ID	Field	Content
1.	Review title	Identifying effective interventions to improve uptake of routine vaccines and the barriers to, and facilitators for, vaccine uptake.
2.	Review questions	What are the most effective interventions for increasing the uptake of routine vaccines? What are the barriers to, and facilitators for, increasing the uptake of routine vaccines?
3.	Objectives	To identify the barriers to, and facilitators to vaccine uptake and effective strategies to improve routine vaccine uptake.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Medline in process • Medline epubs ahead of print • Emcare • Psycinfo • Sociological Abstracts • ASSIA • DARE • Econlit (economic searches) • NHS EED (economic searches) • HTA (economic searches) • Other subject specific databases as appropriate for the quantitative review Searches will be restricted by: • Studies published since 1990 • English language • Human studies

		• Qualitative, Systematic Review, RCT, OECD geographic filters as appropriate Other searches: • Reference searching where appropriate • Citation searching where appropriate • Inclusion lists of systematic reviews • Websites where appropriate The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition being studied	Uptake of vaccines on the routine NHS schedule
6.	Population	Inclusion: • All people who are eligible for vaccines on the routine UK immunisation schedule and their families and carers (if appropriate). • Staff including, but not limited to, those providing advice about or administering vaccines and those people with relevant administrative or managerial responsibilities. Exclusion: None
7.	Interventions and factors of interest	<u>RQ2.1 Quantitative review</u> Interventions including, but not confined to: 1. Information, education and methods of communicating them Interventions to provide information including: • online campaigns including social media and apps • radio campaigns • letters by mail • printed materials (e.g. leaflets) • multi-media campaigns • TV and online advertising (including pop up adverts) • posters • online information exchange- fill in questionnaire and get information Educational interventions (delivery methods): • face-to-face sessions • telephone conversations • social media with responses • interactive multi-media interventions (e.g. case studies on GP websites; e-learning) • interactive community events (e.g. talks with question and answer sessions)

		• 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)
		• multicomponent interventions targeting education
		• vaccine hotlines and special advisory clinics for health professionals
		
		Who provides the information and/or advice and how they do so, including:
		• Vaccine champions:
		  ○ Practitioners
		  ○ Peers
		  ○ Community leaders
		• Interventions to train staff and other people on how best to communicate the information/ run educational sessions.
		• Recommendations to vaccinate from people/groups including:
		  ○ Medical and other staff (for example, GPs, nurse, health visitors, midwives,)
		  ○ Social workers
		  ○ Community leaders
		  ○ Religious leaders
		  ○ Peers
		  ○ Teachers
		
		Information and education can be provided during home visits, during interactions with health and social care workers, at support group meetings for people using other services etc. This may involve providing a contact point for more information.
		
		Types of information include PHE bulletins and local bulletins for providers.
		
		2. Vaccination reminders aimed at providers or individuals including:
		
		Reminder and recall systems (aimed at provider)
		• clinical alerts and prompts
		• national alerts to local teams
		• local recall initiatives
		
		Personal invitation to be vaccinated from:
		• GP
		• community pharmacist
		• health or social care worker
		• from several professionals
		
		Reminders to individuals/ eligible groups by:
		• text messages
		• electronic invitations (via apps)

		• emails • letter • phone calls • posters • postcards 3. Interventions targeting acceptability: • Alternative forms of vaccinations (e.g. injections, formulations) • Alternative settings • Alternative vaccine providers (e.g. doctor administering vaccine instead of nurse) 4. Interventions to improve access including: Expanding access in healthcare, such as: • Reducing distance/time to access vaccinations • Out of hour or drop-in services • Delivering vaccines in clinical settings in which they were previously not provided 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 clinics for specific/ all routine vaccinations • Mass vaccination clinics in community or other settings (e.g. schools) • Walk in or open access immunisation clinics Extended hours clinics • weekends evenings (after 6 pm) • early mornings (before 8 am) • 24-hour access Outreach interventions or mobile services • home or domiciliary or day centre visits • support group meeting visits • residential or care home visits • special school visits • inpatient visits • custodial visits • immigration settings • mobile clinics (e.g. in community) Parallel clinics • Offer vaccination in parallel with regular appointments (e.g. with midwives, clinicians, inpatient and outpatient clinics, long stay wards, etc.) • coordinated timing of other programmes (such as child developmental checks)

		Opportunistic vaccinations: • visits to GP, practice nurse or consultant for other medical conditions including STI clinics, drug and alcohol programmes • having vaccinations provided in hospitals or accident and emergency departments • may involve a dedicated person to administer the vaccines. 5. Interventions to improve infrastructure (targeting processes, staffing and settings): Booking systems • dedicated vaccination lines or online systems Organisation of local provider-based systems: • Local area approaches • Systems and processes in place to work with the community • Practice level approaches • Assigned lead for a specific vaccination programme • Having staff who are competent to deliver vaccinations available in multiple settings • Having staff with responsibilities for training practitioners, answering complex questions, co-ordinating immunisations etc. Systems involved in the recording and identification of eligibility and status (covered in RQ1- see this review protocol for a list of potential interventions) Incentives based interventions: • Incentive (and disincentives for not vaccinating) schemes (for individuals) o voucher schemes (not to cover cost of vaccination or healthcare) o payment to cover travel costs o fines/ penalties for not vaccinating o entry to childcare settings/ schools blocked in the absence of proof of vaccination status • Mandatory vaccination • Incentive schemes (for providers) o targets o quality and outcomes framework o voucher schemes Audit and feedback on uptake rates for providers • Weekly statistics • Content and delivery of feedback • Practical relevance (e.g. how many more people need to be vaccinated to achieve a target number) • Comparison data (e.g. between GP practices) 6. Multicomponent interventions:

		• Interventions which include more than one component and target multiple issues (for example the intervention could include an educational component and changes in the timing of clinics) will be analysed separately, but with other similar multicomponent interventions where possible. • Multicomponent interventions which include more than one component that is targeting a single issue will be included in the relevant category instead. RQ2.2 Qualitative review Barriers to, and facilitators for, routine vaccine uptake including, but not limited to: • Thoughts, views and perceptions of individuals, parents or carers and staff • Issues relating to acceptability • Issues relating to accessibility • Issues relating to infrastructure • Issues relating to mis-information or a lack of information and communication of information • Issues relating to informed refusal • collective benefit / altruistic motives

8.	Comparators	RQ2.1 Quantitative review.
		• Usual approaches to increase vaccine uptake
		• Other interventions to increase vaccine uptake
		  ○ Other interventions targeting same issue/ theme (for example education)
		  ○ Other interventions targeting different issues/ theme (for example education versus infrastructure)
		
		RQ2.2 Qualitative review.
		
		Not applicable

9.	Types of study to be included	RQ1.1 Quantitative review. Systematic reviews of included study designs. Then as needed: • Randomised controlled trials • Non-randomised controlled trials • Controlled before-and-after studies • Interrupted time series • Cohort studies • Before and after studies • Mixed method study designs (quantitative evidence that matches the above study designs only) RQ1.2 Qualitative review • Systematic reviews of included study designs • Qualitative studies that collect data from focus groups and interviews

		• Qualitative studies that collect data from open-ended questions from questionnaires/ surveys • Mixed method study designs (qualitative evidence that matches the above study designs only) For the mixed methods synthesis, published mixed methods studies will also be included if the study does not present quantitative and qualitative evidence separately, but only if the individual study designs meet the inclusion criteria for both the qualitative and quantitative reviews as detailed above.
10.	Other exclusion criteria	Interventions to increase uptake of these vaccines/ conditions: • Selective immunisation programmes, as defined in the Green Book and additional vaccines for people with underlying medical conditions because they do not form part of the routine schedule. • Seasonal vaccinations because they are not part of the routine vaccination schedule, apart from Flu, which is covered by a separate NICE guideline and excluded for this reason (see section 14 for reasons underlying a possible deviation from this exclusion). • Travel vaccines- not on routine schedule • Areas covered by NICE's guideline on tuberculosis. • Catch-up campaigns alongside the introduction of a new vaccine Only papers published in the English language will be included. Questionnaires and surveys will not be included, (apart from those reporting open-ended questions from questionnaires/surveys). Where studies from the USA (or other countries with similar health insurance-based systems) are included in the qualitative reviews any barriers/ facilitators relating to financial incentives (such as payment for vaccines or affording health insurance) will not be recorded as these are not relevant for the UK. In addition, in countries where vaccines or health care are paid for by the user studies looking at any financial incentive-based interventions are excluded.
11.	Context	The Department of Health and Social Care in England has asked NICE to produce a guideline on vaccine uptake in the general population. In recent years, UK vaccination rates have declined, resulting in increases in vaccine preventable diseases, particularly measles. There were 991 confirmed cases in England in 2018 compared with 284 in 2017 and the World Health Organization no longer considers measles 'eliminated' in the UK.

		Reasons for low uptake include poor access to healthcare services; inaccurate claims about safety and effectiveness, which can lead to doubts about vaccines; and insufficient capacity within the healthcare system for providing vaccinations. In addition, problems with the recording of vaccination status and poor identification of people who are eligible to be vaccinated may have contributed to this problem.
12.	Primary outcomes (critical outcomes)	RQ2.1 Quantitative outcomes: Changes in: • Vaccine uptake (overall for a specific vaccine or vaccines and for each dose where a vaccine is administered in multiple doses) RQ2.2. Qualitative outcomes: The outcomes will be generated using emergent coding, but are expected to include the following: • Thoughts, views and perceptions of individuals, parents or carers and staff • Issues relating to acceptability • Issues relating to accessibility • Issues relating to infrastructure • Issues relating to mis-information or a lack of information and communication of information • Issues relating to informed refusal
13.	Secondary outcomes (important outcomes)	RQ2.1 Quantitative outcomes: Changes in: • the proportion of people offered vaccinations • the numbers of people who develop the disease the vaccination was aimed at preventing
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The qualitative review search results and quantitative systematic review search results will be sifted using the EPPI reviewer priority screening functionality, but the whole data base will still be screened in each case. However, when sifting for primary studies for specific sections of the quantitative review priority screening may be used to terminate screening before the end of the search is reached. In this case, at least 50% of the identified abstracts will be screened. After this point, screening will only be terminated if a pre-specified threshold of 500 references is met for a number of abstracts being screened without a single new include being identified. A random 10% sample of the studies remaining in the database when the threshold is met will be additionally screened, to check if a substantial number of relevant studies are not being

		correctly classified by the algorithm, with the full database being screened if concerns are identified. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. Data will be extracted from the included studies into a standardised form (see Developing NICE guidelines: the manual section 6.4) for assessment of study quality and evidence synthesis. Extracted information for the quantitative review will include: study type; study setting; study population and participant demographics and baseline characteristics; details of the intervention and comparator used; study methodology; inclusion and exclusion criteria; recruitment and study completion rates; outcomes and times of measurement and information for assessment of the risk of bias. For the qualitative review, extracted information will include study type; study setting; sample characteristics; study methodology; inclusion and exclusion criteria; themes reported and information for assessment of the risk of bias. If insufficient evidence is identified to make recommendations, we will consult the committee and consider a call for evidence (as detailed in the NICE manual) or include more indirect evidence from other relevant guidelines (for example, the NICE flu guideline).
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using appropriate checklists as described in Developing NICE guidelines: the manual. Systematic reviews will be assessed using the ROBIS checklist. For the quantitative review, randomised controlled trials will be assessed using the Cochrane risk of bias v2.0 checklist. Non-randomised controlled trials and cohort studies will be assessed using the Cochrane ROBINS-I checklist. Controlled/ uncontrolled before and after studies, and interrupted time series will be assessed using the EPOC tool. Any mixed methods studies with quantitative data that can be extracted separately will be assessed using ROBINS-I, Cochrane risk of bias v2.0, or EPOC appropriate. Qualitative studies will be assessed using the CASP qualitative checklist. Any mixed methods studies with qualitative data that can be extracted separately will be assessed using the CASP qualitative checklist. Mixed methods studies where separate quantitative and qualitative data cannot be assessed separately will be assessed using the mixed methods appraisal tool (2018 version).

16.	Strategy for data synthesis	A mixed methods approach will be used to address this topic area. The quantitative and qualitative reviews will be conducted separately (segregated study design) but at the same time. The evidence from the reviews will then be analysed in relation to each other (convergent synthesis of results). (See below for more details. The findings will **not** be integrated by transforming one type of evidence into the other (e.g. quantitative findings into qualitative findings). <u>RQ1.1 Quantitative review</u> Where possible, meta-analyses of outcome data will be conducted for all comparators that are reported by more than one study, with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011). Data will be separated into the groups identified in section 17. Continuous outcomes will be analysed as mean differences, unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all comparators, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions is met: • Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. • The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$. In any meta-analyses where some (but not all) of the data comes from studies at high risk of bias, a sensitivity analysis will be conducted, excluding those studies from the analysis. Results from both the full and restricted meta-analyses will be reported. Similarly, in any meta-analyses where some (but not all) of the data comes from indirect studies, a sensitivity analysis will be conducted, excluding those studies from the analysis. GRADE will be used to assess the quality of the outcomes. Outcomes using evidence from RCTs, non-randomised trials and cohort studies will be rated as high quality initially and downgraded from this point. Controlled before and after studies and interrupted time series will be rated as low quality

		initially. Reasons for upgrading the certainty of the evidence will also be considered. Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically assess the potential for publication bias. Meta-analyses will be carried out separately for each study type per outcome, but the similarities and differences between the results obtained from the different study types will be noted. <u>RQ1.2 Qualitative review:</u> Where multiple qualitative studies are identified for a single question, information from the studies will be combined using a thematic synthesis. By examining the findings of each included study, descriptive themes will be independently identified and coded in NVivo v.11. If there are less than 5 studies, Nvivo v.11 will not be used. Once all of the included studies have been examined and coded, the resulting themes and sub-themes will be evaluated to examine their relevance to the review question, the importance given to each theme, and the extent to which each theme recurs across the different studies. The qualitative synthesis will use these 'descriptive themes' to develop 'analytical themes', which will be interpreted by the reviewer in light of the overarching review questions. Code saturation may be used as a reason to stop extracting data from new qualitative studies. CERQual will be used to assess the confidence we have in the summary findings of each of the identified themes. Evidence from all qualitative study designs (interviews, focus groups etc.) is initially rated as high confidence and the confidence in the evidence for each theme will be downgraded from this initial point. <u>Synthesising the findings of mixed method reviews.</u> Where mixed methods studies are identified that present data in a form that cannot be extracted and analysed separately as quantitative and qualitative data, the results of the studies will be reported separately for each study. Any correlations or discrepancies between the findings of the mixed methods studies and the syntheses of the quantitative and qualitative findings of the above analyses will be noted. <u>Mixed method synthesis of findings</u> <u>from the quantitative and qualitative reviews</u> Where appropriate, a synthesis matrix will be produced to combine results from the different individual analysis methods.

		Findings from one analytical approach will be compared to findings from the second approach, and outcomes paired up if they provided relevant information on the same underlying topic. The agreement between the findings of the two approaches will be qualitatively assessed, with each paired set of findings put into one of the three categories relating to the strength of the identified correlation. The results may be presented as a concept diagram with quantitative findings mapped onto the qualitative ones if this is thought to be informative.

17.	Analysis of sub-groups	<u>RQ2.1. Quantitative review</u>
		
		Results will be separated into the following for analysis:
		
		• Age/time when vaccine is due:
		  ○ During pregnancy
		  ○ 0-5 years
		  ○ 11 to 18 years
		  ○ 65 years and older
		
		• Population groups with potential equality issues:
		  ○ Children excluded from mainstream education (including pupil referral units) and non-attenders.
		  ○ Care home residents or people in long-term care
		  ○ Looked after children
		  ○ Religious groups or groups with special beliefs (e.g. anthroposophical views)
		  ○ Travellers/ gypsies
		  ○ Migrants and asylum seekers
		
		• Settings:
		  ○ care homes (covered above for residents)
		  ○ hospitals
		  ○ community versus healthcare
		  ○ educational settings
		
		• Mandatory versus partially mandatory, opt-outs allowed or completely optional vaccine schedules
		
		• Numbers of doses of vaccines
		
		• Study type: RCT, non-randomised studies (NRTs, CBA, ITS)
		
		• Interventions that are part of a catch up campaign versus interventions that are not part of a catch up campaign
		
		• System levels:
		  ○ health system level (for example clinical commissioning group [CCG], local authority, regional and national level)

		○ service provider level (for example GP practices, practitioners) ○ individual level (for example patients or service users including carers) ○ mixed levels • For interventions that use information/ education to increase uptake the results will also be presented for generic versus tailored interventions. <u>RQ2.2 Qualitative review</u> • Views of individuals, their parents and carers (where relevant) versus staff. • Age/time when vaccine is due: ○ During pregnancy ○ 0-5 years ○ 11 to 18 years ○ 65 years and older • Views of population groups with potential equality issues: ○ Children excluded from mainstream education (including pupil referral units) and non-attenders. ○ Care home residents or people in long-term care ○ Looked after children ○ Religious groups or groups with special beliefs (e.g. anthroposophical views) ○ Travellers, migrants and asylum seekers • Settings: ○ care homes (residents covered above) ○ hospitals ○ community versus healthcare ○ educational settings • Mandatory versus partially mandatory, opt-outs allowed or completely optional vaccine schedules • Views concerning catch up campaigns versus non catch up campaigns • System level issues: ○ health system level (for example clinical commissioning group [CCG], local authority, regional and national level) ○ service provider level (for example GP practices, practitioners) ○ individual level (for example patients or service users) ○ mixed levels

<table>
<tr><td>18.</td><td>Type and method of review</td><td colspan="3">☒ Intervention (multicomponent review)
☐ Diagnostic
☐ Prognostic
☐ Qualitative
☐ Epidemiologic
☐ Service Delivery
☒ Mixed method (all other quantitative reviews)</td></tr>
<tr><td>19.</td><td>Language</td><td colspan="3">English</td></tr>
<tr><td>20.</td><td>Country</td><td colspan="3">England</td></tr>
<tr><td>21.</td><td>Anticipated or actual start date</td><td colspan="3">January 2020</td></tr>
<tr><td>22.</td><td>Anticipated completion date</td><td colspan="3">October 2021</td></tr>
<tr><td rowspan="7">23.</td><td rowspan="7">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td></td><td></td></tr>
<tr><td>Piloting of the study selection process</td><td></td><td></td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td></td><td>h</td></tr>
<tr><td>Data extraction</td><td></td><td></td></tr>
<tr><td>Risk of bias (quality) assessment</td><td></td><td></td></tr>
<tr><td>Data analysis</td><td></td><td></td></tr>
</table>

24.	Named contact	**5a. Named contact** Guideline Updates Team **5b Named contact e-mail** VaccineUptake@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE)
25.	Review team members	From the Guideline Updates Team: • Marie Harris 2006ingh • Toby Mercer • Stephen Sharp • Joshua Pink • Stacey Chang-Douglass • Elizabeth Barrett
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Updates Team which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10139
29.	Other registration details	None
30.	Reference/URL for published protocol	None
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication

		• publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	Vaccine uptake, NHS routine vaccination schedule, interventions and barriers and facilitators.
33.	Details of existing review of same topic by same authors	None
34.	Current review status	☐ Ongoing ☐ Completed but not published ☒ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	None
36.	Details of final publication	www.nice.org.uk