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HPV vaccination and Native Americans: protocol for a systematic review of factors associated with HPV vaccine uptake among American Indians and Alaska Natives in the USA

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ABSTRACT

Introduction The nine-valent human papillomavirus (HPV) vaccine could prevent an estimated 92% of the cancers attributable to HPV types targeted by the vaccine. However, uptake of the HPV vaccine among American Indian and Alaska Native (AI/AN) adolescents has been low. AI/ANs also bear a disproportionate burden of cervical and other HPV-associated cancers. Increasing HPV vaccination rates is a national priority, but reviews and national surveys on HPV vaccination factors are lacking for the AI/AN population. The objective of this systematic review is to assess factors associated with HPV vaccination among AI/ANs in the USA.

Methods and analysis A systematic review is proposed to synthesise the current literature on HPV vaccination factors in AI/ANs from 1 July 2006 until 30 September 2019. As applicable, controlled vocabulary terms, keywords and special features (eg, limits, explode and focus) will be incorporated into database searches. To maximise the identification of relevant studies, citation indexes and databases that index dissertations, preprints and grey literature are included. Studies will be screened and selected independently in two stages. In stage 1, titles and abstracts will be screened. In stage 2, full-text articles will be screened and selected. A data extraction form and quality assessment tool will be piloted, revised and implemented. If available, measures of frequency and association will be presented. A narrative synthesis of the included studies will also be undertaken and reported.

Ethics and dissemination As our review will use publicly available data and publications, an Institutional Review Board review will not be required. We will disseminate the findings from this review through peer-reviewed publication(s) and conference presentation(s).

Potential amendments In the event of amendments to the protocol, we will provide the date, rationale, and description of the change for each amendment.

PROSPERO registration number CRD42020156865.

Strengths and limitations of this study

- This systematic review is one of the first to focus on human papillomavirus vaccination factors among American Indian and Alaska Natives in the USA.
- This protocol follows Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines and outlines the methods to provide transparency of the process.
- We will use a validated tool to appraise the quality of studies in our review.
- Limited and lack of high-quality studies may affect the quality of the evidence synthesised from our review; however, we will search databases, citation indexes and grey literature to ensure the inclusion of all relevant studies.
- We may encounter potential reporting biases, such as bias due to selective non-reporting or publication bias, in our review of included studies.

INTRODUCTION

Rationale

Human papillomavirus (HPV) is the most common sexually transmitted infection in the USA. A national survey to assess the prevalence of the virus from 2011 to 2014 found that more than 42% of American adults over the age of 18 years are infected with HPV.[1] Persistent infection with HPV is causally associated with cervical cancer and certain vulvar, vaginal, anal, penile and oropharyngeal cancers.[2] To prevent HPV-associated cancers and genital warts, safe and effective HPV vaccines have been available and recommended for use in the USA since their introduction in 2006.[3 4] However, vaccine uptake has been suboptimal compared with that of other recommended adolescent immunisations in the USA, with only 65.5% of adolescents having ≥1 vaccine dose as of 2017.[5] HPV vaccine uptake is also below the Healthy People (HP) 2020 target of 80% coverage.[6] The uptake of the HPV vaccine is even lower among American Indian and Alaska Native (AI/AN) adolescents. Coverage data from the National Immunization

Survey—Teen in 2017 showed that AI/AN adolescents had one of the lowest coverages for ≥1 dose of the HPV vaccine at 60.2%. AI/ANs adolescents also had lower coverage than did Hispanic (74.5%), Asian (70.4%), African American (70.0%) and multiracial (65.1%) adolescents.[5]

Reviews have identified several factors that are associated with HPV vaccination in the USA. Some of these factors and interventions include provider recommendation,[7–12] knowledge of HPV and the vaccine,[8 13–15] insurance coverage,[7 13 16 17] and reminder and recall systems.[18–21] Reviews have also reported barriers to vaccination, including vaccine safety concerns,[8 11 12 15 22 23] cost of the vaccine and financial burden,[7 8 11 12 14 23] and low perceived risk of HPV infection.[7 14 22] In addition to these factors, HPV vaccination initiation and completion estimates differ by race and ethnicity in the USA.[5 24–26] Due to the observed differences in coverage, some reviews have centred on specific racial and ethnic groups, including African Americans and Hispanics.[22 27] However, no review on HPV vaccination factors has focused on the AI/AN population in the USA. Even reviews that have assessed racial factors and disparities in vaccination did not include AI/ANs.[26 28 29] Furthermore, analyses of national surveys with questions on HPV vaccination factors, including the National Immunization Survey,[30–32] the National Health Interview Survey,[24] the Health Information National Trends Survey[33] and the National Survey of Family Growth,[34] have combined AI/ANs with other racial groups. Racial and ethnic data are essential to document and facilitate efforts to reduce health disparities. This aggregation of data makes it challenging for AI/AN communities to access meaningful, quality data for their population.

Our proposed systematic review will synthesise the literature and summarise the evidence on HPV vaccination factors for AI/ANs in the USA. This review is essential because AI/ANs bear a disproportionate burden of cervical cancer,[35–37] as well as other HPV-associated cancers.[38] For instance, incidence rates for cervical cancer were 1.6–3.5 times higher in AI/AN women than in white women in the USA.[35–37] Also, HPV vaccination coverage among AI/AN adolescents is comparatively low.[5] Increasing HPV vaccination rates in the USA is a national public health priority aligned with the goals of HP 2020,[6] the President's Cancer Panel[39] and the American Cancer Society, among others. Failure to improve vaccination coverage may increase the burden of preventable cancers among AI/ANs and broaden disparities in this historically underserved population.

Objective

The proposed systematic review focuses on AI/ANs in the USA. The objectives of the review are to identify and assess factors: (1) found to be barriers for HPV vaccination, (2) found to support or enhance HPV vaccination and (3) found not to be associated with HPV vaccination.

METHODS AND ANALYSIS

This review protocol was prepared according to the 2015 guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (see online supplementary file 1).[40] The protocol is registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42020156865).

Eligibility criteria

To be eligible and included in the systematic review, studies will have the following study (population, study design and setting) and report (time frame, geographical location, language and publication type) characteristics.

Population

As this review focuses on the AI/AN population of the USA, we will only include studies that feature or provide results for AI/AN populations. No age or gender restrictions will be placed, as the HPV vaccine is recommended for both men and women, as well as age-eligible adolescents and adults.[41]

Study design

Studies assessing HPV vaccination factors have used different designs.[18 42–45] Therefore, we will include all study designs in our review, except existing reviews, as we are not undertaking an overview of reviews.

Setting

As HPV vaccination factors have been assessed in different settings, including population-based, healthcare, and school and college settings,[42] we will not restrict studies by any type of setting.

Time frame

Studies published from 1 July 2006 until 30 September 2019 will be included, as the US Food and Drug Administration licensed the first HPV vaccine in 2006.[3]

Geographical location

As our population of interest is AI/ANs, we will restrict our studies to the USA only (excluding US territories, such as American Samoa, Guam, Northern Mariana Islands, Puerto Rico and US Virgin Islands).

Language

We will include only studies reported in English, as we are focusing on AI/AN populations living in the USA.

Publication type

As the number of studies focused on AI/AN populations will be limited, we will not restrict by publication type (eg, journal article, conference abstract, dissertation, report and preprint).

Information sources

As we suspected a limited literature on AI/ANs, we searched several resources to maximise the inclusion of all relevant studies. A list of sources that were searched with their brief description is presented in table 1. To minimise the risk of bias, we searched grey literature sources, including dissertations, abstracts, conference papers and posters, and reports from the Tribal Epidemiology Centers; not including these sources may substantially

Table 1 Sources searched for systematic review on human papillomavirus vaccination factors, 1 July 2006 to 5 January 2020

Type	Name	Interface/platform	Coverage range	Search executed	Brief description
Database and Citation Index	MEDLINE and Epub ahead of print, in-process and other non-indexed citations	Ovid	1946 to 5 July 2019	July 8 to 2019 Search updated: October 3 to 2019	Bibliographic database of biomedical literature. Produced by the US National Library of Medicine (NLM).
	PubMed	https://www.ncbi.nlm.nih.gov/pubmed/	1946 to present	July 22 to 2019 Search updated: October 3 to 2019	PubMed covers biomedical literature with citations from MEDLINE indexed journals, journals/manuscripts deposited in PMC and NCBI Bookshelf. Produced by the US NLM.
	Embase	Ovid	1947 to 5 July 2019	July 8 to 2019 Search updated: October 3 to 2019	Bibliographic database indexing biomedical and pharmacological literature from journals and conferences worldwide. Produced by Elsevier.
	Cochrane Central Register of Controlled Trials	Ovid	1991 to present	October 4 to 2019	Bibliographic database of controlled trials. Produced by the Cochrane Library in collaboration with the US NLM, Elsevier and others.
	CINAHL complete	EBSCO	1937 to present	July 22 to 2019	Bibliographic database focused on nursing and allied health literature, including journals, audiovisual materials, books and book chapters, and select conference proceedings.
	ERIC	Ovid	1965 to April 2019	July 22 to 2019	Bibliographic database of education research, including journal articles, reports, books and briefs. Sponsored by the US Department of Education.
	PsycINFO	Ovid	1806 to July (week 1) 2019	July 8 to 2019	Bibliographic database of journal articles, books and book chapters, and dissertations relevant to psychology and related fields. Produced by the American Psychological Association.
	SocINDEX	EBSCO	1895 to present	July 22 to 2019	Bibliographic database focused on sociology research, including journal articles, books and monographs, and conference papers.
	Bibliography of Native North Americans	EBSCO	16th century to present	July 22 to 2019	Bibliographic database covering all aspects of Native American culture, history and life; indexes journals, books and government documents.
	Social work abstracts	EBSCO	1965 to present	July 22 to 2019	Bibliographic database of the social work field. Produced by the National Association of Social Workers.
	Native Health Database	https://hslic-nhd.health.unm.edu/	17th century to present	December 22 to 2019	Database of AI/AN health literature. Produced by the University of New Mexico.
	Indigenous Studies Portal	https://iportal.usask.ca/	16th century to present	December 23 to 2019	Database of Indigenous North American literature. Produced by the University of Saskatchewan.
	Arctic Health Publications Database	https://arctichealth.org/	1787 to present	December 23 to 2019	Database of health information about Alaska Native peoples. Sponsored by the US NLM and maintained by the University of Alaska Anchorage.
	SCI-Expanded	Web of Science	1900 to present	July 8 to 2019	Bibliographic database providing multidisciplinary access to scientific journal literature, including all cited references from indexed articles.
	SSCI	Web of Science	1900 to present	July 8 to 2019	Bibliographic database providing multidisciplinary access to journal literature in the social sciences.
	A&HCI	Web of Science	1975 to present	July 8 to 2019	Bibliographic database providing access to journal literature in disciplines focused on the arts and humanities.
	Emerging Sources Citation Index	Web of Science	2015 to present	July 8 to 2019	Bibliographic database referencing literature from newer journals being considered for indexing in SCI-Expanded, SSCI or A&HCI.

Continued

Table 1 Continued

Type	Name	Interface/platform	Coverage range	Search executed	Brief description
	Scopus	https://www.scopus.com/home.uri	1788 to present	July 22 to 2019	Bibliographic database providing access to journal and conference literature across multiple disciplines. Produced by Elsevier.
Grey literature					
Dissertation	Dissertations and theses	ProQuest	1637 to present	October 4 to 2019	Database of dissertations and theses developed in partnership with academic institutions in the USA, Canada and worldwide.
Abstracts and conferences	Northern Light Life Sciences Conference Abstracts	Ovid	2010–2019 (week 28)	July 22 to 2019	Full-text database of abstracts and posters presented at conferences. Produced by the Northern Light Group.
	PapersFirst	FirstSearch	1993 to present	October 4 to 2019	Bibliographic database of papers presented at meetings worldwide. Produced by the OCLC.
	Proceedings	FirstSearch	1993 to present	October 4 to 2019	Bibliographic database of conference proceedings for meetings held around the world. Produced by OCLC.
Preprints	OSF preprints	https://osf.io/preprints/	1988 to present	December 24 to 2020	Aggregator of various preprint servers.
Reports	Tribal Epidemiology Centers	https://tribalepicenters.org/12-tecs/	–	January 5 to 2020	Data and health reports of AI/ANs from 12 centres.

A&HCI, Arts & Humanities Citation Index; AI/AN, American Indian and Alaska Native; CINAHL, Cumulative Index to Nursing and Allied Health; ERIC, Education Resources Information Center; N/A, Not applicable; NCBI, National Center for Biotechnology Information; NLM, National Library of Medicine; OCLC, Online Computer Library Center; PMC, PubMed Central; SCI-Expanded, Science Citation Index Expanded; SSCI, Social Sciences Citation Index.

limit the number of studies and the proposed review.[46] We will also undertake complementary searching activities, including citation chaining and contacting relevant researchers and health professionals in the field to ask about any unpublished or recently submitted data.

Search strategy

The selection of sources and search strategy was developed in consultation with the Head of Reference and Instructional Services at the University of Oklahoma Health Sciences Center's Robert M. Bird Library (SCC).

When available, controlled vocabulary terms were used to construct searches in all sources. Keywords, such as synonyms and trade names, were also used to capture key concepts; tools such as truncation and proximity searching were employed to ensure a comprehensive search strategy. In developing the strategy, we aimed to strike a balance between comprehensiveness and precision by setting appropriate limits and removing duplicates. Search terms were modified and refined, and the resulting search strategy was piloted in these databases: MEDLINE, Embase, PsycINFO and Web of Science Core Collection's Social Sciences Citation Index, Science Citation Index-Expanded, Arts & Humanities Citation Index and Emerging Sources Citation Index. The refined search strategy for MEDLINE is presented in table 2; search strategies for the other sources are provided in online supplementary file 2. To ensure the inclusion of newer literature, searches were updated in MEDLINE (Ovid), Embase (Ovid) and PubMed.

Study records

Data management

A reference management tool, EndNote (V.X9; Clarivate Analytics, Philadelphia, Pennsylvania, USA), will be used to manage bibliographies and references. Duplicate articles will be identified in and removed from the EndNote library. For title and abstract screening, we will use a web application, Rayyan (Qatar Computing Research Institute, Doha, Qatar).

Selection process

A screening and selection tool was developed and piloted to ensure that relevant studies are included in the review (section II of online supplementary file 3). Screening and selection of studies will be conducted in two stages. In stage 1, two reviewers (SVG and AES) will independently screen all titles and abstracts, as this approach is more precise than screening titles only.[47] We will use the following keywords for screening: HPV vaccine, HPV vaccine or vaccination factors, American Indians, Alaska Natives, Native Americans and race or racial. In stage 2, the tool will be used against the criteria to identify full text of potential articles for inclusion in the review.

A kappa statistic will be calculated to measure agreement between the two reviewers on eligibility decisions. Any discrepancies or disagreements during the selection process will be resolved through discussions; however,

Table 2 Search strategy for MEDLINE, July 2019

Number	Search items	Hits
1	exp Papillomavirus Vaccines	7128
2	((papilloma$ or hpv) adj2 (vaccin$ or immuniz$)).mp.	10458
3	(gardasil$ or ceravix$ or cervarix$ or silgard$).mp.	571
4	or/1 to 3	10492
5	exp American Native Continental Ancestry Group	20720
6	(native american$ or american indian$ or amerind$).mp.	12397
7	(indigenous$ or tribe or tribes or tribal$).mp.	41854
8	(aian or ai an).mp.	806
9	or/5 to 8	63672
10	4 and 9	60
11	l/ 10 yr=2006-current	60
12	remove duplicates from 11	60
13	exp united states	1300858
14	(us or usa or united states).mp.	9358201
15	(Alabama$ or Alaska$ or Arizona$ or Arkansa$ or California$ or Colorado$ or Connecticut$ or Delaware$ or Florid$ or Georgia$ or Hawaii$ or Idaho$ or Illinois$ or Indiana$ or Iowa$ or Kansa$ or Kentuck$ or Louisiana$ or Maine$ or Maryland$ or Massachusetts$ or Michigan$ or Minnesota$ or Mississippi$ or Missouri$ or Montana$ or Nebraska$ or Nevada$ or New Hampshire$ or New Jers$ or New Mexic$ or New York$ or North Carolin$ or North Dakota$ or Ohio$ or Oklahoma$ or Oregon$ or Pennsylvania$ or Rhode Island$ or South Carolin$ or South Dakota$ or Tenness$ or Texa$ or Utah$ or Vermont$ or Virginia$ or Washington$ or West Virginia$ or Wisconsin$ or Wyoming$).mp.	674164
16	or/13 to 15	9780569
17	12 and 16	46
18	12 not 17	14
19	from 18 keep 3	1
20	17 or 19	47
21	exp continental population groups/	208897
22	(race or races or racial$).mp.	131570
23	21 or 22	302873
24	4 and 23	502
25	l/ 24 yr=2006-current	500
26	remove duplicates from 25	499
27	26 not 20	466
28	16 and 27	364

if needed, we will include a third reviewer (AEJ) to aid decision-making and achieve resolution. A PRISMA flow diagram highlighting the number of articles identified, screened, determined eligible and included in the final review will be generated.

Data extraction and items

A data extraction form was developed by adapting and customising questions from the Cochrane Collaboration's intervention reviews for randomized controlled trials (RCTs) and non-RCTs,[48] Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for quantitative studies[49] and Standards for Reporting Qualitative Research (SRQR) guideline[50] (online supplementary file 3). STROBE and SRQR were used as reporting guidelines to provide a minimum list of information needed to ensure that the study can be included in a systematic review.[51]

Data items

Using the data extraction form, some of the key data items that will be obtained from the studies are listed in table 3.

Quality appraisal and bias assessment

To appraise the quality of studies in our review, we will use a modified Mixed Methods Appraisal Tool (MMAT) (V.2018).[52] MMAT was selected to assess the methodological quality of studies. Although several critical appraisal tools exist, most focus on a single design type or have an individual component approach (eg, Cochrane risk-of-bias tool for randomised trials,[53] Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies,[54] Critical Appraisals Skills Programme (CASP) checklist for cohort studies[55] and Joanna Briggs Institute (JBI) checklist for qualitative research[56]). However, MMAT covers quantitative, qualitative and mixed methods studies. MMAT was also selected for its utility (varied coverage) and usability (easy learnability and high efficiency).[57] The appraisal tool has an improved content validity and an inter-rater reliability of 0.72 for Global Quality Score.[52 58]

MMAT contains 2 questions on screening and 25 questions on methodological quality across qualitative, quantitative randomised controlled trials, quantitative non-randomised, quantitative descriptive and mixed methods studies (5 items each). Each item is rated on a categorical scale (yes, no and cannot tell). However, for

Table 3 Data items to be extracted from included articles by study type and section

Study type	Section	Items
All	Study details	Study rationale, question(s), objectives, design, start date, end date, HPV vaccine initiation coverage, HPV vaccine completion coverage, factors found to be barriers for HPV vaccination, factors found to support or enhance HPV vaccination and factors found not to be associated with HPV vaccination.
	Study participants	Population description, US state or region, setting, inclusion criteria, exclusion criteria, method of selection, informed consent, number of participants, age, sex, clinical characteristics, social characteristics and Native American tribe.
	Funding and conflict of interest	Study funding sources and possible conflicts of interest.
Randomised controlled trial	–	Total number randomised, clusters, baseline imbalances, withdrawals and exclusions.
	Intervention and comparison group	Group name, number randomised to group, theoretical basis, duration of treatment period, timing, delivery, providers, cointerventions, economic information, resource requirements, integrity of delivery and compliance.
	Outcome	Outcome name, time points measured, time points reported, outcome definition, person measuring/reporting, unit of measurement, scales, is outcome/tool validated, imputation of missing data, assumed risk estimate and power.
Quantitative study	–	Method of follow-up, criteria for matching, exposure(s), outcome(s), confounder(s), effect modifier(s), measurement method, bias, statistical methods, missing data, outcome data, main results (point estimates and confidence intervals) and limitations reported and not reported.
Qualitative study	–	Qualitative approach, research paradigm, research characteristics and reflexivity, context, sampling strategy, data collection methods, data collection instruments, units of study, data processing methods, data analysis methods and main findings or themes.

HPV, human papillomavirus.

certain MMAT questions, a categorical scale of response may not suffice or may require further elaboration beyond that provided in the accompanying explanation document for MMAT.[59] For instance, the option of 'yes' on MMAT question 3.3 will be defined as the availability of greater than 80% of primary outcome data. Furthermore, if some confounders were addressed in the study, but other known or suspected confounders were omitted, the response for question 3.4 will be marked as 'yes', but additional information and explanation will be provided in the comments section.

We modified the MMAT by including five additional questions (6.1–6.5 in table 4) and expanded the scope to include methodological and reporting criteria involving AI/ANs. The first three questions (6.1, 6.2 and 6.3) were added because they are a requirement of several reporting guidelines, including Consolidated Standards of Reporting Trials,[60] International Committee of Medical Journal Editors,[61] PRISMA[62] and STROBE.[49] The latter two questions (6.4 and 6.5) were adapted from the CONSIDER (consolidated criteria for strengthening reporting of health research involving indigenous peoples) statement to assess whether culturally appropriate methodology had been used.[63] We included the question on data collection and analysis (6.1) to capture the transparency and appropriateness of what was planned and conducted in a study. This question is meant to assess whether the authors of the study: described data collection procedures adequately, offered a rationale for the choice of data collection tool(s), provided validity and reliability of data collection tool(s), addressed the appropriateness of statistical methods used, and gave justification to support their analyses. The discussion of limitations is an important aspect of scientific discourse, as it allows study author(s) to prevent misunderstandings, discuss the quality of evidence and place their findings in context.[64 65] Therefore, in line with other MMATs,[66] we added a question on limitations in the modified MMAT (6.2). We also included a question on ethical concerns (6.3) because conflicts of interest related to funding, especially as it pertains to a pharmacological agent such as a vaccine, can potentially influence the research components (study design, data analysis and interpretation, and whether to publish).[67 68] We adapted two questions (6.4 and 6.5) from two different domains (research relationships and research methodologies) of the CONSolIDated critERtia for strengthening the reporting of health research involving Indigenous Peoples (CONSIDER) statement.[63] The purpose of question 6.4 is to assess whether and how AI/AN stakeholders and participants were involved in research processes, including the design, recruitment, implementation, analysis and interpretation.

Table 4 Modified Mixed Methods Appraisal Tool for appraising the quality of studies, V.2018

		Responses			
Category of study designs	**Methodological quality criteria**	**Yes**	**No**	**Cannot tell**	**Comments**
Screening questions (for all types)	S1. Are there clear research questions?				
	S2. Do the collected data allow to address the research questions?				
	Further appraisal may not be feasible or appropriate when the answer is 'no' or 'cannot tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?				
	1.2. Are the qualitative data collection methods adequate to address the research question?				
	1.3. Are the findings adequately derived from the data?				
	1.4. Is the interpretation of results sufficiently substantiated by data?				
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomised controlled trials	2.1. Is randomisation appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomised controlled trials	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?				
	4.2. Is the sample representative of the target population?				
	4.3. Are the measurements appropriate?				
	4.4. Is the risk of nonresponse bias low?				
	4.5. Is the statistical analysis appropriate to answer the research question?				
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?				
	5.2. Are the different components of the study effectively integrated to answer the research question?				
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?				
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?				
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?				

Continued

Table 4 Continued

Category of study designs	Methodological quality criteria	Responses			
		Yes	No	Cannot tell	Comments
6. Additional questions*	6.1. Are the data collection and analysis methods appropriate?				
	6.2. Are the limitations of the study adequately described?				
	6.3. Are there any ethical concerns or conflict of interest?				
	6.4. Were AI/AN stakeholders and participants involved in the research processes?				
	6.5. Did the methodology consider the physical, social, economic and cultural environment of the AI/AN stakeholders and participants?†				

*These questions are not part of the original MMAT.
†Adapted from the CONSIDER statement.[63]

The question on methodology (6.5) was included to assess whether it incorporated the physical, social, economic and cultural environment of the AI/AN participants. Including these two additional questions (6.4 and 6.5) will allow us to evaluate the context and implications of research for AI/AN participants and communities (in the included studies).

Assessment of studies will be conducted independently by two reviewers (SVG and AES). Any discrepancies or disagreements during the selection process will be resolved through discussions, and if needed, through the help of a third reviewer (AEJ). The data extraction form and quality assessment tool were piloted using three studies identified from the MEDLINE search above. The data extraction form was revised after testing and piloted again using three additional studies.

Data synthesis

As we are not anticipating that the included studies will be homogenous in design and have individual data available, it will not be appropriate to undertake a meta-analysis or analyse quantitative data. However, measures of frequency, such as prevalence, will be reported. For instance, the number and proportion of AI/ANs who have and have not received the HPV vaccine by tribes will be summarised and presented. If available, measures of association, such as odds ratios along with confidence intervals, will be presented.

A narrative synthesis of the included studies will be undertaken and presented. The main elements of the narrative synthesis process, such as the preliminary synthesis of findings and exploring relationships both within and between included studies, will be applied.[69] Preliminary synthesis will be developed through textual description of studies and tabulation of data.[69] For exploring relationships in the data, graphical tools and qualitative case descriptions will be used.[69] Thematic synthesis methodology as described by Thomas and Harden will be used to combine qualitative studies identified in our review.[70] Findings on the facilitators and barriers to HPV vaccination will be further explored. The risk of potential threats to validity, including biases, will be assessed and reported. Any effect modifiers or confounders and their impact on the study findings will also be evaluated.

Patient and public involvement

No patients or the public were involved in the development of this systematic review protocol.

DISCUSSION

To reduce the burden of HPV-associated cancers, there is a need to identify and understand factors that influence vaccine uptake. Prior reviews and national surveys on HPV vaccination factors have assessed different groups, but failed to focus on the AI/AN population that bears a disproportionate burden of HPV-associated cancers. Our systematic review aims to address this gap. The results from this review are anticipated to identify HPV vaccination factors and inform future research, policy and practice on vaccinations for HPV among AI/ANs.

Ethics and dissemination

This systematic review protocol is currently registered in PROSPERO (CRD42020156865). As our review will use publicly available data and publications, an Institutional Review Board review will not be required. We will disseminate the findings from this review through peer-reviewed publication(s) and conference presentation(s).

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Contributors SVG, AEJ and JC initiated the project. SVG and AES designed and piloted the data extraction form, including the screening and selection tool. SCC and SVG developed and implemented the search strategy. AEJ, JS, JP, AC and ALS provided feedback on the methods. SVG developed the first draft of the protocol. All authors reviewed, revised and approved the final protocol.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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REFERENCES

1 McQuillan G, Kruszon-Moran D, Markowitz LE. *Prevalence of HPV in adults aged 18-69: United States, 2011-2014.NCHS data brief*. , 2017: 280, 1–8.
2 Muñoz N, Castellsagué X, de González AB, *et al*. Chapter 1: HPV in the etiology of human cancer. *Vaccine* 2006;24 Suppl 3:1–10.
3 Markowitz LE, Gee J, Chesson H, *et al*. Ten years of human papillomavirus vaccination in the United States. *Acad Pediatr* 2018;18:S3–10.
4 Harper DM, DeMars LR. HPV vaccines - A review of the first decade. *Gynecol Oncol* 2017;146:196–204.
5 Walker TY, Elam-Evans LD, Yankey D, *et al*. National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years - United States, 2017. *MMWR Morb Mortal Wkly Rep* 2018;67:909–17.
6 Office of Disease Prevention and Health Promotion. Immunization and infectious diseases, 2019. Available: https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives [Accessed 1 Aug 2019].
7 Holman DM, Benard V, Roland KB, *et al*. Barriers to human papillomavirus vaccination among US adolescents: a systematic review of the literature. *JAMA Pediatr* 2014;168:76–82.
8 Small SL, Sampselle CM, Martyn KK, *et al*. Modifiable influences on female HPV vaccine uptake at the clinic encounter level: a literature review. *J Am Assoc Nurse Pract* 2014;26:519–25.
9 Bartlett JA, Peterson JA. The uptake of human papillomavirus (HPV) vaccine among adolescent females in the United States: a review of the literature. *J Sch Nurs* 2011;27:434–46.
10 Bratic JS, Seyferth ER, Bocchini JA. Update on barriers to human papillomavirus vaccination and effective strategies to promote vaccine acceptance. *Curr Opin Pediatr* 2016;28:407–12.
11 Radisic G, Chapman J, Flight I, *et al*. Factors associated with parents' attitudes to the HPV vaccination of their adolescent sons : A systematic review. *Prev Med* 2017;95:26–37.
12 Rambout L, Tashkandi M, Hopkins L, *et al*. Self-Reported barriers and facilitators to preventive human papillomavirus vaccination among adolescent girls and young women: a systematic review. *Prev Med* 2014;58:22–32.
13 Kessels SJM, Marshall HS, Watson M, *et al*. Factors associated with HPV vaccine uptake in teenage girls: a systematic review. *Vaccine* 2012;30:3546–56.
14 Ratanasiripong NT. A review of human papillomavirus (HPV) infection and HPV vaccine-related attitudes and sexual behaviors among college-aged women in the United States. *J Am Coll Health* 2012;60:461–70.
15 Wilson L, Rubens-Augustson T, Murphy M, *et al*. Barriers to immunization among newcomers: a systematic review. *Vaccine* 2018;36:1055–62.
16 Fisher H, Trotter CL, Audrey S, *et al*. Inequalities in the uptake of human papillomavirus vaccination: a systematic review and meta-analysis. *Int J Epidemiol* 2013;42:896–908.
17 Gallagher KE, Kadokura E, Eckert LO, *et al*. Factors influencing completion of multi-dose vaccine schedules in adolescents: a systematic review. *BMC Public Health* 2016;16:172.
18 Niccolai LM, Hansen CE. Practice- and community-based interventions to increase human papillomavirus vaccine coverage: a systematic review. *JAMA Pediatr* 2015;169:686–92.
19 Holloway GL. Effective HPV vaccination strategies: what does the evidence say? an integrated literature review. *J Pediatr Nurs* 2019;44:31–41.
20 Smulian EA, Mitchell KR, Stokley S. Interventions to increase HPV vaccination coverage: a systematic review. *Hum Vaccin Immunother* 2016;12:1566–88.
21 Walling EB, Benzoni N, Dornfeld J, *et al*. Interventions to improve HPV vaccine uptake: a systematic review. *Pediatrics* 2016;138:2015-3863.
22 Galbraith KV, Lechuga J, Jenerette CM, *et al*. Parental acceptance and uptake of the HPV vaccine among African-Americans and Latinos in the United States: a literature review. *Soc Sci Med* 2016;159:116–26.
23 Dibble KE, Maksut JL, Siembida EJ, *et al*. A systematic literature review of HPV vaccination barriers among adolescent and young adult males. *J Adolesc Young Adult Oncol* 2019;8:495–511.
24 Agenor M, Perez AE, Peitzmeier SM, *et al*. Racial/Ethnic disparities in human papillomavirus vaccination initiation and completion among U.S. women in the post-Affordable care act era. *Ethn Health* 2018:1–15.
25 Niccolai LM, Mehta NR, Hadler JL. Racial/Ethnic and poverty disparities in human papillomavirus vaccination completion. *Am J Prev Med* 2011;41:428–33.
26 Jeudin P, Liveright E, Del Carmen MG, *et al*. Race, ethnicity, and income factors impacting human papillomavirus vaccination rates. *Clin Ther* 2014;36:24–37.
27 Suárez P, Wallington SF, Greaney ML, *et al*. Exploring HPV knowledge, awareness, beliefs, attitudes, and vaccine acceptability of Latino fathers living in the United States: an integrative review. *J Community Health* 2019;44:844–56.
28 Spencer JC, Calo WA, Brewer NT. Disparities and reverse disparities in HPV vaccination: a systematic review and meta-analysis. *Prev Med* 2019;123:197–203.
29 Jeudin P, Liveright E, del Carmen MG, *et al*. Race, ethnicity and income as factors for HPV vaccine acceptance and use. *Hum Vaccin Immunother* 2013;9:1413–20.
30 Hirth JM, Fuchs EL, Chang M, *et al*. Variations in reason for intention not to vaccinate across time, region, and by race/ethnicity, NIS-Teen (2008-2016). *Vaccine* 2019;37:595–601.
31 Landis K, Bednarczyk RA, Gaydos LM. Correlates of HPV vaccine initiation and provider recommendation among male adolescents, 2014 NIS-Teen. *Vaccine* 2018;36:3498–504.
32 Mohammed KA, Vivian E, Loux TM, *et al*. Factors associated with parents' intent to vaccinate adolescents for human papillomavirus: findings from the 2014 national immunization Survey-Teen. *Prev Chronic Dis* 2017;14:E45.
33 Osazuwa-Peters N, Adjei Boakye E, Mohammed KA, *et al*. Not just a woman's business! understanding men and women's knowledge of HPV, the HPV vaccine, and HPV-associated cancers. *Prev Med* 2017;99:299–304.
34 Liddon NC, Hood JE, Leichliter JS. Intent to receive HPV vaccine and reasons for not vaccinating among unvaccinated adolescent and

young women: findings from the 2006-2008 national survey of family growth. *Vaccine* 2012;30:2676–82.
35 Watson M, Benard V, Thomas C, *et al*. Cervical cancer incidence and mortality among American Indian and Alaska native women, 1999-2009. *Am J Public Health* 2014;104 Suppl 3:S415–22.
36 Foote M, Strickland R, Lucas-Pipkorn S, *et al*. The high burden of cancer among American Indians/Alaska natives in Wisconsin. *WMJ* 2016;115:11–16.
37 Gopalani SV, Janitz AE, Campbell JE. Trends in cervical cancer incidence and mortality in Oklahoma and the United States, 1999-2013. *Cancer Epidemiol* 2018;56:140–5.
38 United States Cancer Statistics. Cancers associated with human papillomavirus in the American Indian and Alaska native population, United States—1999–2015 (Purchased/Referred care delivery Areas-PRCDA, 2018. Available: https://www.cdc.gov/cancer/uscs/pdf/USCS-DataBrief-No6-December2018-508.pdf [Accessed 20 Jul 2019].
39 President's Cancer Panel. *HPV Vaccination for Cancer Prevention: Progress, Opportunities, and a Renewed Call to Action*. Bethesda (MD, 2018.
40 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
41 Petrosky E, Bocchini JA, Hariri S, *et al*. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on immunization practices. *MMWR Morb Mortal Wkly Rep* 2015;64:300–4.
42 Allen JD, Coronado GD, Williams RS, *et al*. A systematic review of measures used in studies of human papillomavirus (HPV) vaccine acceptability. *Vaccine* 2010;28:4027–37.
43 Ferrer HB, Trotter C, Hickman M, *et al*. Barriers and facilitators to HPV vaccination of young women in high-income countries: a qualitative systematic review and evidence synthesis. *BMC Public Health* 2014;14:700.
44 Batista Ferrer H, Audrey S, Trotter C, *et al*. An appraisal of theoretical approaches to examining behaviours in relation to human papillomavirus (HPV) vaccination of young women. *Prev Med* 2015;81:122–31.
45 Garcini LM, Galvan T, Barnack-Tavlaris JL. The study of human papillomavirus (HPV) vaccine uptake from a parental perspective: a systematic review of observational studies in the United States. *Vaccine* 2012;30:4588–95.
46 Hopewell S, McDonald S, Clarke M, *et al*. Grey literature in meta-analyses of randomized trials of health care interventions. *Cochrane Database Syst Rev* 2007;2:Mr000010.
47 Mateen FJ, Oh J, Tergas AI, *et al*. Titles versus titles and Abstracts for initial screening of articles for systematic reviews. *Clin Epidemiol* 2013;5:89–95.
48 The Cochrane Collaboration. Data collection form for intervention reviews: RCTs and non-RCTs, 2014. Available: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=2ahUKEwjG5NPy5uDjAhVmiOAKHXXvBtcQFjAAegQIAhAC&url=https%3A%2F%2Fcommunity.cochrane.org%2Fsites%2Fdefault%2Ffiles%2Fuploads%2Finline-files%2FERC%2520data%2520collection%2520form%2520for%2520intervention%2520reviews%2520for%2520RCTs%2520and%2520non-RCTs.doc&usg=AOvVaw2f0Wx5fM1jBDFLsLBbNpI- [Accessed 30 July 2019].
49 von Elm E, Altman DG, Egger M, *et al*. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Epidemiology* 2007;18:800–4.
50 O'Brien BC, Harris IB, Beckman TJ, *et al*. Standards for reporting qualitative research: a synthesis of recommendations. *Acad Med* 2014;89:1245–51.
51 Equator Network. What is a reporting guideline?Available: http://www.equator-network.org/about-us/what-is-a-reporting-guideline/ [Accessed 31 Jul 2019].
52 Hong QN, Pluye P, Fàbregues S, *et al*. Improving the content validity of the mixed methods appraisal tool: a modified e-Delphi study. *J Clin Epidemiol* 2019;111:e41:49–59.
53 Jørgensen L, Paludan-Müller AS, Laursen DRT, *et al*. Evaluation of the Cochrane tool for assessing risk of bias in randomized clinical trials: overview of published comments and analysis of user practice in Cochrane and non-Cochrane reviews. *Syst Rev* 2016;5:80.
54 Armijo-Olivo S, Stiles CR, Hagen NA, *et al*. Assessment of study quality for systematic reviews: a comparison of the Cochrane collaboration risk of bias tool and the effective public health practice project quality assessment tool: methodological research. *J Eval Clin Pract* 2012;18:12–18.
55 Critical Appraisal Skills Programme.. Casp cohort study checklist, 2018. Available: https://casp-uk.net/wp-content/uploads/2018/01/CASP-Cohort-Study-Checklist_2018.pdf. [Accessed 26 Jul 2019].
56 The Joanna Briggs Institute. Checklist for qualitative research., 2017. Available: https://joannabriggs.org/critical_appraisal_tools [Accessed 26 Jul 2019.].
57 Hong QN, Gonzalez-Reyes A, Pluye P. Improving the usefulness of a tool for appraising the quality of qualitative, quantitative and mixed methods studies, the mixed methods appraisal tool (MMAT). *J Eval Clin Pract* 2018;24:459–67.
58 Pace R, Pluye P, Bartlett G, *et al*. Testing the reliability and efficiency of the pilot mixed methods appraisal tool (MMAT) for systematic mixed studies review. *Int J Nurs Stud* 2012;49:47–53.
59 Quan H, Pierre P, Sergi F. Mixed methods appraisal tool (MMAT) Version, 2018. Available: http://mixedmethodsappraisaltoolpublic.pbworks.com/w/file/fetch/127916259/MMAT_2018_criteria-manual_2018-08-01_ENG.pdf [Accessed 21 Oct 2019].
60 Schulz KF, Altman DG, Moher D, *et al*. Consort 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
61 Drazen JM, Van Der Weyden MB, Sahni P, *et al*. Uniform format for disclosure of competing interests in ICMJE journals. *Lancet* 2009;374:1395–6.
62 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
63 Huria T, Palmer SC, Pitama S, *et al*. Consolidated criteria for strengthening reporting of health research involving Indigenous peoples: the consider statement. *BMC Med Res Methodol* 2019;19:173.
64 Puhan MA, Akl EA, Bryant D, *et al*. Discussing study limitations in reports of biomedical studies- the need for more transparency. *Health Qual Life Outcomes* 2012;10:23.
65 Ioannidis JPA. Limitations are not properly acknowledged in the scientific literature. *J Clin Epidemiol* 2007;60:324–9.
66 Sirriyeh R, Lawton R, Gardner P, *et al*. Reviewing studies with diverse designs: the development and evaluation of a new tool. *J Eval Clin Pract* 2012;18:746–52.
67 Roseman M, Milette K, Bero LA, *et al*. Reporting of conflicts of interest in meta-analyses of trials of pharmacological treatments. *JAMA* 2011;305:1008–17.
68 Sismondo S. How pharmaceutical industry funding affects trial outcomes: causal structures and responses. *Soc Sci Med* 2008;66:1909–14.
69 Popay J, Roberts H, Sowden A, *et al*. *Guidance on the conduct of narrative synthesis in systematic reviews*, 2006.
70 Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol* 2008;8:45.