National Institute for Health and Care Excellence

Final

Flu vaccination: increasing uptake

Evidence reviews for increasing uptake in carers

NICE guideline NG103

Evidence reviews

August, 2018

Final

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

Disclaimer

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Review question 2b (RQ 2b): What interventions to increase access to seasonal flu vaccine are cost effective in increasing uptake of seasonal flu vaccine among carers?

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Introduction

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

This evidence review focuses on the effectiveness and cost-effectiveness of interventions that can be delivered in the community to increase acceptability and uptake of seasonal flu vaccination among carers. Eligibility for free flu vaccination in the UK according to the Green Book is for those carers who are:

i) in receipt of a carer's allowance, as described in the annual Flu Plan, or

ii) the main carer of an older or disabled person whose welfare may be at risk if the carer falls ill, as described in the Flu Plan.

Vaccine uptake among carers is low; in 2017/18 in England it was 40% according to an annual survey of flu vaccination in GP patients[a].

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 review systematically identified studies that fulfilled the criteria specified in Table 1. For full details of the review protocol, see Appendix A. The main outcomes for this review were increasing vaccination uptake, acceptability and cost effectiveness. Additional outcomes of interest include knowledge, awareness, intention, beliefs, adverse outcomes and the views of the target group.

[a] https://www.gov.uk/government/statistics/seasonal-flu-vaccine-uptake-in-gp-patients-winter-2017-to-2018

PICO table

Table 1: PICO inclusion criteria for the review questions on increasing uptake in carers

Population	Carers groups eligible for free vaccination according to the Green book[b]
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 ○ 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

[b] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456568/2904394_Green_Book_Chapter_19_v10_0.pdf

	○ 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 trial designs (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 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 for a summary of studies included in this review.

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, 1377 references were found for these review questions, and full-text versions of 14 citations that seemed potentially relevant to this topic were retrieved. In total 3 studies are included in the effectiveness section of the review with no studies being included in either the qualitative or cost effectiveness review sections (see PRISMA diagram in Appendix M).

Summary of studies included in the effectiveness review

Table 2: Included studies for each review question (RQ1-3)

RQ1a: Information, education, tailoring, flu champions and recommendation by a respected person					
First author, year	**Design**	**Country**	**Setting**	**Population**	**Intervention**
Desbiens, 2005	Before and After (time series)	US	Community *Program of All-Inclusive Care for the Elderly (PACE)*	Carers of elderly adults who have a severe disability living in the community as a PACE program participant.	Recommendations by the PACE programme to access flu shots either within their programme or via their own provider.
RQ2a: Flexible, walk-in/open access, outreach and parallel clinics or other opportunistic approach					
First author, year	**Design**	**Country**	**Setting**	**Population**	**Intervention**
Warner, 2013	Observational (comparative)	UK	Community	Carers who met the Department of Health criteria for vaccination	Influenza vaccination delivered in a Community Pharmacy
Atkins 2016	Before and After	UK	Community pharmacies	Carers who met the Department of Health criteria for vaccination.	Enabling NHS reimbursed pharmacies to provide seasonal flu vaccination to all eligible individuals registered with a London borough primary care trust
RQ3a: Local leadership, reminder-recall, provider prompts, incentives, audit and feedback					
First author, year	**Design**	**Country**	**Setting**	**Population**	**Intervention**
No studies met the intervention inclusion criteria for this question					

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

Synthesis and quality assessment of effectiveness evidence

Only studies with observational study designs were identified for inclusion in this review. The Effective Public Health Practice Project (EPHPP) quality appraisal checklist, as referenced in Appendix H of the NICE methods manual, was applied to each study to assess risk of bias.

Due to limitations in reported data, a pooled meta-analysis of studies could not be undertaken.

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

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. No pooled analyses were conducted for this review of increasing vaccination uptake in carers. Evidence was therefore rated 'not applicable' on this domain.
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

Quality domain	Description
	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 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).

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 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 multi-component and crosses review questions where the data cannot be disaggregated for separate review questions.

ES 1.1 Very low quality evidence from 1 before and after (time series) study with between 170 and 184 participants showed that recommendation from a respected person increased acceptability and uptake of seasonal flu vaccination among carers. Uptake increased significantly year-on-year from 9% at baseline (2000/2001) to 33% in 2001/02 (RR 3.71; 95%CIs 2.19 to 6.30), 44% in 2002/03 (RR 4.99; 95%CIs 3.00 to 8.31) and 62% in 2003/04 (RR 7.05; 95%CIs 4.29 to 11.59) [GRADE profile 1].

ES 2.1 Very low quality evidence from 2 observational descriptive studies suggests that providing vaccination in community pharmacies may improve accessibility of seasonal flu vaccination to carers but may not increase overall uptake. In one study, a significantly greater proportion of those vaccinated in community pharmacies were carers compared with the proportion vaccinated in GP practices (3% vs. 0.4% respectively; $p<0.001$), although the overall proportion of eligible carers who were vaccinated across the two settings was similar (23% at pharmacies and 27% at GP practices). Convenience of access was the major factor for choosing a community pharmacy over their GP practice reported by respondents from all groups who met Department of Health criteria for free flu vaccination; no specific breakdown by eligibility group was reported. In another study with before and after data, widening provision of free vaccination to community pharmacies did not increase uptake among carers by any more than 1% compared with pre-intervention rates. Cross-sectional data showed that approximately 37% of all eligible carers were vaccinated in the first year of the intervention (2013/14). However of those, 22% received their vaccination in a community pharmacy setting, which was a greater proportion than for any other ‘at risk’ group that met Department of Health criteria for free flu vaccination [GRADE profile 2].

Qualitative evidence review

No qualitative studies were identified that met the inclusion criteria for inclusion in this review.

Economic evidence

No health economic evaluations were identified that met the inclusion criteria for inclusion in this review.

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 carers' (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. <u>Cost-effectiveness</u> 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 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.	As noted elsewhere, if large numbers of papers are identified and included at full text, the following may be implemented: • Prioritising evidence with critical or highly important outcomes

	Stage 2. Full text screening 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 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	Exclusion criteria: • 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 i.e. Older people to other groups • Call for Evidence • Expert Testimony	

PICO RQ 1-3 (Carers)

	Details			Additional comments
Study design	**(A)** Comparator studies (effectiveness): • Systematic reviews • Randomised or non-randomised controlled trials • Before and after studies (including before and after surveys) Observational studies were only included if no studies of	**(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

	Details			Additional comments
	effectiveness were identified for particular intervention areas: • Cohort studies • Case-control studies			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 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.

	Details				Additional comments
					Excluded countries (qualitative): Non-OECD, Japan, Korea, South and Central America. If too many studies are identified those European countries where there are significant cultural differences – Eastern Europe will be excluded and priority will be given to UK studies.
Population	Carers				
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 member who shares similar life	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,	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
	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	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 ○ 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	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
		○ 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	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)		

	Details				Additional comments
		to receive flu vaccination from community providers	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 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				

	Details	Additional comments
	○ Vaccine wastage • Cost effectiveness and economic outcomes: ○ Cost per quality-adjusted life year ○ Cost per unit of effect	

Appendix B: Health economic analysis

Please see separate economic modelling report

Appendix C: Research recommendations

See full guideline for prioritised research recommendations

Appendix D: Included evidence study selection

Atkins K, van Hoek A, Watson C et al. (2016) Seasonal influenza vaccination delivery through community pharmacists in England: evaluation of the London pilot. BMJ Open; 6: e009739

Desbiens N. A 5-year experience with influenza prevention and containment in a program of all-inclusive care for elderly adults, American Journal of Infection Control, 33, p.238-42, 2005

Warner J., Portlock J., Smith J., Rutter P. Increasing seasonal influenza vaccination uptake using community pharmacies: experience from the Isle of Wight, England, The International journal of pharmacy practice, 21, p.362-7, 2013.

Appendix E: Economic evidence study selection

No cost effectiveness studies were identified for inclusion in this review

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)
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)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
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)
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)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
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 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)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
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)
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)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
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$.tw. (4089)
168 (follow up adj (study or studies)).tw. (38237)
169 (observational adj (study or studies)).tw. (49507)
170 longitudinal.tw. (145584)
171 prospective.tw. (369555)
172 retrospective.tw. (295058)
173 cross sectional.tw. (180405)
174 or/154-173 (3535459)
175 Meta-Analysis.pt. (62777)
176 Meta-Analysis as Topic/ (14637)
177 Review.pt. (2023681)
178 exp Review Literature as Topic/ (8461)
179 (metaanaly$ 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)

Database: Ovid MEDLINE (R) <1996 to April Week 2 2016>
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)
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)

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 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.1.1 Desbiens 2005

<table>
<tr><th>Study detail</th><th>Inclusion/Exclusion & Patient/Population</th><th>Intervention/Comparator</th><th>Results</th></tr>
<tr>
<td>Full citation
Desbiens, N. A 5-year experience with influenza prevention and containment in a program of all-inclusive care for elderly adults, American Journal of Infection Control, 33, 238-42, 2005

Study type
Before and After (time series)

Aim of the study
To describe the influenza prevention and containment program that has evolved at 1 Program of All-Inclusive Care for the Elderly (PACE) site since its inception and discuss problems with implementation.

Location and setting</td>
<td>Number of participants
Number of carers per year
<table>
<tr><td>Season</td><td>1999 to 2000</td><td>2000 to 2001</td><td>2001 to 2002</td><td>2002 to 2003</td><td>2003 to 2004</td></tr>
<tr><td>Total carers (not health care workers)</td><td>-</td><td>170</td><td>171</td><td>184</td><td>172</td></tr>
</table>
Participant characteristics:
Carers (not health care workers) of elderly adults who have a severe disability living in the community who meet the state Medicaid requirements for nursing home placement and are a participant of the PACE program.
Some live by themselves or in nursing homes or assisted living.

Inclusion criteria
A carer of an elderly adult with a severe disability living in the community as a participant of the PACE program.

Exclusion criteria
Not reported</td>
<td>Intervention / Comparison
A multi-disciplinary team of care providers whose aim is to keep elderly adults who have severe disability living in the community offered caregivers of their elderly patients gratis vaccinations through their program or encouraged / recommended they access vaccinations via their usual provider

No comparator (baseline control).</td>
<td>Percentage known to be immunized.
<table>
<tr><td>Season</td><td>1999 to 2000</td><td>2000 to 2001</td><td>2001 to 2001</td><td>2002 to 2003</td><td>2003 to 2004</td></tr>
<tr><td>Percentage of carers known to be immunized</td><td>-</td><td>9</td><td>33</td><td>44</td><td>62</td></tr>
<tr><td>Total carers (not health care workers)</td><td>-</td><td>170</td><td>171</td><td>184</td><td>172</td></tr>
</table>
</td>
</tr>
</table>

Study detail	Inclusion/Exclusion & Patient/Population	Intervention/Comparator	Results
Tennessee, USA. **Length of study** Five years. **Source of funding** None for study. PACE program offered free flu vaccination.			

Notes

Limitations identified by author

Authors report having made greater efforts to encourage caregivers to receive flu shots, but acknowledge that it is an undeveloped part of the program.

Carers are not patients and receive care under the normal health care system, limiting the extent of impact on carer's choices.

Limitations identified by review team

The primary aim of the study was not to increase uptake of flu vaccine in carers. Reported uptake of flu in carers appears to be a secondary outcome of the study. The intervention is unknown as no details of definition of encouragement or content of intervention are reported.

No data reported on numbers excluded or source of immunization (i.e. own Health Care provider or through PACE program).

No data reported on the methods used to measure number of carers known to be immunized.

Other comments

If the carers or relatives are similar in characteristics to PACE programme participants, potentially many are socially disadvantaged and poor.

G.1.2 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 open. 2016 Feb 1;6(2):e009739. Quality score - Study type Before and after Aim of study To evaluate the effectiveness	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 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	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 to offer inactivated flu vaccines to clinically at risk children from aged 2 and older.	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. 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

<table>
<tr><th colspan="5">Atkins 2016</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>and cost of the pan-London pharmacy initiative, a program that allows administration of seasonal influenza 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</td><td>facilities' (<1% of patients)</td><td></td><td></td><td>Authors note the relatively high use of pharmacy option among carers, suggesting it is due to issues of greater accessibility and convenience although service users were not surveyed as part of this evaluation (only pharmacists and GPs).

<u>NICE post-hoc analysis</u>:

Year 1 of pharmacy initiative (2013/14)

<table><tr><th></th><th>Total % vaccinated*</th><th>% vaccinated at pharmacy*</th><th>% vaccinated at GP practice*</th><th>Pharmacy-admin as % of all vaccinated</th></tr><tr><td>Carers aged<65 years</td><td>37</td><td>8</td><td>29</td><td>21.6</td></tr></table>*estimated from graphs</td></tr>
</table>

Atkins 2016				
Study details	**Inclusion/ Exclusion criteria**	**Population**	**Intervention/Comparator**	**Results**
the London School 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.1.3 Warner 2013

Study detail	Inclusion/Exclusion & Patient/Population	Intervention/Comparator	Results
Full citation Warner J, Portlock J, Smith J, Rutter P. Increasing seasonal	**Number of participants** 356 eligible carers in a total patient population of 45, 647	**Intervention / Comparison** Intervention:	Primary outcomes

Study detail	Inclusion/Exclusion & Patient/Population	Intervention/Comparator	Results
influenza vaccination uptake using community pharmacies: experience from the Isle of Wight, England. The International Journal of Pharmacy Practice, 21, 362-7, 2013 **Study type** Observational descriptive (Comparative). **Aim of the study** To determine whether inclusion of community pharmacies in an influenza vaccination programme improves vaccination rates and is acceptable to patients **Location and setting** Eighteen community pharmacies on the Isle of Wight, compared to GP practices. **Length of study** 23 Weeks. September 2010 to end of February 2011.	**Participant characteristics** Patient characteristics: All patients who met the Department of Health (DoH) criteria for vaccination, except those who were less than 12 years of age, pregnant or immunocompromised. Community pharmacy characteristics: Every pharmacist offering the service had been trained to meet the national standard for vaccination, had received training in basic life support and anaphylaxis treatment and had private consultation rooms meeting or exceeding the requirements set out in the current pharmacy contractual framework. **Inclusion criteria** Patient: met the DoH criteria for vaccination. Community pharmacy: Pharmacy staff had been trained to meet the national standard for vaccination; had training in basic life support and anaphylaxis treatment and Pharmacy had private consultation rooms meeting or exceeding requirements set out in the current pharmacy contractual framework. **Exclusion criteria** Patient: Initially less than 12 years of age; pregnant; or immunocompromised.	Influenza vaccination delivered in a Community Pharmacy. Multicomponent intervention included a public health awareness campaign : window and wall posters in pharmacies; leaflets on influenza distributed to all at risk patients based on types of medication presented for dispensing and opportunistically by pharmacy frontline staff to the general public using the pharmacy. An online data-capture system was locally developed which notified GP practices of their patients vaccinated in community pharmacies. Comparator: Influenza vaccination delivered in a GP practice (usual care).	<table><tr><td>Number of carer influenza vaccinations by location</td><td>n of carers</td></tr><tr><td>By GP</td><td>96</td></tr><tr><td>By Community pharmacies</td><td>83</td></tr><tr><td>Total number vaccinated</td><td>179</td></tr><tr><td>Eligible number of carers</td><td>356</td></tr></table> <table><tr><td>Total number of patients vaccinated through community pharmacies</td><td>2,837</td></tr><tr><td>Percentage of carers of total population vaccinated through community pharmacies</td><td>3 %</td></tr><tr><td>Total number of patients vaccinated by GP</td><td>26,558</td></tr></table>

Study detail	Inclusion/Exclusion & Patient/Population	Intervention/Comparator	Results
Source of funding Isle of Wight Primary Care Trust.	Pharmacy staff had not been trained to meet the national standard for vaccination; or did not have training in basic life support and anaphylaxis treatment and Pharmacy did not have private consultation rooms meeting or exceeding requirements set out in the current pharmacy contractual framework.		<table><tr><td>Percentage of carers of total population vaccinated by GP</td><td>0.4%</td></tr></table> A significantly greater proportion of carers was vaccinated through pharmacies than medical practices (X^2=test p<0.001). Secondary outcomes: Primary Care Trust vaccination rate increased from 64.1% to 70.3%. Accessibility was the key determinant for carers choosing a pharmacy over their medical practice. The cost of the pharmacy service to the commissioner was identical to that of general medical practitioners, in terms of both practitioner reimbursement and vaccine procurement.
Notes <u>Limitations identified by author</u>			

Study detail	Inclusion/Exclusion & Patient/Population	Intervention/Comparator	Results

Only 18 of 30 Community pharmacies met the criteria for being ready to provide vaccination. If more were able to provide the service they would have had a greater penetration of the population.

A program change to allowing those under twelve years of age, and pregnant women to be vaccinated by in Community Pharmacies was made in December 2010, if they had been included from the start, they would have had a bigger impact on these groups.

Limitations identified by review team

No baseline (comparator) measure for carers from previous years.

Carers were not randomized or allocated to receive vaccine from either GP or community pharmacy.

No before and after data to indicate uptake by intervention or by setting so it is not clear if intervention has increased flu vaccine uptake prior to delivery by community pharmacy and if this is due to accessibility. Study reports only number vaccinated by GP or pharmacy number GP practices is not stated.

No costs reported for training/delivery of flu vaccine

Other comments

Adding community pharmacies added an additional 6.2% over previous years. Overall they did 9.7% of the vaccinations, so attract some people who previously attended GP practices for vaccination. However, as noted above the make-up of those additional people in terms of eligible groups or sub-groups was not provided.

No mention of any adverse effects, i.e. attending GP surgeries means the person can be screened for other issues, thus screening opportunities potentially reduced.

Appendix H: Economic evidence tables

No economic studies were identified that met the criteria for inclusion in this review.

Appendix I: GRADE tables

I.1 GRADE profile 1

Review question 1a: What interventions to promote information about, and acceptability of, flu vaccination are the most effective for increasing acceptability and uptake of seasonal flu vaccination among carers?

Outcome: Outcome: Flu vaccination uptake – carers

Quality assessment								Effect	Quality	Rating
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)		
Recommendation from respected person vs. baseline (pre-intervention) [Forest plot Figure 1; ES1.1]										
1[1]	Before and After	Serious [a]	n/a	No serious	Serious [b]	None	170-184	15/170 (9% in (2000/1)) - baseline 56/171 (33% in 2001/2)) – Yr1 81/184 (44% in 2002/3)) – Yr2 107/172 (62% in 2003/4)) – Yr3 ---------- Yr1 (vs baseline) RR 3.71 (2.19 to 6.30)* Yr2 (vs baseline) RR 4.99 (3.00 to 8.31)* Yr3 (vs baseline) RR 7.05 (4.29 to 11.59)*	Very low	Critical

1 Desbiens 2005 [B&A]

a. downgraded 1 level due to potential attrition bias or selective reporting: No data reported on numbers excluded or source of immunization (i.e. own Health Care provider or through PACE program). No data reported on the methods used to measure number of carers known to be immunized.
b. downgraded 1 level: small study sample and low event numbers (<300 total events) reduces certainty in effect

* data from post hoc analysis undertaken by the review team

I.2 GRADE profile 2

Review question 2a (RQ 2a): What interventions to improve access to flu vaccination are the most effective for increasing acceptability and uptake of seasonal flu vaccination among carers?

Outcome: Flu vaccination uptake

Quality assessment										
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants	Relative risk (95% CI)	Quality	Rating
Community pharmacy vs. GP practice [ES2.1]										
2[1,2]	Observational	Very serious [a]	n/a (not pooled)	No serious	Very serious [b]	None	356 eligible carers [1]	**Proportion of carers vaccinated in each setting:** • 23% of eligible carers vaccinated in pharmacy • 27% eligible carers vaccinated in GP practice **Proportion of the total population vaccinated in each setting who were carers:** • 3% of those choosing to be vaccinated in a pharmacy setting were carers • 0.04% those choosing to be vaccinated in a GP setting were carers A significantly greater proportion of the population vaccinated in pharmacies were carers compared to GP practices (X^2=test P<0.001).	Very low	critical
							Not reported [2]	**Overall uptake:** increased <1% among eligible carers aged <65 years (between baseline: 2012/13 and Year 1: 2013/14) **Proportion of registered eligible carers aged <65 years who were vaccinated (Year 1: 2013/14):** • 8% vaccinated in a pharmacy setting • 29% vaccinated in GP practice (estimated from graph)		

								Pharmacy-delivery as % of all vaccinated carers (Year 1: 2013/14): • 21.6% of all vaccinated carers received their vaccination in a pharmacy setting		

1 Warner 2013
2 Atkins 2016

a. downgraded 2 levels due to selective outcome reporting: Warner 2013 indicates an increased number of vaccinations delivered overall but does not provide data at eligible population sub-group level or by setting, despite reporting other data at this level; Atkins 2016 reports pharmacy-reported uptake only in terms of proportions of carers and other eligible groups (sample sizes not stated; no comparisons with GP practice uptake)

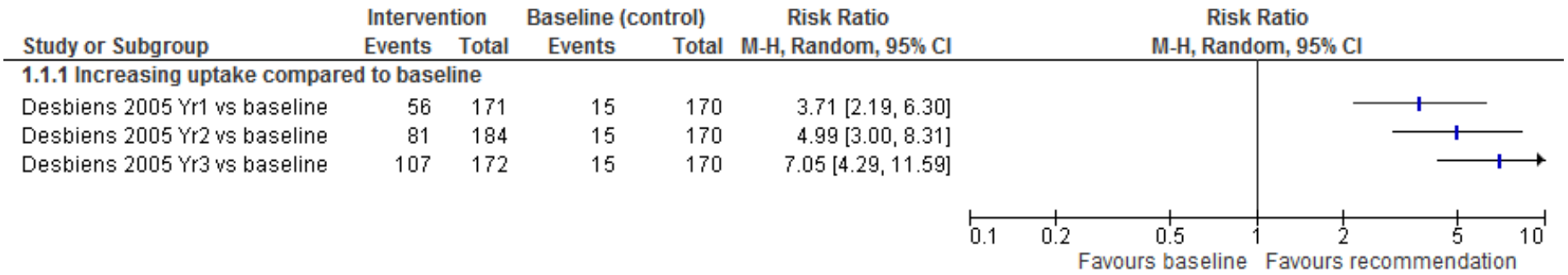
b. downgraded 2 levels: small study sample (<300 total events) reduces certainty in effect (Warner 2013); no comparative data or sample sizes given in Atkins 2016; 95%CIs not reported so imprecision cannot be assessed.

Appendix J: Health economic evidence profiles

No economic studies were identified that met the inclusion criteria for this review.

Appendix K: Forest plots

Figure 1: Change in flu vaccination uptake over time (intervention: recommendation by a respected person) [GRADE profile 1; ES 1.1]



Appendix L:Excluded studies

Study citation	Reason for exclusion
Guzman-Cottrill, Judith A., Phillipi, Carrie A., Dolan, Susan A., Nyquist, Ann-Christine, Win, Amy, Siegel, Jane, Free vaccine programs to cocoon high-risk infants and children against influenza and pertussis, American Journal of Infection Control, 40, 872-876, 2012	No intervention.
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., Schuster, M., Strategies for addressing vaccine hesitancy - A systematic review, Vaccine, 33, 4180-4190, 2015	Systematic review did not match the review questions.
Jefferson, T., Demicheli, V., Influenza vaccination for elderly people and their care workers, Lancet, 369, 1857-1858, 2007	Letter. No data.
Kelly, Nancy R., Kromelis, Michelle R., Jordan, Donna, Merryman, Ruth, Siegel, Jane D., Feasibility of delivering influenza vaccine to household contacts of pediatric patients in a residents' continuity clinic, American Journal of Infection Control, 40, 627-631, 2012	Population: Household contacts, not carers.
Krishna,S., Balas,E.A., Boren,S.A., Maglaveras,N., Patient acceptance of educational voice messages: a review of controlled clinical studies, Methods of information in medicine Methods Inf Med, 41, 360-369, 2002	Data not presented separately for carers.
Lee, Ingi, Thompson, Sarah, Lautenbach, Ebbing, Gasink, Leanne B., Watson, Barbara, Fishman, Neil O., Chen, Zhen, Linkin, Darren R., Effect of accessibility of influenza vaccination on the rate of childcare staff vaccination, Infection control and hospital epidemiology, 29, 465-7, 2008	Population: Healthcare workers. Not carers
Lin, C. J., Nowalk, M. P., Toback, S. L., Rousculp, M. D., Raymund, M., Ambrose, C. S., Zimmerman, R. K., Importance of vaccination habit and vaccine choice on influenza vaccination among healthy working adults, Vaccine, 28, 7706-12, 2010	Population: healthy working adults. No information on carer status.
Macdonald, Laura, Cairns, Georgina, Angus, Kathryn, de Andrade, Marisa, Promotional communications for influenza vaccination: a systematic review, Journal of health communication, 18, 1523-49, 2013	Population included: patients and health care workers, not carers.
Newall, A. T., Jit, M., Beutels, P., Methodological decisions in economic evaluations of childhood influenza vaccination: Findings from a literature review, Value in Health, 14, A273, 2011	Conference abstract. No data.
Shah, Shetal, Caprio, Martha, Trivalent inactivated influenza vaccine compliance rate in neonatal intensive care unit parents, Advances in neonatal care : official journal of the National Association of Neonatal Nurses, 7, 295-8,2007	Population: Household contacts, not carers.
Thomas, D. R., Chantry, K., Aubrey, F., Beaven, S., Bowen, C., Fairley, J., Roberts, A., Cottrell, S., Roberts, R., Influenza immunisation uptake in carers, Vaccine, 26, 6746-6748, 2008	No intervention. Survey.

Appendix M: PRISMA