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Adolescent self-consent for vaccinations: protocol for a mixed methods systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-021335
Article Type:	Protocol
Date Submitted by the Author:	29-Dec-2017
Complete List of Authors:	Batista, Harriet; University of Bristol, Population Health Sciences: Bristol Medical School Hickman, M; University of Bristol, Population Health Sciences: Bristol Medical School Macleod, John; University of Bristol, Population Health Sciences: Bristol Medical School Audrey, Suzanne; University of Bristol, Population Health Sciences: Bristol Medical School
Keywords:	Self-consent, Vaccination, Systematic review, Mixed methods, Adolescents

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1 **TITLE: Adolescent self-consent for vaccinations: protocol for a mixed methods systematic review**

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19

20 **Word count: 2,219**

21

22 **Key words**

23 Self-consent, Vaccination, Systematic review, Adolescents, Mixed Methods

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1
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3 25 **ABSTRACT**

4
5 26 **Introduction:** The recent global expansion of routine adolescent vaccination programmes has the
6
7 27 potential to protect young people against the acquisition of infectious disease and improve their
8
9 28 health. Although in many countries the legal framework supports young people to provide consent
10
11 29 for medical interventions if they are considered competent, written parental consent can act as a
12
13 30 barrier to uptake as it is frequently a condition of adolescent vaccination programmes. The aim of
14
15 31 this systematic review protocol is to document the methods which will be used to identify, appraise
16
17 32 and synthesise the available qualitative and quantitative evidence to address: (i) whether
18
19 33 implementation of adolescent self-consent procedures can increase vaccination uptake, and; (ii) the
20
21 34 barriers and facilitators to implementation of adolescent self-consent procedures.

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23
24 35 **Methods and analysis:** Comprehensive search strategy of all relevant electronic databases for both
25
26 36 qualitative and quantitative studies using predefined inclusion and exclusion criteria. At least two
27
28 37 authors will independently review titles and abstracts, extract data and assess the methodological
29
30 38 quality of eligible primary studies, resolving disagreements by consensus. Quantitative studies will
31
32 39 be reported narratively and where possible pooled in a meta-analysis using a random-effects model.
33
34 40 The findings of qualitative primary studies will be extracted, interpreted and synthesised to identify
35
36 41 overarching themes as well as similarities and differences within those themes.

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38
39 42 **Ethics and dissemination:** As this systematic review involves analysis of secondary data, the study
40
41 43 does not require ethical approvals. We will use our findings to assess whether the evidence supports
42
43 44 the hypothesis that self-consent procedures can increase coverage of adolescent vaccination
44
45 45 programmes. We will identify barriers and facilitators to the implementation of adolescent self-
46
47 46 consent for vaccination, and make recommendations for policy-makers and practitioners in relation
48
49 47 to consent procedures within vaccination programmes for young people.

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51 48 **Systematic review registration:** PROSPERO CRD42017084509

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53 49 **Word count:** 284

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3 51 **Strengths and limitations of this study**
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- 5 52 • The mixed methods systematic review will answer complementary research questions about
6
7 53 self-consent for adolescent vaccination programmes
8
9 54 • Robust systematic review methodology will be used to identify, appraise and synthesise the
10
11 55 relevant qualitative and quantitative literature
12
13 56 • Improvement to uptake of adolescent vaccination programmes by introduction of self-consent
14
15 57 procedures will be assessed in quantitative studies
16
17 58 • Synthesis of qualitative studies will examine barriers and facilitators to self-consent for
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19 59 adolescent vaccination programmes
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21 60 • Findings from this mixed-methods systematic review will inform recommendations for future
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23 61 policy and practice
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63 INTRODUCTION

64 In recent years, the number of routine vaccinations recommended during adolescence have
65 increased, and include vaccines that protect against tetanus, diphtheria, meningitis and human
66 papillomavirus (HPV) acquisition [1, 2]. Provided sufficient coverage is achieved, the expansion of
67 adolescent vaccination programmes may improve young people's health by protecting them from
68 potentially life- threatening infectious diseases.

69
70 The introduction of new adolescent vaccination programmes is relevant to the debate about young
71 people's capacity to provide consent to receive medical treatment. The United Nations Convention
72 on the Rights of the Child recognises the right for all children and young people to participate in
73 decision-making processes which involve them [3]. However, the World Health Organisation (WHO)
74 has acknowledged difficulties over consent for vaccination of adolescents because of their age, and
75 describes current practice through which countries are encouraged to adopt procedures that ensure
76 parents have been informed and agreed to the vaccination [4].

77
78 In most countries, the legal framework for consent requires parental or guardian permission for
79 young people aged below 18 years [4]. However, the age of consent for medical interventions, such
80 as vaccination programmes, is lower in some countries. In the United Kingdom (UK), Canada and
81 Sweden young women are legally able to override parental decisions if they are considered mature
82 enough to make, and understand the consequences of, the decision to vaccinate. In Australia and
83 the United States of America (USA) there are geographic variations of the age (12 to 17 years) that a
84 young person can consent to be vaccinated. Despite young people being supported by the law to
85 provide consent themselves, written parental consent is usually sought. In relation to the HPV
86 vaccination programme, this has been shown to act as an important barrier preventing young
87 women (usually aged 12 to 13 years) receiving the Human Papillomavirus (HPV) vaccine, with

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3 88 implications for vaccination programme coverage [5, 6]. Furthermore, it is a barrier with potential to
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5 89 reinforce health inequalities since lack of written parental consent may also be related to lower
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7 90 socioeconomic status and some ethnic groups [5, 7].
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10 91 To examine the issue of self-consent for the HPV vaccine in more detail, a mixed-methods study has
11
12 92 been funded by the National Institute for Health Research (NIHR) Research for Patient Benefit
13
14 93 Programme (RfPB) in England. The study is examining the practicality, acceptability and impact of
15
16 94 implementing new self-consent procedures for the schools-based HPV vaccination in two local
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18 95 authorities in the south-west of England [8]. There are three elements to the study: statistical
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20 96 analyses of routine data to assess the impact of self-consent on overall uptake levels and in relation
21
22 97 to socio-economic status, ethnicity and type of school; a process evaluation to examine the context,
23
24 98 implementation and response to the new consent procedures, and; a systematic review of the
25
26 99 evidence relating to self-consent for adolescent vaccines. The current protocol focusses on the
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28 100 systematic review which will run alongside, and inform, the other elements of the study.
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32
33 102 An initial scoping search suggested a paucity of peer-reviewed evidence in relation to self-consent
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35 103 procedures for HPV vaccination programmes. Since issues relating to self-consent for the HPV
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37 104 vaccination are likely to be relevant for other vaccinations delivered during adolescence we widened
38
39 105 the scope of the systematic review to identify and collate the evidence across all adolescent
40
41 106 vaccination programmes. We chose to restrict to vaccination programmes, rather than include
42
43 107 studies related to healthcare in general, to ensure the findings were relevant to the programme of
44
45 108 research described above. Therefore, the aim of this mixed-methods systematic review is to identify,
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47 109 appraise and synthesise the available qualitative and quantitative literature to gain understanding as
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49 110 to: (i) whether implementation of adolescent self-consent procedures can increase vaccination
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51 111 uptake, and; (ii) the related barriers and facilitators to implementation of adolescent self-consent
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53 112 procedures.
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3 114 **METHODS AND ANALYSIS**
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5 115 We are using mixed methods methodology within this systematic review to answer complementary
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7 116 research questions within one study. In addition to answering questions of the effectiveness of self-
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9 117 consent interventions at increasing uptake of adolescent vaccination programmes, the systematic
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11 118 review will also synthesise qualitative research comprising the views of young people and relevant
12
13 119 stakeholders to gain understanding of how self-consent procedures can be implemented effectively
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15 120 to increase uptake [9]. The findings from the qualitative and quantitative studies will be integrated
16
17 121 to produce recommendations for future policy and practice [9].
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21
22 123 This review protocol was prepared using the Preferred Reporting Items for Systematic Reviews and
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24 124 Meta-Analyses (PRISMA) Protocol guidelines [10] (Supplementary file 1) and has been registered
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26 125 with the International Prospective Register of Systematic Reviews (PROSPERO) (Registration
27
28 126 number: CRD42017084509).
29

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32 128 **Search strategy**
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34 129 A comprehensive search strategy has been developed to capture all literature relevant to adolescent
35
36 130 self-consent procedures for vaccination programmes by a reviewer (HB-F) experienced in
37
38 131 undertaking systematic reviews in the proposed research field and discussed with members of the
39
40 132 research team. The original search strategy developed for the Embase database has been adapted
41
42 133 for each included database (see below) and comprises a combination of text words and the
43
44 134 following medical subject headings (MeSH) indexing terms: 'child', 'adolescent', 'active
45
46 135 immunization', 'immunization', 'immunization programs', 'mass immunization', 'revaccination',
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48 136 'vaccination', 'diphtheria vaccine', 'diphtheria tetanus vaccine', 'diphtheria pertussis tetanus',
49
50 137 'haemophilus influenzae type b vaccine', 'hepatitis b vaccine', 'meningococcus vaccine', 'rubella
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52 138 vaccine', 'wart virus vaccine', 'papillomavirus vaccines', 'decision making', 'informed consent',
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3 139 'parental consent', 'treatment refusal' (Table 1). Study design filters will not be applied as diverse
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5 140 study designs are eligible for inclusion.

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9 142 **Databases**

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11 143 To ensure all the relevant literature is captured, we will search the following ten databases from
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13 144 inception to January 2018 and re-run six months later (June 2018) to inform the wider research
14
15 145 study as it progresses: Child Development & Adolescent Studies via EBSCOhost, Cochrane Central
16
17 146 Register of Controlled Trials via The Cochrane Library, Cochrane Reviews via The Cochrane Library,
18
19 147 Cumulative Index to Nursing and Allied Health Literature via EBSCOhost, Embase via Ovid, Health
20
21 148 Technology Assessment Database, Medline via Ovid, PsycINFO via Ovid, Social Care Online via Social
22
23 149 Care Institute for Excellence and Web of Science Core Collection: Social Sciences Citation Index and
24
25 150 Conference Proceedings Citation Index- Science. All abstracts will be saved using Endnote X8.

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30 152 **Inclusion and exclusion criteria**

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32 153 Quantitative studies will be eligible if vaccine uptake following implementation of self-consent
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34 154 procedures is reported for young people aged between ten and 18 years [11]. Qualitative studies
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36 155 reporting the views and experiences of key stakeholder in relation adolescent self-consent
37
38 156 procedures will also be included. Relevant stakeholders will vary with context but are likely to
39
40 157 include young people, parents or primary care givers, healthcare professionals, policy makers,
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42 158 community leaders, and teachers.

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47 160 We will include a range of study designs. To determine whether self-consent procedures can
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49 161 increase uptake of vaccination programmes, primary studies reporting parallel group randomised
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51 162 controlled trials, quasi-randomised trials, non-randomised controlled trials, controlled before and
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53 163 after studies, historically controlled studies, and retrospective or prospective cohort studies that
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55 164 include a control group will be eligible. Qualitative studies which use interviews, focus groups,

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3 165 observations, or open-ended questions allowing free-text responses in questionnaires will be
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5 166 included to explore views and behaviours related to young people's self-consent for vaccination.
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9 168 Conference abstracts, reviews, editorials, opinion pieces, dissertations, letters and books will only be
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11 169 included if they present original data. There will be no language or country of origin restriction
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13 170 imposed, and any relevant full text paper that is not written in English will be translated.
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18 172 **Study selection**

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20 173 Two reviewers will independently assess the titles and abstracts against the predefined eligibility
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22 174 criteria. Full-text publications of all potentially relevant articles will be retrieved and examined for
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24 175 relevance. Any disagreements arising will be resolved by discussion. The reference lists and
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26 176 bibliographies from relevant studies and systematic reviews will be hand-searched for additional
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28 177 primary studies not retrieved by the electronic search.
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32 179 We will use the reference management software EndNote X8 to remove duplicates and sort
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34 180 exclusions and inclusions. The search strategy and study selection process will be documented using
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36 181 a PRISMA flow diagram [12].
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41 183 **Data extraction**

42
43 184 At least two reviewers will independently extract data from selected studies using structured and
44
45 185 standardised data extraction forms used in our previous qualitative and quantitative systematic
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47 186 reviews. In instances where multiple publications relate to the same study, these will be reported
48
49 187 together. The following domains will be retrieved: study characteristics (authors, publication year,
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51 188 country, aim, study time period, study design, location, type of setting, data collection period, data
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53 189 collection method, sampling strategy, analysis), participant characteristics (participant age, sample
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55 190 size, vaccination status of participants, socioeconomic indicators, race/ethnicity, gender, and
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3 191 religion) and study results (uptake of vaccine, views and behaviours related to self-consent
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5 192 procedures). Where possible, authors will be contacted for missing or incomplete data.
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7 193 Disagreements will be resolved through discussion.
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11 195 **Risk of bias and quality assessment**

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13 196 For eligible primary studies, quality assessment will be undertaken to illustrate potential sources of
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15 197 bias. As we anticipate the majority of eligible studies will be observational, studies will not
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17 198 automatically be excluded on the basis of 'low' quality assessment if they are considered to
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19 199 contribute relevant information. We propose using the Cochrane Collaboration's handbook for the
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21 200 assessment of risks of bias for systematic review of randomised controlled studies and quasi-
22
23 201 randomised intervention studies [13], the Strengthening the Reporting of Observational Studies in
24
25 202 Epidemiology (STROBE) appraisal tool for observational studies [14], and the Critical Appraisal Skills
26
27 203 Programme criteria adapted for qualitative studies for evaluating qualitative research [15]. Quality
28
29 204 assessment of primary studies will be undertaken independently by two reviewers and then an
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31 205 overall assessment of 'high', 'medium', 'low', or 'unclear' will be assigned and reported.
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36 207 **Data synthesis: Quantitative studies**

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38 208 We anticipate that the primary quantitative studies will be reported narratively as preliminary
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40 209 searches specifically related to HPV vaccination programmes indicated a lack of published studies
41
42 210 and the likelihood of heterogeneity in relation to study design and reported outcomes. However, if
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44 211 sufficiently similar studies are captured we will consider combining individual study results through
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46 212 meta-analyses. To assess the heterogeneity between studies, we will use the Q-statistic and the I^2 -
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48 213 statistics [16]. Evidence of heterogeneity will be classified as weak, moderate and strong for
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50 214 corresponding I^2 of 25%, 50% and 75% respectively. If heterogeneity between studies is classified as
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52 215 weak, analyses will comprise adjusted odds ratios (aORs) where available, with unadjusted odds
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54 216 ratios used if not reported. Analyses will be undertaken using the meta-analysis function [17]
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3 217 available in Stata 15. We do not anticipate sufficient data being available to undertake sub-group
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5 218 analyses.

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9 220 **Data synthesis: Qualitative studies**

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11 221 The socio-ecological model [18] considers that behaviour is shaped by a complex interaction
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13 222 between factors operating at public policy, community, organisational, interpersonal, and
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15 223 intrapersonal levels. In a previous qualitative synthesis, we have shown that young women's access
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17 224 to the HPV vaccine is shaped by decisions at different levels of the socio-ecological model [5]. During
18
19 225 the analysis, we will use the socio-ecological model to provide a framework for understanding how
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21 226 barriers and facilitators operating at different levels of the model can provide access to, or prevent,
22
23 227 young people self-consenting in the context of vaccination programmes.
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27
28 229 To analyse the qualitative data, the methodology for thematic synthesis reported by Thomas and
29
30 230 Harden [19], assisted by the Framework method of qualitative data management [20], will be used.

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32 231 These methods are suited to studies with *a priori* aims and objectives. The overall purpose of the
33
34 232 synthesis will be to 'pool' the results from individual primary studies by initially separating the
35
36 233 findings, coding and interpreting the text, and then combining them through the identification of key
37
38 234 themes across the studies as well as similarities and differences within those themes [21]. Thematic
39
40 235 synthesis will be led by one reviewer reporting to the wider team about interpretation of the data as
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42 236 analysis progresses.
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47 238 Familiarisation with the dataset will begin with reading the full papers. Pertinent sections of the text
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49 239 reported in each primary study will represent the basic units for analysis. Primary charts of the text
50
51 240 will be constructed around key issues using the Framework Matrix within QSR NVivo10 software. For
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53 241 example, initial charts are likely to focus on 'barriers' and 'facilitators' to adolescent self-consent.
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55 242 The primary charts will be retained and revisited as required, but streamlined versions will be
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3 243 produced as the process of coding, summarising and synthesising the data progresses. In subsequent
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5 244 charts, key terms and phrases will be retained while repetition within studies and extraneous text
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7 245 are removed. During this process, overarching themes will be identified, and differences or
8
9 246 similarities explored within these emerging themes.

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12 13 248 **Data synthesis: Interrogation**

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15 249 The final stage of the analysis will aim to firstly comprise testing whether the recommendations
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17 250 developed from the qualitative studies have been addressed in evaluative studies retrieved for the
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19 251 review and, secondly, to examine whether interventions that match the recommendations result in
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21 252 higher uptake in vaccination [9].
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25 26 254 **ETHICS AND DISSEMINATION**

27
28 255 We will not seek ethical approval for this study because the secondary data to be collected cannot
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30 256 be linked to individuals. As far as we are aware, this will be the first systematic review to collate
31
32 257 evidence in relation to adolescent self-consent procedures for vaccination programmes. The review
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34 258 comprises part of a larger study. The findings of this review will inform the larger study evaluating
35
36 259 the practicality, acceptability and impact of new self-consent procedures for the schools-based HPV
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38 260 vaccination programme in the UK. Findings will also be used to make recommendations to improve
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40 261 self-consent procedures for young people in vaccination programmes. We anticipate the results of
41
42 262 this study this may be of interest to national and international stakeholders interested in improving
43
44 263 uptake in adolescent vaccination programmes.
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48 49 265 **FULL REFERENCES**

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21
22 337 **LIST OF ABBREVIATIONS**

23
24 338 HPV: Human Papillomavirus

25
26 339 WHO: World Health Organisation

27
28 340 UK: United Kingdom

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30 341 USA: United States of America

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32 342 PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol

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34 343 PROSPERO: Prospective Register of Systematic Reviews

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36 344 MeSH: Medical Subject Headings

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38 345 STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

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40 346 aOR: Adjusted Odds Ratio

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42 347 OR: Odds Ratio

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47 349 **AUTHORS' CONTRIBUTIONS**

48
49 350 All authors were involved in the conception and design of the research. SA is Principal Investigator;

50
51 351 HB-F is study manager and lead researcher; JM and MH advise on systematic review methodology.

52
53 352 HB-F wrote the first draft and all authors contributed to the final version of the manuscript.

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3 354 **FUNDING STATEMENT**
4

5 355 This work is supported by the National Institute for Health Research for Patient Benefit (NIHR RfPB)
6
7 356 programme (project number PB-PG-0416-20013). The work is also undertaken with the support of
8
9 357 the NIHR Health Protection Research Unit in Evaluation of Interventions. The views and opinions
10
11 358 expressed therein are those of the authors and do not necessarily reflect those of the NIHR RfPB
12
13 359 Programme, the Department of Health, or Public Health England.
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17 361 **COMPETING INTERESTS STATEMENT**
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19 362 The authors declare there are no competing interests.
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364 Table 1. Embase search strategy

1. child/
2. adolescent/
3. ("Young people#" OR "young person#" OR "young offender#" OR adolescent# OR adolescence OR youth# OR minor# OR teen OR teens OR teenage OR teenaged OR teenager# OR juvenile# OR pupil# OR boy# OR girl# OR underage# OR daughter# or son# (school AND dropout#) OR (school AND "drop out#") OR "school aged").mp.
4. active immunization/
5. immunization/
6. immunization programs/
7. mass immunization/
8. revaccination/
9. vaccination/
10. diphtheria vaccine/
11. diphtheria tetanus vaccine/
12. diphtheria pertussis tetanus Haemophilus influenzae type b vaccine/
13. hepatitis B vaccine/
14. meningococcus vaccine/
15. rubella vaccine/
16. wart virus vaccine/
17. Papillomavirus Vaccines/
18. (cervical cancer or diphtheria or diphtheria or diphteria or DtaP or DTP or Hep B or hepatitis or HPV or measles or MenC or MenACWY or meningitis or Meningococcal or Neisseria meningitidis or papillomavirus or pertus* or rubella or rubeola or td?ipv or tetanus or wart virus or whoop*).tw.
19. (policy OR program*)
20. (immuniz* OR immunis* OR immunother* OR inoculat* OR innoculat* OR prophyla* OR revaccinat* OR vaccin*).mp.
21. Decision making/
22. Informed consent/
23. Parental consent/
24. Treatment refusal/
25. (assent* OR competen* OR decision-making OR decision making OR Gillick OR Fraser OR inform* consent OR mental capacity OR minor consent OR parent* consent OR permission* OR presume* consent OR treatment refusal OR self consent OR self-consent OR opt-out OR opt-in).mp.
26. 1 or 2 or 3
27. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
28. 18 and 20
29. 19 and 20
30. 27 or 28 or 29
31. 21 or 22 or 23 or 24 or 25
32. 26 and 30 or 31

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 5:15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	X	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	X	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	X	<input type="checkbox"/>	48, 124-25
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	<input type="checkbox"/>	3-18
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X	<input type="checkbox"/>	345-348
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	X	
Support					
Sources	5a	Indicate sources of financial or other support for the review	X	<input type="checkbox"/>	350-355
Sponsor	5b	Provide name for the review funder and/or sponsor	X	<input type="checkbox"/>	350-355
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	<input type="checkbox"/>	350-355
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	X	<input type="checkbox"/>	63-111

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	<input type="checkbox"/>	30-34, 108-111
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	X	<input type="checkbox"/>	140-168
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	X	<input type="checkbox"/>	140-148
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	X	<input type="checkbox"/>	360
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	<input type="checkbox"/>	148, 177-178
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	X	<input type="checkbox"/>	170-203
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	<input type="checkbox"/>	181-191
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	X	<input type="checkbox"/>	181-191
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	<input type="checkbox"/>	189
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	<input type="checkbox"/>	193-203
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	X	<input type="checkbox"/>	205-215
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	X	<input type="checkbox"/>	205-215

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	X	<input type="checkbox"/>	205-215
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X	<input type="checkbox"/>	206-208, 217-249
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	X	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	X	

BMJ Open

Adolescent self-consent for vaccinations: protocol for a mixed methods systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-021335.R1
Article Type:	Protocol
Date Submitted by the Author:	26-Mar-2018
Complete List of Authors:	Batista, Harriet; University of Bristol, Population Health Sciences: Bristol Medical School Hickman, M; University of Bristol, Population Health Sciences: Bristol Medical School Macleod, John; University of Bristol, Population Health Sciences: Bristol Medical School Audrey, Suzanne; University of Bristol, Population Health Sciences: Bristol Medical School
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	Self-consent, Vaccination, Systematic review, Mixed methods, Adolescents

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3 1 **TITLE: Adolescent self-consent for vaccinations: protocol for a mixed methods systematic review**

4
5 2

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39 19

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41 20 **Word count: 2,219**

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43 21

44
45 22 **Key words**

46
47 23 Self-consent, Vaccination, Systematic review, Adolescents, Mixed Methods

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49 24

1
2
3 25 **ABSTRACT**
4

5 26 **Introduction:** The recent global expansion of routine adolescent vaccination programmes has the
6
7 27 potential to protect young people against the acquisition of infectious disease and improve their
8
9 28 health. Although in many countries the legal framework supports young people to provide consent
10
11 29 for medical interventions if they are considered competent, written parental consent can act as a
12
13 30 barrier to uptake as it is frequently a condition of adolescent vaccination programmes. The aim of
14
15 31 this systematic review protocol is to document the methods which will be used to identify, appraise
16
17 32 and synthesise the available qualitative and quantitative evidence to address: (i) whether
18
19 33 implementation of adolescent self-consent procedures can increase vaccination uptake, and; (ii) the
20
21 34 barriers and facilitators to implementation of adolescent self-consent procedures.
22

23
24 35 **Methods and analysis:** Comprehensive search strategy of all relevant electronic databases for both
25
26 36 qualitative and quantitative studies using predefined inclusion and exclusion criteria. At least two
27
28 37 authors will independently review titles and abstracts, extract data and assess the methodological
29
30 38 quality of eligible primary studies, resolving disagreements by consensus. Quantitative studies will
31
32 39 be reported narratively and where possible pooled in a meta-analysis using a random-effects model.
33
34 40 The findings of qualitative primary studies will be extracted, interpreted and synthesised to identify
35
36 41 overarching themes as well as similarities and differences within those themes.
37

38
39 42 **Ethics and dissemination:** As this systematic review involves analysis of secondary data, the study
40
41 43 does not require ethical approvals. We will use our findings to assess whether the evidence supports
42
43 44 the hypothesis that self-consent procedures can increase coverage of adolescent vaccination
44
45 45 programmes. We will identify barriers and facilitators to the implementation of adolescent self-
46
47 46 consent for vaccination, and make recommendations for policy-makers and practitioners in relation
48
49 47 to consent procedures within vaccination programmes for young people.
50

51 48 **Systematic review registration:** PROSPERO CRD42017084509
52

53 49 **Word count:** 284
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3 51 **Strengths and limitations of this study**
4

5 52 • The mixed methods systematic review will answer complementary research questions about
6
7 53 self-consent for adolescent vaccination programmes
8

9 54 • Robust systematic review methodology will be used to identify, appraise and synthesise the
10
11 55 relevant qualitative and quantitative literature
12

13 56 • Lack of primary studies and heterogeneity of eligible studies in terms of study design, population
14
15 57 and reporting may limit our ability to infer conclusions in relation to the research questions
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59 INTRODUCTION

60 In recent years, the number of routine vaccinations recommended during adolescence have
61 increased, and include vaccines that protect against tetanus, diphtheria, meningitis and human
62 papillomavirus (HPV) acquisition [1, 2]. Provided sufficient coverage is achieved, the expansion of
63 adolescent vaccination programmes may improve young people's health by protecting them from
64 potentially life- threatening infectious diseases.

65
66 The introduction of new adolescent vaccination programmes is relevant to the debate about young
67 people's capacity to provide consent to receive medical treatment. The United Nations Convention
68 on the Rights of the Child recognises the right for all children and young people to participate in
69 decision-making processes which involve them [3]. However, the World Health Organisation (WHO)
70 has acknowledged difficulties over consent for vaccination of adolescents because of their age, and
71 describes current practice through which countries are encouraged to adopt procedures that ensure
72 parents have been informed and agreed to the vaccination [4].

73
74 In most countries, the legal framework for consent requires parental or guardian permission for
75 young people aged below 18 years [4]. However, the age of consent for medical interventions, such
76 as vaccination programmes, is lower in some countries. In the United Kingdom (UK), Canada and
77 Sweden young women are legally able to override parental decisions if they are considered mature
78 enough to make, and understand the consequences of, the decision to vaccinate. In Australia and
79 the United States of America (USA) there are geographic variations of the age (12 to 17 years) that a
80 young person can consent to be vaccinated. Despite young people being supported by the law to
81 provide consent themselves, written parental consent is usually sought. In relation to the HPV
82 vaccination programme, this has been shown to act as an important barrier preventing young
83 women (usually aged 12 to 13 years) receiving the Human Papillomavirus (HPV) vaccine, with

1
2
3 84 implications for vaccination programme coverage [5, 6]. Furthermore, it is a barrier with potential to
4
5 85 reinforce health inequalities since lack of written parental consent may also be related to lower
6
7 86 socioeconomic status and some ethnic groups [5, 7].
8
9

10 87 To examine the issue of self-consent for the HPV vaccine in more detail, a mixed-methods study has
11
12 88 been funded by the National Institute for Health Research (NIHR) Research for Patient Benefit
13
14 89 Programme (RfPB) in England. The study is examining the practicality, acceptability and impact of
15
16 90 implementing new self-consent procedures for the schools-based HPV vaccination in two local
17
18 91 authorities in the south-west of England [8]. There are three elements to the study: statistical
19
20 92 analyses of routine data to assess the impact of self-consent on overall uptake levels and in relation
21
22 93 to socio-economic status, ethnicity and type of school; a process evaluation to examine the context,
23
24 94 implementation and response to the new consent procedures, and; a systematic review of the
25
26 95 evidence relating to self-consent for adolescent vaccines. The current protocol focusses on the
27
28 96 systematic review which will run alongside, and inform, the other elements of the study.
29
30

31 97

32
33 98 An initial scoping search suggested a paucity of peer-reviewed evidence in relation to self-consent
34
35 99 procedures for HPV vaccination programmes. Since issues relating to self-consent for the HPV
36
37 100 vaccination are likely to be relevant for other vaccinations delivered during adolescence we widened
38
39 101 the scope of the systematic review to identify and collate the evidence across all adolescent
40
41 102 vaccination programmes. We chose to restrict to vaccination programmes, rather than include
42
43 103 studies related to healthcare in general, to ensure the findings were relevant to the programme of
44
45 104 research described above. Therefore, the aim of this mixed-methods systematic review is to identify,
46
47 105 appraise and synthesise the available qualitative and quantitative literature to gain understanding as
48
49 106 to: (i) whether implementation of adolescent self-consent procedures can increase vaccination
50
51 107 uptake, and; (ii) the related barriers and facilitators to implementation of adolescent self-consent
52
53 108 procedures.
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3 1094
5 110 **METHODS AND ANALYSIS**

6
7 111 We are using mixed methods methodology within this systematic review to answer complementary
8
9 112 research questions within one study. In addition to answering questions of the effectiveness of self-
10
11 113 consent interventions at increasing uptake of adolescent vaccination programmes, the systematic
12
13 114 review will also synthesise qualitative research comprising the views of young people and relevant
14
15 115 stakeholders to gain understanding of how self-consent procedures can be implemented effectively
16
17 116 to increase uptake [9]. The findings from the qualitative and quantitative studies will be integrated
18
19 117 to produce recommendations for future policy and practice [9].
20

21
22 118

23
24 119 This review protocol was prepared using the Preferred Reporting Items for Systematic Reviews and
25
26 120 Meta-Analyses (PRISMA) Protocol guidelines [10] (Supplementary file 1) and has been registered
27
28 121 with the International Prospective Register of Systematic Reviews (PROSPERO) (Registration
29
30 122 number: CRD42017084509).
31

32 123

33
34 124 **Search strategy**

35
36 125 A comprehensive search strategy has been developed to capture all literature relevant to adolescent
37
38 126 self-consent procedures for vaccination programmes by a reviewer (HB-F) experienced in
39
40 127 undertaking systematic reviews in the proposed research field and discussed with members of the
41
42 128 research team. The original search strategy developed for the Embase database has been adapted
43
44 129 for each included database (see below) and comprises a combination of text words and the
45
46 130 following medical subject headings (MeSH) indexing terms: 'child', 'adolescent', 'active
47
48 131 immunization', 'immunization', 'immunization programs', 'mass immunization', 'revaccination',
49
50 132 'vaccination', 'diphtheria vaccine', 'diphtheria tetanus vaccine', 'diphtheria pertussis tetanus',
51
52 133 'haemophilus influenzae type b vaccine', 'hepatitis b vaccine', 'meningococcus vaccine', 'rubella
53
54 134 vaccine', 'wart virus vaccine', 'papillomavirus vaccines', 'decision making', 'informed consent',
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3 135 'parental consent', 'treatment refusal' (Table 1). Study design filters or restrictions by setting will not
4
5 136 be applied as the study aims to be inclusive in relation to study design and settings eligible for
6
7 137 inclusion.
8

9 138

10 11 139 **Databases**

12
13 140 To ensure all the relevant literature is captured, we will search the following ten databases from
14
15 141 inception to January 2018 and re-run six months later (June 2018) to inform the wider research
16
17 142 study as it progresses: Child Development & Adolescent Studies via EBSCOhost, Cochrane Central
18
19 143 Register of Controlled Trials via The Cochrane Library, Cochrane Reviews via The Cochrane Library,
20
21 144 Cumulative Index to Nursing and Allied Health Literature via EBSCOhost, Embase via Ovid, Health
22
23 145 Technology Assessment Database, Medline via Ovid, PsycINFO via Ovid, Social Care Online via Social
24
25 146 Care Institute for Excellence and Web of Science Core Collection: Social Sciences Citation Index and
26
27 147 Conference Proceedings Citation Index- Science. All abstracts will be saved using Endnote X8.
28

29
30 148

31 32 149 **Inclusion and exclusion criteria**

33
34 150 Quantitative studies will be eligible if vaccine uptake following implementation of self-consent
35
36 151 procedures is reported for young people aged between ten and 18 years [11]. Qualitative studies
37
38 152 reporting the views and experiences of key stakeholders in relation adolescent self-consent
39
40 153 procedures will also be included. Studies related to consent procedures solely targeting parents of
41
42 154 adolescents, or early childhood and adult vaccination programmes will not be eligible for inclusion.
43
44 155 Relevant stakeholders will vary with context but are likely to include young people, parents or
45
46 156 primary care givers, healthcare professionals, policy makers, community leaders and teachers.
47

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50
51 158 We will include a range of study designs. To determine whether self-consent procedures can
52
53 159 increase uptake of vaccination programmes, primary studies reporting parallel group randomised
54
55 160 controlled trials, quasi-randomised trials, non-randomised controlled trials, controlled before and
56
57

1
2
3 161 after studies, historically controlled studies, and retrospective or prospective cohort studies that
4
5 162 include a control group will be eligible. Qualitative studies which use interviews, focus groups,
6
7 163 observations, or open-ended questions allowing free-text responses in questionnaires will be
8
9 164 included to explore views and behaviours related to young people's self-consent for vaccination.

10
11 165

12
13 166 Conference abstracts, reviews, editorials, opinion pieces, dissertations, letters and books will only be
14
15 167 included if they present original data. There will be no language or country of origin restriction
16
17 168 imposed, and any relevant full text paper that is not written in English will be translated.

18
19 169

20 21 22 170 **Study selection**

23
24 171 Two reviewers will independently assess the titles and abstracts against the predefined eligibility
25
26 172 criteria. Full-text publications of all potentially relevant articles will be retrieved and examined for
27
28 173 relevance. Any disagreements arising will be resolved by discussion. The reference lists and
29
30 174 bibliographies from relevant studies and systematic reviews will be hand-searched for additional
31
32 175 primary studies not retrieved by the electronic search.

33
34 176

35
36 177 We will use the reference management software EndNote X8 to remove duplicates and sort
37
38 178 exclusions and inclusions. The search strategy and study selection process will be documented using
39
40 179 a PRISMA flow diagram [12].

41
42 180

43 44 45 181 **Data extraction**

46
47 182 At least two reviewers will independently extract data from selected studies using structured and
48
49 183 standardised data extraction forms used in our previous qualitative and quantitative systematic
50
51 184 reviews. In instances where multiple publications relate to the same study, these will be reported
52
53 185 together. The following domains will be retrieved: study characteristics (authors, publication year,
54
55 186 country, aim, study time period, study design, location, type of setting, data collection period, data

1
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3 187 collection method, sampling strategy, analysis, participant characteristics (participant age, sample
4
5 188 size, vaccination status of participants, socioeconomic indicators, race/ethnicity, gender, and
6
7 189 religion) and study results (uptake of vaccine, psychological outcomes, healthcare service use,
8
9 190 incidence of vaccine preventable disease, views and behaviours related to self-consent procedures,
10
11 191 authors' reported conflicts of interest and study funding sources). We will also record data relating
12
13 192 to the possible harms resulting from self-consent procedures (e.g. conflict with parents, healthcare
14
15 193 professional anxiety). Where possible, authors will be contacted for missing or incomplete data.
16
17 194 Disagreements will be resolved through discussion.
18
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195

196 **Risk of bias and quality assessment**

197 For eligible primary studies, quality assessment will be undertaken to illustrate potential sources of
198 bias. As we anticipate the majority of eligible studies will be observational, studies will not
199 automatically be excluded on the basis of 'low' quality assessment if they are considered to
200 contribute relevant information. We propose using: the Cochrane Collaboration's handbook for the
201 assessment of risks of bias for systematic review of randomised controlled studies and quasi-
202 randomised intervention studies [13] Risk Of Bias in Non Randomised Studies of Interventions
203 (ROBINS-I) [14] ;, the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional
204 Studies [15], and; the Critical Appraisal Skills Programme criteria adapted for qualitative studies for
205 evaluating qualitative research [16]. Quality assessment of primary studies will be undertaken
206 independently by two reviewers and recorded in an excel spreadsheet. An overall assessment of
207 'high', 'medium', 'low', or 'unclear' will be assigned and reported.
208

209

209 **Data synthesis: Quantitative studies**

210 We anticipate that the primary quantitative studies will be reported narratively as preliminary
211 searches specifically related to HPV vaccination programmes indicated a lack of published studies
212 and the likelihood of heterogeneity in relation to study design and reported outcomes. However, if

1
2
3 213 sufficiently similar studies are captured we will consider combining individual study results through
4
5 214 meta-analyses. To assess the heterogeneity between studies, we will use the Q-statistic and the I^2 -
6
7 215 statistics [17]. Evidence of heterogeneity will be classified as weak, moderate and strong for
8
9 216 corresponding I^2 of 25%, 50% and 75% respectively. If heterogeneity between studies is classified as
10
11 217 weak, analyses will comprise adjusted odds ratios (aORs) where available, with unadjusted odds
12
13 218 ratios used if not reported. Analyses will be undertaken using the meta-analysis function [18]
14
15 219 available in Stata 15. We do not anticipate sufficient data being available to undertake sub-group
16
17 220 analyses. However, if sufficient data were reported we propose two sub-group analyses to compare
18
19 221 impact of self-consent procedures by: (i) setting (healthcare vs. school) and (ii) age of participants
20
21 222 (less than 14 years old vs. 14 years and greater).
22
23

24 223

25 224 **Data synthesis: Qualitative studies**

26
27
28 225 The socio-ecological model [19] considers that behaviour is shaped by a complex interaction
29
30 226 between factors operating at public policy, community, organisational, interpersonal and
31
32 227 intrapersonal levels. In a previous qualitative synthesis, we have shown that young women's access
33
34 228 to the HPV vaccine is shaped by decisions at different levels of the socio-ecological model [5]. During
35
36 229 the analysis, we will use the socio-ecological model to provide a framework for understanding how
37
38 230 barriers and facilitators operating at different levels of the model can provide access to, or prevent,
39
40 231 young people self-consenting in the context of vaccination programmes.
41
42

43 232

44
45 233 To analyse the qualitative data, the methodology for thematic synthesis reported by Thomas and
46
47 234 Harden [20], assisted by the Framework method of qualitative data management [21], will be used.

48
49 235 These methods are suited to studies with *a priori* aims and objectives. The overall purpose of the
50
51 236 synthesis will be to 'pool' the results from individual primary studies by initially separating the
52
53 237 findings, coding and interpreting the text, and then combining them through the identification of key
54
55 238 themes across the studies as well as similarities and differences within those themes [22]. Thematic
56
57
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59

239 synthesis will be led by one reviewer reporting to the wider team about interpretation of the data as
240 analysis progresses.

241

242 Familiarisation with the dataset will begin with reading the full papers. Pertinent sections of the text
243 reported in each primary study will represent the basic units for analysis. Primary charts of the text
244 will be constructed around key issues using the Framework Matrix within QSR NVivo10 software. For
245 example, initial charts are likely to focus on 'barriers' and 'facilitators' to adolescent self-consent.
246 The primary charts will be retained and revisited as required. Streamlined versions will be produced
247 as the process of coding, summarising and synthesising the data progresses. In subsequent charts,
248 key terms and phrases will be retained while repetition within studies and extraneous text are
249 removed. During this process, overarching themes will be identified, and differences or similarities
250 explored within these emerging themes.

251

252 **Data synthesis: Interrogation**

253 The final stage of the analysis will aim, firstly, to test whether the recommendations developed from
254 the qualitative studies have been addressed in evaluative studies retrieved for the review and,
255 secondly, to examine whether interventions that match the recommendations result in higher
256 uptake in vaccination [9].

257

258 **Patient and public involvement**

259 The Bristol Young People's Advisory Group (YPAG) comprises young people aged ten to 17 years who
260 are interested in healthcare and research. They meet regularly to help researchers with their
261 projects and have been consulted about the design of the wider study and participant materials.
262 They will also be invited to an event at the end of the study to consider findings and
263 recommendations with the young people, parents, immunisation nurses and school staff involved in
264 the study.

265

266 ETHICS AND DISSEMINATION

267 We will not seek ethical approval for this study because the secondary data to be collected cannot
268 be linked to individuals. As far as we are aware, this will be the first systematic review to collate
269 evidence in relation to adolescent self-consent procedures for vaccination programmes. The review
270 comprises part of a larger study. The findings of this review will inform the larger study evaluating
271 the practicality, acceptability and impact of new self-consent procedures for the schools-based HPV
272 vaccination programme in the UK. Findings will also be used to make recommendations to improve
273 self-consent procedures for young people in vaccination programmes. We anticipate the results of
274 this study this may be of interest to national and international stakeholders interested in improving
275 uptake in adolescent vaccination programmes.

276

277 FULL REFERENCES

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3 352
4 353 **LIST OF ABBREVIATIONS**
5
6 354 HPV: Human Papillomavirus
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8 355 WHO: World Health Organisation
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10 356 UK: United Kingdom
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12 357 USA: United States of America
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14 358 PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol
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16 359 PROSPERO: Prospective Register of Systematic Reviews
17
18 360 MeSH: Medical Subject Headings
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20 361 STROBE: Strengthening the Reporting of Observational Studies in Epidemiology
21
22 362 aOR: Adjusted Odds Ratio
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24 363 OR: Odds Ratio
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26 364 YPAG: Young Person's Advisory Group
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31 366 **AUTHORS' CONTRIBUTIONS**

32
33 367 All authors were involved in the conception and design of the research. SA is Principal Investigator;
34
35 368 HB-F is study manager and lead researcher; JM and MH advise on systematic review methodology.
36
37 369 HB-F wrote the first draft and all authors contributed to the final version of the manuscript.
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41 371 **FUNDING STATEMENT**

42
43 372 This work is supported by the National Institute for Health Research for Patient Benefit (NIHR RfPB)
44
45 373 programme (project number PB-PG-0416-20013). The work is also undertaken with the support of
46
47 374 the NIHR Health Protection Research Unit in Evaluation of Interventions. The work was also
48
49 375 undertaken with the support of The Centre for the Development and Evaluation of Complex
50
51 376 Interventions for Public Health Improvement (DECIPHer), a UKCRC Public Health Research Centre of
52
53 377 Excellence. Joint funding (MR/KO232331/1) from the British Heart Foundation, Cancer Research UK,
54
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3 378 Economic and Social Research Council, Medical Research Council, the Welsh Government and the
4
5 379 Wellcome Trust, under the auspices of the UK Clinical Research Collaboration, is gratefully
6
7 380 acknowledged. The views and opinions expressed therein are those of the authors and do not
8
9 381 necessarily reflect those of the NIHR RfPB Programme, the Department of Health, or Public Health
10
11 382 England.

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15 384 **COMPETING INTERESTS STATEMENT**

16
17 385 The authors declare there are no competing interests.

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387 Table 1. Embase search strategy

1. child/
2. adolescent/
3. ("Young people#" OR "young person#" OR "young offender#" OR adolescent# OR adolescence OR youth# OR minor# OR teen OR teens OR teenage OR teenaged OR teenager# OR juvenile# OR pupil# OR boy# OR girl# OR underage# OR daughter# or son# (school AND dropout#) OR (school AND "drop out#") OR "school aged").mp.
4. active immunization/
5. immunization/
6. immunization programs/
7. mass immunization/
8. revaccination/
9. vaccination/
10. diphtheria vaccine/
11. diphtheria tetanus vaccine/
12. diphtheria pertussis tetanus Haemophilus influenzae type b vaccine/
13. hepatitis B vaccine/
14. meningococcus vaccine/
15. rubella vaccine/
16. wart virus vaccine/
17. Papillomavirus Vaccines/
18. (cervical cancer or diphtheria or diphtheria or diphteria or DtaP or DTP or Hep B or hepatitis or HPV or measles or MenC or MenACWY or meningitis or Meningococcal or Neisseria meningitidis or papillomavirus or pertus* or rubella or rubeola or td?ipv or tetanus or wart virus or whoop*).tw.
19. (policy OR program*)
20. (immuniz* OR immunis* OR immunother* OR inoculat* OR innoculat* OR prophyla* OR revaccinat* OR vaccin*).mp.
21. Decision making/
22. Informed consent/
23. Parental consent/
24. Treatment refusal/
25. (assent* OR competen* OR decision-making OR decision making OR Gillick OR Fraser OR inform* consent OR mental capacity OR minor consent OR parent* consent OR permission* OR presume* consent OR treatment refusal OR self consent OR self-consent OR opt-out OR opt-in).mp.
26. 1 or 2 or 3
27. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
28. 18 and 20
29. 19 and 20
30. 27 or 28 or 29
31. 21 or 22 or 23 or 24 or 25
32. 26 and 30 or 31

PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 5:15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	X	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	X	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	X	<input type="checkbox"/>	48, 120-21
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	<input type="checkbox"/>	3-18
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X	<input type="checkbox"/>	362-365
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	X	
Support					
Sources	5a	Indicate sources of financial or other support for the review	X	<input type="checkbox"/>	367-377
Sponsor	5b	Provide name for the review funder and/or sponsor	X	<input type="checkbox"/>	367-377
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	<input type="checkbox"/>	367-377
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	X	<input type="checkbox"/>	59-107

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	<input type="checkbox"/>	32-34, 104-107
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	X	<input type="checkbox"/>	147-166
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	X	<input type="checkbox"/>	147-166
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	X	<input type="checkbox"/>	382
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	<input type="checkbox"/>	145, 175-176
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	X	<input type="checkbox"/>	168-177
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	<input type="checkbox"/>	179-192
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	X	<input type="checkbox"/>	183-192
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	<input type="checkbox"/>	183-192
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	<input type="checkbox"/>	194-205
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	X	<input type="checkbox"/>	207-220
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	X	<input type="checkbox"/>	207-220

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	X	<input type="checkbox"/>	217-220
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X	<input type="checkbox"/>	208-210, 222-254
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	X	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	X	

BMJ Open

Adolescent self-consent for vaccinations: protocol for a mixed methods systematic review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-021335.R2
Article Type:	Protocol
Date Submitted by the Author:	19-Apr-2018
Complete List of Authors:	Batista, Harriet; University of Bristol, Population Health Sciences: Bristol Medical School Hickman, M; University of Bristol, Population Health Sciences: Bristol Medical School Macleod, John; University of Bristol, Population Health Sciences: Bristol Medical School Audrey, Suzanne; University of Bristol, Population Health Sciences: Bristol Medical School
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	Self-consent, Vaccination, Systematic review, Mixed methods, Adolescents

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1 **TITLE: Adolescent self-consent for vaccinations: protocol for a mixed methods systematic review**

2

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4 Professor Matthew Hickman, Population Health Sciences, Bristol Medical School, University of

5 Bristol.

6 Professor John Macleod, Population Health Sciences, Bristol Medical School, University of Bristol.

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19

20 **Word count: 2,219**

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22 **Key words**

23 Self-consent, Vaccination, Systematic review, Adolescents, Mixed Methods

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1
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3 25 **ABSTRACT**
4

5 26 **Introduction:** The recent global expansion of routine adolescent vaccination programmes has the
6
7 27 potential to protect young people against the acquisition of infectious disease and improve their
8
9 28 health. Although in many countries the legal framework supports young people to provide consent
10
11 29 for medical interventions if they are considered competent, written parental consent can act as a
12
13 30 barrier to uptake as it is frequently a condition of adolescent vaccination programmes. The aim of
14
15 31 this systematic review protocol is to document the methods which will be used to identify, appraise
16
17 32 and synthesise the available qualitative and quantitative evidence to address: (i) whether
18
19 33 implementation of adolescent self-consent procedures can increase vaccination uptake, and; (ii) the
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21 34 barriers and facilitators to implementation of adolescent self-consent procedures.
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24 35 **Methods and analysis:** Comprehensive search strategy of all relevant electronic databases for both
25
26 36 qualitative and quantitative studies using predefined inclusion and exclusion criteria. At least two
27
28 37 authors will independently review titles and abstracts, extract data and assess the methodological
29
30 38 quality of eligible primary studies, resolving disagreements by consensus. Quantitative studies will
31
32 39 be reported narratively and where possible pooled in a meta-analysis using a random-effects model.
33
34 40 The findings of qualitative primary studies will be extracted, interpreted and synthesised to identify
35
36 41 overarching themes as well as similarities and differences within those themes.
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39 42 **Ethics and dissemination:** As this systematic review involves analysis of secondary data, the study
40
41 43 does not require ethical approvals. We will use our findings to assess whether the evidence supports
42
43 44 the hypothesis that self-consent procedures can increase coverage of adolescent vaccination
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45 45 programmes. We will identify barriers and facilitators to the implementation of adolescent self-
46
47 46 consent for vaccination, and make recommendations for policy-makers and practitioners in relation
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49 47 to consent procedures within vaccination programmes for young people.
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51 48 **Systematic review registration:** PROSPERO CRD42017084509
52

53 49 **Word count:** 284
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3 51 **Strengths and limitations of this study**
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5 52 • The mixed methods systematic review will answer complementary research questions about
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7 53 self-consent for adolescent vaccination programmes
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9 54 • Robust systematic review methodology will be used to identify, appraise and synthesise the
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11 55 relevant qualitative and quantitative literature
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13 56 • Lack of primary studies and heterogeneity of eligible studies in terms of study design, population
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15 57 and reporting may limit our ability to infer conclusions in relation to the research questions
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59 INTRODUCTION

60 In recent years, the number of routine vaccinations recommended during adolescence have
61 increased, and include vaccines that protect against tetanus, diphtheria, meningitis and human
62 papillomavirus (HPV) acquisition [1, 2]. Provided sufficient coverage is achieved, the expansion of
63 adolescent vaccination programmes may improve young people's health by protecting them from
64 potentially life- threatening infectious diseases.

65
66 The introduction of new adolescent vaccination programmes is relevant to the debate about young
67 people's capacity to provide consent to receive medical treatment. The United Nations Convention
68 on the Rights of the Child recognises the right for all children and young people to participate in
69 decision-making processes which involve them [3]. However, the World Health Organisation (WHO)
70 has acknowledged difficulties over consent for vaccination of adolescents because of their age, and
71 describes current practice through which countries are encouraged to adopt procedures that ensure
72 parents have been informed and agreed to the vaccination [4].

73
74 In most countries, the legal framework for consent requires parental or guardian permission for
75 young people aged below 18 years [4]. However, the age of consent for medical interventions, such
76 as vaccination programmes, is lower in some countries. In the United Kingdom (UK), Canada and
77 Sweden young women are legally able to override parental decisions if they are considered mature
78 enough to make, and understand the consequences of, the decision to vaccinate. In Australia and
79 the United States of America (USA) there are geographic variations of the age (12 to 17 years) that a
80 young person can consent to be vaccinated. Despite young people being supported by the law to
81 provide consent themselves, written parental consent is usually sought. In relation to the HPV
82 vaccination programme, this has been shown to act as an important barrier preventing young
83 women (usually aged 12 to 13 years) receiving the Human Papillomavirus (HPV) vaccine, with

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3 84 implications for vaccination programme coverage [5, 6]. Furthermore, it is a barrier with potential to
4
5 85 reinforce health inequalities since lack of written parental consent may also be related to lower
6
7 86 socioeconomic status and some ethnic groups [5, 7].
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10 87 To examine the issue of self-consent for the HPV vaccine in more detail, a mixed-methods study has
11
12 88 been funded by the National Institute for Health Research (NIHR) Research for Patient Benefit
13
14 89 Programme (RfPB) in England. The study is examining the practicality, acceptability and impact of
15
16 90 implementing new self-consent procedures for the schools-based HPV vaccination in two local
17
18 91 authorities in the south-west of England [8]. There are three elements to the study: statistical
19
20 92 analyses of routine data to assess the impact of self-consent on overall uptake levels and in relation
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22 93 to socio-economic status, ethnicity and type of school; a process evaluation to examine the context,
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24 94 implementation and response to the new consent procedures, and; a systematic review of the
25
26 95 evidence relating to self-consent for adolescent vaccines. The current protocol focusses on the
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28 96 systematic review which will run alongside, and inform, the other elements of the study.
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33 98 An initial scoping search suggested a paucity of peer-reviewed evidence in relation to self-consent
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35 99 procedures for HPV vaccination programmes. Since issues relating to self-consent for the HPV
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37 100 vaccination are likely to be relevant for other vaccinations delivered during adolescence we widened
38
39 101 the scope of the systematic review to identify and collate the evidence across all adolescent
40
41 102 vaccination programmes. We chose to restrict to vaccination programmes, rather than include
42
43 103 studies related to healthcare in general, to ensure the findings were relevant to the programme of
44
45 104 research described above. Therefore, the aim of this mixed-methods systematic review is to identify,
46
47 105 appraise and synthesise the available qualitative and quantitative literature to gain understanding as
48
49 106 to: (i) whether implementation of adolescent self-consent procedures can increase vaccination
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51 107 uptake, and; (ii) the related barriers and facilitators to implementation of adolescent self-consent
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53 108 procedures.
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3 1094
5 110 **METHODS AND ANALYSIS**

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7 111 We are using mixed methods methodology within this systematic review to answer complementary
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9 112 research questions within one study. In addition to answering questions of the effectiveness of self-
10
11 113 consent interventions at increasing uptake of adolescent vaccination programmes, the systematic
12
13 114 review will also synthesise qualitative research comprising the views of young people and relevant
14
15 115 stakeholders to gain understanding of how self-consent procedures can be implemented effectively
16
17 116 to increase uptake [9]. The findings from the qualitative and quantitative studies will be integrated
18
19 117 to produce recommendations for future policy and practice [9].
20

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22 118

23
24 119 This review protocol was prepared using the Preferred Reporting Items for Systematic Reviews and
25
26 120 Meta-Analyses (PRISMA) Protocol guidelines [10] (Supplementary file 1) and has been registered
27
28 121 with the International Prospective Register of Systematic Reviews (PROSPERO) (Registration
29
30 122 number: CRD42017084509).
31

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34 124 **Search strategy**

35
36 125 A comprehensive search strategy has been developed to capture all literature relevant to adolescent
37
38 126 self-consent procedures for vaccination programmes by a reviewer (HB-F) experienced in
39
40 127 undertaking systematic reviews in the proposed research field and discussed with members of the
41
42 128 research team. The original search strategy developed for the Embase database has been adapted
43
44 129 for each included database (see below) and comprises a combination of text words and the
45
46 130 following medical subject headings (MeSH) indexing terms: 'child', 'adolescent', 'active
47
48 131 immunization', 'immunization', 'immunization programs', 'mass immunization', 'revaccination',
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50 132 'vaccination', 'diphtheria vaccine', 'diphtheria tetanus vaccine', 'diphtheria pertussis tetanus',
51
52 133 'haemophilus influenzae type b vaccine', 'hepatitis b vaccine', 'meningococcus vaccine', 'rubella
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54 134 vaccine', 'wart virus vaccine', 'papillomavirus vaccines', 'decision making', 'informed consent',
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3 135 'parental consent', 'treatment refusal' (Table 1). Study design filters or restrictions by setting will not
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5 136 be applied as the study aims to be inclusive in relation to study design and settings eligible for
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7 137 inclusion.
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10 11 139 **Databases**

12
13 140 To ensure all the relevant literature is captured, we will search the following ten databases from
14
15 141 inception to January 2018 and re-run six months later (June 2018) to inform the wider research
16
17 142 study as it progresses: Child Development & Adolescent Studies via EBSCOhost, Cochrane Central
18
19 143 Register of Controlled Trials via The Cochrane Library, Cochrane Reviews via The Cochrane Library,
20
21 144 Cumulative Index to Nursing and Allied Health Literature via EBSCOhost, Embase via Ovid, Health
22
23 145 Technology Assessment Database, Medline via Ovid, PsycINFO via Ovid, Social Care Online via Social
24
25 146 Care Institute for Excellence and Web of Science Core Collection: Social Sciences Citation Index and
26
27 147 Conference Proceedings Citation Index- Science. All abstracts will be saved using Endnote X8.
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31 32 149 **Inclusion and exclusion criteria**

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34 150 Quantitative studies will be eligible if vaccine uptake following implementation of self-consent
35
36 151 procedures is reported for young people aged between ten and 18 years [11]. Qualitative studies
37
38 152 reporting the views and experiences of key stakeholders in relation adolescent self-consent
39
40 153 procedures will also be included. Studies related to consent procedures solely targeting parents of
41
42 154 adolescents, or early childhood and adult vaccination programmes will not be eligible for inclusion.
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44 155 Relevant stakeholders will vary with context but are likely to include young people, parents or
45
46 156 primary care givers, healthcare professionals, policy makers, community leaders and teachers.
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51 158 We will include a range of study designs. To determine whether self-consent procedures can
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53 159 increase uptake of vaccination programmes, primary studies reporting parallel group randomised
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55 160 controlled trials, quasi-randomised trials, non-randomised controlled trials, controlled before and
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3 161 after studies, historically controlled studies, and retrospective or prospective cohort studies that
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5 162 include a control group will be eligible. Qualitative studies which use interviews, focus groups,
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7 163 observations, or open-ended questions allowing free-text responses in questionnaires will be
8
9 164 included to explore views and behaviours related to young people's self-consent for vaccination.

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13 166 Conference abstracts, reviews, editorials, opinion pieces, dissertations, letters and books will only be
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15 167 included if they present original data. There will be no language or country of origin restriction
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17 168 imposed, and any relevant full text paper that is not written in English will be translated.

18
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20 21 22 170 **Study selection**

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24 171 Two reviewers will independently assess the titles and abstracts against the predefined eligibility
25
26 172 criteria. Full-text publications of all potentially relevant articles will be retrieved and examined for
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28 173 relevance. Any disagreements arising will be resolved by discussion. The reference lists and
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30 174 bibliographies from relevant studies and systematic reviews will be hand-searched for additional
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32 175 primary studies not retrieved by the electronic search.

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36 177 We will use the reference management software EndNote X8 to remove duplicates and sort
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38 178 exclusions and inclusions. The search strategy and study selection process will be documented using
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40 179 a PRISMA flow diagram [12].

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43 44 45 181 **Data extraction**

46
47 182 At least two reviewers will independently extract data from selected studies using structured and
48
49 183 standardised data extraction forms used in our previous qualitative and quantitative systematic
50
51 184 reviews. In instances where multiple publications relate to the same study, these will be reported
52
53 185 together. The following domains will be retrieved: study characteristics (authors, publication year,
54
55 186 country, aim, study time period, study design, location, type of setting, data collection period, data

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3 187 collection method, sampling strategy, analysis, participant characteristics (participant age, sample
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5 188 size, vaccination status of participants, socioeconomic indicators, race/ethnicity, gender, and
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7 189 religion) and study results (uptake of vaccine, psychological outcomes, healthcare service use,
8
9 190 incidence of vaccine preventable disease, views and behaviours related to self-consent procedures,
10
11 191 authors' reported conflicts of interest and study funding sources). We will also record data relating
12
13 192 to the possible harms resulting from self-consent procedures (e.g. conflict with parents, healthcare
14
15 193 professional anxiety). Where possible, authors will be contacted for missing or incomplete data.
16
17 194 Disagreements will be resolved through discussion.
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196 **Risk of bias and quality assessment**

197 For eligible primary studies, quality assessment will be undertaken to illustrate potential sources of
198 bias. As we anticipate the majority of eligible studies will be observational, studies will not
199 automatically be excluded on the basis of 'low' quality assessment if they are considered to
200 contribute relevant information. We propose using: the Cochrane Collaboration's handbook for the
201 assessment of risks of bias for systematic review of randomised controlled studies and quasi-
202 randomised intervention studies [13] Risk Of Bias in Non Randomised Studies of Interventions
203 (ROBINS-I) [14] ;, the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional
204 Studies [15], and; the Critical Appraisal Skills Programme criteria adapted for qualitative studies for
205 evaluating qualitative research [16]. Quality assessment of primary studies will be undertaken
206 independently by two reviewers and recorded in an excel spreadsheet. An overall assessment of
207 'high', 'medium', 'low', or 'unclear' will be assigned and reported.
208

209

209 **Data synthesis: Quantitative studies**

210 We anticipate that the primary quantitative studies will be reported narratively as preliminary
211 searches specifically related to HPV vaccination programmes indicated a lack of published studies
212 and the likelihood of heterogeneity in relation to study design and reported outcomes. However, if

1
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3 213 sufficiently similar studies are captured we will consider combining individual study results through
4
5 214 meta-analyses. To assess the heterogeneity between studies, we will use the Q-statistic and the I^2 -
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7 215 statistics [17]. Evidence of heterogeneity will be classified as weak, moderate and strong for
8
9 216 corresponding I^2 of 25%, 50% and 75% respectively. If heterogeneity between studies is classified as
10
11 217 weak, analyses will comprise adjusted odds ratios (aORs) where available, with unadjusted odds
12
13 218 ratios used if not reported. Analyses will be undertaken using the meta-analysis function [18]
14
15 219 available in Stata 15. We do not anticipate sufficient data being available to undertake sub-group
16
17 220 analyses. However, if sufficient data were reported we propose two sub-group analyses to compare
18
19 221 impact of self-consent procedures by: (i) setting (healthcare vs. school) and (ii) age of participants
20
21 222 (less than 14 years old vs. 14 years and greater).
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224 **Data synthesis: Qualitative studies**

225 The socio-ecological model [19] considers that behaviour is shaped by a complex interaction
226 between factors operating at public policy, community, organisational, interpersonal and
227 intrapersonal levels. In a previous qualitative synthesis, we have shown that young women's access
228 to the HPV vaccine is shaped by decisions at different levels of the socio-ecological model [5]. During
229 the analysis, we will use the socio-ecological model to provide a framework for understanding how
230 barriers and facilitators operating at different levels of the model can provide access to, or prevent,
231 young people self-consenting in the context of vaccination programmes.
232

232

233 To analyse the qualitative data, the methodology for thematic synthesis reported by Thomas and
234 Harden [20], assisted by the Framework method of qualitative data management [21], will be used.

235 These methods are suited to studies with *a priori* aims and objectives. The overall purpose of the
236 synthesis will be to 'pool' the results from individual primary studies by initially separating the
237 findings, coding and interpreting the text, and then combining them through the identification of key
238 themes across the studies as well as similarities and differences within those themes [22]. Thematic

239 synthesis will be led by one reviewer reporting to the wider team about interpretation of the data as
240 analysis progresses.

241

242 Familiarisation with the dataset will begin with reading the full papers. Pertinent sections of the text
243 reported in each primary study will represent the basic units for analysis. Primary charts of the text
244 will be constructed around key issues using the Framework Matrix within QSR NVivo10 software. For
245 example, initial charts are likely to focus on 'barriers' and 'facilitators' to adolescent self-consent.
246 The primary charts will be retained and revisited as required. Streamlined versions will be produced
247 as the process of coding, summarising and synthesising the data progresses. In subsequent charts,
248 key terms and phrases will be retained while repetition within studies and extraneous text are
249 removed. During this process, overarching themes will be identified, and differences or similarities
250 explored within these emerging themes.

251

252 **Data synthesis: Interrogation**

253 The final stage of the analysis will aim, firstly, to test whether the recommendations developed from
254 the qualitative studies have been addressed in evaluative studies retrieved for the review and,
255 secondly, to examine whether interventions that match the recommendations result in higher
256 uptake in vaccination [9].

257

258 **Patient and public involvement**

259 The Bristol Young People's Advisory Group (YPAG) comprises young people aged ten to 17 years who
260 are interested in healthcare and research. They meet regularly to help researchers with their
261 projects and have been consulted about the design of the wider study and participant materials.
262 They will also be invited to an event at the end of the study to consider findings and
263 recommendations with the young people, parents, immunisation nurses and school staff involved in
264 the study.

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5 266 **ETHICS AND DISSEMINATION**

6
7 267 We will not seek ethical approval for this study because the secondary data to be collected cannot
8
9 268 be linked to individuals. As far as we are aware, this will be the first systematic review to collate
10
11 269 evidence in relation to adolescent self-consent procedures for vaccination programmes. The review
12
13 270 comprises part of a larger study. The findings of this review will inform the larger study evaluating
14
15 271 the practicality, acceptability and impact of new self-consent procedures for the schools-based HPV
16
17 272 vaccination programme in the UK. Findings will also be used to make recommendations to improve
18
19 273 self-consent procedures for young people in vaccination programmes. We anticipate the results of
20
21 274 this study this may be of interest to national and international stakeholders interested in improving
22
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24 275 uptake in adolescent vaccination programmes.
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3 352
4 353 **LIST OF ABBREVIATIONS**
5
6 354 HPV: Human Papillomavirus
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8 355 WHO: World Health Organisation
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10 356 UK: United Kingdom
11
12 357 USA: United States of America
13
14 358 PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol
15
16 359 PROSPERO: Prospective Register of Systematic Reviews
17
18 360 MeSH: Medical Subject Headings
19
20 361 STROBE: Strengthening the Reporting of Observational Studies in Epidemiology
21
22 362 aOR: Adjusted Odds Ratio
23
24 363 OR: Odds Ratio
25
26 364 YPAG: Young Person's Advisory Group
27
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31 366 **AUTHORS' CONTRIBUTIONS**

32
33 367 All authors were involved in the conception and design of the research. SA is Principal Investigator;
34
35 368 HB-F is study manager and lead researcher; JM and MH advise on systematic review methodology.
36
37 369 HB-F wrote the first draft and all authors contributed to the final version of the manuscript.
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40

41 371 **FUNDING STATEMENT**

42
43 372 This work is supported by the National Institute for Health Research for Patient Benefit (NIHR RfPB)
44
45 373 programme (project number PB-PG-0416-20013). The work is also undertaken with the support of
46
47 374 the NIHR Health Protection Research Unit in Evaluation of Interventions. The work was also
48
49 375 undertaken with the support of The Centre for the Development and Evaluation of Complex
50
51 376 Interventions for Public Health Improvement (DECIPHer), a UKCRC Public Health Research Centre of
52
53 377 Excellence. Joint funding (MR/KO232331/1) from the British Heart Foundation, Cancer Research UK,
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378 Economic and Social Research Council, Medical Research Council, the Welsh Government and the
379 Wellcome Trust, under the auspices of the UK Clinical Research Collaboration, is gratefully
380 acknowledged. The views and opinions expressed therein are those of the authors and do not
381 necessarily reflect those of the NIHR RfPB Programme, the Department of Health, or Public Health
382 England.

383

384 **COMPETING INTERESTS STATEMENT**

385 The authors declare there are no competing interests.

386

For peer review only

387 Table 1. Embase search strategy

1. child/
2. adolescent/
3. ("Young people#" OR "young person#" OR "young offender#" OR adolescent# OR adolescence OR youth# OR minor# OR teen OR teens OR teenage OR teenaged OR teenager# OR juvenile# OR pupil# OR boy# OR girl# OR underage# OR daughter# or son# (school AND dropout#) OR (school AND "drop out#") OR "school aged").mp.
4. active immunization/
5. immunization/
6. immunization programs/
7. mass immunization/
8. revaccination/
9. vaccination/
10. diphtheria vaccine/
11. diphtheria tetanus vaccine/
12. diphtheria pertussis tetanus Haemophilus influenzae type b vaccine/
13. hepatitis B vaccine/
14. meningococcus vaccine/
15. rubella vaccine/
16. wart virus vaccine/
17. Papillomavirus Vaccines/
18. (cervical cancer or diphtheria or diphtheria or diphteria or DtaP or DTP or Hep B or hepatitis or HPV or measles or MenC or MenACWY or meningitis or Meningococcal or Neisseria meningitidis or papillomavirus or pertus* or rubella or rubeola or td?ipv or tetanus or wart virus or whoop*).tw.
19. (policy OR program*)

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20. (immuniz* OR immunis* OR immunother* OR inoculat* OR innoculat* OR prophyla* OR revaccinat* OR vaccin*).mp.
21. Decision making/
22. Informed consent/
23. Parental consent/
24. Treatment refusal/
25. (assent* OR competen* OR decision-making OR decision making OR Gillick OR Fraser OR inform* consent OR mental capacity OR minor consent OR parent* consent OR permission* OR presume* consent OR treatment refusal OR self consent OR self-consent OR opt-out OR opt-in).mp.
26. 1 or 2 or 3
27. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
28. 18 and 20
29. 19 and 20
30. 27 or 28 or 29
31. 21 or 22 or 23 or 24 or 25
32. 26 and 30 or 31

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PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 5:15

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	X	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	X	
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	X	<input type="checkbox"/>	48, 120-21
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X	<input type="checkbox"/>	3-18
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	X	<input type="checkbox"/>	362-365
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	X	
Support					
Sources	5a	Indicate sources of financial or other support for the review	X	<input type="checkbox"/>	367-377
Sponsor	5b	Provide name for the review funder and/or sponsor	X	<input type="checkbox"/>	367-377
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X	<input type="checkbox"/>	367-377
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	X	<input type="checkbox"/>	59-107

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	X	<input type="checkbox"/>	32-34, 104-107
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	X	<input type="checkbox"/>	147-166
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	X	<input type="checkbox"/>	147-166
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	X	<input type="checkbox"/>	382
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X	<input type="checkbox"/>	145, 175-176
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	X	<input type="checkbox"/>	168-177
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	X	<input type="checkbox"/>	179-192
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	X	<input type="checkbox"/>	183-192
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	X	<input type="checkbox"/>	183-192
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	X	<input type="checkbox"/>	194-205
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	X	<input type="checkbox"/>	207-220
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	X	<input type="checkbox"/>	207-220

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	X	<input type="checkbox"/>	217-220
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X	<input type="checkbox"/>	208-210, 222-254
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input type="checkbox"/>	X	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	X	