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Sociodemographic Differences In Human Papillomavirus Vaccine Impact: A Systematic Review

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Table of Contents

List of Figures and Tables

Abstract

IMPORTANCE: The majority of literature related to disparities in human papillomavirus (HPV) vaccination has been focused on sociodemographic differences in vaccine uptake. Now nearly ten years after the introduction of the vaccine, and with a better understanding of disparities in uptake, a small but growing body of evidence is beginning to examine the impacts of the vaccination campaign. Monitoring disparities in the impact of the vaccine is crucial in order to better understand the full implications of the vaccine and to properly guide future programs and recommendations.

OBJECTIVE: To systematically review the literature on the impact of the human papillomavirus vaccine on HPV-related outcomes, and to assess the potential differences in impact by various sociodemographic characteristics.

EVIDENCE REVIEW: We systematically searched the global literature using keyword searches of the Medline, PubMed, and Web of Science databases between January 1, 2007 and January 31st, 2016 to identify studies that met our inclusion criteria. Using a standardized protocol, two investigators independently abstracted information on relevant study characteristics including principle outcomes, methods, sociodemographic characteristics of the study population, and the statistical methods used by the authors to account for these factors. The quality of studies (potential for bias and confounding) was assessed by review of participant selection or recruitment procedures, and potential confounders considered in the statistical analyses. A total of 3,713 records were screened and 45 published studies were included. Results were summarized by method of statistical analysis.

FINDINGS: Of the 45 included articles, 22 articles did not collect information on sociodemographic variables and 23 collected at least one sociodemographic variable. Variables collected varied between studies and countries with the most commonly assessed being race, ethnicity, education, urbanization and geographic region of residence. Of the studies that collected sociodemographic information, the statistical methods used to account for these factors included adjusting (n=15), stratifying (n=5), stratifying and then adjusting (n=1), or no further analysis (n=2). Two of the stratified analyses found differences in outcome measures based on sociodemographic characteristics such as ethnicity, screening venue, poverty, and urban versus nonurban residence. Findings indicated that HPV 16/18 prevalence decreased across all screening venues and that there was a significant decrease among white women but the decrease among black women was less marked and not significant. Further, there was a strong and significant decline in CIN2+/AIS among census tracts that had a lower proportion of the population living in poverty, in nonurban counties, and of Black and Hispanic race/ethnicity. The remaining three studies that used a stratified analysis found no differences in the outcome measures.

CONCLUSION AND RELEVANCE: In order to gain a better understanding of the impact of the HPV vaccine on related outcomes, efforts should be made to conduct stratified analyses whenever sociodemographic information is available. Further, this review indicates that a higher overall uptake of the vaccine may reduce potential disparities in impact and therefore future efforts should focus on improving vaccine coverage.

Introduction/Background

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States with about 79 million Americans currently infected and nearly 14 million new infections each year [1]. It is estimated that up to 80% of individuals will acquire HPV at some point in their lifetime with about 50% of people acquiring it from their first sexual partner[2]. It has been recognized that HPV is a necessary cause of cervical cancer and while many infections are asymptomatic, persistent infection may result in outcomes such as genital warts and several cancers including cervical, anal, vaginal, vulvar, penile, and oropharyngeal [2]. There are more than 50 anogenital types of HPV and of those, 18 are considered to be high-risk due to their strong association with cervical cancer [3].

Since 2006, the United States Food a Drug Administration (FDA) has approved three vaccines that protect against HPV-16 and HPV-18, which are known to cause 70% of invasive cervical cancers [3]. The bivalent HPV2 vaccine (Cervarix) prevents infection with HPV 16/18 and the quadrivalent HPV4 vaccine (Gardasil) provides additional protection against HPV-6 and HPV-11 [4]. In December 2014, the FDA approved a 9-valent vaccine (Gardasil 9) that protects against HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 [4]. Current recommendations from the Advisory Committee on Immunization Practices (ACIP) are for routine vaccination for adolescent females and males aged 11 or 12, and a catch-up period for those not previously vaccinated through the age of 21 for males and age 26 for females [5].

Thus far, the majority of literature related to disparities in HPV vaccination has been focused on sociodemographic differences in vaccine uptake. Current trends in the U.S. indicate that initiation of the HPV vaccine is highest among Hispanic adolescents, followed by black adolescents, with white adolescents having the lowest vaccine uptake overall [6]. In addition, by 2011 Hispanic adolescents had the highest percentage of initial vaccine coverage as well as the greatest increase in vaccine coverage since the introduction of the vaccine [6]. However, compared to Hispanic and non-Hispanic white females, black females had a lower rate of vaccine series completion [7]. In looking at vaccine uptake by poverty status, a 2014 CDC report showed that vaccine series initiation among girls living below the national poverty line was higher than that of girls living above the poverty line [7]. Nonetheless, the rate of series completion is lower among adolescents below poverty than for those living above poverty [8]. Finally, Mehta et al. described in 2012 how publicly insured (77%) and uninsured (85%) women were more likely than privately insured women (48%) to report no history of vaccination [9].

Now nearly ten years after the introduction of the first vaccines for HPV, a small but growing body of evidence is beginning to examine the impacts of the vaccination campaign. The purpose of this article is to systematically review the literature on the impact of the human papillomavirus vaccine on HPV-related outcomes, and to assess the potential differences in impact by various sociodemographic characteristics. Results can be used to identify potential disparities and areas for future programs and research that aim to understand the full impact of the vaccine.

Methods

This systematic review is registered in PROSPERO (registration number is CRD42016036465), an international database of prospectively registered systematic reviews in health and social care [10]. The review protocol is available on the Centre for Reviews and Dissemination website.

We systematically reviewed the global literature and report it according to the PRISMA guidelines [11]. Our primary search was conducted in the MEDLINE database with a combination of the following Medical Subject Heading (MeSH) terms, title, or abstract words: ("papillomavirus infections", or "uterine cervical dysplasia", or "adenocarcinoma in situ", or "cervical intraepithelial neoplasia", or ("cervical or cervix" adj "dysplasia or neoplasia or lesion")) and ("papillomavirus vaccines", or "HPV vaccine", or "human papillomavirus vaccine", or "HPV vaccination", or "human papillomavirus vaccination"). In addition to using the search terms to identify additional eligible articles in the PubMed database, we also conducted a cited reference search in Web of Science and searched the references of eligible articles. Databases were searched for relevant articles published from January 1, 2007 through January 31st, 2016. In order to identify eligible articles, the inclusion criteria below were applied first to the titles and abstracts of articles and then to full-text articles in order to determine final inclusion status. Conference abstracts were excluded from this review.

The primary inclusion criteria was that articles had to report data about vaccine impact using at least one primary endpoint including anogenital warts, histopathologically confirmed high-grade cervical lesions (cervical intraepithelial neoplasia [CIN] 2 or higher), or HPV infection. Studies were excluded for the following reasons: (1) not a source of primary data (news articles, recommendations, editorials, etc.), (2) no trends or data from a pre- and post-vaccine era, (3) randomized control trials of vaccine efficacy, and (4) duplicate articles. If more than one exclusion criteria applied, only the first criteria was listed as dictated by the numerical order above. Further, if more than one publication from the same data source and research team was available, we included both articles as analyses may have changed over time.

A standardized form was created to extract the relevant study characteristics for all included studies. For each study, we collected information about country or region of study, study population, setting, principle outcomes, methods, and if applicable, whether or not the authors collected information of sociodemographic characteristics, reported sociodemographic characteristics of the study population, and how the authors accounted for these factors. Two authors reviewed each article independently and discrepancies were resolved through discussion in order to achieve consensus regarding the accuracy of data extraction. The quality of studies (potential for bias and confounding) was assessed by review of participant selection or recruitment procedures, and potential confounders considered in the statistical analyses. No formal meta-analysis was performed due to a small number of eligible studies that could be included and heterogeneity of outcome measures.

Results

In our search, we identified 3,713 abstracts, of which 45 met our inclusion criteria[12-56] (Figure 1) and all of the included studies had sufficient methodological quality to be qualitatively described (Appendix A). Characteristics of the included studies are summarized in Table 1. Studies were done in 11 high-income countries including Australia, New Zealand, the United States, Sweden, Denmark, England, Germany, Scotland, Belgium, the Netherlands and Canada. The endpoints varied widely in each study but included prevalent HPV infections (n=3), type specific infections (including vaccine-type specific) (n=7), high-grade cervical abnormalities (CIN2+/AIS) (n=5), genital warts (n=25), atypia or worse (n=2), cervical abnormalities (n=1), incident abnormal events (CIN 1-3) (n=1), and general cervical cytology and histology results (n=1). Of the 45 included articles, 22 articles did not collect information on sociodemographic variables and 23 collected at least one sociodemographic variable. Variables collected varied between studies and countries with the most commonly assessed being race, ethnicity, education, urbanization and geographic region of residence. Of the studies that collected sociodemographic information, the statistical methods used to account for these factors included adjusting (n=15), stratifying (n=5), stratifying and then adjusting (n=1), or no further analysis (n=2).

Adjusted Analyses

In total, 15 studies used adjusted analyses when presenting findings on their primary outcomes. Among these studies, 8 papers presented both crude and adjusted measures[19,25,27,34,38,42,48,51,55] while the remaining 7 papers presented only the adjusted estimates. Within the 8 studies that presented crude and adjusted data, 4 studies made some indication that there was little to no difference between the two estimates and therefore the potential for confounding was unlikely[19,25,51,55]. In addition, there was usually a limited discussion, if any, about the role of potential confounders. Where a discussion was presented, it was a more general discussion about confounding and was not specific to sociodemographic factors.

Stratified Analyses

There were 5 studies that presented stratified analyses[40,43,47,52,53] and 1 study that first stratified and then adjusted in the absence of effect modification[29]. Sociodemographic factors collected and used in the stratified analysis varied and included some regionally specific characteristics.

Two of the five stratified studies found differences in outcome measures based on the variables used in the analyses. One study from England assessed the prevalence of vaccine-type HPV infections and stratified the analysis based on the screening venue (general practice, youth clinic, or family planning Community Sexual Health Services) and ethnicity[40]. When looking at the prevalence of type 16/18 infection by ethnicity, the authors reported that from the pre-immunization to the post-immunization period, there was a significant decrease in prevalence among white women (19.7% to 6.7%) but the decrease among black women was less marked and not significant (14.9% to 9.4%)[40]. Further, they reported a reduction in the prevalence of HPV 16/18 among 16-18 year olds of 76% in the GP clinics, 64% in community sexual health services centers, and 55% in youth clinics from the pre- to the post-immunization periods[40]. The significance of this finding was not reported. The second paper was a 2013 paper from the United States that assessed CIN2+/AIS trends over time in Connecticut[43]. The analysis was stratified by ethnicity (proportion of black and Hispanic), poverty as defined by the percentage of

population in each census tract living below the federal poverty level, and urban versus nonurban residence[43]. The main finding from the stratified analysis was that there was a strong and significant decline in census tracts that had a lower proportion of the population living in poverty, in nonurban counties, and of Black and Hispanic race/ethnicity[43]. The authors discuss that the reason for this disparity is not clear but may reflect a higher prevalence of vaccine-type strains (HPV 16/18) among White women and women living in low poverty areas[43].

The remaining three studies that used a stratified analysis found no differences in the outcome measures based on the various sociodemographic factors that they considered. Two studies from Australia looked at trends in genital warts in years pre- and post-vaccine[52,53]. The first study conducted a stratified analysis by indigenous status and concluded that the fall in genital warts admissions in young females (15-24) after implementation of the National HPV Vaccination Program (NHVP) was comparable for indigenous and non-indigenous females[52]. The second study stratified by two variables including residency inside or outside of a major city and an Index of Relative Socioeconomic Disadvantage (IRSD)[53]. IRSD is a measure that uses characteristics such as income, unemployment, occupation skill level and housing to create a score that is then placed into a ranking[53]. The authors found that there were no significant differences in the estimated reductions between women living in more versus less disadvantaged areas and that the reduction in genital warts admissions among young men were similar for those residing in and outside of major cities[53]. Finally, a study from Boston, USA also looked at trends in genital warts and concluded from their stratified analysis that there were significant declines in the rate of genital warts following the introduction of the vaccine and that the declines warts were similar for males and females of all race/ethnicities[47].

Other Analyses

Finally, 2 articles collected sociodemographic characteristics of race/ethnicity[24,31] and insurance[31] but only used the data for descriptive purposes and did not further account for them in the statistical analysis.

Discussion

The current body of literature surrounding uptake of the HPV vaccine in the United States suggests that there are potential disparities in who is initiating and completing the vaccine series. With this kind of evidence at hand, it is important to consider that there may be disparities in the impact of the vaccine. This review of 45 studies revealed that approximately half of the studies collected information related to sociodemographic characteristics of the study population and of those, yet only 5 studies conducted a stratified analysis in order to examine the potential role of these factors on their outcomes of interest. While reporting sociodemographic characteristics of the study population provides some insight, an adjusted statistical analysis takes away the ability to determine the role that a secondary factor may have on the outcome of interest. A stratified analysis is almost always useful and allows researchers to learn more about the complex relationships between variables of interest. Further, this approach provides a better understanding of the potential strength of an association in various strata of the potentially confounding variable rather than from a single estimate, such as in an adjusted analysis. It is our recommendation that when sociodemographic information is available, stratified analyses should be considered in order to gain a better understanding of the impact that the vaccine may be having on different

populations. Further, an analysis that both stratifies and then controls for additional characteristics may provide the most information and allow researchers to focus solely on one variable at a time, although these kinds of analyses were not seen in this body of literature.

There are a number of reasons why more research has not been done in this area regarding disparities in the HPV vaccine impact. First, the relevant data may not be available to do a stratified analysis. Many of the large-scale surveillance studies used population level data or extracted data from claims forms and medical chart reviews. In this situation, it may be more difficult to link sociodemographic characteristics to the population compared to a study where participants are enrolled, followed prospectively, and actively participate in providing information to the researchers. Next, it may be important to consider the baseline vaccine uptake in a population in order to gauge if disparities in the outcomes are likely to occur. For example, in the United States, coverage with at least one dose of the vaccine was at 60.0% in 2014 but complete coverage with the 3-dose series remained low at 39.7%[57]. In contrast, in 2014 it was estimated that 88.1% of females in grade 9 in England[58] and between 70.1% to 75.6% of females in Australia had completed the HPV vaccine series[53]. With these differences in mind, it may make sense that a stratified analysis from the U.S. demonstrated differences in the decline of CIN2+/AIS by measures of race/ethnicity, poverty, and area of residence[43], while in the two stratified analyses from Australia, there were no differences in the outcome for different populations[52,53]. This may suggest that in a population where vaccine uptake is low, the potential for disparities is higher than in a population with more widespread coverage. However, this suggestion does not hold true for all the stratified analyses presented here and thus continued surveillance is needed in order to better understand the role of vaccine uptake on disparities in HPV-related outcomes.

In addition to differences in vaccine uptake, it is important to consider other factors that may contribute to disparities in vaccine impact. Most notably, Hariri et al. described differences in HPV type distribution by a number of sociodemographic variables. The main finding from this study was that cervical lesions associated with HPV types 16/18 were less common in non-Hispanic blacks (41.9%), and Hispanics (46.3%) compared to non-Hispanic whites (59.1%) and these differences were statistically significant[59]. Further, Niccolai et al. added in 2013 that in addition to black race and Hispanic ethnicity, higher area-based poverty was a salient predictor of lower HPV 16/18 positivity among women who were diagnosed with high-grade cervical lesions[60]. Together, these findings suggest that current HPV vaccines may have a lower impact on particular populations thus further perpetuating disparities that may already exist. Second-generation vaccines, such as the 9-valent vaccine, may provide additional benefit for some racial/ethnicity and socioeconomic groups and thus continued surveillance is of the utmost importance.

Limitations

This systematic review does have some limitations that need to be acknowledged. The existing published studies did not allow for a quantitative meta-analysis and to be as comprehensive as possible and aid in the wide dissemination of findings, we did not exclude any study on the basis of quality. However, based on our quality review of the included studies, no studies fell into a low quality range and should all, therefore, provide robust and unique evidence to our potential

understanding of HPV vaccine impact. In addition, there is always a conceivable risk of publication bias in a review of this nature due to the inclusion of only peer-reviewed, full-text articles. Finally, the studies included in this review were all from high-income countries and therefore the conclusions made cannot be further generalized to other middle- or low-income countries, as we do not currently have a strong understanding of the HPV vaccine landscape in those locations.

Conclusion

This review provides a systematic and comprehensive summary of the impacts of the HPV vaccine on HPV-related outcomes and the potential disparities in those outcomes that have been identified in the literature. While the body of literature is growing, continued surveillance is needed to measure vaccine impact and monitor health disparities. In order to gain a better understanding of the impact of the HPV vaccine on related outcomes, efforts should be made to conduct stratified analyses whenever sociodemographic information is available. Further, this review indicates that a higher overall uptake of the vaccine may reduce potential disparities in impact and therefore future efforts should focus on improving vaccine coverage.

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Figure 1. Flow Diagram (Preferred Reporting Items for Systematic Review and Meta-Analyses) of Articles Considered for Inclusion

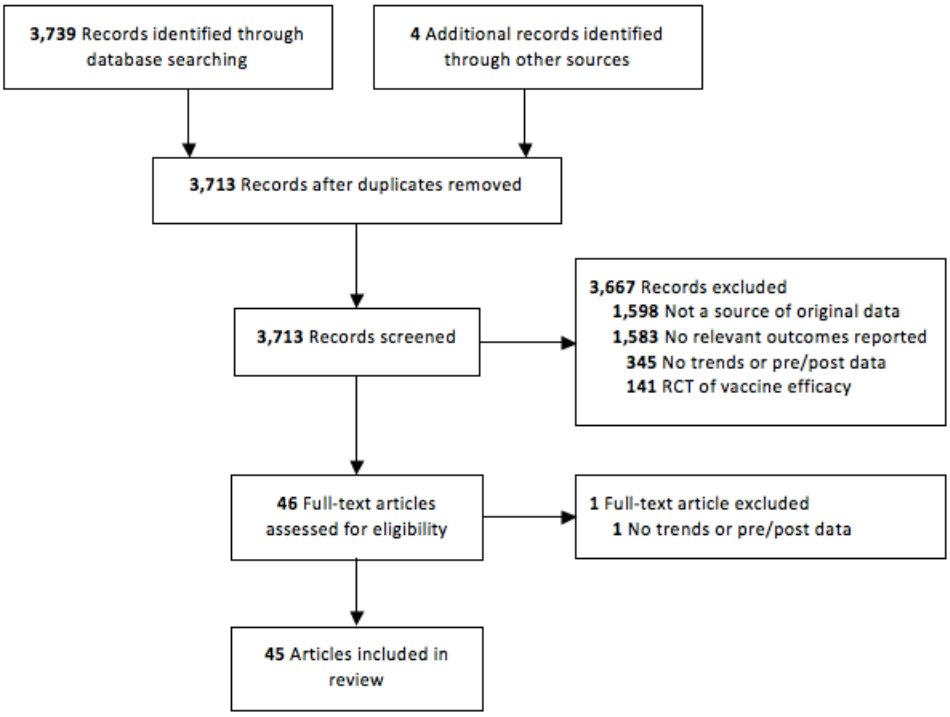


Table 1: Characteristics of Included Studies

Study ID	Location and Collection Dates	Study Population and Sample Size	Setting	Principal Outcomes	Collected SDC*?	What measures?	Statistical Analysis
Fairley 2009 STI	Melbourne, Australia January 1, 2004-December 31, 2008	Men and women, any age, n=36,055	Melbourne Sexual Health Centre (public sexual health clinic)	Genital warts	N	--	--
Brotherton 2011 Lancet	Victoria, Australia January 2003-December 2009	Women, any age, n=>2.7 million	Victorian Cervical Cytology Registry, participating in national cervical cancer screening program	High and low grade cervical abnormalities	N	--	--
Donovan 2011 Lancet	Australia (8 locations) January 2004-December 2009	New patients, men and women, any age n=112,083	Sentinel surveillance at sexual health clinics	Genital warts	N	--	--
Oliphant 2011 NZMA	Auckland, New Zealand January 1, 2007-June 30, 2010	New patients, men and women, any age n=40,793	Auckland Sexual Health Services clinic	Genital warts	N	--	--
Read 2011 STI	Melbourne, Australia July 1, 2004-June 30, 2011	New patients, men and women, any age n=52,454	Melbourne Sexual Health Centre (public sexual health clinic)	Genital warts	N	--	--
Bauer 2012 AJPH	California 2007-2010	Males and females all ages, n=1,754,000 female and 258,000 male clients annually	California Family Planning Access Care and Treatment (Family PACT) program	Genital warts	N	--	--
Cummings 2012 Vaccine	Indianapolis, Indiana Pre: 1999-2005, Post: 2010	Women age 14-17 n=Pre:150, Post: 75	3 urban primary care clinics	Type-specific HPV infection	Y	Race	Nothing (didn't account for it at all, just used to describe)

Kahn 2012 Pediatrics	Cincinnati, Ohio Pre: Oct 2006-May 2007, Post: Dec 2009-June 2010	Women age 13-26 who had sexual contact n=Pre: 368, Post: 409	Hospital-based adolescent clinic and community health center associated with the health department	Vaccine-type specific	Y	Race, ethnicity, insurance	Adjusted
Leval 2012 JID	Sweden 2006-2010	Men and women, ages 10-44, n=varied per year, >4 million	Data linkage with Prescribed Drug Register and National Patient Register	Genital warts	N	--	--
Tabrizi 2012 JID	Australia (Perth, Sydney, Melbourne) Pre: 2005-2007, Post: 2010-2011	Women age 18-24 attending pap screen, n=606	Family planning clinics in the 3 cities	HPV prevalence	Y	SES measure (including variables such as education and median income), residential area, education	Adjusted
Ali 2013 BMC ID	Australia 2000-2011	Men and women age 15-44, n=6,950	Extracted data from all private hospitals	Genital warts (inpatient treatment)	N	--	--
Ali 2013 BMJ	Australia January 2004-December 2011	Men and women, any age, n=85,770	Attended any of the 8 sexual health clinics enrolled for the first time	Genital warts	N	--	--
Baadrup 2013 STD	Jutland and Funen, Denmark, 1996-2011	Men and women, any age, with new infection, n=18,574 in Jutland and Funen from 1996-2010, and 17,309 in Denmark from 2006-2011	Danish National Patient Register	Genital warts	N	--	--
Blomberg 2013 CID	Denmark, Oct 2006-May 2012	Girls born in birth cohorts from 1989-1999, n=399,770	National Patient Register- data linkage	Genital warts	N	--	--
Flagg 2013 AJPH	United States January 2003-December 2010	Privately insured persons, male and females, ages 10-39, with continuous health insurance in a given year, n=between 5 and 13 million persons per year	Truven Health Analytics Marketscan Commercial Claims and Encounters Database	Anogenital warts	Y	Geographic region, MSA vs. non-MSA, type of health insurance (capitated vs. non)	Stratified and then adjusted in the absence of effect modification

Gertig 2013 BMC	Victoria, Australia April 1, 2007-December 31, 2011	Women age 17 or younger in 2007 with a pap screening n=38,956	Data linkage from the Victorian Cervical Cytology Registry	High-grade cervical abnormalities CIN 2+/AIS	Y	Socioeconomic disadvantage, remoteness	Adjusted
Howell-Jones 2013 JID	England 2002-2011	Males and females, age 15-24 n=not reported	General practices and genitourinary medicine clinics	Genital warts	N	--	--
Leval 2013 JNCI	Sweden January 2006-December 2010	Women age 10-44, n=2,209,263	Data linkage, population registers	Genital warts	Y	Maternal and paternal education	Adjusted
Markowitz 2013 JID	United States 2003-2010	Females age 14-59 n=2003-2006: 4150, 2007-2010: 4253	NHANES, nationally representative of the civilian, noninstitutionalized US population	HPV infection	Y	Race/ethnicity, poverty index	Adjusted
Mesher 2013 Vaccine	Seven regions in England 2008 and October 2010-June 2012	Sexually active females, 16-24, undergoing screening for chlamydia n=Post: 4,178	Patients visiting their community sexual health services, general practitioners, and youth clinics	Vaccine type HPV infection (16/18)	Y	Screening venue, ethnicity	Stratify
Mikolajczyk 2013 STD	Germany 2005-2008	Men and women, ages 10-79 n=not reported	German Pharmacoepidemiological Research Database	Anogenital warts	N	--	--
Niccolai 2013 CEBP	Connecticut, US 2008-2011	Women, ages 21-39 n=8,146 cases	Statewide surveillance registry	CIN 2+/AIS	Y	Ethnicity (proportion black and Hispanic), poverty, urban/nonurban	Stratify
Nsouli-Maktabi 2013	United States January 1, 2000-December 21, 2012	Men and women, age 17+, who served in the active component of the US Armed Forces n=varied per year, >1.5 million	Defense Medical Surveillance System	Genital warts	N	--	--
Baldur-Felskov 2014 JNCI	Denmark 2006-2012	All girls and women born in Denmark from 1989-1999, n=399,244	Data linkage from Civil Registration System	(1) Atypia or worse, (2) CIN 2 or worse	Y	Mother's highest education and disposable income	Adjusted

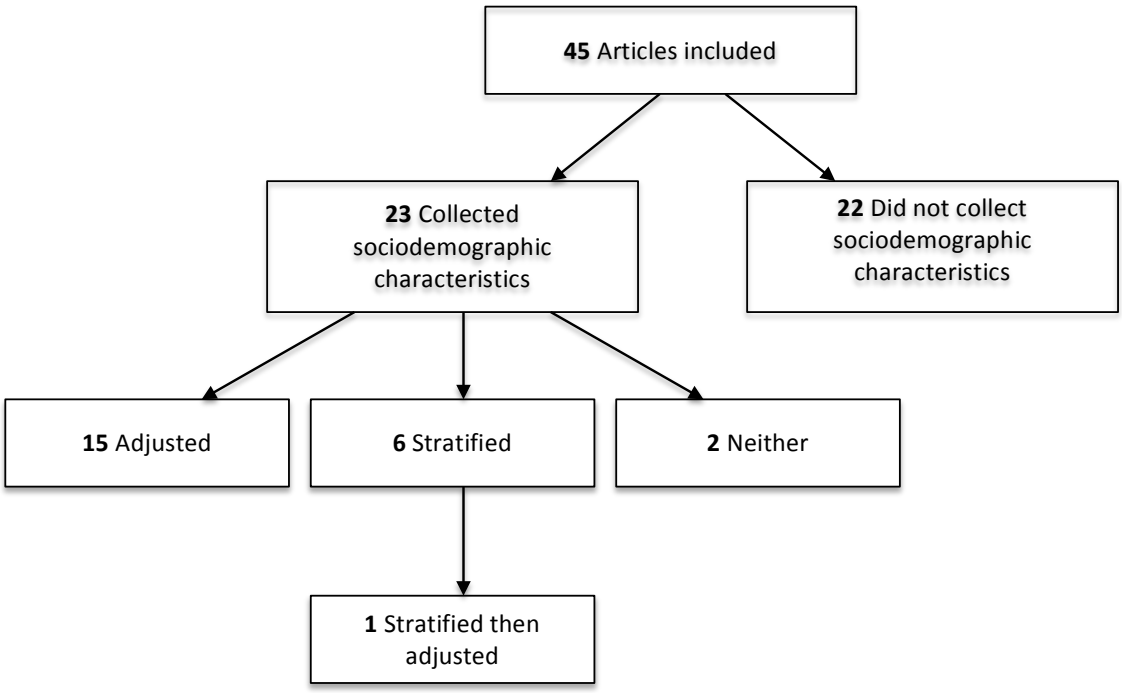
Baldur-Felskov 2014 Cancer	Denmark January 1, 2000-March 1, 2013	Females age 12+, n=>2 million between 2000-2012	National pathology data bank	(1) Atypia or worse, (2) CIN 2 or worse	N	--	--
Harrison 2014 PLOS One	Australia July 2000-June 2012	Anyone age 15+ presenting to one of the randomly chosen general practitioners n=1,175,879 patient encounters	Cross-sectional national study: Bettering Evaluation and Care of Health Program	Genital warts	N	--	--
Kavanagh 2014 BJC Cancer	Scotland 2009-2012	Women age 20-21 attending cervical screening appointment, n=4,729	Scottish Cervical Screening Call and Recall System	Type-specific HPV 16/18, 31, 33, 45	Y	Scottish Index of Multiple Deprivation	Adjusted
Liu 2014 STI	Australia 2001, 2011	Women age 18-39 n=2001: 4,874, 2011: 2,394	In 2001, Australian Study of Health and Relationships (random digit dial) and in 2011, cross-sectional random digit dial	Genital warts	Y	Education, aboriginality, state of residence	Adjusted
Pollock 2014 BJC	Scotland 2008-May 2013	Women born between 1988-1992 who were age 20-21 during 2008-2012 n=106,052	Scottish Cervical Screening Program- data linkage	Incident abnormal histological events (CIN 1, 2, 3)	Y	SIMD- Scottish index of multiple deprivations	Adjusted
Sando 2014	Denmark Jan 2001-Dec 2011	All people, age 15-34 n=not reported	National registries: Register of Medical Products Statistics and National Patient Register	Anogenital warts	N	--	--
Soderlund-Strand 2014 CEBP	Skane region, Sweden Baseline 2008, follow-up 2012-2013	Men and women any age n=2008: 44,146 2012: 5,224, 2013: 5,815	Lab data from all patients screened for chlamydia in the specific region	HPV infection	N	--	--
Tabrizi 2014 Lancet	Sydney, Melbourne, Perth Australia Oct 2005-July 2007, Aug 2010-Nov 2012	Women age 18-24 n=Pre: 202, Post: 1,058	Attended one of the 6 family planning clinics in the 3 metropolitan areas for pap screening	Vaccine-targeted and "closely related" HPV types	Y	Socioeconomic disadvantage, residential area, education	Adjusted

Blomberg 2015 CID	Denmark 2006-2012	All girls in Denmark born 1985-1999, n=550,690	Data linkage from Civil Registration System	Genital warts	Y	Maternal education level and disposable income at the start of the follow-up	Adjusted
Brotherton 2015 CCC	Victoria, Australia 2000-2013	Women of all ages n= >8 million pap screenings	Victorian Cervical Cytology Registry	High grade cervical abnormalities (CIN2+)	N	--	--
Chow 2015 Lancet	Melbourne, Australia July 1, 2004-June 30, 2014	Women age 25 or younger, n=1,202	Attended the Melbourne Sexual Health Centre and had a diagnosis of chlamydia	Vaccine-targeted HPV types	N	--	--
Chow 2015 STI BMJ	Melbourne, Australia July 1, 2004-June 30, 2014	All new patients, n=81,939	Attending Melbourne Sexual Health Center	Genital warts	N	--	--
Dominiak-Felden 2015 PLOS ONE	Belgium January 2006-December 2013	Men and women age 16-59 n=Between 907,047 and 1,284,493	Retrospective cohort using MLOZ reimbursement database	Genital warts	Y	VE only: Household income, and region of residence	Adjusted
Dorton 2015 Obstetrics and Gynecology	Boston February 26, 2007-March 10, 2014	Women age 26 or younger at first visit, n=1,392	Patients who presented to the Center for Lower Genital Tract Disease at 2 institutions in Boston	Cervical cytology and histology results (diagnosis for clinical care)	Y	Race/ethnicity, language, insurance, concern about insurance or financial matters	Adjusted
Hariri 2015 Cancer	US (CA, CT, NY, OR) January 2008-December 2012	Women age 18-39 n=9,119 cases	Catchment areas in 4 states	CIN2+/AIS	Y	Race/ethnicity, insurance	Nothing (didn't account for it at all, just used to describe)
Mollers 2015 Vaccine	Netherlands 2009-2012	Girls age 14-16 who were eligible for National Vaccination catch-up in 2009-2010, n=1,668	Enrolled in the HPV Amongst Vaccinated and Non-vaccinated Adolescents (HAVANA) study	Incident and persistent HPV infections with 16/18/31/45	Y	Ethnicity, education, urbanization	Adjusted

Ogilvie 2015 IJC	BC, Canada, January 1, 2004-December 31, 2012	Young women age 15-22, n=not reported	Data linkage study, BC Cancer Agency database and BC Centre for Disease Control Data Screening program	CIN 2 and CIN 2+	N	--	--
Perkins 2015 STD	Boston Jan 2004-Dec 2013	Men & women, age 16-26, n=45,787	Urban medical center and 6 affiliated community health centers	Genital warts	Y	Language, race, public insurance	Stratify
Smith 2015 JID	Australia 1999-2011	Men & women 12-69 years, n=39,350	National Hospital Morbidity Data	Genital warts	Y	Indigenous status	Stratify
Smith 2015 Pediatrics	Ontario, Canada Sept 1, 2005-2012	All girls in grade 8 during 2005/2006-2008/2009 n=260,493	Population-based cohort, administrative health database	Cervical dysplasia and anogenital warts	Y	Residency (urban vs. rural), income	Adjusted
Smith 2016 BMC ID	Australia July 2004-June 2011	Males and females aged 10-39 at admission n=not reported	National Hospital Morbidity Data (comprehensive national database)	Genital warts	Y	Index of relative socioeconomic disadvantage, resident inside or outside major cities	Stratify

*SDC: Sociodemographic characteristics

Figure 2. Flow Diagram of Articles Collecting Sociodemographic Information



Appendix A: Assessment of Quality and Confounding

Study ID	Country	Type of Study Population	Subjects Included	Selection Bias Rating	Potential Confounders Considered
Fairley 2009 STI	Melbourne, Australia	Clinic-based (total)	Men and women all ages	Medium	None
Brotherton 2011 Lancet	Victoria, Australia	Total population (national)	Women, any age	Low	None
Donovan 2011 Lancet	Australia (8 locations)	Clinic-based (total)	New patients, men and women, any age	Medium	None
Oliphant 2011 NZMA	Auckland, New Zealand	Clinic-based (total)	New patients, men and women, any age	Medium	None
Read 2011 STI	Melbourne, Australia	Clinic-based (total)	New patients, men and women, any age	Medium	Number of sex partners
Bauer 2012 AJPH	California	Clinic-based (total)	Males and females all ages	Medium	None
Cummings 2012 Vaccine	Indianapolis, Indiana	Clinic-based (sample)	Women age 14-17	High	None
Kahn 2012 Pediatrics	Cincinnati, Ohio	Clinic-based (sample)	Women age 13-26 who had sexual contact	High	Propensity score
Leval 2012 JID	Sweden	Total population (national)	Men and women 10-44	Low	None
Tabrizi 2012 JID	Australia (Perth, Sydney, Melbourne)	Clinic-based (sample)	Women age 18-24 attending pap screen	High	Age, hormonal contraceptive use, region, socioeconomic group, smoking status
Ali 2013 BMC ID	Australia	Total population (select)	Men and women age 15-44	Low	None
Ali 2013 BMJ	Australia	Clinic-based (total)	Men and women, any age	Medium	None
Baadrup 2013 STD	Jutland and Funen, Denmark	Total population (national)	All men and women, any age, with new infection	Low	None
Blomberg 2013 CID	Denmark	Total population (national)	Girls born in birth cohorts from 1989-1999	Low	None
Flagg 2013 AJPH	United States	Population-based (sample)	Privately insured persons, male and females ages 10-39, with continuous health insurance in a given year	Medium	None
Gertig 2013 BMC	Victoria, Australia	Total population (regional)	Women age 17 or younger in 2007 with a pap screening	Low	Remoteness, SES, age at first screening

Howell-Jones 2013 JID	England	Clinic-based (total)	Males and females age 15-24	Medium	Chlamydia diagnoses rate, primary care trust
Leval 2013 JNCI	Sweden	Total population (national)	Women age 10-44	Low	Age and parental education level as a proxy for socioeconomic status
Markowitz 2013 JID	United States	Population-based (sample)	Females age 14-59	Medium	Race/ethnicity, lifetime number of sex partners
Mesher 2013 Vaccine	Seven regions in England	Clinic-based (sample)	Sexually active females, 16-24, undergoing screening for chlamydia	High	Sexual history, age, venue type, ethnicity, chlamydia positivity
Mikolajczyk 2013 STD	Germany	Clinic-based (total)	Men and women ages 10-79	Medium	Calendar time
Niccolai 2013 CEBP	Connecticut, US	Total population (regional)	Women ages 21-39	Low	None
Nsouli-Maktabi 2013	United States	Total population (select)	Men and women, age 17 and older, who served in the active component of the US Armed Forces	Medium	None
Baldur-Felskov 2014 JNCI	Denmark	Total population (national)	All girls and women born in Denmark from 1989-1999	Low	Mother's highest education and disposable income
Baldur-Felskov 2014 Cancer	Denmark	Total population (national)	Females age 12 and older	Low	None
Harrison 2014 PLOS One	Australia	Clinic-based (sample)	Anyone age 15+ presenting to one of the randomly chosen general practitioners	High	None
Kavanagh 2014 BJC Cancer	Scotland	Population-based (sample)	Women age 20-21 attending cervical screening appointment	Medium	Cohort year, number of doses received, Scottish Index of Multiple Deprivations
Liu 2014 STI	Australia	Population-based (sample)	Women age 18-39	Medium	Age, country of birth, state of residence, education, aboriginality
Pollock 2014 BJC	Scotland	Total population (national)	Women born between 1988 and 1992 who were age 20-21 during 2008-2012	Low	Cohort year, age in months, Scottish Index of Multiple Deprivations
Sando 2014	Denmark	Total population (national)	All people ages 15-34	Low	None
Soderlund-Strand 2014 CEBP	Skane region, Sweden	Total population (regional)	Men and women any age	Low	None

Tabrizi 2014 Lancet	Sydney, Melbourne, Perth Australia	Clinic-based (sample)	Women age 18-24	High	Age, hormonal contraceptive use
Blomberg 2015 CID	Denmark	Total population (national)	All girls in Denmark born 1985-1999	Low	Attained age and calendar time
Brotherton 2015 CCC	Victoria, Australia	Total population (regional)	Women of all ages	Low	None
Chow 2015 Lancet	Melbourne, Australia	Clinic-based (sample)	Women age 25 or younger	High	None
Chow 2015 STI BMJ	Melbourne, Australia	Clinic-based (total)	All new patients	Medium	Number of partners in the past 12 months
Dominiak-Felden 2015 PLOS ONE	Belgium	Clinic-based (total)	All men and women age 16-59	Medium	Household income, region of residence
Dorton 2015 Obstetrics and Gynecology	Boston	Clinic-based (total)	Women age 26 or younger at first visit	Medium	Race/ethnicity, language, number of pregnancies, gonorrhea, smoking status
Hariri 2015 Cancer	US (CA, CT, NY, OR)	Total population (regional)	Women age 18-39	Low	Age
Mollers 2015 Vaccine	Netherlands	Total population (select)	Girls age 14-16 who were eligible for National Vaccination catch-up in 2009-2010	Medium	Age, urbanization degree, ethnicity, ever smoked, current smoking, anticonception use, ever had sexual intercourse, age of partner, lifetime number of sex partners
Ogilvie 2015 IJC	British Columbia, Canada	Population-based (regional)	Young women age 15-22	Low	None
Perkins 2015 STD	Boston	Clinic-based (total)	Men and women 16-26	Medium	None
Smith 2015 JID	Australia	Total population (national)	Men and women 12-69 years	Low	None
Smith 2015 Pediatrics	Ontario, Canada	Total population (regional)	All girls in grade 8 during 2005/2006-2008/2009	Low	Birth category, recent indicator of sexual behavior, neighborhood income quintile, Hepatitis B vaccination
Smith 2016 BMC ID	Australia	Total population (national)	Males and females aged 10-39 at admission	Low	None