><td>29</td><td>18</td></tr>
</table>
Participant characteristics</td>
<td>Intervention / Comparison
A multi-practice audit of influenza and pneumococcal vaccination in high-risk groups as part of the annual clinical governance programme.
The aim of the audit was to compare vaccination coverage between practices, assess practices' ability to target vaccination to high risk groups and to improve vaccination of these risk groups through appropriate interventions.
The initial audit was carried out in May 2000 and repeated April 2001. Practices were asked to collect vaccination data for three tracer conditions: CHD, diabetes, splenectomy; as well as patients aged 65yrs+.

For each condition, participating practices recorded if patients have</td>
<td>Primary outcomes
The authors noted that statistically significant and clinically important improvements occurred in vaccination rates for patients with CHD, and diabetes but not splenectomy, where initial vaccination rates were already high. The greatest improvement of 24% occurred for influenza vaccination of patients over 65 years.

Improvement in vaccination uptakes of practices taking part in both phases of the audit:
<table>
<tr><td>Risk group</td><td>Phase 1 (%) flu vac uptake</td><td>Phase 2 (%) flu vac uptake</td><td>Median standard (phase 1, 2)</td><td>Mean (95% CI)</td><td>P value</td></tr>
<tr><td>CHD</td><td>58.3</td><td>77.5</td><td>70,70</td><td>19.2 (14.4</td><td><0.001</td></tr>
</table>
</td>
</tr>
</table>

Siriwardena 2004			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
a single PCT to improve influenza and pneumococcal vaccination uptake in high risk groups as a component of a clinical governance programme. Location and setting Primary care Trust, UK Length of study 1yr Source of funding	Inclusion criteria All practices in West Lincolnshire PCT (n=39) were invited to participate Exclusion criteria -	received influenza or pneumococcal vaccination. Practices used their own staff, receptionists or nurses to collect data in reprinted form and these together with their target standards to the Primary care Audit Group (PCAG). This data was analysed and anonymised summary data, graphs and results were fed back to practices. Information on good practice was distributed to practices as well as example protocols for influenza and pneumococcal vaccination. Advice given to practices included: Initiating, updating and maintaining chronic disease registers. Use and implement written protocols for adult vaccination. Ensure adequate vaccine supplies, sufficient refrigerator space and maintenance of the cold chain are important.	<table><tr><td></td><td></td><td></td><td></td><td>to 24.0)</td><td></td></tr><tr><td>Diabetes</td><td>57.6</td><td>74.5</td><td>75,70</td><td>16.9 (10.2 to 23.6)</td><td><0.001</td></tr><tr><td>Splen-ectomy</td><td>70.6</td><td>76.6</td><td>100,100</td><td>6.1 (-2.5 to 14.7)</td><td>0.155</td></tr></table>*no participant figures were provided regarding flu vaccination Secondary outcomes

Siriwardena 2004			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Trent Focus assisted with funding for ANS and West Lincolnshire PCT and Lincolnshire Health Authority funded the audit programme and Lincolnshire PCAG.		Simultaneous vaccination is a good way of increasing coverage of high risk groups. Tight stock control and efficient discounting of and claiming for vaccines ensure the vaccination program is profitable. A coordinated approach, agreed on by all personnel in the practice, including Drs, practice and district nurses, receptionists and practice managers works best. A poster campaign and advice printed on repeat prescriptions each winter will help raise patient awareness. Recommendation by a health professional and a consistent message has been shown consistently to improve vaccination rates. Practices were encouraged to discuss their results and how they could increase vaccination uptake within their primary teams. An explanation of computer searches and reimbursement were disseminated. A variety of local	

Siriwardena 2004			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
		and national awareness raising and reminder initiatives were undertaken.	
Limitations identified by author Only just over half of the practices participated in both phases of the audit. The study could not account for secular trends or the Hawthorne effect and participating practices may have differed in enthusiasm from those which did not participate. The methodology was not designed to assess the effect of audit or feedback but rather the capability ad extent to which participating practices might improve performance with the aid of audit and feedback. The national influenza campaign is likely to have had an important effect on influenza vaccination rates. Limitations identified by review team No further			

G.1.17 Walter 2008

Walter 2008			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year Walter 2008 Quality score	Clinical risk group Asthma Number of participants	Intervention / Comparison 2 interventions were performed: postcard reminders including an additional education	Primary outcomes Postcard Plus vs regular postcard (usual care)

<table>
<tr><th colspan="4">Walter 2008</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>+

Study type RCT and before and after
(2 interventions were implemented and measured individually)

Aim of the study
To evaluate the addition of a safety message about influenza vaccine to the standard vaccine reminder as well as the</td>
<td>8912 asthmatics sent a postcard in 2002-03

Postcard reminder intervention
8355 participants sent reminders in both study years (2002/03 and 2003/04);

4154 were sent postcard reminders including an additional educational message (Postcard Plus) (2003/04)

4201 were sent standard postcard reminders (2003/04)

Practice improvement intervention
15 primary care practices in total;
8 participated in practice improvement
7 acted as control practices

Participant characteristics</td>
<td>message (Postcard Plus) and a practice improvement intervention

Postcard Plus

Participants received a regular postcard reminder about influenza vaccination that also contained the following education statement:
“A recent national study by the American Lung Association showed that influenza vaccination does not worsen the symptoms associated with asthma”

Control participants received a regular postcard reminder about influenza vaccination
(no specifics provided)

Participants received postcards during each of the influenza seasons studied (posted 27th Nov 2002 and 4th Nov 2003)

Practice improvement</td>
<td>The vaccine coverage rate did not vary by type of vaccine reminder (regular postcard or postcard Plus) when analysed both for the entire vaccination season or for the period after the vaccine reminder was posted)

<table>
<tr><td></td><td colspan="2">Postcard plus</td><td colspan="2">Regular postcard</td></tr>
<tr><td></td><td>Uptake</td><td>Total</td><td>Uptake</td><td>Total</td></tr>
<tr><td>Yr1 (n=8912</td><td>3463</td><td>4440</td><td>3443</td><td>4472</td></tr>
<tr><td>Yr2 (n=8355)</td><td>3157</td><td>4154</td><td>3277</td><td>4201</td></tr>
</table>
*analysis undertaken by the review team using postcard survey responses for flu vac % coverage

Practice improvement
There was a mean increase in influenza vaccination across all sites (control and intervention) of 4.3% (SD=3.8%)

Intervention sites had a mean increase of 4.5% (SD=3.8%)

Control sites had a mean increase of 4.0% (SD=4.6%)

<table>
<tr><td>Intervention practice</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td></tr>
</table>
</td>
</tr>
</table>

Walter 2008

Study detail	Inclusion/Exclusion and Patient population	Intervention\Comparators	Results

Study detail

implantation of a practice improvement process to enhance influenza vaccination rates among asthmatic patients.

Location and setting

Primary care practices: 9 family medicine practices, 4 internal medicine practices and 2 paediatric practices, within the Duke University Health System, North

Inclusion/Exclusion and Patient population

		Flu vac coverage rate	
		02/03	03/04
Age			
3-49	5761 (65%)	17	21
50-65	1784 (20%)	30	30
6m-2yr	296 (3%)	28	36
>65	1071 (12%)	42	44
% Fem	63		
% white	51		
Insurance status			
private	71%		
Medicaid or medicare	26%		

Characteristics of both interventions:

Mean age = 38yrs

Inclusion criteria

Intervention\Comparators

Before the 2003-2004 influenza immunisation season, practice specific and aggregate coverage rates for influenza vaccination were shared with the 8 intervention practices

Perceived barriers to influenza immunisation were discussed at each intervention practice.

Face-to-face meetings between study staff and the intervention practices were performed in order to establish at least 1 proposed strategy for improving the practice-specific influenza immunisation rate.

A variety of interventions were implemented across the 8 sites. Some interventions were already being utilise as described in the following table:

Intervention Practice								
Intervention	1	2	3	4	5	6	7	8

Results

Increase in vaccination coverage from year 1-year 2 (%)	0	2	4	7	4	8	2	9
Control practice	1	2	3	4	5	6	7	8
Increase in vaccination coverage from year 1-year 2 (%)	1	0	1	10	1	11	4	

(Refer to intervention table for interventions implemented by each practice number)

Secondary outcomes

None

<table>
<tr><th colspan="4">Walter 2008</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Carolina, USA.

Length of study
2 years (across 2002-2003 and 2003-2004 influenza seasons)

Source of funding
Agency for Healthcare Research and Quality grant R21HS13511-02</td>
<td>Asthma diagnosis
Living within the state of North Carolina

Exclusion criteria
Living in institutions (eg prisons, orphanages)</td>
<td>
<table>
<tr><td>Chart reminders</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>+</td></tr>
<tr><td>Patient educational materials</td><td>+</td><td></td><td>+</td><td>+</td><td>+/ ✓</td><td></td><td>+</td><td>+</td></tr>
<tr><td>Mail or telephone reminders</td><td></td><td>+</td><td>+</td><td></td><td></td><td>+</td><td></td><td>✓</td></tr>
<tr><td>Expanded access in clinical settings (evening or weekend clinics)</td><td>✓</td><td></td><td>+</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
</table>
+ = implemented as part of the study
✓ = already in use
</td>
<td></td>
</tr>
<tr><td colspan="4"><u>Limitations identified by author</u>
Influenza vaccination coverage among the asthmatic population in this study was at least 10% higher in both years of the study than what was historically observed in the same population the year before the study started.
The fall 2003 influenza epidemic attracted intense media coverage, leading to an increase demand for influenza vaccine and local disruptions in the supply of the vaccine due to a rapid depletion of available vaccine.</td></tr>
</table>

Walter 2008			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
The use of the administrative database likely underestimated vaccine coverage, as over 40% of those who received vaccine as reported by both the postcard survey and handheld survey (not from database) received influenza vaccine at a place other than their primary providers office. The higher vaccine coverage rates ascertained by the postcard survey reflect response bias. Limitations identified by review team Multiple interventions were performed simultaneously, making it unclear which interventions achieved the results. Participation was rewarded with a payment £1500-£2000 quarterly in arrears Other comments This study contains qualitative data which has been excluded from the review as it is not an appropriate study type for qualitative data (closed ended survey)			

G.2 Effectiveness – systematic reviews

G.2.1 Aigbogun 2015

Aigbogun 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year Aigbogun NW, Hawker JI et al (2015) Quality score ++ Study type Systematic Review Aim of the study To conduct a systematic review of studies that have	Clinical risk group Children with high risk conditions Number of included studies 18 studies were included in the review Participant characteristics Most of the studies (nine) were carried out on children with asthma, four were on children with HRCs, one covered children with onco-haematological malignancies, one was on children with rheumatic disease and one was a theoretical paper. Inclusion criteria Articles were included if the studies reported on children aged between 6 months and 19 years with one or more high-risk conditions and interventions were specifically to improve influenza vaccination rates in these children.	Study details Two databases (PubMed and SCOPUS) were searched using the following combination of keywords – Influenza AND vaccination OR immunisation OR children AND asthma OR malignancy OR high-risk AND reminder (asthma is the commonest chronic condition in children, and malignancy is a common indication for influenza vaccination). There were no time or language restrictions in the search. The search was last conducted on 18/03/2014. A total of 916 citations were retrieved (839 from PubMed and 77from Scopus). Duplicates were removed (a total of 45), leaving 871 studies. Abstracts of studies were selected for screening if the titles identified the paper as relevant to the research question. A total of 840 articles were excluded at this stage.	Primary outcomes The 18 studies included one systematic review of a specific intervention in asthmatic children (All primary studies were extracted by the NICE team)), seven RCTs, six before-and-after studies, one non-randomized controlled trial, one retrospective cohort study, one quasi-experimental post-test study, and one letter to editors. Most of the studies (nine) were carried out on children with asthma, four were on children with high risk conditions, one on children with onco-haematological malignancies, one on children with rheumatic disease and one was a theoretical paper. The studies examined various types of interventions, including multi-component strategies, letter reminders, telephone recall, and a combination of letters and telephone calls. One used an Electronic Health Record (EHR) plus letter reminder and/or phone calls and an Asthma Education Tool (AET) in two

Aigbogun 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
examined interventions aimed at improving influenza vaccination in children with high risk conditions. Location and setting Various. Mostly US studies Length of study N/A Source of funding Health Protection Agency/Pub	Exclusion criteria Articles were excluded if they focused only on influenza vaccination in healthcare staff, the elderly, healthy children, adults with high risk conditions or on vaccinations other than influenza in healthy children or children with high risk conditions.	Abstracts of 31 articles were then screened – based on the inclusion/exclusion criteria above – from which 13 studies were selected for inclusion in the review. Five additional studies were identified from reviewing the reference lists of the initial thirteen, bringing the total number of included studies to 18. The quality of the RCTs was assessed using CASP as well as the Jadad/Oxford quality scoring system. Of the seven RCTs, five used appropriate randomization methods and described them fully, while the other two mentioned randomization but did not describe the method in detail. Five of the studies did not use blinding of participants or assessors, probably due to the nature of the interventions. Five of the seven studies gave a full account of participants, including numbers of participants that progressed from the start to the end of each intervention. Other study types were assessed using the CASP checklist alone.	separate studies. Authors also reported a study involving a letter plus additional Saturday influenza vaccination clinics, one involving clinician screen alerts, another involving the use of an automatic best practice reminder in patients' EHRs and one involving year-round scheduling for influenza vaccination. Please see below for a full extraction table The reviewers conclude that: There is good evidence that reminder letters can improve influenza immunisation uptake in children with HRCs. There is a lack of evidence that multiple reminder letters are more effective than single letters. There is weak evidence that telephone recall improves uptake and good evidence that a known clinician making the call and the patient's usual specialist clinic administering the vaccine is the best combination. It is not clear if telephone reminders are more effective than reminder letters. There is weak evidence that adding a telephone reminder to a reminder letter may

Aigbogun 2015			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
lic Health England			increase uptake further. Studies of provider based interventions were limited. There is weak evidence that an asthma education tool is effective as a single intervention, but it is not clear if it is more effective than reminder letters or if adding them to reminders would further increase uptake. Secondary outcomes None.
Limitations identified by author This review does not include a meta-analysis because the heterogeneity caused by the different study methods, study populations and intervention programmes made it impossible to meaningfully combine the data. Most of the studies were undertaken in the United States, except two studies that were conducted in Italy. There were no reported studies from other parts of the world, including the UK, where the extensive primary care system managed by general practitioners and funded from general taxation could readily lend itself to a large, randomized study. Limitations identified by review team Study is conducted according to SR methodology but includes various types of study, including an opinion piece. This seriously compromises its integrity. The search was simple and unstructured and does not identify the key conditions that are considered ‘high risk’, in fact, nowhere in the paper is ‘high risk conditions’ defined.			

G.2.1.1 Aigbogun 2015 (extraction table) - Children with Chronic Conditions (asthma, oncological, rheumatic disease, cystic fibrosis + other conditions)

Aigbogun 2015 (systematic review: extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Jones Cooper 2012	SR reviewed and all primary studies extracted below				Reminder/recall (10 studies)	SR
Fiks 2009 Edu	935	5809	657	5338	Education 30 min slide show	B&A
Fiks 2009 Edu + provider prompts	1173	6110	767	5329	Education plus EHC provider prompts	
Martin 2008 yr1 (2003 v 2006)	76	169	16	122	Asthma education and action plan (one copy to parent and one on medical record	B&A
Martin 2008 yr2 (2004 v 2007)	107	180	23	150		
Walter 1997 (95/96 vs 96/97 season) [e]	35	264	28	264	UC (Letter) vs, UC + Saturday clinics (Increase access)	B&A
Paul 2006 Infants	940	1265	552	1365	Routine flu season appointments vs. year round appointments	Retrospective cohort
Paul 2006 Children	522	1489	309	1332		
Szilagyi 1992	19	63	4	61	Letter Reminders	RCT
Kemper 1993	20	43	11	53		RCT
Daley 2004	391	920	237	931		RCT

[e] Data extracted from Jones Cooper 2012 p.331

Aigbogun 2015 (systematic review: extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Moore 2006	66	114	359	820		Quasi experimental
Dombkowski 2012	310	1007	242	994		RCT
Cecinati 2010 known & oncology	31	71	11	71	Telephone Recall	Randomised before and after (control = before year)
Cecinati 2010 known & paediatric	27	64	12	64		
Cecinati 2010 unknown & paediatric	34	70	19	70		
Esposito 2009 unknown & vaccination clinic	46	93	33	93		Randomised before and after (control = before year)
Esposito 2009 known & vaccination clinic	48	97	37	97		
Esposito 2009 unknown & asthma clinic	58	95	38	95		
Gaglani 2001	297	925	50	925	Letter plus telephone call	B&A
Martin 2006 yr1	372	827	70	536	Letter and/or telephone call	B&A
Martin 2006 yr 2	441	742	70	536		

Aigbogun 2015 (systematic review: extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Zimmerman 2006 yr1	385	2935	127	1219	EHC, electronic vaccine record reminders	B&A study (Control = before yr)
Zimmerman 2006 yr2	619	3311	127	1219		
Patwarden 2011	271	778	207	1246	EHC provider prompts	B&A
Multi-component						
Britto 2007	4813	8117	4684	10719	MC: increase contacts, more clinic times/access, web-based registry, provider prompts and patient reminders in clinic, recall phone calls.	nRCT
Britto 2006	762	1296	Not reported	Not reported	MC: Tracking system, phone calls, pharmacy collaboration, postcard reminders – Children's hospital medical centre.	B&A

G.2.2 Ndiaye 2005

Ndiaye 2005			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year Ndiaye SM, Hopkins DP et al (2005) Quality score + Study type Systematic Review Aim of the study To conduct a systematic review of studies that have examined interventions aimed at improving influenza, pneumococc	Clinical risk group People with heart disease, lung disease, diabetes, renal dysfunction, haemoglobinopathies, immunosuppression, and/or people living in nursing homes and other chronic care facilities. Children and adolescents (aged 6 months to 18 years) receiving long-term aspirin therapy and therefore at risk for experiencing Reye syndrome after influenza infection Women who are pregnant during flu season. Number of included studies 35 studies were included in the review. 18 primary studies met the criteria for inclusion in this review – and were extracted Participant characteristics Of the 35 included studies, 25 examined interventions aimed at improving influenza vaccination coverage. 23 studies evaluated interventions implemented in combination, 17 examined interventions aimed at improving influenza vaccination coverage. Inclusion criteria	Study details Published studies were searched for in 12 electronic databases and in reference lists from retrieved papers. Two reviewers abstracted identified studies and difference in assessment of study design and quality of execution were resolved by consensus of the team. 'The general methods for conducting systematic reviews for the Community Guide have been described in detail elsewhere. The methods used to conduct these systematic reviews and to organise the evidence of effectiveness is based on a format recommendation from the Task Force The studies examined various types of interventions, including the following, for which studies aimed at improving influenza vaccination coverage were identified: Single component: Client reminder systems Provider reminder systems Provider assessment and feedback	Primary outcomes Please see below for a full extraction table of studies included according to the review protocol (n=18). The reviewers conclude that the studies provide evidence that interventions combined across categories are effective in increasing vaccination coverage in adult populations at high risk. More specifically they report: Strong evidence of effectiveness in studies evaluating interventions to enhance access to vaccination services (expanding access in healthcare settings, reducing client out-of-pocket costs) combined with provider or system based interventions (provider reminders, providers assessments and feedback, standing orders) and/or interventions to increase client demand for vaccination services (client education, client reminders) Insufficient evidence to determine the effectiveness of combinations that did not include one or more interventions to enhance access to vaccination services

Ndiaye 2005			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
al disease and hepatitis B vaccination coverage Location and setting Various, mainly USA Length of study N/A Source of funding -	Articles were included if they: were published between 1980 and August 2001 as a journal article in English. Evaluated an intervention to deliver influenza, pneumococcal disease and hepatitis B vaccination in a population at risk or included information on risk populations as part of larger vaccination effort. Included changes in vaccination coverage as an outcome measurement. Exclusion criteria	Multicomponent: Client education + client reminder Client reminder + expanded access Client reminders + provider reminders Provider education + provider feedback Client education + client reminder + expanded access Client education + provider education + provider feedback Client education + expanded access + reduced client out of pocket costs Client reminders + provider reminders + provider feedback Standing orders + expanded access + reduced client out of pocket costs (free vaccination) Client education + client reminder + expanded access + reduced client out of pocket costs (free vaccination) Client education + client reminder + reduced client out of pocket costs (free vaccination) Client education + provider reminders + standing orders + expanded access	Insufficient evidence to determine the effectiveness of provider education as an option for combinations of provider-or system-based interventions. Secondary outcomes None.
Limitations identified by author			

Ndiaye 2005			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
The available evidence on effectiveness was not stratified by targeted vaccine or by targeted indication (e.g. medical, occupational, behavioural, other). Data was organised by intervention or combination of intervention implemented or evaluated. Within this format, further stratification by vaccine or targeted indication resulted in insufficient evidence to support more specific conclusion on effectiveness. The conceptual categories adopted for this review consolidate the evidence on effectiveness of the specific interventions within that category; however, this obscures information about the contribution of any specific intervention to a combined effort. Category based conclusion on effectiveness supports a significantly greater number of specific intervention combinations than were demonstrated in the qualifying studies. <u>Limitations identified by review team</u> The targeted indications for influenza vaccines is wider than that in the UK. Only those relevant to the UK have been extracted. Many of the studies were from the US, where the healthcare system relies on payment or health insurance. Behaviour may be substantially different in the UK where vaccination is free for risk groups.			

G.2.2.1 Ndiaye 2005 (extraction table) – High Risk Adults

Ndiaye 2005 (systematic review extraction table)						
	Experimental (intervention)		**Control (usual care/no intervention/other intervention)**			
Study	**Events (n)**	**Total (n)**	**Events (n)**	**Total (n)**	**Intervention**	**Study Type**
Larson 1982	79	199	17	84[f]	No intervention vs. Personalised postcard reminder	RCT

[f] Data extracted from Jacobsen & Szilagyi 2005 Cochrane Review p.61

Ndiaye 2005 (systematic review extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Becker 1989 provider prompt only	32	350	31	350[g]	UC vs, UC + provider prompts	RCT
Chambers 1991	177	432	95	432		RCT
Davidson 1984	68	170	37	205		Retrospective cohort
Gelfman 1986	286	381	11	381		Before and After
Harris 1990 Nurse initiated reminder	65	150	3	25		Retrospective cohort
Harris 1990 computer reminder	89	150	3	25		
McDonald 1992 yr1	22	61	9	54		cRCT (cluster randomised at provider level)
McDonald 1992 yr2	19	61	10	54		
McDonald 1992 yr3	26	61	14	54		
Multicomponent						
					Demand + Provider	
Barton 1990	80	143	30	111	UC (client reminder-postcard) vs. UC + provider prompts + provider feedback	Retrospective Cohort
Turner 1990	83	177	71	246	Provider prompts vs. provider prompts + client reminder (postcard)	Cluster RCT (GP)

[g] Data extracted from primary paper abstract Becker et al 1989

Ndiaye 2005 (systematic review extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Van Essen 1997	23250	250000 (118 GP practices)	27000	300000 (124 GP practices)	GP education, participant education, mail prompts, special vaccination hours and provider feedback (prescriptions filled)	cB&A
					Access + Demand	
Baker 1998h Generic postcard	2684	6169	835	2057	UC (increased access + client education) vs. UC + generic postcard	RCT
Baker 1998 Personalised postcard	2795	6252	835	2057	UC (increased access + client education) vs. UC + personalised postcard	
Baker 1998 Tailored letter	2780	6151	835	2057	UC (increased access + client education) vs. UC + tailored letter	
Brimberry 1998 Mail reminder	26	267	5	131	UC vs. UC + mail reminder	RCT
Brimberry 1998 telephone reminder	24	258	5	131	UC vs. UC + phone reminder	
Brimberry Mail vs telephone (intensity subgroups analysis)	26	267	24	258	UC + mail reminder vs. UC + phone reminder	
Carter 1986	41	114	28	121	UC (increased access + client reminder) vs. UC + Client and Provider education (posters and brochures) + provider feedback	RCT

[h] Data extracted from primary paper Baker et al 1998 (free access PMC)

Ndiaye 2005 (systematic review extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Moran 1996 (Int 1)	46	198	6	67	Increased access + reduced out of pocket expenses vs. Increased access + reduced out of pocket expenses + client reminder (postcard) + Education brochure	RCT
Moran 1996 (Int 2)	52	198	6	67	Increased access + reduced out of pocket expenses vs. Increased access + reduced out of pocket expenses + client reminder (postcard) + Incentive (lottery ticket)	
Moran 1996 (Int 3)	52	198	6	67	Increased access + reduced out of pocket expenses vs. Increased access + reduced out of pocket expenses + client reminder (postcard) + Education brochure + Incentive (lottery ticket)	
Spaulding 1991	131	519	50	549	Increased access + reduced out of pocket expenses vs. Increased access + reduced out of pocket expenses + client reminder (postcard)	RCT
					Access + Demand + Provider	

Ndiaye 2005 (systematic review extraction table)						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Hogg 1996 (Int 1)	23	252	20	132	UC (provider prompts + reduced out of pocket costs) vs. UC + Client Education (letter and general preventative information)	Cluster RCT
Hogg 1996 (Int 2)	36	204	20	132	UC (provider prompts + reduced out of pocket costs) vs. UC + Client reminder	
Jans 2000	278	455	76	152	UC (no info?) vs. UC+ provider edu + provider feedback	
Nichol 1990	156	267	208	697	UC (client education and expanded access i.e. walk in clinic) vs. UC + client reminder + provider prompts + standing order (nurse vaccination)	nRCTi
Nichol 1998 (Durability of intervention effect-subgroup analysis)	347	500	261	500	UC (client education and expanded access i.e. walk in clinic) + client reminder + provider prompts + standing order (nurse vaccination)-Year 1 vs. UC + client reminder + provider prompts + standing order (nurse vaccination)-Year 10	B&A (10 year follow-up)

[i] Per protocol analysis

G.2.3 Wong 2016

Wong 2016			
Study detail	**Inclusion/Exclusion and Patient population**	**Methods/Interventions**	**Results**
Author/year Wong, 2016 Quality score ++ Study type Systematic Review Aim of the study To identify and evaluate interventions used to improve immunisation uptake among pregnant women.	Clinical risk group Pregnancy Included studies The initial search yielded 2941 articles → duplicates removed: 1565 → title and abstract screening: 25 → full paper screening: 11 11 studies met the selection criteria and were reviewed here. All studies were published between 2007-2014 Participants Sample sizes varied from 126 to 21,292 participants (mean=2531) 2/11 studies recruited post-natal participants	Methods: This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. Search strategy Electronic databases including PubMed, MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials were searched, including articles published from May 2004 to August 2014. The following search terms were used in all fields regardless of publication date and language: #1: vaccine*(truncation OR immune* #2: influenza* OR flu #3: preg* OR matern* A manual search of reference lists of relevant publications was also performed. Study selection 2 reviewers screened studies by titles, then by abstracts and then by a full paper review; the relevance and eligibility of each study was determined through discussions between the 2 reviewers.	Primary outcomes No study solely assessed the effectiveness of interventions to enhance access to influenza vaccination. One moderate quality RCT showed that an influenza pamphlet, with or without a verbalized benefit statement, improved the vaccination rate (RD = 0.26; RD = 0.39). The other reviewed RCTs showed discordant results, with RDs ranging from −0.15 to 0.03. Although all observational studies significantly improved vaccination rates (RDs ranged from 0.03 to 0.44), the quality of the evidence varied. The authors concluded that the evidence of effect available was not substantial enough show an increase of influenza vaccination rate in pregnant women to allow clear indicators for success.

Wong 2016			
Study detail	**Inclusion/Exclusion and Patient population**	**Methods/Interventions**	**Results**
Location and setting 9 of the studies were conducted in the USA, 1 in Canada and 1 in Australia. Antenatal outpatient clinics; primary care outpatient clinics; tertiary hospitals and multispecialty medical organisations Source of funding -	9/11 studies included only pregnant women who had antenatal medical appointments Participants ranged from 14-50 yrs old Participants were Hispanic, Caucasian, African-American, Asian or multiracial Inclusion criteria All original research articles that reported on interventions to increase influenza vaccine uptake during pregnancy. A historical or concurrent control group was necessary for inclusion. Study outcome measure was influenza vaccination rate in all included studies. Exclusion criteria Study protocols and conference abstracts	Bias evaluation Risk of bias of RCTs was assessed using the Cochrane Collaboration method. Risk bias was assessed by considering: - Sequence generation - Allocation concealment - Blinding - Handling of incomplete outcome data - Selective outcome reporting - 'Other' potential threats to validity For each outcome, the GRADE criteria were also used to assess the risk of bias; this took into account consistency; directness; precision and risk of bias Observational studies were assessed using the Newcastle-Ottawa Scale. Studies were appraised across 3 categories: - Selection of cohorts - Comparability of cohorts - Ascertainment of the exposure of interest for cohort studies Evidence quality RCTs: 1 was 'high'; 2 were 'moderate'; 1 was 'low' Observational studies: 2 scored 3/9; 1 scored 4/9; 3 scored 5/9; 1 scored 7/9	They recommend that clinicians provide influenza pamphlets to pregnant women with a verbalized statement about the benefits of influenza vaccine to new-borns. They highlight that further high-quality RCTs are needed to develop successful maternal influenza vaccination programs. This includes increased clarity in reporting the content of interventions to help to improve the comparability and generalizability of the published studies. Please see below for a full extraction table

Wong 2016			
Study detail	**Inclusion/Exclusion and Patient population**	**Methods/Interventions**	**Results**
		Interventions Broadly, interventions were to overcome provider/system barriers (physician focused); to increase demand (pregnant woman focused) or to enhance vaccination access The following table shows which interventions were studied across the included articles:	

	Study number										
Intervention type	1	2	3	4	5	6	7	8	9	10	11
Provider reminder		✓	✓					✓	✓		
Standing order						✓	✓				
Provider feedback*						✓					
Provider education			✓			✓	✓	✓			
Pregnant woman reminder**										✓	
Pregnant woman education***	✓		✓	✓	✓			✓		✓	✓
Extend service location							✓	✓			
Increase stock			✓								

Wong 2016			
Study detail	**Inclusion/Exclusion and Patient population**	**Methods/Interventions**	**Results**
		*included delivering reports to clinics on their vaccination rates and providing education to improve knowledge and attitudes of healthcare staff towards vaccination **using text message in conjunction with education ***including mass media campaigns, via the Internet, through posters and leaflets and through lectures and workshops	
Limitations identified by author In 4 studies, the standard care groups included pregnant women that were recruited prior to 2004 in the US and prior to 2007 in Canada and the intervention groups included participants recruited after the change in the vaccination recommendations. Thus, in these studies, the groups observed over time may not be comparable. Limitations identified by review team “Given the broad heterogeneity in the study design and types of interventions, we did not conduct a quantitative pooled analysis” 4 studies did not provide the participant characteristics			

G.2.3.1 Wong 2016 (extraction table) – Pregnant Women

Wong 2016						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Klatt 2012	393	645	267	639	Usual antenatal care vs. UC + provider prompt (antenatal clinic)	B&A (B=control)
Sherman 2012	445	836	74	504		Retrospective cohort
Mouzoon 2010 Int yr 1	427	2231	222	8813	Routine antenatal vs. routine antenatal and provider interventions including education, standing orders and provider feedback *hurricane Ike during the pregnancy – lower rates attributed to this.	Retrospective cohort
Mouzoon 2010 Int yr 2	579	2035	222	8813		
Mouzoon 2010 Int yr 3	633	2040	222	8813		
Mouzoon 2010 Int yr 4	603	2111	222	8813		
Mouzoon 2010 Int yr 5	949	2039	222	8813		
Mouzoon 2010 Int yr 6	760*	2032	222	8813		
Frew (gain framed) 2014	11	45	8	20	Usual care (vaccine information sheet) vs. UC plus gain framed messages (Int 1) or loss framed messages (Int 2)	RCT
Frew (loss framed) 2014	10	42	8	20		
Meharry 2013 Int 1	35	48	12	25	Usual antenatal care vs. UC + education pamphlet (Int 1) or UC + education pamphlet + verbalized benefit statement	RCT
Meharry 2013 Int 2	31	36	12	25		

Wong 2016						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
					"vaccinating pregnant women also protects the infant" (Int 2)	
Moniz 2013	34	104	31	100	Usual antenatal care + weekly SMS general health messages vs. UC + weekly SMS general health messages + importance of flu vaccination	RCT
Stockwell 2013	284	576	269	577	Usual care (routine automated telephone reminders) vs. UC + SMS education + additional reminders	RCT
Yudin 2010	103	182	11	58	UC (routine antenatal care) vs. UC + educational pamphlet	B&A
McCarthy 2012	96	240	60	199	UC (routine antenatal care) vs. UC + multicomponent education campaign including provider education, provider prompts, participant education and increased access	B&A
Ogburn 2007 Int 1	7	220	1	95	UC (routine antenatal care) vs. UC + provider education, increased clinic access and nurse screening protocol	Retrospective Cohort

Wong 2016						
	Experimental (intervention)		Control (usual care/no intervention/other intervention)			
Study	Events (n)	Total (n)	Events (n)	Total (n)	Intervention	Study Type
Ogburn 2007 Int 2	71	192	1	95	UC (routine antenatal care) vs. Int 1 + standing orders (nurse to administer vaccine)	
Panda 2011	149	480	99	520	UC (routine antenatal care) vs. UC + multicomponent education program including provider education, provider prompts, participant education, participant reminders and increased access (vaccination @ antenatal clinic)	B&A

G.3 Access

G.3.1 Atkins 2016

Atkins 2016				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
Full citation Atkins K, van Hoek AJ, Watson C, Baguelin M, Choga L, Patel A, Raj T, Jit M, Griffiths U. Seasonal influenza vaccination delivery through community pharmacists in England: evaluation of the London pilot. BMJ	Inclusion criteria Eligibility criteria for vaccination: Aged 65yrs or over Pregnant women Long-stay care home residents Carers (as specified in the Green Book) Patients with chronic disease (as	Number of participants: Unknown – all eligible individuals registered with a GP in a London borough primary care trust Participant characteristics: Unknown	Intervention: In 2013/2014, NHS England, in consultation with North East London Local Pharmaceutical Committee and Pharmacy London, began the 'pharmacy initiative'. This enabled pharmacists to provide the seasonal flu vaccine to eligible individuals. The NHS reimbursed pharmacies when they vaccinated an individual aged 13 years or older with inactivated flu vaccine, belonging to any of the first 5 eligibility groups (left). From 2014/2015, the initiative was expanded to allow pharmacies	Flu vaccination rate: The following groups increased uptake of flu vaccination by 1% or less between 2012/13 and 2013/14 seasons: ○ Kidney disease ○ Immunosuppression ○ Respiratory disease ○ Neurological disease ○ Liver disease ○ Carers ○ Pregnant women The probability that individuals received their vaccine in pharmacies varied between 2% in chronic kidney or liver disease patients, and 22% for carers. The probability that any individual within each group became vaccinated at a pharmacy was between 1% for patients with kidney or liver disease and 8% for carers.

Atkins 2016				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
open. 2016 Feb 1;6(2):e009739. Quality score - Study type Before and after Aim of study To evaluate the effectiveness and cost of the pan-London pharmacy initiative, a program that allows administration of seasonal influenza	specified in the Green Book, excluding morbid obesity) Exclusion criteria Excluded from analysis were: 'Frontline healthcare staff' (7% of patients) 'Householders of immunocompromised individuals' (<1% of patients) Those 'living in long-stay accommodation facilities'		to offer inactivated flu vaccines to clinically at risk children from aged 2 and older.	Total number of vaccines administered 2013/14= 68,220 Total number of vaccines administered 2014/15= 108,186 Vaccine uptake rates (all risk groups) 2011-12- 60.1% 2012-13- 60.4% 2013-14 - 60.5% (First year of pharmacy initiative) Change from previous year non-significant t=0.84

Atkins 2016				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
vaccination to eligible patients at pharmacies. Location and setting Community pharmacies in all London boroughs Source of funding NHS England (London Region); the NIHR Health Protection Research Unit (HPRU); Immunisation at the London School	(<1% of patients)			

Atkins 2016				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
of Hygiene and Tropical Medicine; MRC grant (MR/J003999/ 1).				
Limitations identified by author: Results may not be generalisable to other areas of the country or the national pharmacy delivery programme Limitations identified by review team: GP ImmForm data (used to collect the total number receiving vaccination from GPs and pharmacies), stratified by ages 16-64, whereas Sonar data (used to record only pharmacy provided vaccinations) was stratified by ages 13-64, increasing the population of those eligible to receive the vaccine at a pharmacy compared to the GP. Other Other data reported in this study is out of scope for this evidence review. Overall vaccination uptake data includes a large proportion of over 65's which cannot be disaggregated; costs of providing the service are reported; completeness of vaccine recording is reported and GP and pharmacist opinions were reported, but recorded using a survey.				

G.3.2 Rai and Wood 2017

<table>
<tr><th colspan="5">Rai & Wood 2017</th></tr>
<tr><th>Study details</th><th>Inclusion/ Exclusion criteria</th><th>Population</th><th>Intervention/Comparator</th><th>Results</th></tr>
<tr>
<td>Full citation
Rai and Wood (2017) Effectiveness of community pharmacies in improving seasonal influenza uptake – an evaluation using the Donabedian framework. Journal of Public Health pp.1-7. https://doi.org/10.1093/pubmed/fdx078

Quality score
-

Study type</td>
<td>Inclusion:
Adults eligible for NHS flu vaccination, as specified in the Green Book:
• Aged 65yrs or over
• In a clinical risk group (CRG)
• Registered carers

Exclusion:
None noted.</td>
<td>Number of participants (patients):
269,355 eligible patients (aged 18-64yr in a CRG in 2014-15) registered with a GP practice in the area served by the pharmacy scheme.

Participant characteristics:
Not reported

Pharmacy participation
Scheme open to all 652 pharmacies in the area (area covered 7 CCGs).

376 (57.7%) pharmacies were approved to provide the vaccination</td>
<td>Intervention:
Flu vaccination service commissioned by NHSE regional team for Birmingham, Solihull and Black Country for 2014/15 flu season. Scheme enabled pharmacists to provide the seasonal flu vaccine to eligible adults.

Pharmacies made own arrangements for training, ensuring supplies of vaccine, adrenaline and collection of sharps.

Limited promotion of the service - two flu posters sent out per practice and distributed to local pharmacies, but not all participating pharmacies received or displayed a poster.</td>
<td>Flu vaccination rate:
Comparison of NHS flu vaccinations provided by GP practices and community pharmacies to people aged 18-64yrs in a CRG in 2013-14 and 2014-15

<table>
<tr><th></th><th>2013-14 (before pharmacy intervention)</th><th>2014-15 (after pharmacy intervention)</th></tr>
<tr><td>Total no. of eligible patients (18-64yrs) in a CRG</td><td>247,641</td><td>269,355</td></tr>
<tr><td>No. vaccinated in general practice (as % of all vaccinated)</td><td>130,838 (100%)</td><td>136,137 (97.4%)</td></tr>
<tr><td>No. vaccinated in community pharmacy (as % of all vaccinated)</td><td>n/a</td><td>3,574 (2.6%)</td></tr>
<tr><td>Overall uptake among eligible patients aged 18-64yrs in CRG (%)</td><td>130,838 / 247,641 (52.8%)</td><td>139,711 / 269,355 (51.9%)</td></tr>
</table>
</td>
</tr>
</table>

Rai & Wood 2017				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
Mixed methods with B&A analysis of uptake **Aim of study** To evaluate whether a community pharmacy flu vaccination service was effective in achieving an increased uptake **Length of follow-up** 2014-5 flu season **Location and setting**		service on submission of signed SLA to commissioners. Of these, 61pharmacies (16.2%) did not subsequently vaccinate anyone. Active sample = 315 pharmacies.	**Comparator:** Uptake rates in 2013/14, before introduction of scheme. **Data collection** Uptake data recorded on PharmOutcomes (by pharmacy, GP, CCG and risk group). ImmForm used by GP practices to record vaccination activity (GPs expected to update patient records with notifications received from pharmacies). Patient satisfaction Satisfaction data recorded on PharmOutcomes. Pharmacist experience Surveys sent to all participating pharmacies	Pre- vs. post-intervention overall vaccination uptake 52.8% vs. 51.9%; *RR = 0.98 (95%CI: 0.98 to 0.99) Note: Participating pharmacies administered a total of 8,743 vaccinations in 2014-15, of which 3,574 (40.9%) were to those in a CRG aged 18-64yrs, 231 (2.6%) to registered carers and the remainder (4.938; 56.5%) were to those aged 65yrs+. Comparative (pre- vs. post-intervention) data on uptake among patients aged 65yrs+ not extracted as outside scope of review. Data on carer uptake not reported pre-intervention so comparative analysis could not be undertaken. The two large chain pharmacies (n=155 pharmacy sites in total) delivered 45% of all vaccinations. Authors note that 689 (7.9%) of vaccinations were administered to 'new' patients (= 'never vaccinated' / 'not vaccinated for at least 2 years' / 'previously vaccinated privately') – no details reported of what proportion of 'new' patients were people aged 18-64yrs in a CRG. **Patient satisfaction:**

Rai & Wood 2017				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
West Midlands, UK **Source of funding** Service commissioned by NHSE regional team for Birmingham, Solihull and Black Country.			about experiences of set-up. Non-active pharmacies contacted about reasons for not participating. <u>Pharmacy audit</u> High & low performing pharmacies, those with GP complaints and those with median uptake rates were selected for audit visits (n=30) to assess compliance with Service Level Agreement (SLA).	93.7% of the 8,743 responded (no breakdown by eligibility group). Satisfaction was high and almost all respondents stated they would use the service again in future. Convenience and accessibility were main drivers for using the pharmacy service (78.3% of respondents) – no appointment needed, convenient opening hours and close proximity to shops or work. **Pharmacy & GP opinions and experiences:** 61 pharmacies signed up but didn't vaccinate, citing: - short lead time for training and set-up - worry about upsetting local GPs. GP complaints were mainly about: - ineligible patients being vaccinated - notifications for people not registered at their practice - wasting appointment / staff time when patients already booked for flu vaccine at surgery attended pharmacy instead. Concerns were raised about negative impact on GP uptake, vaccine stock and missed opportunities for over-65 health checks. However, no reports of left over vaccine stock or financial loss at end of flu season.

Rai & Wood 2017				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
				No major issues with data loss between pharmacies and GP recording on ImmForm, although information had to be inputted manually at GP surgeries so there is potential for data loss without close monitoring and clear agreement for activity transfer between systems. There were gaps in distribution of active pharmacies across the area. The most active pharmacies were all located in urban locations with high footfall (e.g. high streets or near shopping centres). *RR calculated by reviewer.
Limitations identified by author: Primary care complaints / opinions were reactive – not based on systematic survey. Low response rate to pharmacist survey about service set-up (34%). Small sample size for pharmacy audit (9.5%) Limitations identified by team: Gaps in distribution of participating pharmacies mean that target population had inequitable access to the service; degree to which uptake was affected by accessibility cannot be ascertained. Differences in 'eligible' target population (denominator) between pre- and post-intervention periods not explained; if due to additional risk groups becoming eligible for flu vaccination in 2014-15 this may explain reduction in overall uptake (if people were not made aware they were now eligible)				

G.4 Qualitative studies

G.4.1 Colley 2008

Colley 2008				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Colley, 2008 Quality score ++ Study type Aim of the study To look at adults under 65 years of age with a long-term condition and to explore their views about influenza	CRG: Diabetes, coronary heart disease, chronic renal disease, immunosuppression Data collection Semi-structured interviews with an interview topic guide, covering their knowledge about influenza, including its potential problems and their knowledge about the vaccine including possible side effects. Further questions explored their reasons for accepting or declining the vaccination and whether family, friends or healthcare professionals had influences their decision A purposeful sample was selected from the target population chosen on the bias of whether or not individuals had received the	Inclusion criteria 18-65yr olds with a long term illness (specifically: Diabetes, coronary heart disease, chronic renal disease or immunosuppression) Exclusion criteria Children Patients with severe mental health problems Patients in poor physical health (such as those with terminal cancer)	Participant numbers 12 Participant characteristics Male: 4 Age: 33-62 (median age 52.5) White British: 10; Asian: 1; East European: 1 Diabetes: 5 Renal disease: 1 Cardiac: 4 Respiratory: 2 50% had had the influenza	Perception of risk: Vaccinated group: Saw themselves in a high-risk group, with this being a reason for having the vaccination “Ever since I was diagnosed with heart disease, I’ve had (influenza) every autumn” “It takes me a long time to get rid of a cold being a diabetic, so that’s why [I have the vaccination]” Unvaccinated group: The majority did not consider themselves in the at risk category “At the moment I don’t really need it” 1 knew that diabetes was a risk factor, but felt that the risk would increase when she was older: “I am only 34 and there are far more vulnerable people in this country that need vaccination more than I do. So I give me dose to some elderly patient who could probably do with it, I’m still able to fight it off”

Colley 2008				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
vaccination and identify what factors influences their decision to accept or refuse it Location and setting Most interviews were carried out at the respondent homes; 2 were conducted at a surgery. Both relatively affluent suburban areas and deprived inner-city areas; UK	influenza vaccination. 50% chosen had had the vaccine, 50% had not. Method of analysis Systematic steps of grounded theory guided the analysis After transcription of the tapes, mind-mapping techniques identified concepts. Common themes were then identified and results presented according to these themes.		vaccination, 50% had not	Another respondent felt that having had 2 kidney transplants, other health issues seemed less significant: "Even if I had my arm cut off my first concern would be my kidney, so everything else is irrelevant to me" Side effects: For most, in both groups, the knowledge of side effects did not affect their decision Vaccinated group: "I think there have been really positive benefits in that I don't worry too much about Flu anymore" Unvaccinated group: Only 2 respondents thought that the vaccination caused significant side effects. This did affect their decision to not get vaccinated: "My parents, religiously had the flu vaccine… it always mucked them about in one way or another, which is my prime reason for not having it"

Colley 2008				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Source of funding Unknown				One respondent felt that the vaccination was not effective Others thought that the vaccination had minor side effects but this did not affect their decision not to have it: “I think everything has side effects… it wouldn’t bother me” “Most medication has some side effect, so no, it probably wouldn’t put me off” Advice from healthcare professionals: Vaccinated group: Several respondents stated that a nurse or a doctor had influenced their decision: “I assume that if I go to the doctor or nurse it’s a professional view of the people they have so I accept that they’re going to be right” “I think you’re only putting yourself at risk by not taking up the advice that’s given to you” “If I’m told to have it I will have it” Unvaccinated group:

Colley 2008				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
				4 had never received information about flu vaccination 1 said that she would definitely have it if her GP advised her to, another said she might have it if she was given more information: "If someone suggested it would be a good idea, I would do it" "I'd consider it if I had more information about the vaccine… someone with expert knowledge to discuss it with, not just say 'You should have it'"
Limitations identified by author The sample size was small due to time limitations There was a poor response to invitation letters from non-white, non-British respondents, therefore results cannot be generalised to these groups Limitations identified by review team "patients with poor physical health, such as those with terminal cancer, excluded" – there is no clear definition of who would be excluded or included provided, given that the target population are within a clinical risk group, it could be that an unknown proportion of those being targeted were excluded for their health being too poor				

G.4.2 Evans 2016

<table>
<tr><th>Study details</th><th>Research parameters</th><th>Inclusion/ exclusion</th><th>Study Population</th><th>Results</th></tr>
<tr>
<td>Full citation
Evans 2016

Quality score
+
Study type
Mixed methods study

Aim of the study
Insight into challenges that face community pharmacies to take an expanded role in flu vaccination and other primary care services</td>
<td>Data collection
Purposive sample of 43 pharmacies with a balance of geographical distribution, ownership, dispensing volumes and proportion of vaccinations given to people not vaccinated in previous flu season.
Analysis
Quantitative: descriptive analysis of pharmacy activity data including number of vaccinations</td>
<td>Inclusion:
Sampling frame was pharmacists at pharmacies who provided at least one vaccination during 2013-14 flu season. Pharmacies stratified by quintiles on basis of number of vaccinations provided and pharmacists in highest and second lowest eligible for participation

Exclusion:
Pharmacists in the 2nd 3rd and 5th quintiles of vaccination volume</td>
<td>Participant numbers
44 pharmacists invited for interview and 16 responded for interviews (Response rate 36.4%)

Participant characteristics
8 pharmacists provided high number of vaccinations and 8 provided a low number of vaccinations
50% male
Postgrad qualification: NONE (n=7), DIPLOMA/CERTIFICATE (N=6), MASTERS/PhD (N=3)
Position in pharmacy: Owner (n=5), Manager (n=7), Employee (n=4)
Pharmacy type: Independent (n=7), Multiple location (n=9)
Employment status: Full-time (n=12), Part-time (n=4)</td>
<td>Flu vaccination rate:
No. of NHS flu vaccinations provided by community pharmacies in Wales by eligibility criteria 2013-14 (n=7861)
<table>
<tr><th></th><th>N (%) of all pharmacy-delivered flu vaccinations</th></tr>
<tr><td>≥65 yrs of age</td><td>4081 (51.9)</td></tr>
<tr><td>Chronic resp disease (<65yrs)</td><td>1564 (19.9)</td></tr>
<tr><td>Diabetes (<65yrs)</td><td>639 (8.1)</td></tr>
<tr><td>Carer (<65yrs)</td><td>571 (7.3)</td></tr>
<tr><td>Chronic heart disease (<65yrs)</td><td>280 (3.6)</td></tr>
<tr><td>Pregnancy</td><td>233 (3.0)</td></tr>
<tr><td>Immunosuppressed (<65yrs)</td><td>174 (2.2)</td></tr>
<tr><td>Chronic neurological disease (<65yrs)</td><td>95 (1.2)</td></tr>
<tr><td>Other (as specified in patient group direction)</td><td>76 (1.0)</td></tr>
<tr><td>Household contact of immunocompromised person</td><td>40 (0.5)</td></tr>
<tr><td>Chronic kidney disease (<65yrs)</td><td>38 (0.5)</td></tr>
<tr><td>Designated first aider (<65yrs)</td><td>34 (0.4)</td></tr>
</table>
</td>
</tr>
</table>

Study details	Research parameters	Inclusion/ exclusion	Study Population	Results
Length of follow-up Oct 2013-Mar 2014 Location and setting Wales, UK Source of funding No funding received from public, commercial or not-for profit sectors				<table><tr><td>Chronic liver disease (<65yrs)</td><td>20 (0.3)</td></tr><tr><td>Long-stay residential care hoe residents</td><td>10 (0.1)</td></tr><tr><td>Community first responder</td><td>6 (0.1)</td></tr></table> 1960/7861 (24.9%) reported not being vaccinated in the 2012-13 flu season Acceptability Three themes emerged: Pharmacy factors, public awareness and external factors as factors influencing the vaccination rates Pharmacy factors- workload was an important determinant of the number of vaccinations. In particular having more than one pharmacist present helped by preventing disruption to the other activities: ''We've got two pharmacists here so it means that dispensing continues without disrupting the normal day-to day activities'' Other pharmacy numbers included extended trading hours, pharmacy location, staff support, flexibility to offer vaccinations, identifying patients, planning approach, impact on other services, Number of consultation rooms available

Study details	Research parameters	Inclusion/ exclusion	Study Population	Results
				Public awareness factors included word of mouth and availability of promotional material ''We could have more proactively promoted it (the service) but didn't particularly want to step on the GPs toes'' External factors included financial incentives for pharmacist, GP relationships, vaccine availability, administrative burden, and commissioning processes ''we didn't actually get the Patient Group Direction until the week the service started''
Notes: Limitations identified by author: Measurement of the performance of pharmacies in numbers of vaccines given, which assumes that all pharmacies serve a broadly similar at-risk population. Participants were volunteers who may have overstated their enthusiasm or how well the service was received by patients or understated GP resistance, particularly if they believed this was critical to ensuring that they were commissioned in the future. All participants were providing NHS flu vaccinations and findings cannot be applied to all pharmacies Limitations identified by review team: Patients from CRGs were vaccinated the data is not collected in a manner to directly attribute vaccination to any members of this population				

G.4.3 Maher 2014

Maher 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Maher, 2014 Quality score + Study type Qualitative Aim of the study To investigate the knowledge, attitudes, beliefs, and practices of general	CRG Pregnancy Data collection Purposeful samples were used to ensure diversity. 44 general practitioners were selected to be invited Interviews were conducted in person Method of analysis 4 researchers conducted analysis; they met to discuss emergent concepts, themes and issues across the dataset and a conceptual framework was developed to capture this.	Inclusion criteria None mentioned Exclusion criteria None mentioned	Participant numbers 17 Participant characteristics General practitioners 9 female, 8 male 10 from small practices, 7 from large practices	GPs risk perception of influenza infection during pregnancy: Overall, the GPs were not concerned about the risks associated with influenza during pregnancy 1/3 did not consider influenza during pregnancy to be a serious risk for the mother or the baby 2/3 thought there was an increased risk associated, mentioning miscarriage or premature labour Some thought that the risks of infection were specifically associated with the H1N1 strain of the 2009 pandemic Many did not have direct experience of a pregnancy patient contracting influenza and having serious consequences and this in turn decreased their perception of the risk Many did not know that pregnancy alone placed a woman in a high-risk category “I'm aware that if women get the influenza virus during pregnancy complications are much higher, the severity of the influenza is much higher and so we ought to be vaccinating women during pregnancy”.

Maher 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
practitioners in the Sydney and South-Western Sydney Local Health Districts in Australia towards influenza vaccination during pregnancy Location and setting In GPs place of practice, Sydney, Australia				"I guess the same (risks) as anyone who doesn't have a pregnancy. Whether it brings on pre-term labour, possibly, but I am not aware of any specific problems directly related to the pregnancy". "I think with the number of people (pregnant women) who catch the flu and the number of people who don't have any problems with it….I see it's a small amount of risk involved". GPs knowledge, attitudes and beliefs about influenza vaccination during pregnancy: Most were aware of the recommendations of influenza vaccination during pregnancy, but not confident on all aspects, particularly in relation to timings "The thing that surprised us is why suddenly there is a push for vaccinating for flu in pregnant woman….most of us are quite surprised that it is recommended". Most identified vaccination during pregnancy as beneficial in preventing consequences such as miscarriage or premature labour. Very few mentioned the benefits for the baby.

Maher 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Source of funding Unknown				More than half had significant concerns about the safety of the vaccine during pregnancy Vaccination in pregnancy is relatively new and many needed a longer period of time where this was practiced without adverse outcomes before they could be confident that the vaccine was completely safe for pregnant women. A number were concerned that if they provided the vaccine and an adverse event subsequently happened (related or not to the vaccine), that women would blame the vaccine and hold the practitioner liable. “I think it is more of an unknown and you tend to be more conservative about what you give [pregnant] patients”. “With the small amount of risk involved [with influenza] I don’t see that the benefits [of the vaccination] outweigh the risks”. “My understanding is it category B in pregnancy. Which is a little bit of grey area…. If it was Category A I would be much more likely to recommend it.” (In Australia, Category B2 drugs have only have taken by a limited number of pregnant women, and studies in animals are lacking, but available data shows no evidence of harmful effects on the foetus)

Maher 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
				"We have to wait and see whether the information is correct. Most times after a few years you find out that the information might not be that accurate." "I just think if they had the flu injection, then whether it was a day, a month, or at any stage after getting the vaccine, that if anything went wrong like foetal death or early labour, I know that they would look at pointing the finger at the flu vaccine as the cause. Whether it is or not. So it is safer as a doctor not to do that". Those confident that the vaccine is safe were either more informed about the evidence regarding safety or were more willing to trust that the vaccine is safe, based on the fact that it is recommended under the national immunisation guidelines Most felt they needed more information and were under confident in their knowledge Many reported challenges in staying aware of recent research and evidence

Maher 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
				GPs approach to promoting and providing influenza vaccination during pregnancy: Some reported that influenza vaccination was not often a high priority "It's not high on my priority. I think around March [autumn], when the flu vaccines come out, you tend to be much more likely to bring it up with patients, or they will bring it up with you." Many would ultimately leave the decision regarding vaccination to their patient "We just advise them. If they accept that's fine" A strong doctor-patient relationship is an important factor in patients accepting the vaccine
<u>Limitations identified by author</u> Only 17 of the 44 invited participated (20 estimated as needed to reach saturation) Responses of GPs may have been affected by the fact that the interviewer is a New South Wales public health employee <u>Limitations identified by review team</u> Lack of information regarding inclusion/exclusion criteria, but as all participants are GPs, this is unlikely to make any difference to the conclusions.				

G.4.4 Marsh 2014

Marsh 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Marsh, 2014 Quality score - Study type Qualitative Aim of the study To explore message framing of targeted messaging for pregnant women to receive the influenza vaccination Location and setting OB/GYN clinics within the Grady Health System, Emory Health System and surrounding urban and suburban areas of Atlanta Source of funding Partially supported by a Kaiser Permanente Georgia community benefits grant and a	CRG Pregnancy Data collection Project staff randomly approached women at OB/GYN clinics. Interviews were conducted in assigned areas for up to 1hr. Responses were routinely read back to participants to ensure correct interpretation of results. Interviews examined perceived benefits of influenza immunisation compared to risks of not obtaining vaccination. They explored what information women would need before getting the flu shot. Also explored was why or why not they would get an influenza vaccine during pregnancy. Method of analysis Thematic categories and coding scheme were developed through independent content review of all transcripts, followed by	Inclusion 18-50 Self-identified African American Currently pregnant Could read and write English Could provide informed written consent Exclusion Women who had already had an influenza or Tdap vaccine during their	Number of participants 21 Participant characteristics 8-36 weeks pregnant African American 19-39 yrs (mean age 24.5)	Vaccination in pregnancy: Most women considered influenza vaccination in pregnancy either harmful or unnecessary “Well it was a couple people that I read and they were saying that sometimes it could mess up something in the baby, sometimes it can mess up the development… so I don’t want to try it.” “cause…they tell you do not take anything except for Tylenol so it kinda makes it seem like you probably shouldn’t be getting vaccines.” Women showed interest in knowing more about influenza vaccination during pregnancy

Marsh 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
grant from the Centre for Disease Control and prevention, Grant 5P01TP000300 to the Emory Preparedness and Emergency Response Research Centre, Emory University (Atlanta, Georgia)	discussion among the research team about emergent themes. Initially, 2 coders reviewed a small sample of printed materials and independently coded the materials i to establish pre-test reliability and refine unclear areas. Analyses utilised the constant comparative approach within the grounded theory process model. Themes were elicited by independent review of all transcripts followed by discussion. Subsequent axial coding was conducted, facilitating the emergence of thematic linkages among variables.	current pregnancy		Concerns overwhelmingly revolved around the vaccine efficacy and risks and benefits for the foetus rather than themselves "If anything else is happening you want to know, is the baby okay? That's always the first thing…that's the main concern before themselves." Women expressed strong willingness for influenza immunisation if their doctors described the risks and benefits to the infant Positive framing (benefits) vs Negative framing (risks):

Marsh 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
				Positive framing of vaccination uptake messages was highly preferred: "…your emotions are already all over the place and last thing you want to hear is…not getting this could cause serious complications, might kill you, might kill the baby… " Strong willingness was shown by 20/21 of the women (95%) to get vaccinated if the benefits to the infant were clearly communicated Communication approaches: Women identified their community networks – specifically other women's experiences, media and

Marsh 2014				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
				primarily their doctor - as trusted sources of information Participants mentioned that public messages in media do not do a good job of explaining who is at risk and who should get vaccinated as a priority 1 participant insisted on the need to get more information "My doctor just said get it cause it's flu season, but I didn't know nothing about it…and every time I get shot I like to ask, what, how it helps me…and my doctor didn't tell me."
Limitations identified by author Convenience sampling of women from 1 city is not representative of the larger population Intention, as opposed to actual behaviour was measured; there is no data to support the claims made that positive framing or targeting health promotion to the benefits for the child is the most effective Limitations identified by review team No others				

G.4.5 Meharry 2013

Meharry 2013				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Meharry 2013 Quality score + Study type Qualitative Aim of the study To gain an in-depth understanding of the reasons why pregnant	CRG Pregnancy Data collection Potential participants were identified through the daily patient census and recruited for interview systematically, starting in room 1 on the census list. Participants completed a brief written	Inclusion In 3rd trimester or new mothers on the postpartum unit 18 yrs + Receiving care at a designated site Conversant in English or Spanish Exclusion Participants were	Participant numbers 60 Participant characteristics Age: 18-45yrs Private insurance: 43 Public insurance: 17 Household income <$50,000: 29 Household income >$50,000: 20 (11 not disclosed) Comorbidities: -Asthma: 11 -Diabetes:2 -Other:1 -None:46	Differing degrees of influence affect action to vaccinate: Influence of healthcare personnel If providers explain the threat of influenza and recommend maternal vaccination, most women accept the vaccine “For me, I trust my doctor. If you don’t trust your doctor, you may as well not go to them. So, you know, he told me I should get it and I listened to him.” Other women perceive an indifferent provider as a barrier to vaccination “The doctor just asked if you wanted the vaccine and when you said no, she didn’t follow-up with any information.” Influence of family and friends Family members influence the women’s perceptions of whether to vaccinate or not Influence of self Women may value their own opinion more than the provider

Meharry 2013				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
women accept or reject the seasonal influenza vaccine Location and setting 2 post-partum units and adjoining hospital-based prenatal clinics in North-western USA Source of funding	questionnaire and semi-structured interview consisting of 15 questions, with an open ended query segment. Interviews lasted 5-10 minutes of average Method of analysis For thematic analysis, 3 specialists in maternal and child nursing first analysed the 60 transcripts independentl	excluded if considered ill by the clinical co-ordinator; had an unstable infant or failed to complete both the questionnair e and interview		Conveniently located venue for vaccination reduces barriers to uptake: The majority of women seeking vaccination did eventually locate one. Wasting time and energy locating a vaccine is a major barrier for pregnant women and several eventually become fed-up. Two-for-One benefit is a pivotal piece of knowledge for future vaccination: Women who are aware of their susceptibility, severity of illness, and benefits of a safe and effective vaccine, are more likely to accept the influenza vaccine. In particular, women who are knowledgeable of the two-for-one benefit to protect them from illness and to transfer immunity to the new born are more likely to accept the vaccine. “I thought it was something I should do, for the health of the baby…and myself carrying the baby” The majority of women in this study are unaware of the conferral of protection from the vaccinated mother to the foetus and infant after birth. Furthermore, when they garner this ‘two-for-one’ knowledge from the interviewer’s questioning

Meharry 2013				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
	y to understandin g their meaning in context and identify patterns.20% of transcripts were independentl y coded into meaningful segments. Specialists then reviewed each other's coded descriptions and minor discrepancies were amended. A codebook was developed to provide a			they are more earnest to take action and vaccinate in a future pregnancy. Several women and providers appear unaware of the threat of illness and appropriate action to reduce the threat. "I didn't know the risks and I didn't want to do anything to harm the baby" Fear if I do, fear if I don't and no action when I fear both: Fear of vaccine Women who reject the vaccine perceive a potential threat to themselves or their foetus. "My main concern is that we don't know the side effects on the babies" Fear of influenza Some perceive an increase in susceptibility and influenza complications if not vaccinated Fear of vaccine and influenza

Meharry 2013				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
	framework for the categories. All data were then applied to the codebook and the entire data set was reviewed in full.			Those who fear the vaccine and influenza, typically wait for more compelling information form their provider or availability of a vaccine. When the information or the vaccine does not come forth as expected, the women default to no action. Women who verbalise 'no need' fear the vaccine: Women less nervous about the threat of influenza feel there's no need to get it; these women do not have symptoms, do not perceive a threat and therefore do not take preventive action to reduce the threat
Limitations identified by author Only a specific time period was used so this may not represent all possible responses Women's responses were influenced by the widespread media attention and threat of H1N1 Limitations identified by review team Interviewer was likely known to the participants (nurse midwife)				

G.4.6 O'Grady 2015

O'Grady 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year O'Grady, 2015 Quality score ++ Study type Qualitative Aim of the study To inform studies investigating the understanding of the determinants of vaccination, accounting for the	Data collection Yarning circles (informal focus group which is culturally friendly and recognised by aboriginal people) were held in settings and at a time convenient to participants A semi-structured interview guide based on the theory of planned behaviour	Inclusion 28 weeks pregnant or more or less than 16 weeks post birth 17 yr + Willing and able to adhere to al protocol requirements Had sufficient verbal English to permit questionnaire completion at study entry Exclusion 'No specific exclusion criteria'	Participant numbers 7 Participant characteristics Aboriginal and Torres Strait Islander women 21-34 years	All participants were aware of influenza; overall the participants were supportive of influenza vaccination during pregnancy, particularly if it was thought to benefit both the mother and the unborn child. "Yeah, I basically find it's very important to have it that is like, it's not mainly for your health, but if you're like your kids end up gettin sick too, it's good for them to have it too… ….like when you don't have it you're more sicker than when you do have it…like it calms it down a lot….." Participants were interested in the safety of the vaccine, what products were used to make the vaccine and wanted to understand the risks of vaccination to self and the foetus. All but 1 indicated they would be willing to be vaccinated. 5 of the participants were not aware that influenza vaccination was recommended and available free for pregnant women. The majority reported their health service providers had not discussed influenza vaccination with them during their pregnancy. 2 members discussed doctor-led education sessions, which would strengthen the relationship between doctors and patients.

O'Grady 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
heterogeneity of the Australian Aboriginal and Torres Strait Islander population Location and setting Queensland, Australia (both towns with large Aboriginal and Torres Strait Islander communities) Source of funding Project grant from the Lowitja Institute. KFO is	was used to inform the conversations. Attitudes, subjective norms and perceived behavioural control were themes that were explored by researchers. Method of analysis Narrative summaries of the transcripts and major themes determined			Indicated that should just give the vaccine at the time the person was there as the steps required to get vaccinated (ie go to pharmacy, come back to clinic etc) were difficult to complete given competing priorities) "When you go in there they have to give you all these descriptions and all that but they don't do nothing about it… they should just say if you wanted to get the needle, they should just pull out the needle …". The participants wanted to hear more from the doctor, not others, about vaccination during pregnancy.

O'Grady 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
supported by a NHMRC Career Development Fellowship (1045157) and a Queensland Government Smart Futures Fellowship. LM & KH are supported by an Australian Post-Graduate Award and Supervisor Top Up Scholarship through the NHMRC Centre for Research	and presented			

O'Grady 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Excellence in Lung Health for Aboriginal and Torres Strait Islander Children. LMcH is supported by a conjoint scholarship through UQ and QLD Health.				
Limitations identified by author Small sample size Limitations identified by review team 1 participant was a practising aboriginal health worker; this may have influenced others in the group or skewed results as a more complete understanding of vaccination during pregnancy would be expected from this participant				

G.4.7 Sampson 2011

Sampson 2011				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Sampson, 2011 Quality score - Study type Qualitative Aim of the study To explore parental reasons for non-uptake of influenza vaccination in young at-risk groups.	CRG Chronic respiratory disease Chronic heart disease Chronic renal disease Chronic liver disease Chronic neurological disease Diabetes mellitus Immunosuppression	Inclusion Parents of children eligible for vaccination aged 2-16 yrs, and who did not receive influenza vaccination over a 7 month period (1 September-31 March) Exclusion Children no longer registered in the practice on or before 31 March.	Participant number 7 Participant characteristics None provided other than parent of child within CRGs investigated	Barriers to vaccination Uncertainty about indication for vaccination: A proportion of parents expressed doubt, scepticisms or a lack of knowledge about the relevance of the vaccination for their child '[Child's] asthma had seemed to be "dormant" for several years so we didn't think a flu jab was necessary. Also, we thought as her asthma is quite mild she wasn't high risk.' Challenges with access: A lack of personal invitation from the practice, difficulties gaining an appointment and the challenges of intercurrent illnesses compounding appointment difficulties were barriers expressed. "…as he wasn't asked to come we were unsure of his eligibility for the vaccine" "the clinic was busy and it was well into November before I could get an appointment. By the time she was unwell with

Sampson 2011				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
The study hypothesis was that exploration of parental reasons for non-uptake may reveal important barriers to an effective influenza vaccination programme. Location and setting General practice in Inverness, Scotland Source of funding This study was	Data collection Questionnaire which could be completed either in writing, or in a telephone interview or a face-to-face interview Method of analysis Written responses and audio recording of interviews were transcribed. Text was analyses manually by 2 researchers	Eligible children who turned 17 on or before 31 March. Parents who did not consent to taking part in the study Non-responders to invitation Participants who were unaware that influenza vaccination was recommended for their child		chest infections, or if not had temperatures. [Child] did actually get her flu jab last winter but it was actually February before she was well enough to have it” Lack of parental priority Some parents felt they paced a lack of priority on ensuring that their child was protected by influenza vaccination, despite apparently being aware of the potential benefits “I actually meant to but did not get round to it” Issues relating to health beliefs There was a group of parents who chose not to vaccinate based on their health beliefs “Media scares about vaccines are hard to shake off, and I think have an impact on one’s perception of vaccines in general. So while there’s not to my knowledge been anything scary said about the flu jab per se, I still feel a bit uneasy about another vaccine for small bodies. I suppose promoting the positives might help convince some people.”

Sampson 2011				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
supported by a NHS Highland Research and Development Endowment fund	independently to capture and code the themes that arose. Themes were compared and an enhanced set of themes was produced.			Some parents expressed difficulty in accepting that the vaccination is as important for children with chronic health problems as it is for older people "The focus is more on older… it's difficult to imagine a child getting the Flu and being very ill" "We feel that he is young to be starting to give him this kind of injection" Concerns were also expressed about the vaccine itself – whether in some way it will make an influenza-like illness more likely or whether it could have an adverse impact on the development of their child's immune system
Limitations identified by author The research was carried out in 1 practice by researchers who were the GPs of the participants giving potential for researcher bias The sample size of 7 was small The initial search carried out to identify the children of participants was dependent on the accuracy of coding and robustness of the coding system of the medical practice Demographics of the practice populations in Inverness may not be representative of the wider UK population. The study site is an urban practice and the results may not be applicable to rural or more deprived inner-city populations				

Sampson 2011				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Limitations identified by review team Unknown which CRGs the children of the 7 participants falls in to; no participant characteristics data reported.				

G.4.8 Schindler 2012

Schindler 2012				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Schindler, 2012 Quality score - Study type Qualitative	CRG Pregnancy Data collection Semi-directed interviews After 263 women filled out a questionnaire, women were selected so as to	No inclusion/ exclusion criteria reported.	Participant number 29 Participant characteristics 19-40 yrs (mean 34 yrs) 5 had been vaccinated against flu Variety of nationalities and professions	Reasons for vaccination decision: Some considered influenza dangerous for different types of population that were a priori weak or vulnerable; for example, the elderly, children and people with chronic diseases “In some cases, depending on the patient’s age, say his medical history…It depends on the patient, but [influenza] can be very serious” The women believed that flu was not a threat for people in good health. They evaluated the risk according to the person’s health and the risk of complications that could lead to death.

Schindler 2012				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Aim of the study To examine Swiss pregnant women's representations of the risk associated with seasonal flu and its vaccination Location and setting Maternity unit of a hospital, Switzerland Source of funding Unknown	represent a variety of ages, national origins and professional activities, while targeting the women most likely to detail their arguments around the theme studied. Data was collected in March 2011, while these women were in the maternity unit, 3-5 days after giving birth.			Pregnancy alone was not considered as a reason for vaccination. "We hear that pregnant women are at risk, but I think that pregnancy women who have no health problems won't have anything serious because of the flu" It was thought by some that certain lifestyle habits and some knowledge of hygiene indications guaranteed good health. Others noted that such individual measures did not necessarily protect against flu Attitudes towards risks associated with vaccination: There was an expression of fears concerning the effects of the flu vaccination during pregnancy: "I'm not against vaccines…We know there's always a risk. Even if it's minimal, there's always a risk"

Schindler 2012				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
	The interview guide topics were defined to question: disease risks; means of protection; motivations and obstacles to vaccination and attitudes towards vaccination Method of analysis The interviews were conducted by 2 physicians. The interviews were fully transcribed and then			"I think there's always a risk in taking a medication and when getting vaccinated. But I think that it's better to be vaccinated than to fall ill" "I believe that during my pregnancy I don't really want to run a risk that I judge to be…not reasonable" Attitudes towards healthcare professionals delivering information on vaccination: Most women thought it was the physician who had the responsibility of informing patients "I was so preoccupied by the baby's growth, a good diet, etc., during the pregnancy. So if the doctor doesn't bring it up, I couldn't have thought about it" "It's the responsibility of the doctor or the midwife to say that: if there are dangers, do you want to protect yourself against them?"

Schindler 2012				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
	coded using ATLAS.ti qualitative analysis software.			If the message was clear and delivered with conviction, participants said they would follow the recommendations Conversely, doubt arose in some women when the message was not delivered with conviction "She didn't suggest [vaccination] while I was doing the exam. Then all of a sudden, when I was walking down the hallway to leave, she tells me: "I don't know if you would be interested…" and she talks to me a little bit about [vaccination] in the hallway. I thought, if it had really been serious maybe she would have talked about it right away"
Limitations identified by author Research was conducted in a hospital setting and by physicians. This probably heightened the absence of a strong anti-vaccination position, since it is likely that the women who opposed vaccination did not accept to be interviewed or relativized their reservations in the situation of an interview with a representative of the medical institution. The post-partum situation was also unfavourable to more in-depth interviews that would have allowed the ambivalence and questions of the respondents to progressively emerge. Participants were interviewed in March 2011, 1 year after the H1N1 pandemic. It was clear from interviews that attitudes intermingled seasonal flu and H1N1 flu. Limitations identified by review team				

Schindler 2012				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
There is possible selection bias as participants were selected according to their likelihood to detail their arguments. This is a subjective form of selection and could bias researchers to choose participants based on likely desired outcomes from these participants				

G.4.9 Wiley 2015

Wiley 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Author name and year Wiley, 2015 Quality score + Study type Qualitative Aim of the study	CRG Pregnancy Data collection Grounded theory methodology was used. Collection included a cycle of data collection via interviews and analysis, followed by	No inclusion/exclusion criteria reported	Participant number 20 Participant characteristics No characteristics reported	('The system' in this section refers to either health care providers, the hospital, clinic or the government) Access to information: Women reported a significant level of trust in the system "…and it's obviously been researched, well, I believe it is, because it's coming through the hospital and not just through some pamphlet sitting on the side…" Some women drew on the experiences and opinions of other people for their decision making: "Talking to friends who've had babies and that kind of thing had more of an influence on my pregnancy than the relationship I have with [my GP]"

Wiley 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
To gain an understanding of risk perception of influenza and vaccination against influenza, through the eyes of pregnant women Location and setting Antenatal clinics in 3 hospitals in New South Wales, Australia; hospitals were an inner city Sydney	subsequent interviews and analysis cycles. 20 in-depth interviews were conducted (9 face to face, 11 by telephone) using a semi-structured interview schedule which evolved with each iteration of the grounded theory data collection or analysis cycle. Recruitment was ceased when			Most women accessed information online, with almost all of them reporting they would use Google to search for influenza relation information. A preference for information arising from the system (such as government websites) was made, compared to other sources such as social media. "Only if it's like a specific website . . . recommended by the government or something . . . not like a dodgy website . . . because I believe that they would, like, source the right information, and they would look into it a little bit more and tell me what's right and what's wrong." Some women however were interested in what other pregnant women thought and did, turning to social media such as blogs. They valued accounts of personal experiences as well as more official sources of knowledge "If there's something I'm really unsure about, I'll go on the Internet. I'll, I'll read blogs about it. I'll read questions that other people have asked about it." Some women said that it was an expectation they had of their health care professional to tell them what was required. Healthcare provider advice was also important in how prioritised vaccinations were.

Wiley 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
hospital, in the Western suburbs of Sydney and a rural referral hospital. Source of funding Research was funded by a grant from the Financial Markets Foundation for Children (Grant 2010-099). Julie Leask is supported by a NHMRC Career Developme nt	theoretical saturation was reached. Women were asked their perception of disease risk for influenza and their information needs and sources, and their feelings about receiving the influenza vaccine while pregnant. All interviews were recorded and transcribed. Method of analysis Line-by-line coding was used,			Some women thoughts there was a sufficient amount of information provided to them regarding vaccination, others felt they had not been provided with any during their pregnancy. Barriers to vaccination: A recurring theme among the participants was the view that pregnancy is a time of competing priorities, and this could interfere with obtaining the flu vaccine "Because you've got so many other things going on that it's not something that you're thinking about, you know? They're saying take this, take that, and make sure you do this, don't do that, don't eat this, don't eat that, so there's so many things that you've got to remember while you're pregnant. That's just another thing that is put to the side and not even thought of because you're just so busy thinking about everything else." Women generally relied on the system to provide them with vaccines in some way, either through clinics, the hospital or their GP Many women saw influenza as a mild disease. Several spontaneously expressed a concern that they cannot take

Wiley 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
Fellowship (APP1053473).	followed by focuses coding to capture emergent themes from the transcripts. Axial coding was then used to deduce the relationships between the emergent themes. Negative cases in the data were used as an indication that the emergent themes required refinement. Refinement of themes			medication to relieve flu symptoms if they are pregnancy, rather than worry about the severity of symptoms or the possibility of hospitalisation. Perception of risk: When asked about their thoughts on the risks of influenza during pregnancy, most women framed their response in relation to their foetus's health. Influenza during pregnancy was perceived as a disease of the mother rather than one which directly afflicts the foetus and therefore, of comparatively lower consequence.

Wiley 2015				
Study details	**Research Parameters**	**Inclusion/ Exclusion criteria**	**Population**	**Results**
	involved an iterative process of moving in and out of the data, based on the findings of additional interviews until no new themes were identified and divergent cases were no longer found.			
Limitations identified by author The results cannot be taken as representative of all pregnant women, The inclusion of women from other location might have yielded themes not identified here; Did not seek to explicitly explore the needs of specific cultural groups Limitations identified by review team No reported participant characteristics				

Appendix H: Economic evidence tables

H.1.1 Skedgel 2011

<table>
<tr><th colspan="4">Skedgel 2011</th></tr>
<tr><th>Study detail</th><th>Inclusion/Exclusion and Patient population</th><th>Intervention\Comparators</th><th>Results</th></tr>
<tr>
<td>Author/year
Skedgel C, Langley JM, MacDonald NE et al (2011)

Quality score
-

Study type
Incremental cost-effectiveness analysis (CUA)</td>
<td>Clinical risk group
Pregnant women

Number of participants
Baseline event rates were derived from an analysis of a population-based cohort of 134,188 pregnancies, covering the period 1990-2003 (based on study by Dodds et al, 2007). The average annual cohort of pregnant women was 10,316 (for simplicity this was round to 10,000)

Participant characteristics
Pregnant women, including those with one or more co-morbidities (including pre-existing diabetes, respiratory disease (including asthma), heart disease, renal disorder or anaemia)
Inclusion criteria</td>
<td>Intervention / Comparison
The evaluation compared:
targeted vaccination of pregnant women with one or more co-morbidities
universal vaccination of all pregnant women
no vaccination strategies
The decision tree characterised costs and consequences over a 1yr horizon, including the acquisition and administration costs of vaccination and the costs and quality-of-life consequences of influenza related events and vaccination-related adverse effects. As all events in the evaluation occurred within one year, neither costs nor outcomes were discounted.
The evaluation also included a risk of Guillain-Barre syndrome following</td>
<td>Primary outcomes
<table><tr><th></th><th>No vaccination</th><th>Targeted strategy</th><th>Universal Vaccination</th></tr><tr><td>Women vaccinated</td><td>0</td><td>1002</td><td>10,000</td></tr><tr><td>Cohort costs</td><td>$344,878</td><td>$335,392</td><td>$426,536</td></tr><tr><td>Incremental cost (95% CI)</td><td>-</td><td>$9,485 ($65,993-$14,177)</td><td>$91,143 ($22,546-$152,454)</td></tr><tr><td>Total cohort QALYs</td><td>9,492.23</td><td>9,492.55</td><td>9,494.83</td></tr></table></td>
</tr>
</table>

Skedgel 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Aim of the study Development of an economic model to estimate the cost-effectiveness of different flu vaccination strategies (targeted vs universal) for pregnant women. Location and setting Public health clinics or routine family practitioner, Canada	Exclusion criteria	influenza vaccination or an influenza event with or without vaccination. Effectiveness of vaccination: data was taken from single randomised prospective study of lab-confirmed influenza in pregnant women with and without vaccination. Costs: The cost of vaccine acquisition was based on costs to the Nova Scotia Dept of Health and Wellness. Family practitioner delivery costs were based on the 2010 Nova Scotia fee schedule Public health delivery costs were based on the average cost per vaccination at clinics conducted by the Dept of Health and wellness and were consistent with previously published Canadian costs The costs of influenza related physician utilisation was derived from the 2005/06 Nova Scotia physician claims database. Hospital costs were derived from the 2006/07 Ontario Case Cost Initiative database. The annual costs of GBS was taken from a US evaluation	<table><tr><td>Incremental QALYs (95% CI)</td><td>-</td><td>0.32 (0.06-0.88)</td><td>2.28 (0.44-6.18)</td></tr><tr><td>Cost per QALY</td><td>-</td><td>Dominant</td><td>$39,942</td></tr><tr><td>Gained budget impact*</td><td>-</td><td>-$9,485</td><td>$81,658</td></tr></table> * Budget impact is relative to a no-vaccination strategy and may therefore be less than incremental cost. Relative to a no-vaccination strategy, a targeted vaccination strategy for pregnant women (with at least one co-morbidity) delivered as part of a routine FP visit was cost saving. Relative to the targeted strategy, the universal strategy had an incremental cost-effectiveness of $39,942 per QALY gained. Threshold analysis on vaccine effectiveness showed: that the targeted strategy would be economically dominant (cost saving, improved outcomes) over no vaccination with a vaccine

Skedgel 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Length of study 1 year Source of funding Capital Health Research Fund		Costs were adjusted to 2010 Canadian dollars based on the consumer price index, health component. The evaluation took a health system payer perspective. Outcomes: The key outcome in the evaluation was the quality of life improvement due to influenza-related events prevented. Baseline utility (no influenza) was 0.95, reflecting the average utility of all individuals more than 12yrs of age with no chronic conditions. Utility weights for influenza-related illness were derived from a Canadian study by O'Brien et al. Economic Analysis: Evaluation was conducted as an incremental costs-effectiveness analysis, comparing each vaccination strategy to the next best alternative. Key economic outcomes were the net cost of vaccination (vaccination costs less event costs avoided), net QALYs gained and the incremental cost per QALY.	effectiveness (i.e. relative risk) less than 0.76 and would meet a $50,000 per QALY gained threshold with an effectiveness less than 0.84. A universal strategy would meet a $50,000 threshold with an effectiveness less than 0.68 and a $100,000 threshold with an effectiveness less than 0.80. One-way sensitivity analysis on mode of delivery suggest: The targeted strategy would remain dominant relative to the no vaccination strategy when delivered by public health clinics The universal strategy would be strongly costs effective, bordering on dominant, relative to the targeted strategy. If vaccination required an additional FP visit: The targeted vaccination strategy would lose it dominance and have a cost-effectiveness of $62,796. The cost-effectiveness of the universal strategy would increase to more than $150,000. One-way sensitivity analysis on mode of delivery suggests that:

Skedgel 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
		All costs and outcomes were reported on the basis of the average annual cohort of pregnant women, calculated as the total number of pregnancies observed over 1990-2003 divided by the number of years of observation. Sensitivity Analysis: The base case scenario assumed all vaccinations were delivered by a family practitioners as part of a routine visit, but sensitivity analyses considered alternative modes of delivery (extra FP visit, public health clinics). Threshold analyses were conducted on key parameters to identify the threshold values necessary to meet specific cost-effectiveness targets. One-way sensitivity analyses were conducted on other key parameters. Probabilistic sensitivity analysis was used to incorporate uncertainty into the economic evaluation.	The targeted strategy would remain dominant relative to the no-vaccination strategy when delivered by public health clinics. The universal strategy would be strongly cost-effective, bordering on dominant, relative to the targeted strategy.
Limitations identified by author It was not possible to reliably identify and exclude vaccinated women from the cohort when calculating baseline event rates but since only 2.6% of pregnant women in Nova Scotia were vaccinated over the period covered by our data; this is unlikely to have influenced the estimates.			

Skedgel 2011			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Although illness attributed it influenza was not laboratory confirmed in this study, our incidence rates are consistent with estimates from another study with a different design. Limitations identified by review team Other comments			

H.1.2 Teufel (2015)

Teufel (2015)			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Author/year Teufel II RJ, Basco Jr WT and Simpson, KN. Quality score -	Clinical risk group Children with asthma Number of participants Participant characteristics Hypothetical cohort of children aged 1-14 years. Inclusion criteria Hospitalised children with asthma	Intervention / Comparison A decision tree was constructed to represent an intervention to assess and deliver influenza vaccinations to hospitalized pediatric patients with asthma. A literature survey provided estimates for the decision tree assumptions. In the decision analysis, various rates of screening for influenza vaccine status were investigated to determine the	Primary outcomes Existing data showed that only 29% of asthmatics receive the influenza vaccine in a given year. This decision analysis demonstrated that even modest increases in the screening rate for influenza vaccine status among hospitalized patients with asthma can result in clinically significant increases in UTD status. For example:

Teufel (2015)			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Study type Cost-effectiveness analyses Aim of the study To determine the potential clinical benefit and cost savings of delivering influenza vaccination to hospitalized children with asthma. Location and setting Hospitals, USA	Exclusion criteria Children aged 0-11 months (excluded because of the low likelihood that this age group was at risk for influenza complicated by asthma)	effects on final up-to-date (UTD) status in a hypothetical cohort. The cost-effectiveness analysis was used to determine potential cost savings resulting from the modelled increase in UTD status. A number of assumptions were made from literature searches regarding consequences of influenza: Prevalence of influenza in school aged children: 45% Morbidity associated with influenza: 150 clinic visits and 100 antibiotic prescriptions per 1000 children Age adjusted risk: 360 hospitalisations/ 100,000 children The lowest and highest estimates of these assumptions were input into the model also to conduct sensitivity analysis	screening just 20% of those with asthma who are hospitalized would result in 35% ultimately being UTD for that influenza season; 40% screening would result in 41% being UTD; 60% screening would result in 47% being UTD; 80% screening would result in 53% being UTD; 100% screening would result in 59% being UTD. The cost savings for this intervention would be: $5.45/child assessed and $9.19/child vaccinated. Sensitivity analysis demonstrated the results to be robust and generalizable.

Teufel (2015)			
Study detail	**Inclusion/Exclusion and Patient population**	**Intervention\Comparators**	**Results**
Length of study 1year Source of funding -			
Limitations identified by author Limitations identified by review team No range for reporting on the assumptions of risk of hospitalisation from influenza in this cohort has been previously reported in the literature, therefore a standard 25% increase and decrease was used in sensitivity analysis Other comments Price calculations were performed according to US dollars in 2006			

Appendix I: GRADE tables

I.1 GRADE profile 1

Outcome: Flu vaccination uptake

Quality assessment								Effect	Quality	Rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Educational Video vs Control video (hand washing) – pregnant women [Forest plot Figure 1; ES1.1]										
1[1]	RCT	No serious	n/a	No serious	Very serious [a]	None	105	RR 1.13 (0.60 to 2.14)	Low	Critical
Patient educational manual vs Control pamphlet – people with COPD [ES 1.2]										
1[2]	nRCT	Serious [b]	n/a	No serious	Serious [c]	None	249	% Change in flu vaccination rate: Lower socioeconomic disadvantage participants: Intervention: +2% vs. control: 0% (p=0.44) Higher socioeconomic disadvantage participants: Intervention: +4% vs. control: 0% (p=0.13)	Low	critical
Educational Message Framing: 'loss' (risk-negative) framing vs 'gain' (risk-positive) framing: uptake post-intervention – people with chronic respiratory or cardiac disease [Forest plot Figure 2; ES1.3]										
1[3]	RCT	Serious [d]	n/a	No serious	Very serious [a]	None	292	Immediate post-intervention uptake RR 1.02 (0.85 to 1.21)	Very Low	critical

								Uptake 3 months post-intervention RR 0.95 (0.81 to 1.11)		
Pharmacy provided flu vaccine programme vs year preceding programme implementation – pregnant women, care home residents, carers, patients with chronic disease (Atkins 2016) [ES 2.1]; eligible adults (18-64 years) in CRGs (Rai & Wood 2017) [Forest plot Figure 16; ES2.2]										
1[4]	Before and after	Serious [e]	n/a	Serious [f]	Serious [g]	None	Unknown	Pre-intervention uptake 60.4% Post-intervention uptake: 60.5% Difference is non-significant (t=0.84)	Very Low	critical
1[5]	Before and after	Serious [h]	n/a	No serious	No serious	None	Pre-n=247,641; Post-n=269,355	Post-intervention uptake RR = 0.98 (95%CI: 0.98 to 0.99)*	Very Low	critical

1 Goodman 2015
2 Harris 2006
3 O'Connor 1996
4 Atkins 2016
5 Rai & Wood 2017

a downgraded 2 levels due to 95%CI crossing both the upper and lower MID thresholds (RR 0.95 and RR1.05)
b downgraded 1 level due to high rate of invitation but low level of uptake (selection bias) and non-randomised allocation resulting in significant difference in mean socioeconomic deprivation between intervention and control groups
c downgraded 1 level: imprecision not estimable as 95%CI not reported; small study sample (<300 total events) reduces certainty in effect
d downgraded 1 level - factors not controlled for that were seen to reduce the effect of positive message framing intervention (perceived risk of flu, physician advice); health care workers and patients have different drivers for flu vaccination this is not considered in the analysis; differences in flu vaccination drivers between work-based and personal physicians
e downgraded 1 level due to inconsistency and no provision of population numbers
f downgraded 1 level due to study including populations outside of scope (people age 65+) which could not be disaggregated.
g downgraded 1 level; imprecision not estimable as 95%CI and sample size not reported

h downgraded 1 level – difference in size of eligible target population (denominator) between pre- and post-intervention periods not explained; gaps in geographical distribution of participating pharmacies means not all patients in target population had equal access to the intervention.

* data from post hoc analysis undertaken by the review team

I.2 GRADE profile 2

Outcome: Intention to be vaccinated for seasonal flu

Quality assessment								Effect	Quality	Rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Message framing: 'Gain' (risk-positive) vs Control (neutral) vaccination education message (adjusted pairwise regression) – pregnant women [ES1.4]										
1[1]	RCT	Serious [a]	n/a	No serious	Very serious [b]	None	164	OR 1.25 (0.49 to 3.25)	Very low	critical
Message framing: 'Loss' (risk-negative) vs Control (neutral) vaccination education message (adjusted pairwise regression) – pregnant women [ES1.4]										
1[1]	RCT	Serious [a]	n/a	No serious	Very serious [b]	None	166	OR 0.48 (0.17 to 1.35)	Very low	critical

1 Frew 2014

a downgraded 1 level due to lack of methodological detail regarding randomisation, difference in sample regarding intention (participation bias); survey instrument measuring intent to immunise may not reflect actual immunisations
b downgraded 2 levels due to very wide 95%CIs for OR

* data from post hoc analysis undertaken by the review team

I.3 GRADE profile 3

Outcome: Flu vaccination uptake

Quality assessment								Effect	Quality	Rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Mail and mail + telephone reminder vs usual care – people with hypertension [Forest plot Figure 5; ES3.2]										
1[1]	RCT	Serious [a]	n/a	Serious [b]	No serious	None	885	RR 1.52 (1.24 to 1.81)*	Low	critical
Postcard reminder vs usual care – people with asthma or COPD [Forest plot Figure 6; ES3.1]										
2[2-3]	RCT	Serious [c]	No serious	No serious	No serious	None	20,641	RR 1.00 (0.97 to 1.03)*	Moderate	critical

								No significant difference between mail reminder + phone call and mail reminder only, vs usual care mail reminder only: RR 1.37 (1.07 to 1.77); mail + phone reminder: RR 1.68 (1.31 to 2.16)		
Enhanced SMS (with reminder option for 'intenders' or tailored educational message for 'non-intenders') vs 'usual' SMS (no reminder or tailoring) - pregnant women [Forest plot Figure 3; ES3.3]										
1[4]	RCT	Serious [d]	n/a	No serious	Serious [e]	None	3,905	<u>Prior intent and vaccinated / still intends to</u> RR 1.08 (1.02 to 1.14)* <u>No prior intent and vaccinated / intends to</u> RR 0.94 (0.84 to 1.04)*	Low	critical
Tailored SMS reminder vs usual care (standard practice flu campaign with no additional reminder) – people in clinical risk groups [Forest plot Figure 4; ES3.4]										
1[5]	cRCT	Serious [f]	n/a	No serious	No serious	None	102,257	RR 1.03 (1.02 to 1.05)	Moderate	critical
Practice audit vs usual care (pre-audit) - targeted clinical risk groups [ES3.4]										
1[6]	Before and after	Very serious [g]	n/a	Serious [h]	No serious	None	39 practices	CHD: Mean difference 19.2% (14.4 to 24); p<0.001	Very Low	critical
1[6]	Before and after	Very serious [g]	n/a	Serious [h]	No serious	None	39 practices	Diabetes: Mean difference 16.9% (10.2 to 23.6); p<0.001	Very low	critical
1[6]	Before and after	Very serious [g]	n/a	Serious [h]	No serious	None	39 practices	Post-splenectomy: Mean difference	Very low	critical

								6.1% (-2.5 to 14.7); p=0.155		

1 Minor 2010
2 Shoup 2015
3 Walter 2008
4 Jordan 2015
5 Herrett 2016
6 Siriwardena 2004

a downgraded 1 level due to lack of participant information, patients vaccination history was unclear across study arms (history is a key factor related to uptake);
b downgraded 1 level as 29% of sample were aged over 65 years; participants had hypertension and may not all fall into one of the clinical risk groups specified in the review protocol
c downgraded 1 level Shoup 2015 subject to possible confounding; Walters 2008 possible confounding due to media coverage of 2003 flu pandemic
d downgraded 1 level due to large non-reponse rate, lack of demographic detail and self-reported datae downgraded 1 level due to a large non-response rate, lack of demographic detail and self-reported data
e downgraded 1 level – 95%CIs cross either upper MID threshold (RR 1.05) for baseline intention group, or lower MID threshold (RR 0.95) for 'no intention' at baseline group
f downgraded 1 level due contamination between arms: a third of control practices sent text messages and 10% of intervention practices failed to send a message
g downgraded 2 levels – only 50% practices participated in both phases of the audit; study did not account for secular trends or Hawthorne effect; method not designed to assess the effect of audit or feedback; confounding from national influenza campaign
h downgraded 1 level as some of the sample were aged over 65 years

* data from post hoc analysis undertaken by the review team

I.4 GRADE profile 4

Outcome: Flu vaccination uptake

Quality assessment								Effect	Quality	Rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Multicomponent pharmacy-based intervention (including standardised training of pharmacists on providing injections and the use and safety monitoring of influenza vaccination) vs. control (no intervention) – people with chronic conditions [Forest plot Figure 7; ES123.1]										
1[1]	cRCT	Serious [a]	n/a	Serious [b]	No serious	None	26,408	RR 0.75 (0.74 to 0.77)	Low	critical
Multicomponent general practice-based intervention (including education, audit and feedback) vs. baseline data collection, audit and written feedback alone – people with CHD, diabetes or post-splenectomy [Forest plot Figure 8; ES 123.2]										
1[2]	cRCT	No serious	No serious	Serious [c]	Serious [d]	None	10,703	RR 1.06 (1.03 to 1.08)*	Low	critical
Multicomponent interventions including education, posters, vaccine champion, peer to peer vaccination and provider maps vs Usual care – pregnant women [Forest plot Figure 9; ES 123.4]										
1[3]	cRCT	Serious [e]	n/a	No serious	Very serious [f]	None	300	RR 1.47 (0.71 to 3.07)*	Very Low	critical
Subgroup analysis (Chamberlain 2015): recollection of individual intervention components vs Usual care –pregnant women [Forest plot Figure 9; ES123.4]										

1[3]	cRCT	Serious [e]	n/a	No serious	Very serious [f]	None	137	Educational brochure RR 2.57 (0.93 to 7.11)	Very Low	critical
1[3]	cRCT	Serious [e]	n/a	No serious	Serious [g]	None	137	iPad based education RR 3.17 (1.07 to 9.44)	Low	critical
1[3]	cRCT	Serious [e]	n/a	No serious	Very serious [f]	None	137	Lapel Badge RR 2.48 (0.93 to 6.57)	Very Low	critical
1[3]	cRCT	Serious [e]	n/a	No serious	Serious [h]	None	137	ObGyn recommend RR 16.88 (1.03 to 276.05)	Low	critical
1[3]	cRCT	Serious [e]	n/a	No serious	Very serious [f]	None	137	Reminder poster RR 3.01 (0.71 to 12.74)	Very Low	critical
Multicomponent intervention including audit and feedback, educational materials, seminars, monthly support and monitoring vs Usual care (no intervention) – people with end-stage renal disease [123.5]										
1[4]	cRCT	Serious [i]	n/a	No serious	Serious [j]	None	6,460	adjusted % difference in vaccine uptake: 8.86% (0.36 to 17.37); p=0.04	Low	critical
Multi-component intervention (including patient and provider education and enhanced clinical informatics) vs Usual care (pre-intervention rate) – immunocompromised children undergoing chemotherapy or stem cell transplant [Forest plot Figure 10; ES123.3]										
1[5]	Before and after	No serious	n/a	No serious	No serious	None	1,128	Uptake of 2 vaccinations: RR 1.45 (1.30 to 1.63)	Low	critical

								Uptake of 1 vaccination: RR 1.41 (1.29 to 1.55)		
Subgroup analysis (Freedman 2015): Multi-component intervention (as above) vs Usual care (pre-intervention rate) - analysis by condition for uptake of 1 or more vaccinations										
1[5]	Before and after	No serious	n/a	No serious	No serious	None	400	Leukaemia / Lymphoma RR 1.23 (1.10 to 1.39)	Low	critical
1[5]	Before and after	No serious	n/a	No serious	Serious [g]	None	285	Brain Tumour RR 1.53 (1.23 to 1.90)	Very low	critical
1[5]	Before and after	No serious	n/a	No serious	Very serious [f]	None	91	Stem Cell Transplant RR 1.33 (0.97 to 1.89)	Very low	critical
1[5]	Before and after	No serious	n/a	No serious	No serious	None	352	Solid tumour RR 1.56 (1.29 to 1.88)	Low	Critical

1 Marra 2014
2 Siridawena 2002
3 Chamberlain 2015
4 Bond 2011
5 Freedman 2015

a downgraded 1 level due lack of detail regarding control; potential confounding by H1N1 pandemic; data for population of interest (2-64 year olds) only at year 2
b downgraded 1 level – 29% of the sample population were over 65, data on intervention impact could not be disaggregated
c downgraded 1 level as some of the sample were aged 65 years and over
d downgrade 1 level – 95%CI crosses upper MID threshold (RR 1.05)

e downgrade 1 level due to small cRCT powered to find a larger absolute difference between study groups than was observed, potential bias from cluster randomisation especially with small participant numbers and rate of vaccine uptake, practices differed in vaccine availability in 3 out of 5 clusters
f downgrade 2 levels – 95%CI crosses both lower and upper MID thresholds (RR 0.95 and RR 1.05)
g downgrade 1 level – small study sample (total events<300) reduces certainty in effect estimate
h downgrade 1 level - 95%CI crosses upper MID threshold (RR 1.05)
i downgraded 1 level - possible confounding due to control and experimental cluster communicating; inconsistencies in data collection across clusters
j downgraded 1 level - 95%CI crosses upper MID (5% relative increase in uptake)

* data from post hoc analysis undertaken by the review team

I.5 GRADE Profile 5

Outcome: Increasing uptake of seasonal flu vaccination in children with chronic conditions [Aigbogun 2015-SR]

Quality assessment								Effect	Quality	Outcome rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Information and Educational approaches (RQ1)										
Education vs. Usual care – children with asthma [Forest plot Figure 11; SR-ES1.1]										
2[1-2]	B&A	Serious [a]	Serious [b]	No serious	No serious	None	23,207	RR 1.90 (1.43 to 2.53)	Very Low	critical
Increasing Access (RQ2)										
Increasing access (Saturday clinics + reminder letter) vs. Reminder letter only – children with asthma [Forest plot Figure 11; SR-ES2.1]										

1[3]	B&A	No serious	n/a	No serious	Very serious [c]	None	264	RR 1.25 (0.78 to 1.99)	Very Low	critical
Increasing access (year round appointments) vs. Usual care (routine flu season appointments) – all infants + children with asthma [Forest plot Figure 11; SR-ES2.2]										
1[4]	Retrospective cohort	No serious	Serious [d]	No serious	No serious	None	5,451	RR 1.68 (1.38 to 2.04)	Very low	critical
Provider approaches i.e. invitation or changes to local practices (RQ3)										
Letter reminders vs. Usual Care – children in clinical risk groups [Forest plot Figure 11; SR-ES3.1]										
5[5-9]	RCT & Quasi-experimental	No serious	Serious [e]	No serious	No serious	None	5,006	RR 1.53 (1.25 to 1.89)	Moderate	critical
Telephone recall (personal call from paediatrician) vs. Usual care (standard anonymous reminder) – children in clinical risk groups [Forest plot Figure 11; SR-ES3.2]										
2[10-11]	rB&A	No serious	No serious	No serious	No serious	None	490	RR 1.62 (1.33 to 1.98)	Low	critical
Letter and/or Telephone call vs. Usual care – children with asthma [Forest plot Figure 11; SR-ES3.3]										
2[12-13]	B&A	No serious	Serious [f]	No serious	No serious	Upgraded [g]	4,491	RR 4.49 (3.34 to 6.04)	Low	critical
Provider Prompts (RQ3)										

Provider Prompts vs No Provider Prompts [Forest plot Figure 11; SR-ES3.4]										
2[14-15]	B&A	No serious	Serious [h]	No serious	No serious	None	10,113	RR 1.69 (1.26 to 2.26)	Very Low	critical
Multicomponent Interventions										
Reminders, telephone recall, provider prompts, increased access vs Usual care – children in clinical risk groups [Forest plot Figure 11; SR-ES123.1]										
1[16]	nRCT	No serious	n/a	Serious [i]	No serious	None	18,836	RR 1.36 (1.32 to 1.40)	Moderate	critical

1 Fiks 2009 [B&A]
2 Martin 2008 [B&A]
3 Walter 1997 [B&A]
4 Paul 2006 [Retrospective cohort]
5 Daley 2004 [RCT]
6 Dombowski 2012 [RCT]
7 Kemper 1993 [RCT]
8 Moore 2006 [Quasi-experimental]
9 Szilagyi 1992 [RCT]
10 Cecinati 2010 [randomised B&A]
11 Esposiito 2009 [randomised B&A]
12 Gagliani 2001 [B&A]
13 Martin 2006 [B&A]
14 Patwarden 2011 [B&A]
15 Zimmerman 2006 [B&A]
16 Britto 2007 [nRCT]

a downgraded 1 level - Martin (2008) uses ‘before and after’ study design and is a much smaller study than the cRCT included in the analysis (Fiks 2009)

b downgraded 1 level due to heterogeneity I^2 = 92%
c downgraded 2 levels as 95%CIs cross both upper and lower MID thresholds (RR 0.95 and RR 1.05)
d downgraded 1 level due to heterogeneity I^2 = 87%
e downgraded 1 level due to heterogeneity I^2 = 75%
f downgraded 1 level due to heterogeneity I^2 = 77%h downgraded 1 level due to heterogeneity I^2 = 77%
g upgraded 1 level as both observational studies show consistently large effect size
h downgraded 1 level due to heterogeneity I^2 = 88%
i downgraded 1 level - crosses review question PICO

I.6 GRADE Profile 6

Outcome: Increasing uptake of seasonal flu vaccination in adults from clinical risk groups [SR – Ndiaye 2005]

Quality assessment								Effect	Quality	Outcome rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Provider approaches i.e. invitation or changes to local practices (RQ3)										
Personalised postcards vs. usual care – people in clinical risk groups [Forest plot Figure 12; SR-ES3.5]										
1[1]	cRCT	No serious	n/a	No serious	Serious [a]	None	183	RR 1.96 (1.24 to 3.10)	Moderate	critical
Mail reminder vs. telephone reminder vs. control (no reminder) – people in clinical risk groups [Forest plot Figure 12; SR-ES3.6]										

1[12]	RCT	No serious	n/a	No serious	Very serious [b]	None	525	Mail vs. no reminder: RR 2.55 (1.0 to 6.49) Telephone vs. no reminder: RR 2.44 (0.95 to 6.24) Mail vs. telephone: RR 1.05 (0.62 to 1.77)	Low	critical
Provider Prompts										
Provider Prompts vs. Usual care – people in clinical risk groups [Forest plot Figure 12; SR-ES3.7]										
2[2-3]	RCT	No serious	Serious [c]	No serious	Very serious [d]	None	1564	1.44 (0.81 to 2.56)	Very Low	critical
3[4-6]	B&A, Retrospective cohort	Serious [e]	Serious [f]	No serious	No serious	None	1487	5.70 (1.18 to 27.53)	Very Low	critical
Multi-component										
Multi-component (Demand + Provider incentives) vs. Usual Care – people in clinical risk groups [Forest plot Figure 12; SR-ES123.2]										
1[9]	Cluster RCT,	No serious	NA	No serious	Serious [a]	None	423	1.62 (1.26 to 2.09)	Moderate	critical
3[8,10]	Retrospective cohort, cB&A	Serious [g]	Serious [h]	No serious	Very serious [i]	None	55,0254	1.43 (0.73 to 2.82)	Very Low	critical
Multicomponent (Access + Demand) vs. Usual Care – people in clinical risk groups [Forest plot Figure 12; SR-ES123.3]										
5[11-16]	RCT	No serious	Serious [j]	No serious	No serious	None	27,628	RR 1.40 (1.22 to 1.62)	Moderate	critical

Multicomponent (Access + Demand + Provider incentives) vs. Usual care – people in clinical risk groups [SR-ES123.4]										
3[16-18]	cRCT, nRCT	Serious [k]	Serious [l]	No serious	Very serious [i]	None	2,291	RR 1.21 (0.80 to 1.82)	Very low	critical
Durability of effect of multicomponent (Access + Demand + Provider incentives) Year 10 vs. Year 1 [Forest plot Figure 14; SR-ES123.5]										
1[18]	B&A	No serious	n/a	No serious	No serious	None	1,000 - 1,197	Year 10 vs Year 1 (post-intervention) RR 0.75 (0.68 to 0.83) Year 10 vs. Baseline (pre-intervention) RR 1.75 (1.52 to 2.01)	Low	critical

1 Larson 1982 [RCT]
2 Becker 1989 [RCT]
3 Chamber 1991 [RCT]
4 Davidson 1984 [Retrospective cohort]
5 Gelfman 1986 [B&A]
6 Harris 1990 [Retrospective cohort]
7 McDonald 1992 [RCT]
8 Barton 1990 [retrospective cohort)
9 Turner 1990 [Cluster RCT]
10 Van Essen 1997 [controlled B&A]
11 Baker 1998 [RCT]
12 Brimberry 1998 [RCT]
13 Carter 1986 [RCT]
14 Moran 1996 [RCT]
15 Spaulding 1991 [RCT]
16 Hogg 1996 [B&A]
17 Jans 2000 [B&A]
18 Nichol 1990 [B&A]

a downgraded 1 level - small study sample (<300 total vaccination events) reduces certainty in effect
b downgraded 2 levels due to wide 95%CIs for each effect, crossing one or both MID thresholds (RR 0.95 and RR 1.05)
c downgraded 1 level due to heterogeneity I^2 = 80%
d downgraded 2 levels - 95% CIs cross both lower and upper MID thresholds (RR 0.95 and RR 1.05)
e downgraded 1 level due lack of randomisation in Davidson (1984), Gelfman (1986) and Harris (1990)
f downgraded 1 level due to heterogeneity I^2 = 96%
g downgraded 1 level due to lack of randomisation in Barton (1990) and Van Essen (1997)
h downgrade 1 level due to heterogeneity I^2 = 94%
i downgraded 2 levels - 95% CIs cross both lower and upper MID thresholds (RR 0.95 and RR 1.05)
j downgraded 1 level due to heterogeneity I^2 = 85%
k downgraded 1 level due to lack of randomisation in Jans (2000) and Nichol (1990)
l downgraded 1 level due to heterogeneity I^2 89%

I.7 GRADE Profile 7

Outcome: Increasing uptake of seasonal flu vaccination in Pregnant Women [SR – Wong 2016]

Quality assessment								Effect	Quality	Outcome rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Educational approaches (RQ1)										
Educational information vs. Standard antenatal care – pregnant women [Forest plot Figure 15; SR-ES1.2]										

2[1-2]	RCT and B&A	Serious [a]	No serious	No serious	Serious [b]	None	374	RR 1.96 (1.32 to 2.91)	Very Low	critical
Message framing (gain- or loss-framed) vs. Standard vaccine information – pregnant women [Forest plot Figure 15; SR-ES1.3]										
1[3]	RCT	Serious [c]	n/a	No serious	Serious [d]	None	126	RR 0.60 (0.35 to 1.03)	Low	critical
Provider approaches i.e. invitation or changes to local practices (RQ3)										
SMS vs. Usual Care – pregnant women [Forest plot Figure 15; SR-ES3.8]										
2[4-5]	RCT	Serious [e]	No serious	No serious	Very serious [f]	None	1,357	RR 1.06 (0.94 to 1.19)	Very low	critical
Provider prompts vs. Usual Care – pregnant women [Forest plot Figure 15; SR-ES3.9]										
2[6-7]	B&A and Retrospective cohort	No serious	Serious [g]	No serious	Very serious [f]	None	2,624	RR 2.29 (0.88 to 5.95)	Very Low	critical
Multicomponent										
Multicomponent (Education + Standing orders + feedback to providers) vs. Usual antenatal care (pre-intervention) – pregnant women [Forest plot Figure 15; SR-ES123.6]										
1[8]	Retrospective cohort	No serious	n/a	No serious	No serious	None	21,302	Yr 1 RR 7.60 (6.50 to 8.88) Yr 2 RR 11.29 (9.75 to 13.08) Yr 3 RR 12.32 (10.65 to 14.24) Yr 4 RR 11.34 (9.80 to 13.13) Yr 5 RR 18.48 (16.10 to 21.21) Yr 6 RR 14.85 (12.89 to 17.11)	Low	critical

Multicomponent (Education + Access) vs. Usual care – pregnant women [Forest plot Figure 15; SR-ES123.7]										
1[9]	B&A	No serious	n/a	No serious	Serious [h]	None	439	RR 1.33 (1.02 to 1.77)	Very Low	critical
Multicomponent (Education + Access + Nurse activities) vs. Usual care – pregnant women [Forest plot Figure 15; SR-ES123.8]										
1[10]	Retrospective cohort	No serious	n/a	No serious	Very serious [f]	None	602	RR 10.54 (0.77 to 143.80)	Very Low	critical
Multicomponent (Education + Access + reminders + provider prompts) vs. Usual care – pregnant women [Forest plot Figure 15; SR-ES123.9]										
1[11]	B&A	No serious	n/a	No serious	Serious [b]	None	248	RR 1.63 (1.31 to 2.04)	Very Low	critical

1 Meharry 2013 [RCT]
2 Yudin 2010 [B&A]
3 Frew 2014 [RCT]
4 Moniz 2013 [RCT]
5 Stockwell 2013 [RCT]
6 Klatt 2012 [B&A]
7 Sherman 2012 [Retrospective cohort]
8 Mouzoon 2010 [Retrospective cohort)
9 McCarthy 2012 [B&A]
10 Ogburn 2007 [Retrospective cohort]
11 Panda 2011 [B&A]

a downgraded 1 level due poor reporting of allocation concealment and performance bias due to inadequate blinding in Meharry (2013)
b downgraded 1 level - small study sample (<300 total vaccination events) reduces certainty in effect
c downgraded 1 level due to bias as incomplete data resulted in per protocol analysis

d downgraded 1 level – 95%CI crosses lower MID threshold (RR 0.95)
e downgraded 1 level as risk of bias due to unclear blinding in Stockwell (2013)
f downgrade 2 levels – 95%CI crosses both lower and upper MID thresholds (RR 0.95 and RR 1.05)
g downgrade 1 level due to heterogeneity I^2 = 98%h downgraded 1 level – 95%CI crosses upper MID threshold (RR 1.05)

I.8 GRADE profile 8

Outcome: Increasing uptake of seasonal flu vaccination in clinical risk groups

Quality assessment								Effect	Quality	Outcome rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk or other (95% CI)		
Provider incentives (RQ3)										
Increasing pay performance targets via QoF vs. Usual pay performance target – people with CHD vs. other control clinical risk groups [ES3.5]										
1[1]	cB&A	Very serious [a]	n/a	No serious	No serious	None	8,212-8,403 (per annum dependent on season)	Mean reported achievement** co-efficient % (95% CI) ranged from 0.94 (0.83 to 1.05) to 1.19 (1.06 to 1.31) across the four season study	Very Low	critical
Removing pay for performance vs. Usual pay performance target – adults with asthma [ES3.6]										
1[2]	B&A	Serious [b]	n/a	No serious [c]	No serious	None	Not reported	Adjusted back transformed mean difference between 2005/06 season and 2011/12 season: -0.07% (-1.01 to -0.39).	Very low	critical

1 Kontopantelis 2012 [cB&A]
2 Kontopantelis 2014 [B&A]

a downgraded 2 levels for risk of bias, no blinding, baseline characteristics not reported and no comparative assessment of baseline characteristics or uptake so unsure if bias or cofounding introduced, also potential for contamination of outcomes as lower threshold of 3 control CRGs increase at same time which may have effected outcomes
b downgraded 1 level due to risk bias from contamination i.e. other routes for QoF payment due to ~25% of population over 65 and ~19% another CRG
c downgraded 1 level due to indirectness - due to large proportion of >65s in the sample as it was ALL patients with asthma over 16 years not those aged 16-64 years

** mean reported achievement for CHD patients (i.e. number of patients immunised/number with condition and not exception reporting)

Appendix J: Health economic evidence profiles

Please see separate modelling report

Appendix K: Forest plots

Includes post-hoc analysis data for single studies, where undertaken by review team.

Figure 1: Educational video vs. Control video for flu vaccination uptake - GRADE profile 1 [ES1.1]

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Fixed, 95% CI
Goodman et al 2015	15	53	13	52	1.13 [0.60, 2.14]

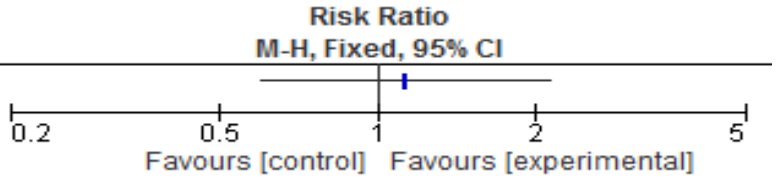


Figure 2: Message framing Gain framed (control) vs Loss Framed (experimental) - GRADE profile 1 [ES1.3]

Study or Subgroup	Experimental (-ve) Events	Experimental (-ve) Total	Control (+ve) Events	Control (+ve) Total	Risk Ratio M-H, Fixed, 95% CI
O Connor 1996 Immediate Vac	91	144	92	148	1.02 [0.85, 1.21]
O Connor 1996 Vacc by Dec	94	144	102	148	0.95 [0.81, 1.11]

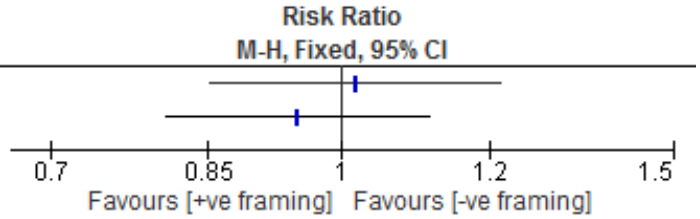


Figure 3: Enhanced SMS messages (with reminder option for 'intenders' or tailored 'educational message for non-intenders) vs. 'usual' SMS (no reminder or tailoring) for pregnant women: events = had vaccinated or intended to vaccinate at follow-up - GRADE profile 3 [ES 3.3]

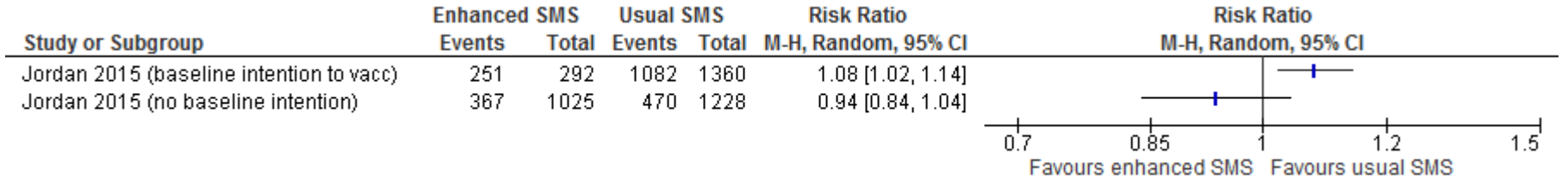


Figure 4: Tailored SMS message reminder to people in clinical risk groups in addition to standard flu campaign vs. control (no additional reminder) - GRADE profile 3 [ES3.4]

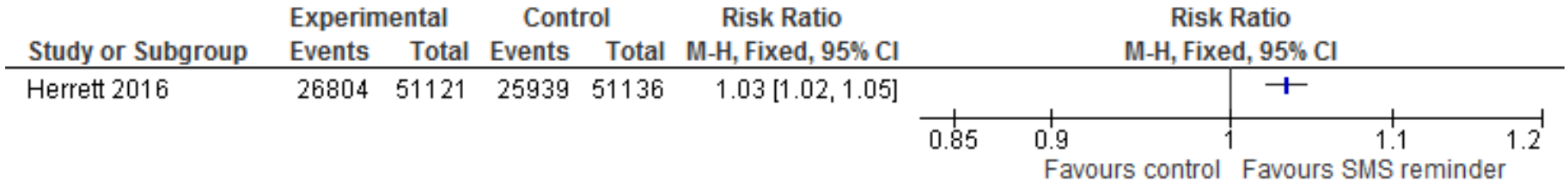


Figure 5: Letter and mail reminder vs. usual care - GRADE profile 3 [ES 3.2]

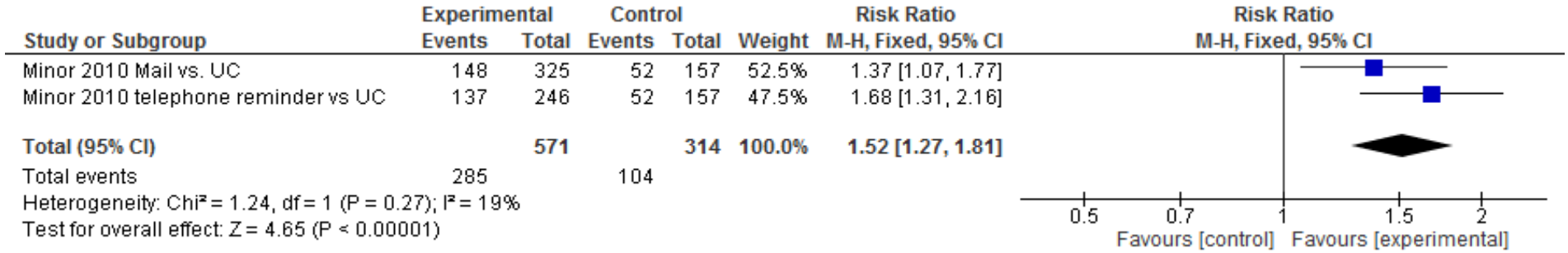


Figure 6: Postcard reminder vs usual care - GRADE profile 3 [ES 3.1]

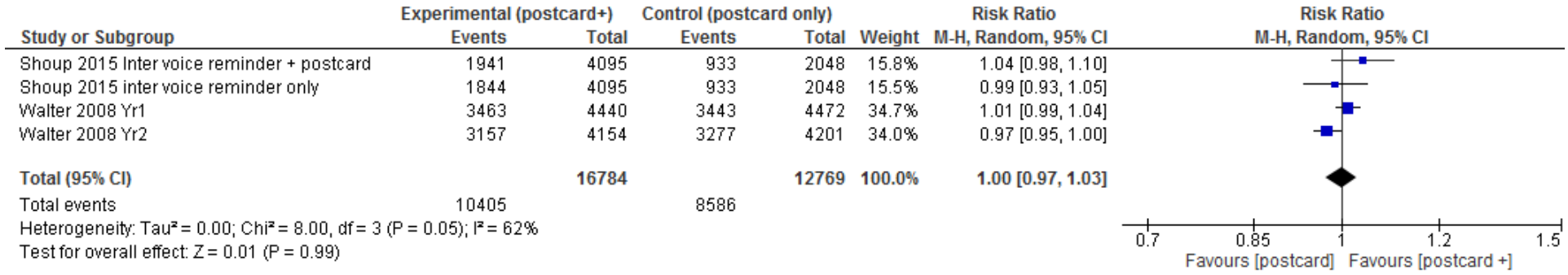


Figure 7: Multicomponent intervention (including standardised training of pharmacists on providing injections and the use of safety monitoring of influenza vaccination) vs. usual care - GRADE profile 4 [ES 123.1]

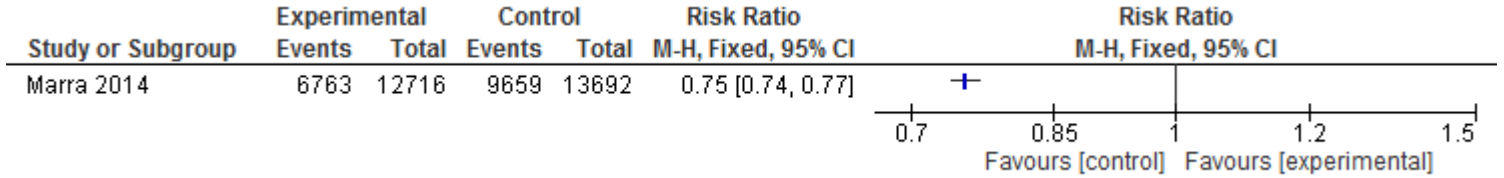


Figure 8: Multicomponent interventions (Outreach education plus, clinical care audits) vs usual care (by condition) - GRADE profile 4 [ES123.2]

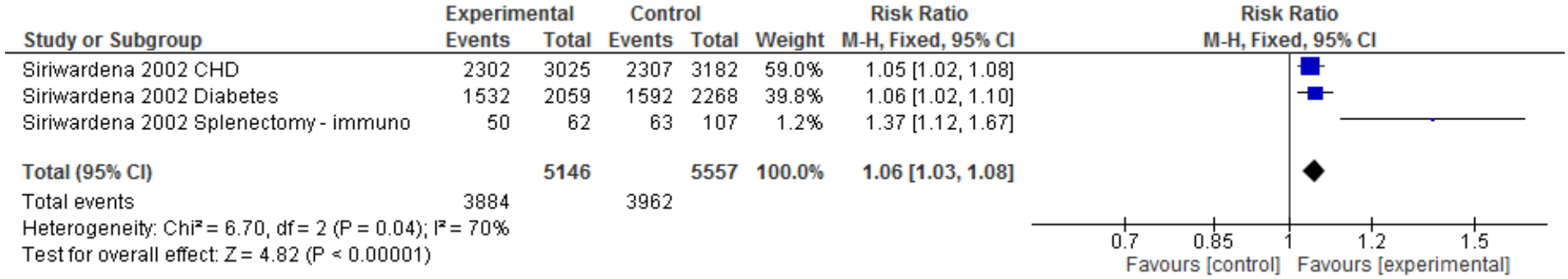


Figure 9: Multicomponent intervention (including posters, education, vaccine champion and obstetrician/gynaecologist recommendation) vs usual care – main findings and by recollection of intervention components) - GRADE profile 4 [ES 123.4]

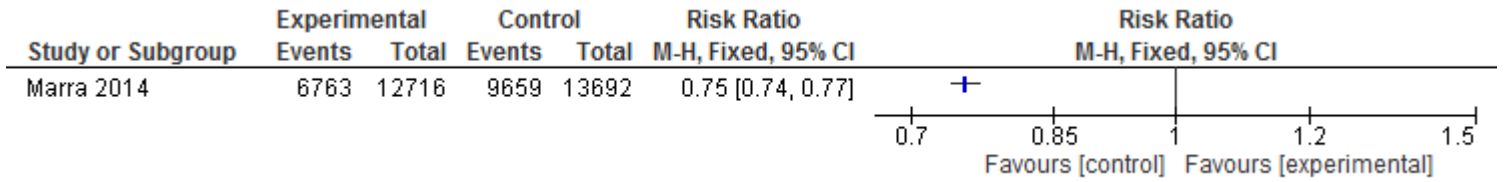


Figure 10: Multicomponent interventions (including patient provider education and enhanced clinical informatics) vs usual care for the uptake of two vaccinations (main results) and subgroup analysis for uptake of 1 vaccination) - GRADE Profile 4 [ES 123.3]

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Fixed, 95% CI
1.9.1 All conditions + 2 vaccs (main results)					
Freedman 2014 (all conds; x 2 vac)	418	648	213	480	1.45 [1.30, 1.63]
1.9.2 All conditions + 1 vaccination					
Freedman 2014 (all conds; x 1+)	502	648	263	480	1.41 [1.29, 1.55]
1.9.3 Leukemia/Lymphoma +1 vaccination					
Freedman 2014 Leuk/Lymph x1+vac	224	258	100	142	1.23 [1.10, 1.39]
1.9.4 Solid tumors +1 vaccination					
Freedman 2014 solid tum x1+ vac	136	187	77	165	1.56 [1.29, 1.88]
1.9.5 Brain tumors +1 vaccination					
Freedman 2014 Brain x1+ vac	116	164	56	121	1.53 [1.23, 1.90]
1.9.6 Stem cell transplants +1 vaccination					
Freedman 2014 Stem Cell Trans x1+ vac	26	39	26	52	1.33 [0.94, 1.89]

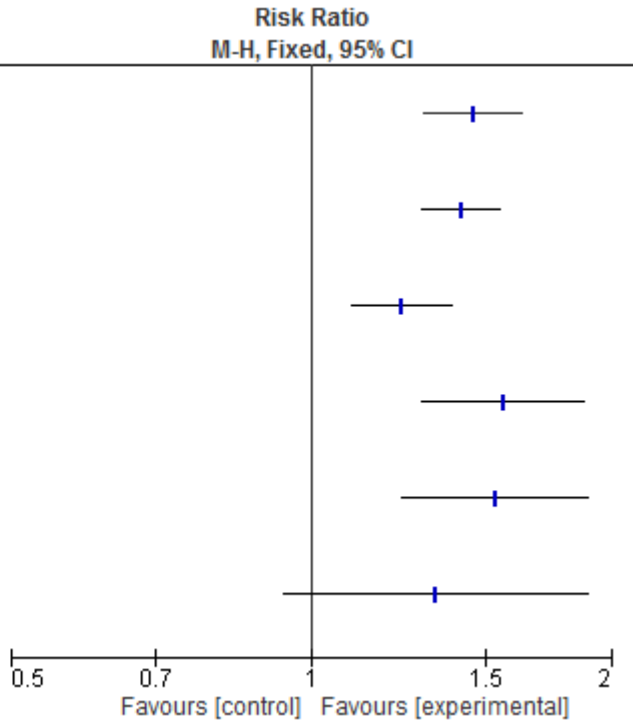
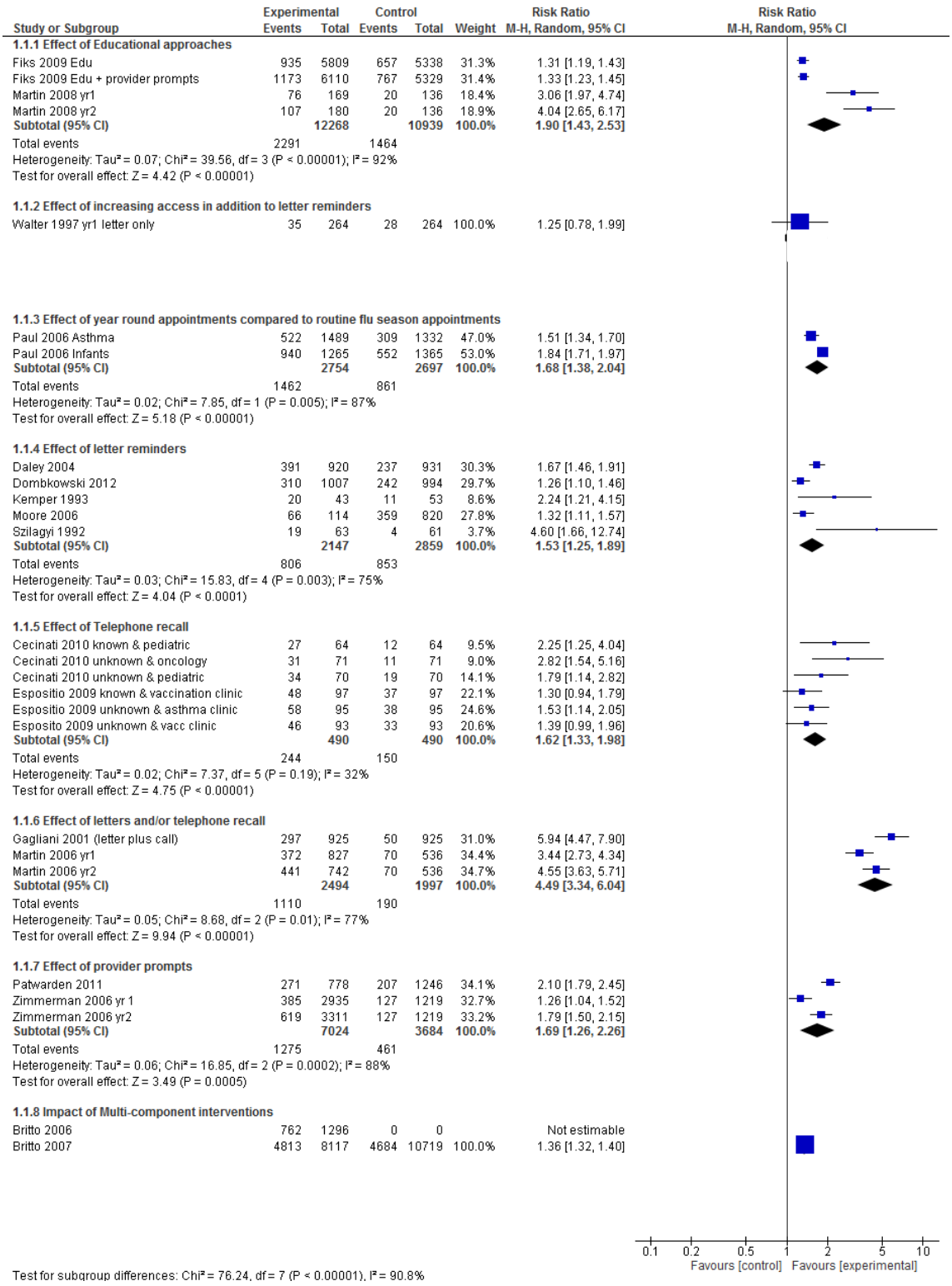


Figure 11: Aigbogun 2015 (SR) [linked GRADE Profile 5]



As noted in the section on Synthesis and quality assessment of effectiveness evidence, a general approach was taken to pool data from RCTs with data from observational studies where the same outcome was being investigated under conditions which were considered to be sufficiently similar. Although observational studies may introduce more bias than RCTs, it has been suggested that this issue might be outweighed by the potential of including observational studies to improve inferences from RCT trials, particularly where RCT evidence is limited. Increased sample size may provide additional evidence to choose a correct treatment for a condition (Shrier et al. 2007)[j]. In order to test whether this was appropriate in each case, a sensitivity analysis was undertaken to determine the relative impact of the different study types on the overall direction of the pooled results. Additionally this was acknowledged in the GRADE profiles by using 'Low' as the starting point for rating the quality of any pooled analyses that combined data from observational studies and RCTs. Where pooling showed a direction of effect that differed from the direction of effect of unpooled results, or where only similar study types were pooled (i.e. RCT only, or observational only), the decision was made not to pool different study types and to report results separately within the evidence statement. Table 1 below shows those analyses where pooling all study types may have been inappropriate due to impact on effect.

Table 1: Outcomes not pooled for review of vaccination uptake in clinical risk groups

Identifier	Studies	Reason for not pooling	Related evidence statement
Figure 12, 2.1.2 Effect of provider prompts	Becker 1989 Chambers 1991 Davidson 1985 Gelfman 1986 Harris 1990	Pooling shows effect. RCTs alone show no effect, and observational studies alone show an effect.	SR-ES 3.7
Figure 12, 2.1.3 Impact of multi-component interventions (Demand + Provider)	Barton 1990 Turner 1990 Van Essen 1997	Pooling shows no effect. RCTs alone show an effect, and observational studies alone show no effect.	SR-ES123.2

[j] Shrier, I., Boivin, J., Steele, R. J. et al. 2007. Should Meta-Analyses of Interventions Include Observational Studies in Addition to Randomized Controlled Trials? A Critical Examination of Underlying Principles. *American Journal of Epidemiology,* 166 (10); 1203-1209.

Figure 12: Ndiaye 2005 (SR) [linked GRADE profile 6]

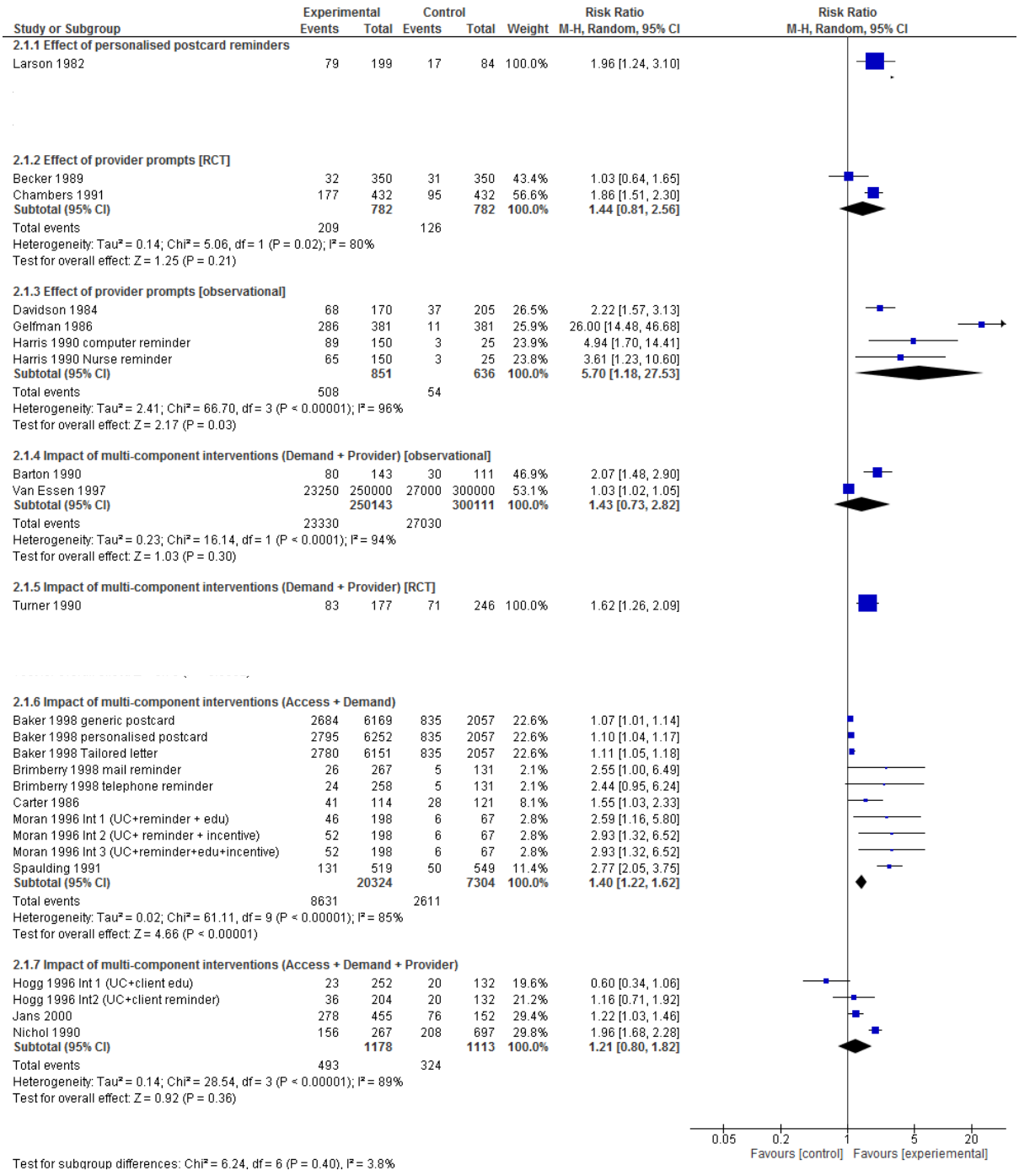


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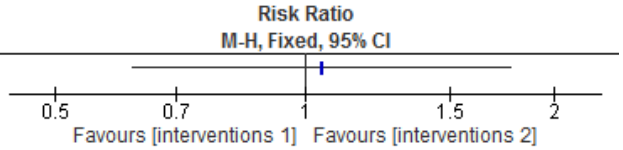
Figure 13: Mail vs phone reminder – GRADE profile 6 [SR-ES3.6]

Study or Subgroup	Intervention 2 (interven) Events	Total	Intervention 1 (control) Events	Total	Risk Ratio M-H, Fixed, 95% CI
Brimberry 1998 mail vs phone (intensity subgroup)	26	267	24	258	1.05 [0.62, 1.77]



Source: Ndiaye 2005

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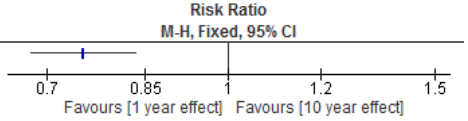
Figure 14: Durability of intervention effect – GRADE profile 6 [SR-ES123.5]

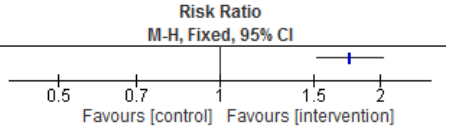
10 year post-intervention vs 1 year post-intervention – uptake of flu vaccination

Study or Subgroup	Experimental Events	Total	Control Events	Total	Risk Ratio M-H, Fixed, 95% CI
Nichol 1998 (durability of intervention effect)	261	500	347	500	0.75 [0.68, 0.83]



2 *10 year post-intervention vs. control (pre-intervention baseline) – uptake of flu vaccination*

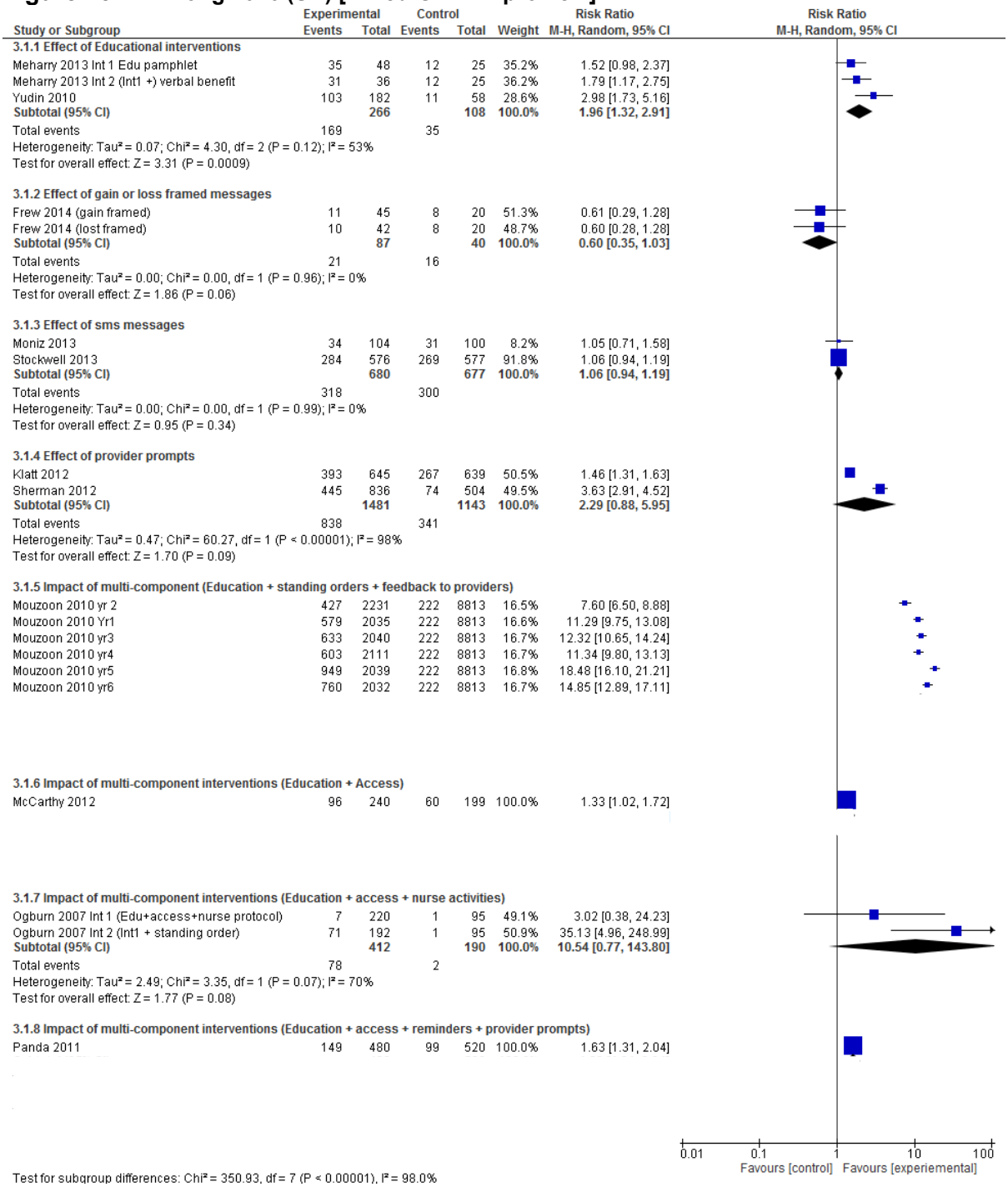
Study or Subgroup	Experimental Events	Total	Control Events	Total	Risk Ratio M-H, Fixed, 95% CI
Nichol 1990 (baseline) vs 1998 (yr 10)	261	500	208	697	1.75 [1.52, 2.01]



3

4 *Source: Ndiaye 2005*

Figure 15: Wong 2016 (SR) [linked GRADE profile 7]



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1
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Figure 16 Extended access (community pharmacy scheme) vs. pre-intervention (GP ractice vaccination only) – GRADE profile 1 [ES2.2]

	Intervn (pharmacy access)		Control (no pharm access)		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% C
Rai & Wood 2017	139711	269355	130838	247641	0.98 [0.98, 0.9

3

Appendix L:Excluded studies

Study citation	Reason for exclusion
Adams Angela, Hall Mellisa, and Fulghum Janis. (2014). Utilizing the Health Belief Model To Assess Vaccine Acceptance Of Patients on Hemodialysis. Nephrology Nursing Journal, pp.393-407.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Annonymous. (2012). The effectiveness and cost of different methods of reminders for annual influenza immunization among adults with asthma and chronic obstructive pulmonary disease. Https://clinicaltrials.gov/show/NCT01852656, pp..	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Basra Kamy. (2014). Behind the scenes of the 'Be a flu hero' social media campaign. British Journal of School Nursing, pp.452-453.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Baxter David. (2013). Approaches to the vaccination of pregnant women: experience from Stockport, UK, with prenatal influenza. Human vaccines &, and immunotherapeutics, pp.1360-3.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Beigi Richard H, Wiringa Ann E, Bailey Rachel R, Assi Tina-Marie, and Lee Bruce Y. (2009). Economic value of seasonal and pandemic influenza vaccination during pregnancy. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, pp.1784-92.	No relevant outcomes reported
Blank P R, Schwenkglenks M, and Szucs T D. (2009). Disparities in influenza vaccination coverage rates by target group in five European countries: trends over seven consecutive seasons. Infection, pp.390-400.	Not a relevant population
Blitz Daina A, Mallen Jonathan R, Kwiatkowski Thomas G, Rabin Jill M, Dlugacz Yosef D, and Silverman Robert A. (2015). Not for industry only: medical students and office-based academic detailing the PIVOT (Pregnant women Influenza Vaccine Optimization Team) initiative. Advances in medical education and practice, pp.323-7.	No relevant outcomes reported
Blommaert A, Bilcke J, Vandendijck Y, Hanquet G, Hens N, and Beutels P. (2014). Cost-effectiveness of seasonal influenza vaccination in pregnant women, health care workers and persons with underlying illnesses in Belgium (Provisional abstract). Vaccine, pp.6075-6083.	No relevant outcomes reported
Bodeker Birte, Betsch Cornelia, and Wichmann Ole. (2016). Skewed risk perceptions in pregnant women: the case of influenza vaccination. BMC Public Health, pp.1308.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Brewer N T, and Hallman W K. (2006). Subjective and objective risk as predictors of influenza vaccination during the vaccine shortage of 2004-2005. Clinical Infectious Diseases, pp.1379-1386.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)

Study citation	Reason for exclusion
Britto M T, Schoettker P J, Pandzik G M, Weiland J, and Mandel K E. (2007). Improving influenza immunisation for high-risk children and adolescents. Quality and Safety in Health Care, pp.363-368.	Duplicate (included in an included systematic review, Aigbogun 2015)
Britto Maria T, Pandzik Geralyn M, Meeks Connie S, and Kotagal Uma R. (2006). Combining evidence and diffusion of innovation theory to enhance influenza immunization. Joint Commission journal on quality and patient safety / Joint Commission Resources, pp.426-32.	Duplicate (included in an included systematic review, Aigbogun 2015)
Brown M, Sheppeard V, Gabriel S, and Thomas J. (2013). Description of the Western Sydney and Nepean Blue Mountains local health districts' influenza prevention programme. Internal medicine journal, pp.760-6.	Not a relevant population
Bryan C, and Boren S A. (2008). The use and effectiveness of electronic clinical decision support tools in the ambulatory/primary care setting: A systematic review of the literature. Informatics in Primary Care, pp.79-91.	No relevant outcomes reported
Bull L. (2004). Practical advice for pneumococcal and influenza vaccination programmes. Nurse 2 Nurse, pp.48-49.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Bundy D G, Persing N M, Solomon B S, King T M, Murakami P N, Thompson R E, Engineer L D, Lehmann C U, and Miller M R. (2013). Improving immunization delivery using an electronic health record: The immprove project. Academic pediatrics, pp.458-465.	No relevant outcomes reported
Burrows R. (2008). Running super-efficient flu clinics. Independent Nurse, pp.41-43.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Cameron Kenzie, Roloff Michael, Friesema Elisha, Brown Tiffany, Jovanovic Borko, Hauber Sara, and Baker David. (2013). Patient knowledge and recall of health information following exposure to 'facts and myths' message format variations. Patient Education and Counseling, pp.381-387.	Not a relevant population
Camurdan M O, Camurdan A D, Beyazova U, and Bideci A. (2012). The rate of seasonal influenza vaccination in diabetic children, the effect of recommendation and the factors influencing the acceptance of recommendation: An interventional study. Balkan Medical Journal, pp.434-439.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Cella M T, Corona G, Tuccillo E, and Franco G. (2005). [Assessment of efficacy and economic impact of an influenza vaccination campaign in the personnel of a health care setting]. Medicina del lavoro, pp.483-9.	Not a relevant population
Cho Bo-Hyun, Asay Garrett R. Beeler, Lorick Suchita A, Tipton Meredith L, Dube Nancy L, and Messonnier Mark L. (2012). Costs of school-located influenza vaccination clinics in Maine during the 2009-2010 H1N1 pandemic. Journal of School Nursing, pp.336-343.	Not a relevant intervention
Churm Linda. (2014). Innovative delivery of flu immunisation. Primary Health Care, pp.29-31.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)

Study citation	Reason for exclusion
Ciancio Bruno Christian, and Rezza Giovanni. (2014). Costs and benefits of influenza vaccination: more evidence, same challenges. BMC public health, pp.818.	No relevant outcomes reported
Daley Matthew F, Barrow Jennifer, Pearson Kellyn, Crane Lori A, Gao Dexiang, Stevenson John M, Berman Stephen, and Kempe Allison. (2004). Identification and recall of children with chronic medical conditions for influenza vaccination. Pediatrics, pp.26-33.	Duplicate (included in an included systematic review, Aigbogun 2015)
Daley Matthew F, Beaty Brenda L, Barrow Jennifer, Pearson Kellyn, Crane Lori A, Berman Stephen, and Kempe Allison. (2005). Missed opportunities for influenza vaccination in children with chronic medical conditions. Archives of pediatrics &, and adolescent medicine, pp.986-91.	No relevant outcomes reported
Daniels Nicholas A, Juarbe Teresa, Rangel-Lugo Martha, Moreno-John Gina, and Pérez-Stable Eliseo J. (2004). Focus group interviews on racial and ethnic attitudes regarding adult vaccinations.. Journal of the National Medical Association, 96(11), pp.1455-1461.	Not a relevant population
Deprez R, Kinner A, Millard P, Baggott L, Mellett J, and Loo J L. (2009). Improving quality of care for patients with chronic obstructive pulmonary disease. Population Health Management, pp.209-215.	Observational study with intervention covered by included effectiveness study
Doe S, Pathare S, Kelly C A, Heycock C R, Binding J, and Hamilton J. (2007). Uptake of influenza vaccination in patients on immunosuppressant agents for rheumatological diseases: a follow-up audit of the influence of secondary care. Rheumatology (Oxford, and England), pp.715-6.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Dombkowski Kevin J, Cowan Anne E, Potter Rachel C, Dong Shiming, Kolasa Maureen, and Clark Sarah J. (2014). Statewide pandemic influenza vaccination reminders for children with chronic conditions. American Journal of Public Health, pp.39-44.	Not a relevant intervention
Dombkowski Kevin J, Harrington Laura B, Dong Shiming, and Clark Sarah J. (2012). Seasonal influenza vaccination reminders for children with high-risk conditions: a registry-based randomized trial. American journal of preventive medicine, pp.71-5.	Duplicate (included in an included systematic review, Aigbogun 2015)
Dombkowski Kevin J, Leung Sonia W, and Clark Sarah J. (2007). Provider attitudes regarding use of an immunization information system to identify children with asthma for influenza vaccination. Journal of public health management and practice : JPHMP, pp.567-71.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Dube E, Gagnon D, Kiely M, Boulianne N, and Landry M. (2015). Acceptability of live attenuated influenza vaccine by vaccine providers in Quebec, Canada. Human Vaccines and Immunotherapeutics, pp.956-960.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Dunlap A M, and Rudenko A W. (2012). Evaluating the difference in preventive vaccination uptake in patients with diabetes mellitus. Annals of Pharmacotherapy, pp.609-610.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)

Study citation	Reason for exclusion
Duval Linda, George Cheryl, Hedrick Nellie, Woodruff Sandra, and Kleinpeter Myra A. (2011). Network 13 partnership to improve the influenza, pneumococcal pneumonia, and hepatitis B vaccination rates among dialysis patients. Advances in peritoneal dialysis. Conference on Peritoneal Dialysis, pp.106-11.	Not a relevant intervention
Eckert L O, and Hoppe K K. (2011). Achieving high coverage of H1N1 influenza vaccine in an ethnically diverse obstetric population: Success of a multifaceted approach. Infectious diseases in obstetrics and gynecology, pp..	Not a relevant intervention
Esposito Susanna, Pelucchi Claudio, Tel Francesca, Chiarelli Gabriella, Sabatini Caterina, Semino Margherita, Marseglia Gian Luigi, De Mattia Domenico, and Principi Nicola. (2009). Factors conditioning effectiveness of a reminder/recall system to improve influenza vaccination in asthmatic children. Vaccine, pp.633-5.	Duplicate (included in an included systematic review, Aigbogun 2015)
Falconer M, Baxter D, and Davenport D. (2008). HCAs and immunisation training: results of a pilot programme. Nursing in Practice, pp.58-62.	Not a relevant intervention
Farmer J, Iversen L, and Peterkin G. (2001). Acceptability and uptake of a community-based flu immunisation programme. Health Bulletin, pp..	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Fiks A G, Grundmeier R W, Biggs L M, Localio A R, and Alessandrini E A. (2007). Impact of clinical alerts within an electronic health record on routine childhood immunization in an urban pediatric population. Pediatrics, pp.707-714.	Not a relevant population
Fiks Alexander G, Hunter Kenya F, Localio A Russell, Grundmeier Robert W, Bryant-Stephens Tyra, Luberti Anthony A, Bell Louis M, and Alessandrini Evaline A. (2009). Impact of electronic health record-based alerts on influenza vaccination for children with asthma. Pediatrics, pp.159-69.	Duplicate (included in an included systematic review, Aigbogun 2015)
Fitch Pamela, and Racine Andrew. (2004). Parental beliefs about vaccination among an ethnically diverse inner-city population. Journal of the National Medical Association, pp.1047-50.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Fleming Douglas M, and Elliot Alex J. (2008). Health benefits, risks, and cost-effectiveness of influenza vaccination in children. The Pediatric infectious disease journal, pp.154-8.	No relevant outcomes reported
Fleurier A, Pelatan C, Willot S, Ginies J L, Breton E, Bridoux L, Segura J F, Chaillou E, Jobert A, Darviot E, Cagnard B, Delaperriere N, Grimal I, Carre E, Wagner A C, Sylvestre E, and Dabadie A. (2015). Vaccination coverage of children with inflammatory bowel disease after an awareness campaign on the risk of infection. Digestive and Liver Disease, pp.460-464.	No relevant outcomes reported
Frank Oliver, Litt John, and Beilby Justin. (2004). Opportunistic electronic reminders. Improving performance of preventive care in general practice. Australian family physician, pp.87-90.	Not a relevant population

Study citation	Reason for exclusion
Franzini L, Boom J, and Nelson C. (2007). Cost-Effectiveness Analysis of a Practice-Based Immunization Education Intervention. Ambulatory Pediatrics, pp.167-175.	Not a relevant population
Frew Paula M, Saint-Victor Diane S, Owens Lauren E, and Omer Saad B. (2014). Socioecological and message framing factors influencing maternal influenza immunization among minority women. Vaccine, pp.1736-44.	Duplicate (included in an included systematic review, Wong 2016)
Fuchs J. (2006). The provision of pharmaceutical advice improves patient vaccination status. Pharmacy Practice, pp.163-167.	Not a relevant population
Gaglani M, Riggs M, Kamenicky C, and Glezen W P. (2001). A computerized reminder strategy is effective for annual influenza immunization of children with asthma or reactive airway disease. The Pediatric infectious disease journal, pp.1155-60.	Duplicate (included in an included systematic review, Aigbogun 2015)
Gaglani Manjusha J. (2002). Rationale and approach to target children with asthma for annual influenza immunization. Seminars in pediatric infectious diseases, pp.97-103.	Review not directly answering question
Garcia-Altes A. (2013). Systematic review of economic evaluation studies: Are vaccination programs efficient in Spain?. Vaccine, pp.1656-1665.	Not a relevant intervention
Giannattasio A, Lo Vecchio A, Franzese A, Prisco F, Femiano P, and Guarino A. (2010). Redundancy of roles by physicians in charge of paediatric diabetes is a barrier to flu immunisation. Archives of Disease in Childhood, pp.399-400.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Gill J M, Ewen E, and Nsereko M. (2001). Impact of an electronic medical record on quality of care in a primary care office. Delaware medical journal, pp.187-94.	Observational study with intervention covered by included effectiveness study
Gill James M, and DiPrinzio Marie J. (2004). The Medical Society of Delaware's Uniform Clinical Guidelines for diabetes: did they have a positive impact on quality of diabetes care?. Delaware medical journal, pp.111-22.	Not a relevant intervention
Gisbert J P, and Chaparro M. (2013). Vaccination strategies in patients with IBD. Nature Reviews Gastroenterology and Hepatology, pp.277-285.	No relevant outcomes reported
Gnanasekaran Sangeeth K, Finkelstein Jonathan A, Hohman Katherine, O'Brien Megan, Kruskal Benjamin, and Lieu Tracy. (2006). Parental perspectives on influenza vaccination among children with asthma. Public health reports (Washington, and D.C. : 1974), pp.181-8.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Gorham M W, Smith C R, Smith S K, Wong L, and Kreze O. (2015). Vaccinations in sickle cell disease: An audit of vaccination uptake in sickle cell patients attending Newham University Hospital. Vaccine, pp.5005-5011.	Not a relevant intervention
Guevara J, and Wolf F. (2001). Benefits of asthma education programs. Pediatrics, pp.1496.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Hall Jennifer L, and Katz Ben Z. (2005). Cost of influenza hospitalization at a tertiary care children's hospital and its impact on the cost-benefit analysis of the recommendation for universal	Not a relevant population

Study citation	Reason for exclusion
influenza immunization in children age 6 to 23 months. The Journal of pediatrics, pp.807-11.	
Harris M, Smith B J, Veale A, Esterman A, Frith P A, and Selim P. (2009). Providing patients with reviews of evidence about COPD treatments: a controlled trial of outcomes. Chronic respiratory disease, pp.133-40.	Duplicate of included study
Hebert Kathy, Marzouka George, Arcement Lee, Julian Elyse, Cortazar Frank, Dias Andre, and Tamariz Leonardo. (2010). Prevalence of vaccination rates in systolic heart failure: a prospective study of 549 patients by age, race, ethnicity, and sex in a heart failure disease management program. Congestive heart failure (Greenwich, and Conn.), pp.278-83.	Not a relevant intervention
Henry T, Smith S, and Hicho M. (2013). Treat to goal: Impact of clinical pharmacist referral service primarily in diabetes management. Hospital Pharmacy, pp.656-661.	Not a relevant intervention
Hess R, Fischer G, Weimer M, Clark S, Zieth C, Dong X X, and Roberts M S. (2012). Intensity of messaging necessary to encourage patients to access the PHR: Preliminary results fromthe smart-phrstudy. Journal of general internal medicine, pp.231.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Hilton S, Hunt K, and Petticrew M. (2007). Gaps in parental understandings and experiences of vaccine-preventable diseases: a qualitative study. Child: Care, and Health and Development, pp.170-179.	No relevant outcomes reported
Holbrook A, Thabane L, Keshavjee K, Dolovich L, Bernstein B, Chan D, Troyan S, Foster G, and Gerstein H. (2009). Individualized electronic decision support and reminders to improve diabetes care in the community: COMPETE II randomized trial. CMAJ, pp.37-44.	No relevant outcomes reported
Holt T A, Thorogood M, and Griffiths F. (2012). Changing clinical practice through patient specific reminders available at the time of the clinical encounter: Systematic review and meta-analysis. Journal of general internal medicine, pp.974-984.	Review not directly answering question
Houle S K. D, Grindrod K A, Chatterley T, and Tsuyuki R T. (2013). Publicly funded remuneration for the administration of injections by pharmacists: An international review. Canadian Pharmacists Journal, pp.353-364.	No relevant outcomes reported
Hueston William J. (2010). Does having a personal physician improve quality of care in diabetes?. Journal of the American Board of Family Medicine : JABFM, pp.82-7.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Ishola D A, Jr Permalloo, N Cordery, and R J Anderson. (2013). Midwives' influenza vaccine uptake and their views on vaccination of pregnant women. Journal of public health (Oxford, and England), pp.570-7.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Jacobson Vann Julie, C , and Szilagyi Peter. (2005). Patient reminder and recall systems to improve immunization rates. Cochrane Database of Systematic Reviews.	Duplicate (included in Jones and Cooper 2013 SR which is included in an included systematic review, Aigbogun 2015)

Study citation	Reason for exclusion
Jarrett C, Wilson R, O'Leary M, Eckersberger E, Larson H J, Eskola J, Liang X, Chaudhuri M, Dube E, Gellin B, Goldstein S, Larson H, MacDonald N, Manzo M L, Reingold A, Tshering K, Zhou Y, Duclos P, Guirguis S, Hickler B, and Schuster M. (2015). Strategies for addressing vaccine hesitancy - A systematic review. Vaccine, pp.4180-4190.	Review not directly answering question
Jit M, Cromer D, Baguelin M, Stowe J, Andrews N, and Miller E. (2010). The cost-effectiveness of vaccinating pregnant women against seasonal influenza in England and Wales. Vaccine, pp.115-122.	No relevant outcomes reported
Jit Mark, Newall Anthony T, and Beutels Philippe. (2013). Key issues for estimating the impact and cost-effectiveness of seasonal influenza vaccination strategies. Human vaccines &, and immunotherapeutics, pp.834-40.	No relevant outcomes reported
Jolin L. (2009). Speeding up flu vaccinations. Practice Nursing, pp.632.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Jones Cooper, Sorelle N, and Walton-Moss Benita. (2013). Using reminder/recall systems to improve influenza immunization rates in children with asthma. Journal of pediatric health care : official publication of National Association of Pediatric Nurse Associates &, and PractitionersJ Pediatr Health Care, pp.327-333.	Duplicate (included in an included systematic review, Aigbogun 2015)
Karthikeyan A, and Agwu J C. (2008). Uptake of influenza vaccination among children with diabetes--a re-audit. The Journal of infection, pp.158-9.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Karve Sudeep, Misurski Derek, Herrera-Taracena Guillermo, and Davis Keith L. (2013). Annual all-cause healthcare costs among influenza patients with and without influenza-related complications: analysis of a United States managed care database. Applied health economics and health policy, pp.119-28.	No relevant outcomes reported
Kavanagh P L, Sobota A E, McClure E S, Sprinz P G, and Adams W G. (2014). Using an electronic health record-based registry to improve pediatric sickle cell care. Journal of Clinical Outcomes Management, pp.159-168.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
KEMPER KJ, and GOLDBERG H. (1993). DO computer-generated reminder letters improve the rate of influenza immunization in an urban pediatric clinic?. American Journal of Diseases of Children, 147(7), pp.717-718.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Keren Ron, Zaoutis Theoklis E, Saddlemire Stephanie, Luan Xian Qun, and Coffin Susan E. (2006). Direct medical cost of influenza-related hospitalizations in children. Pediatrics, pp.1321-7.	No relevant outcomes reported
Kharbanda E O. (2015). Helping mothers to get the message about influenza: Are texts the future for increased immunization?. Expert Review of Vaccines, pp.333-335.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
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Study citation	Reason for exclusion
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Klatt Timothy E, and Hopp Elizabeth. (2012). Effect of a best-practice alert on the rate of influenza vaccination of pregnant women. Obstetrics and gynecology, pp.301-5.	Duplicate (included in an included systematic review, Wong 2016)
Krishna S, Balas E A, Boren S A, and Maglaveras N. (2002). Patient acceptance of educational voice messages: a review of controlled clinical studies. Methods of information in medicineMethods Inf Med, pp.360-369.	No relevant outcomes reported
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Kyaw M, Wayne B, and Chalmers J. (2002). Influenza and pneumococcal vaccine distribution and use in primary care and hospital settings in Scotland: coverage, practice and policies. Epidemiology &, and Infection, pp.445-455.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
La Vela S, Legro M, and Weaver F. (2004). Staff influenza vaccination: lessons learned. SCI Nursing, pp.153-157.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Laney M, and Bayley E. (2002). Incidence of adult immunization for influenza and pneumonia in a preadmission testing unit. How perianaesthesia nurses can encourage vaccination uptake. 31 refs. Journal of PeriAnesthesia Nursing, pp.325-336.	Not a relevant population
Lanternier F, Henegar C, Mouthon L, Blanche P, Guillevin L, and Launay O. (2008). Low influenza-vaccination rate among adults receiving immunosuppressive therapy for systemic inflammatory disease. Annals of the rheumatic diseases, pp.1047.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
LaVela Sherri L, Cameron Kenzie A, Priebe Michael, and Weaver Frances M. (2008). Development and testing of a vaccination message targeted to persons with spinal cord injuries and disorders. The journal of spinal cord medicine, pp.44-52.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
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Linay Denise, and Winter Denise. (2012). Protect against flu. Midwives, pp.21.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)

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Logue Everett, Dudley Patricia, Imhoff Trisha, Smucker William, Stapin Jan, DiSabato John, and Schueller Christine. (2011). An opt-out influenza vaccination policy improves immunization rates in primary care. Journal of health care for the poor and underserved, pp.232-42.	Observational study with intervention covered by included effectiveness study
Long M, Kappelman M, Martin C, Chen W, Anton K, and Sandler R. (2012). A randomized trial of electronic (e-mail) educational prevention messages within the ccfa partners cohort. Inflammatory bowel diseases, pp.28.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Loughlin Susan M, Mortazavi Ali, Garey Kevin W, Rice Gary K, and Birtcher Kim K. (2007). Pharmacist-managed vaccination program increased influenza vaccination rates in cardiovascular patients enrolled in a secondary prevention lipid clinic. Pharmacotherapy, pp.729-33.	Observational study with intervention covered by included effectiveness study
Lynch Janet R, Frankovich Edith, Tetrick Claire A, and Howard Andrew D. (2010). Improving influenza vaccination in dialysis facilities. American journal of medical quality : the official journal of the American College of Medical Quality, pp.416-28.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
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Macabeo B, Akin L, Caliskan Z, Altinel S, and Satman I. (2015). Cost-Effectiveness of Increasing the Influenza Vaccination Rate in Adults with Type 2 Diabetes in Turkey. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, pp.609.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Mak Donna B, Regan Annette K, Joyce Sarah, Gibbs Robyn, and Effler Paul V. (2015). Antenatal care provider's advice is the key determinant of influenza vaccination uptake in pregnant women. The Australian &, New Zealand journal of obstetrics &, and gynaecology, pp.131-7.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
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Marshall Bruce C, Henshaw Carmen, Evans Dee Anne, Bleyl Kristin, Alder Stephen, and Liou Theodore G. (2002). Influenza vaccination coverage level at a cystic fibrosis center. Pediatrics, pp.80-0.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)

Study citation	Reason for exclusion
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Meharry Pamela M, Cusson Regina M, Stiller Robert, and Vazquez Marietta. (2014). Maternal influenza vaccination: evaluation of a patient-centered pamphlet designed to increase uptake in pregnancy. Maternal and Child Health Journal, pp.1205-14.	Duplicate of an included study (Meharry 2013)
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Mersereau Patricia W, Layton Christine M, Smith Lucia Rojas, Kendrick Juliette S, Mitchell Elizabeth W, Amoozegar Jacqueline B, and Williams Jennifer L. (2012). Prenatal care providers and influenza prevention and treatment: lessons from the field. Maternal and Child Health Journal, pp.479-485.	Not a relevant intervention
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Moniz Michelle H, Hasley Steve, Meyn Leslie A, and Beigi Richard H. (2013). Improving influenza vaccination rates in pregnancy through text messaging: a randomized controlled trial. Obstetrics and gynecology, pp.734-40.	Duplicate (included in an included systematic review, Wong 2016)

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Mouzoon Melanie E, Munoz Flor M, Greisinger Anthony J, Brehm Brenda J, Wehmanen Oscar A, Smith Frances A, Markee Julie A, and Glezen W Paul. (2010). Improving influenza immunization in pregnant women and healthcare workers. The American journal of managed care, pp.209-16.	Duplicate (included in an included systematic review, Wong 2016)
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Nemeth L S, Ornstein S M, Jenkins R G, Wessell A M, and Nietert P J. (2012). Implementing and evaluating electronic standing orders in primary care practice: A PPRNet study. Journal of the American Board of Family Medicine, pp.594-604.	Observational study with intervention covered by included effectiveness study
Niroshan Siriwardena A, Rashid A, Johnson M, Hazelwood L, and Wilburn T. (2003). Improving influenza and pneumococcal vaccination uptake in high-risk groups in Lincolnshire: A quality improvement report from a large rural county. Quality in Primary Care, pp.19-28.	Observational study with intervention covered by included effectiveness study
Nosyk B, Sharif B, Sun H, Cooper C, and Anis A H. (2011). The cost-effectiveness and value of information of three influenza vaccination dosing strategies for individuals with human immunodeficiency virus. PloS one, pp.27059.	No relevant outcomes reported
Ogburn Tony, Espey Eve L, Contreras Valeria, and Arroyo Patricia. (2007). Impact of clinic interventions on the rate of influenza vaccination in pregnant women. The Journal of reproductive medicine, pp.753-6.	Duplicate (included in an included systematic review, Wong 2016)
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Panda Britta, Stiller Robert, and Panda Alexander. (2011). Influenza vaccination during pregnancy and factors for lacking compliance with current CDC guidelines. The journal of maternal-fetal &, neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, and the International Society of Perinatal Obstetricians, pp.402-6.	Duplicate (included in an included systematic review, Wong 2016)
Parry Michael F, Grant Brenda, Iton Anthony, Parry Patricia D, and Baranowsky Diane. (2004). Influenza vaccination: a collaborative effort to improve the health of the community. Infection control and hospital epidemiology, pp.929-32.	Not a relevant population
Patel Pankaj H, Welsh Cindy, and Foggs Michael B. (2004). Improved asthma outcomes using a coordinated care approach in a large medical group. Disease management : DM, pp.102-11.	No relevant outcomes reported
Patwardhan Anjali, Kelleher Kelly, Cunningham Dennis, Menke James, and Spencer Charles. (2011). The use of a mandatory best practice reminder in the electronic record improves influenza vaccination rate in a pediatric rheumatology clinic. Clinical Governance, pp.308-319.	Duplicate (included in an included systematic review, Aigbogun 2015)
Paul I M, Eleoff S B, Shaffer M L, Bucher R M, Moyer K M, and Gusic M E. (2006). Improving Influenza Vaccination Rates for Children Through Year-round Scheduling. Ambulatory Pediatrics, pp.230-234.	Duplicate (included in an included systematic review, Aigbogun 2015)
Peasah Samuel K, Azziz-Baumgartner Eduardo, Breese Joseph, Meltzer Martin I, and Widdowson Marc-Alain. (2013). Influenza cost and cost-effectiveness studies globally--a review. Vaccine, pp.5339-48.	Not a relevant intervention
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Pielak K, McIntyre C, and Tu A. (2010). Identifying attitudes, beliefs and reported practices of nurses and doctors as immunization providers. Journal of Advanced Nursing, pp.1602-1611.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
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Real Kevin, Kim Sujin, and Conigliaro Joseph. (2013). Using a validated health promotion tool to improve patient safety and increase health care personnel influenza vaccination rates. American Journal of Infection Control, pp.691-696.	Not a relevant population
Rees Susan, Stevens Linda, Drayton Jennifer, Engledow Nikki, and Sanders Jayne. (2011). Improving Inpatient Pneumococcal and Influenza Vaccination Rates. Journal of Nursing Care Quality, pp.358-363.	Not a relevant population
Riley Margaret, Galang Susan, and Green Lee A. (2011). The impact of clinical reminders on prenatal care. Family medicine, pp.560-5.	Observational study with intervention covered by included effectiveness study
Roberts C, Casey D, and Roberts R. (2000). Influenza vaccine uptake in nursing homes. Practice Nurse, pp.112-116.	Not a relevant intervention
Roberts D H, Gilmartin G S, Neeman N, Schulze J E, Cannistraro S, Ngo L H, Aronson M D, and Weiss J W. (2009). Design and measurement of quality improvement indicators in ambulatory pulmonary care: Creating a "culture of quality" in an academic pulmonary division. Chest, pp.1134-1140.	Observational study with intervention covered by included effectiveness study
Roberts Scott, Hollier Lisa M, Sheffield Jeanne, Laibl Vanessa, and Wendel George D. (2006). Cost-effectiveness of universal influenza vaccination in a pregnant population. Obstetrics and gynecology, pp.1323-9.	No relevant outcomes reported
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Russell Grant, Sutton Judy, Reid Graham J, Beynon Charlene, Cohen Irene, and Huffman David. (2003). Universal influenza immunization. Were Ontario family physicians prepared?. Canadian family physician Medecin de famille canadien, pp.1315-21.	Not a relevant population
Rutter F. (2008). Targeting residential homes against influenza. Journal of Community Nursing, pp.16-18.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Ryan James, Zoellner York, Gradl Birgit, Palache Bram, and Medema Jeroen. (2006). Establishing the health and economic impact of influenza vaccination within the European Union 25 countries. Vaccine, pp.6812-22.	No relevant outcomes reported
Saravana S. (2004). Uptake of influenza vaccination in rheumatology patients [1]. Rheumatology.43 (8) (pp 1055), and 2004.Date of Publication: August 2004., pp.1055-.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Sarnoff R, and Rundall T. (1998). Meta-analysis of effectiveness of interventions to increase influenza immunization rates among	Not a relevant population

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Satman Ilhan, Akalin Sema, Cakir Bekir, Altinel Serdar, and dia V A. X. Study Group. (2013). The effect of physicians' awareness on influenza and pneumococcal vaccination rates and correlates of vaccination in patients with diabetes in Turkey: an epidemiological Study "diaVAX". Human vaccines &, and immunotherapeutics, pp.2618-26.	Observational study with intervention covered by included effectiveness study
Savage J, Muller F, and Ormerod A D. (2011). Awareness and uptake of recommended vaccines among immunosuppressed patients. The journal of the Royal College of Physicians of Edinburgh, pp.202-5.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Shavell Valerie I, Moniz Michelle H, Gonik Bernard, and Beigi Richard H. (2012). Influenza immunization in pregnancy: overcoming patient and health care provider barriers. American journal of obstetrics and gynecology, pp.67-74.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Sherman Melissa J, Raker Christina A, and Phipps Maureen G. (2012). Improving influenza vaccination rates in pregnant women. The Journal of reproductive medicine, pp.371-6.	Duplicate (included in an included systematic review, Wong 2016)
Simondsen K A, and Hayney M S. (2011). Maternal influenza vaccination: Protecting two lives with one vaccine. Journal of the American Pharmacists Association, pp.665-667.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Smith J. (2001). Running a successful influenza campaign. Nursing in Practice, pp.73-75.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Sobota Amy E, Kavanagh Patricia L, Adams William G, McClure Elizabeth, Farrell Delmaude, and Sprinz Philippa G. (2015). Improvement in influenza vaccination rates in a pediatric sickle cell disease clinic. Pediatric blood &, and cancer, pp.654-7.	Observational study with intervention covered by included effectiveness study
Soo Wern Fern, and Tan Ngiap Chuan. (2014). The influence of caregivers' knowledge and understanding of asthma aetiology on domiciliary management of children with asthma. Singapore medical journal, pp.132-6.	Not a relevant setting
Steciwko A, Reksa D, Pokorna-Kalwak D, Sapilak B J, and Brydak L B. (2007). Influenza - Prevention or therapy? Decision based on economical reasons and epidemiological data. Family Medicine and Primary Care Review, pp.11-18.	No relevant outcomes reported
Stenqvist Karin, Hellvin Mari-Anne Andersson, Hellke Per, Hoglund Dag, and von Sydow Helen. (2006). Influenza work on the regional level in Sweden: an integrated program for vaccination of risk groups, surveillance and pandemic planning which focuses on the role of the health care worker. Vaccine, pp.6712-6.	Not a relevant population
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Swenson Carolyn J, Appel Alicia, Sheehan Moira, Hammer Anne, Fenner Zita, Phibbs Stephanie, Harbrecht Marjie, and Main Deborah S. (2012). Using information technology to improve adult immunization delivery in an integrated urban health system. Joint Commission journal on quality and patient safety / Joint Commission Resources, pp.15-23.	Observational study with intervention covered by included effectiveness study
Tahrani A A, McCarthy M, Godson J, Taylor S, Slater H, Capps N, Moulik P, and Macleod A F. (2007). Diabetes care and the new GMS contract: The evidence for a whole county. British Journal of General Practice, pp.483-485.	Observational study with intervention covered by included effectiveness study
Taylor E. (2007). Project based approach to increasing uptake of influenza vaccine in an underachieving GP practice. British Journal of Infection Control, pp.8-12.	Not a relevant population
Thornton H. (2000). A simple influenza campaign for young people with diabetes. Journal of Diabetes Nursing, pp.8-11.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Tran Catherine, and Pitts Judy. (2007). Improving influenza vaccine compliance through patient education for patients with cystic fibrosis. Journal of pediatric health care : official publication of National Association of Pediatric Nurse Associates &, and Practitioners, pp.57-61.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Trogdon Justin G, Nurmagambetov Tursynbek A, and Thompson Hope F. (2010). The economic implications of influenza vaccination for adults with asthma. American journal of preventive medicine, pp.403-10.	No relevant outcomes reported
Turner D A, Wailoo A J, Cooper N J, Sutton A J, Abrams K R, and Nicholson K G. (2006). The cost-effectiveness of influenza vaccination of healthy adults 50-64 years of age. Vaccine, pp.1035-43.	Not a relevant population
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Vinograd I, Baslo R, Eliakim-Raz N, Farbman L, Taha A, Sakhnini A, Lador A, Stemmer S M, Gafter-Gvili A, Fraser D, Leibovici L, and Paul M. (2014). Factors associated with influenza vaccination among adult cancer patients: a case-control study. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases, pp.899-905.	Not a relevant intervention
Wallis David H, Chin Jennifer L, Sur Denise K. C, and Lee Michael Y. (2006). Increasing rates of influenza vaccination during pregnancy: a multisite interventional study. Journal of the American Board of Family Medicine : JABFM, pp.345-9.	Observational study with intervention covered by included effectiveness study
Walsh A J, Weltman M, Burger D, Vivekanandarajah S, Connor S, Howlett M, Radford-Smith G, Selby W, Veillard A S, Grimm M C, Travis S P.L, and Lawrance I C. (2013). Implementing guidelines on the prevention of opportunistic infections in inflammatory bowel disease. Journal of Crohn's &, and colitisJ Crohns Colitis, pp.449-.	Not a relevant population
Walsh J A, Maher C, Rappuoli R, and Giudice G. (2011). Economic implications of influenza and influenza vaccine. Influenza Vaccines for the Future, pp.425-440.	No relevant outcomes reported
Walsh Judith M. E, Gildengorin Ginny, Green Lawrence W, Jenkins Jason, and Potter Michael B. (2012). The FLU-FOBT Program in community clinics: durable benefits of a randomized controlled trial. Health Education Research, pp.886-894.	Not a relevant intervention
Walter E, Sung J, Kahn Meine E, Drucker R P, and Clements D A. (1997). Lack of effectiveness of a letter reminder for annual influenza immunization of asthmatic children. The Pediatric infectious disease journal, pp.1187-8.	Duplicate (included in an included systematic review, Wong 2016)
Warmington V, and James C. (2003). Hitting the mark: achieving target influenza vaccination. Nursing in Practice, pp.51-52.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Warner Jane Carole. (2012). Overcoming barriers to influenza vaccination. Nursing Times, pp.25-27.	Not a relevant study type (letter, opinion piece, editorial, commentary, conference abstract)
Weaver F M, Goldstein B, Evans C T, Legro M W, LaVela S, Smith B, Miskevics S, and Hammond M C. (2003). Influenza vaccination among veterans with spinal cord injury: Part 2. Increasing vaccination rates. Journal of Spinal Cord Medicine, pp.210-218.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Webb H, Street J, and Marshall H. (2014). Incorporating immunizations into routine obstetric care to facilitate Health Care Practitioners in implementing maternal immunization. Human Vaccines and Immunotherapeutics, pp.1114-1121.	No relevant outcomes reported

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Weber Valerie, Bloom Frederick, Pierdon Steve, and Wood Craig. (2008). Employing the electronic health record to improve diabetes care: a multifaceted intervention in an integrated delivery system. Journal of general internal medicine, pp.379-82.	Observational study with intervention covered by included effectiveness study
Weitzel K W, and Goode J V. (2000). Implementation of a pharmacy-based immunization program in a supermarket chain. Journal of the American Pharmaceutical Association (Washington, andD.C. : 1996), pp.252-6.	Not a relevant population
Welch V L, Oster N V, Gazmararian J A, Rask K, Schild L, Cutler C, Spettell C, and Reardon M. (2006). Impact of a diabetes disease management program by race and ethnicity. Disease Management and Health Outcomes, pp.245-252.	Not a relevant intervention
Werker G R, Sharif B, Sun H, Cooper C, Bansback N, and Anis A H. (2014). Optimal timing of influenza vaccination in patients with human immunodeficiency virus: A Markov cohort model based on serial study participant hemoagglutination inhibition titers. Vaccine, pp.677-684.	Not a relevant intervention
Wilson R J, Paterson P, Jarrett C, and Larson H J. (2015). Understanding factors influencing vaccination acceptance during pregnancy globally: A literature review. Vaccine, pp.6420-6429.	Review not directly answering question
Wood Nicholas J, and Cashman Patrick M. (2011). Influenza immunisation program at three tertiary paediatric hospitals in NSW in 2010. New South Wales public health bulletin, pp.230-2.	Not a relevant study type (cross-sectional survey, epidemiological study, correlation study, narrative review)
Wright Adam, Poon Eric G, Wald Jonathan, Feblowitz Joshua, Pang Justine E, Schnipper Jeffrey L, Grant Richard W, Gandhi Tejal K, Volk Lynn A, Bloom Amy, Williams Deborah H, Gardner Kate, Epstein Marianna, Nelson Lisa, Businger Alex, Li Qi, Bates David W, and Middleton Blackford. (2012). Randomized controlled trial of health maintenance reminders provided directly to patients through an electronic PHR. Journal of general internal medicine, pp.85-92.	Not a relevant population
Yamin Dan, Balicer Ran D, and Galvani Alison P. (2014). Cost-effectiveness of influenza vaccination in prior pneumonia patients in Israel. Vaccine, pp.4198-205.	Not a relevant population
Yudin Mark H, Salaripour Maryam, and Sgro Michael D. (2010). Acceptability and feasibility of seasonal influenza vaccine administration in an antenatal clinic setting. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC, pp.745-8.	Not a relevant intervention
Yudin Mark H, Salripour Maryam, and Sgro Michael D. (2010). Impact of patient education on knowledge of influenza and vaccine recommendations among pregnant women. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC, pp.232-7.	Duplicate (included in an included systematic review, Wong 2016)

Study citation	Reason for exclusion
Yuen Carol Yuet Sheung, and Tarrant Marie. (2014). Determinants of uptake of influenza vaccination among pregnant women - a systematic review. Vaccine, pp.4602-13.	No relevant outcomes reported
Zakrzewski Leanne, Sur Denise K, and Agrawal Nisha. (2014). Staff versus physician vaccine protocols for influenza immunization during pregnancy. Journal of the American Board of Family Medicine: JABFM, pp.56-60.	No relevant outcomes reported

Appendix M: Prisma