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Estimated prevalence of human papillomavirus among Nigerian women: A systematic review and meta-analysis

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Abstract

HPV prevalence in Nigeria has been challenging to quantify given regional population heterogeneity and differences in diagnostic methodology. We conducted a systematic review and meta-analysis of 17 studies, each of which summarized HPV prevalence in women residing in six geopolitical zones of Nigeria. The estimated pooled prevalence (effect size) of HPV in Nigeria was 32% (CI: 23-41%). HPV prevalence was 29% (CI: 20-39%) among studies that detected HPV by genotype. HPV prevalence among studies that used serologic detection was 38% (CI: 12-65%). When stratified by region, a study in the South East (SE) geopolitical zone reported the highest prevalence of 71% (CI: 61-80%) while a study in the South South (SS) geopolitical zone reported the lowest prevalence of 4.9% (CI: 3-9%). HPV prevalence in Nigeria was high. Heterogeneity between study regions and differing HPV detection methods both contribute to variation in estimates. Using pooled estimates serves to inform future strategies for epidemiologic surveillance and future design of HPV and cervical cancer prevention initiatives. *(Afr J Reprod Health 2022; 26[6]:89-96).*

Keywords: Human papillomavirus, Nigeria, cervical cancer, prevalence

Résumé

La prévalence du VPH au Nigeria a été difficile à quantifier étant donné l'hétérogénéité régionale de la population et les différences dans la méthodologie de diagnostic. Nous avons effectué une revue systématique et une méta-analyse de 17 études, chacune d'entre elles résumant la prévalence du VPH chez les femmes résidant dans six zones géopolitiques du Nigéria. La prévalence combinée estimée (taille de l'effet) du VPH au Nigeria était de 32 % (IC : 23-41 %). La prévalence du VPH était de 29 % (IC : 20-39 %) parmi les études qui ont détecté le VPH par génotype. La prévalence du VPH parmi les études qui ont utilisé la détection sérologique était de 38 % (IC : 12-65 %). Lorsqu'elle est stratifiée par région, une étude dans la zone géopolitique du Sud-Est (SE) a rapporté la prévalence la plus élevée de 71 % (IC : 61-80 %) tandis qu'une étude dans la zone géopolitique du Sud-Sud (SS) a rapporté la prévalence la plus faible de 4,9 %. (IC : 3-9 %). La prévalence du VPH au Nigéria était élevée. L'hétérogénéité entre les régions d'étude et les différentes méthodes de détection du VPH contribuent toutes deux à la variation des estimations. L'utilisation d'estimations groupées sert à éclairer les futures stratégies de surveillance épidémiologique et la conception future des initiatives de prévention du VPH et du cancer du col de l'utérus. *(Afr J Reprod Health 2022; 26[6]:89-96).*

Mots-clés: Virus du papillome humain, Nigéria, cancer du col de l'utérus, prevalence

Introduction

Cervical cancer remains the fourth most common malignancy diagnosed among women worldwide, and the second most common malignancy in less developed regions. In 2018, there were approximately 570,000 diagnosed cases and 311,000 deaths globally[1]. Approximately 85% of deaths from cervical cancer occur in low-income and middle-income countries, with a death rate 18 times that of wealthier countries[2]. These figures are likely an underestimate, as many cases and deaths go undiagnosed or unreported.

There has been substantial evidence linking cervical cancer to sexually acquired Human Papillomavirus (HPV) infection, particularly with HPV genotypes 16 and 18, which cause 70% of cervical cancers and precancerous lesions[3]. HPV burden in low-income countries is among the highest in the world, especially in Sub-Saharan Africa. Worldwide studies from the literature have included Sub-Saharan African countries in their

analyses. However, often there remains a paucity of data that reflects the country's regional heterogeneity. For example, in one study, researchers conducted a pooled analysis of HPV prevalence worldwide, using 11 countries[4]. Nigeria was represented by one study conducted in an urban, densely populated, religiously and ethnically homogeneous region. In this example, generalizing HPV prevalence may not only lead to an inaccurate estimation of disease burden, but may also present challenges to subsequent surveillance strategies.

Several studies within Nigeria have since characterized HPV prevalence in multiple regions of the country, with much variation. While these studies have aided tremendously in understanding national disease presence, an overall pooled HPV prevalence for the country of Nigeria has been challenging to quantify. This is possibly due to regional population heterogeneity, differences in diagnostic methodology, and variations in strategies for disease screening and surveillance. The overall prevalence of cervical cancer in Nigeria remains poorly understood for similar reasons. Accessibility and availability of cervical cancer screening tools varies tremendously throughout the country. In this study, we estimate the pooled prevalence of HPV in women living in Nigeria by conducting a systematic review and meta-analysis of 17 individual studies conducted in various regions throughout Nigeria.

Methods

The research group consisted of 4 individuals; one physician scientist, one epidemiologist, one librarian specialist, and one medical student researcher. Each member of the group was involved in identifying, screening, and determining inclusion and exclusion eligibility for each article. All members of the group then independently reviewed articles that were both included and excluded to avoid bias. Qualitative analysis and synthesis of each study included a careful review of each article's study design and research methodology. Members were involved in evaluating and discussing each article. Evaluations of the reviewers were generally concordant. A total of five databases were used to complete this search, over a total of two months in 2017. Databases included PubMed, Web of Science Centre for Agriculture and Bioscience (CAB) International Collection, Web of Science Core Collection, Embase, and Google Scholar.

We conducted a systematic review and meta-analysis of 17 studies using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocols and guidelines. We also incorporated the Meta-Analysis of Observational Studies in Epidemiology Guidelines for Reporting (MOOSE). Figure 1 shows the PRISMA Flow Diagram, which depicts the different phases of systematic review.

A slightly different strategy was used for each database, due to variations in syntax requirements for Boolean search methodologies. In an effort to include all available studies, contact with the authors of the studies was sometimes necessary, and was generally limited to clarifications or requests for full-text articles. Published abstracts were not included in the analysis due to insufficient information to include in analysis.

Each study summarized HPV prevalence in Human Immunodeficiency Virus (HIV) uninfected women residing in various regions of Nigeria at the time of the study. HIV uninfected women were chosen in this study because the literature strongly suggests a disproportionately increased prevalence of HPV among HIV infected women. As such, including HIV infected women in this analysis would have potentially artificially inflated the effect size of the study. A random effects model was used to establish an estimated pooled HPV prevalence. We calculated prevalence estimates with 95% confidence intervals and performed heterogeneity testing using the chi-squared test. The question addressed by our study was: what is the estimated pooled prevalence of HPV for women in Nigeria?

Criteria for inclusion were cross-sectional, case control, cohort, or randomized control trials that reported population specific HPV prevalence. Studies must have taken place in one of the six geopolitical zones in Nigeria. Data must have been collected on or after January 1, 2006. Additionally, specific mention of the type of diagnostic test used in the study was required.

Criteria for exclusion were abstracts, studies that included HIV patients in the prevalence estimate, studies using the same study population data as another article included for our meta-analysis, or studies that used data collected prior to January 1, 2006. Our search did not yield articles published in other languages. Stata 13.1 statistical

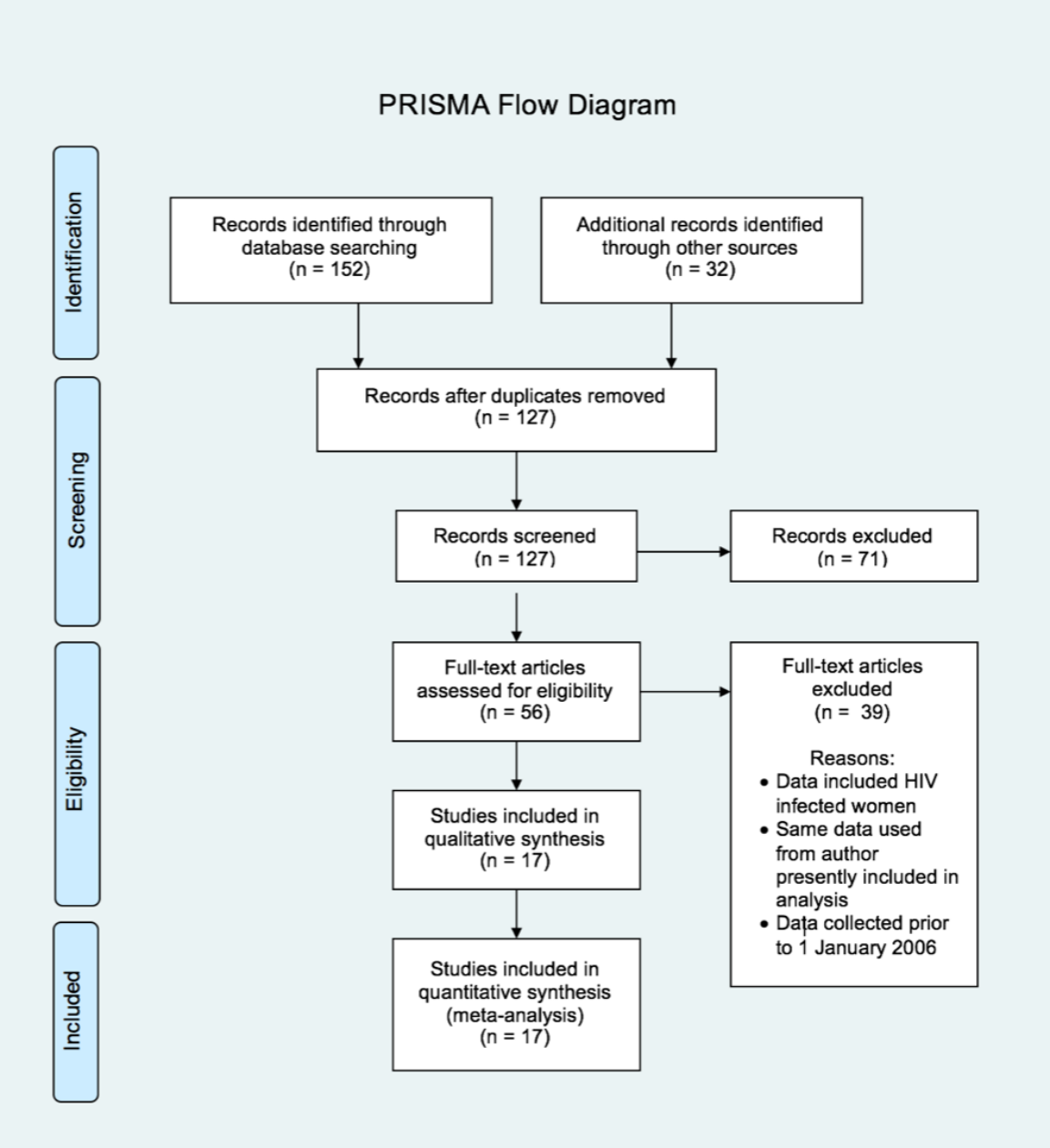

Figure 1: PRISMA flow diagram

software package was used for data analysis and generation of two figures.

Results

Adherence to PRISMA protocols yielded 17 studies eligible for systematic review. All 17 studies took place in one of six geopolitical zones in Nigeria. Table 1 shows the summary characteristics of all studies, including study type. In the North Central (NC) zone, there were 5 studies used, two of which were by Adebamowo[5-6], in addition to studies by Akarolo-Anthony[7], Famooto[8], and Modibbo[9]. Each of these studies had an estimated prevalence of 21.3%, 41.5%, 37%, 24.3%, and 9.9% respectively. The North East (NE) zone had one study by Manga *et al*[10] with an estimated prevalence of 48.1%. The North West (NW) zone included studies by Aminu[11], Auwal[12], and Pimentel[13] with estimated prevalence of 42.9%, 76%, and 15.3% respectively. The South South (SS) zone included studies by Kennedy[14] and Okonko[15] with estimated prevalence of 10% and 4.9% respectively. The South East (SE)

Table 1: Study characteristics

Study by Zone(year)	Study Type	*n*	Mean age (SD)	Estimated Prevalence (%)
NORTH CENTRAL				
Adebamowo(2017)	Cohort Study	535	38 (8)	21.3
Adebamowo(2017)	Cohort Study	11500	39 (10)	41.5
Akarolo-Anthony(2014)	Cross Sectional	275	38 (8)	37
Famooto(2013)	Case Control	267	36.5 (7.6)	24.3
Modibbo(2017)	Randomized Control Trial	293	40.8 (1.3)	9.9
NORTH EAST				
Manga(2015)	Cross Sectional	208	39.6 (10.4)	48.1
NORTH WEST				
Aminu(2014)	Cross Sectional	350	not included	42.9
Auwal(2013)	Cross Sectional	50	28	76
Pimentel(2013)	Cross Sectional	144	38.9 (13.5)	15.3
SOUTH SOUTH				
Kennedy(2016)	Cross Sectional	80	39 (5)	10
Okonko(2015)	Cross Sectional	182	29.35	4.9
SOUTH EAST				
Ngwu(2015)	Cross Sectional	90	34 (9)	71.1
SOUTH WEST				
Adekunle(2014)	Cross Sectional	91	29.35 (1.04)	6.6
Fahadunsi(2013)	Cross Sectional	111	42.9 (10.9)	21.6
Gage(2012)	Cross Sectional	1282	45	14.7
Kalawole(2015)	Cross Sectional	200	not included	67.5
Okunade(2017)	Cross Sectional	200	36.1 (7.4)	36.5

zone included one study by Ngwu[16] with an estimated prevalence of 71.1%. The South West (SW) zone included studies by Adekunle[17] Fahadunsi[18], Gage[19], Kalawole[20], and Okunade[21] with estimated prevalence of 6.6%, 21.6%, 14.7%, 67.5%, and 36.5% respectively. The publication year for each study can also be found in Table 1.

Studies used in this meta-analysis were stratified in two ways: (1) by detection method and (2) by location. First, studies were stratified based on HPV detection method used (Figure 2). Strata specific I^2 and *P* values not shown. The estimated prevalence proportion (PP) when detected by genotype was 0.29. The I^2 was 99.0% and the *P* value was <0.001. The PP when detected by serotype was 0.38. The I^2 was 99.2% and the *P* value was <0.001. The *P* value for heterogeneity between these two strata was $P = .521$. The pooled overall PP of HPV in Nigerian women, when stratified by detection method was .32 or 32% prevalence. The overall I^2 was 99.04 and $P<0.001$. Next, studies were stratified by location based upon six geopolitical zones in Nigeria (Figure 3). The PP in SW was .29. The I^2 was 98.6% and the *P* value was <.001. The PP in NC was .27. The I^2 was 99.1% and the *P* value was <.001. The PP in SS was 0.06. There was no I^2 or *P* value due to there being few studies in the SS stratum. The PP in NE was 0.48. There was no I^2 or *P* value due to there being one single study in the SE stratum. The PP in NE was .48. There was no I^2 or *P* value for similar reasons. The PP in NW was .22. There was no I^2 or *P* value due to there being few studies in the SS stratum. The *P* value for heterogeneity between these six strata was $P<0.001$. The pooled overall PP of HPV in Nigerian women, stratified by region was .32 or 32% prevalence. The I^2 was 99.04 and $P<0.001$.

Discussion

We conducted a systematic review and meta-analysis of HPV among women living in Nigeria. We found 17 studies, and stratified them in two variations: (1) by detection method and (2) by location. Both variations yielded the same overall PP of .32 or an estimated HPV prevalence of 32%. When stratifying by detection method, the serotype stratum yielded a higher prevalence estimate than the genotype stratum by 9%. This likely reflects one of the major differences between genotype and serotype detection. HPV serologic detection identifies individuals with current or past

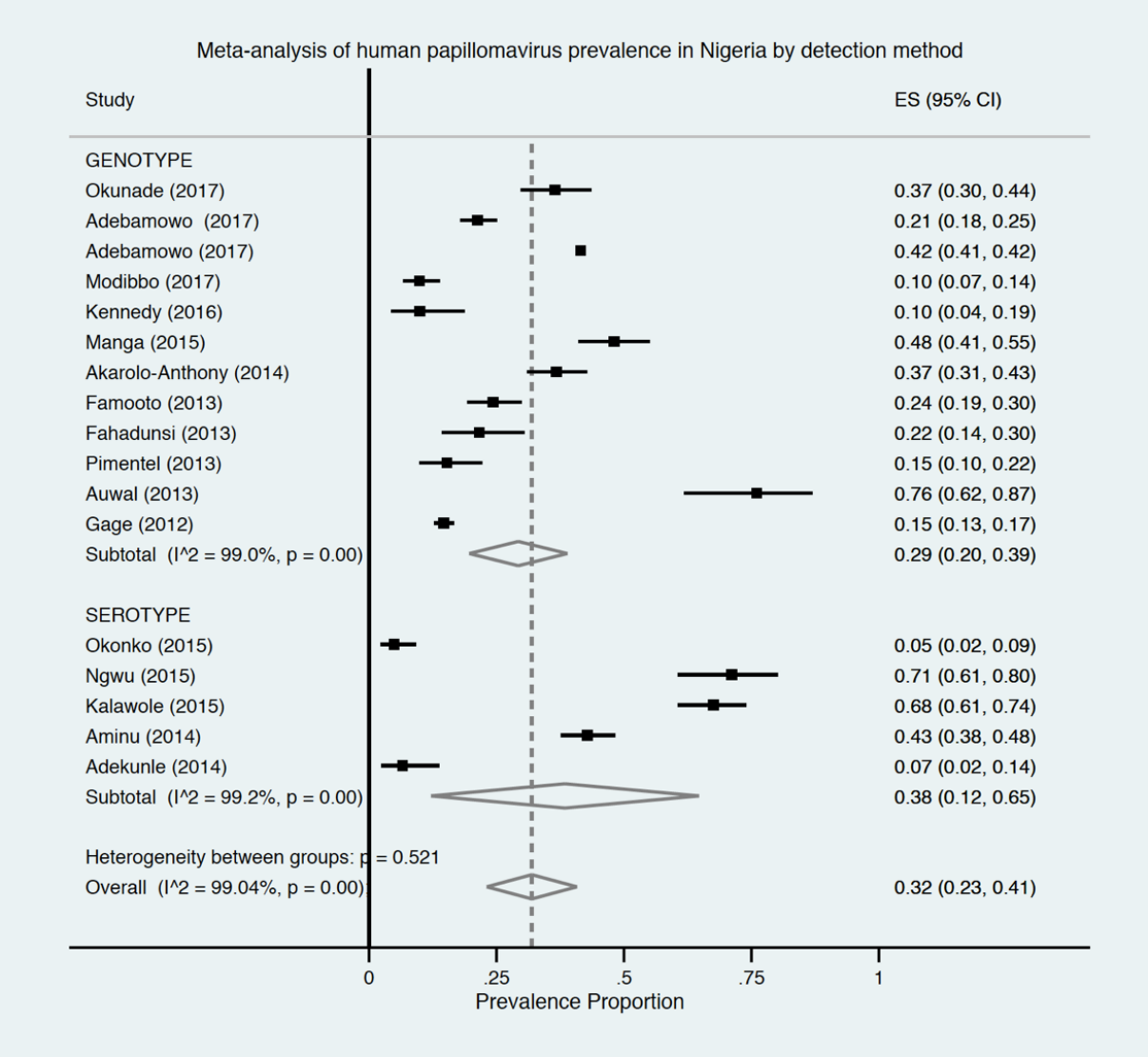

Figure 2: Meta-analysis of human papillomavirus prevalence by detection method

infections, whereas genotypic detection identifies genetic material from a current infection. Nonetheless, serology remains a widely used method for HPV detection in Nigeria.

Our estimated prevalence is two times the prevalence reported in a global study including Nigeria[4] and significantly distinct from those reported in other studies[22-24] in the literature. Prevalence studies in East African countries like Ethiopia[25], Uganda[26], and Tanzania[27] have reported prevalence ranges from 10 to 74%, with some reports similar to our 32% estimate. Our analysis of multiple studies reflecting variations in methodological detection and regional demographics likely represents a more comprehensive, generalizable estimate of HPV prevalence among women in Nigeria.

The implications of our findings are broad, as a high HPV prevalence naturally increases concern for increased incidence and prevalence of HPV-related cancers, especially cervical cancer in this population. Development of screening and vaccination programs are critical to preventing cervical cancer related morbidity and mortality. Currently, national implementation of an HPV vaccination program remains an obstacle in Nigeria and vaccinations outside of those offered in early childhood are not universally accessible. Financial, educational, and legislative barriers have been cited as contributing factors[28], leaving millions

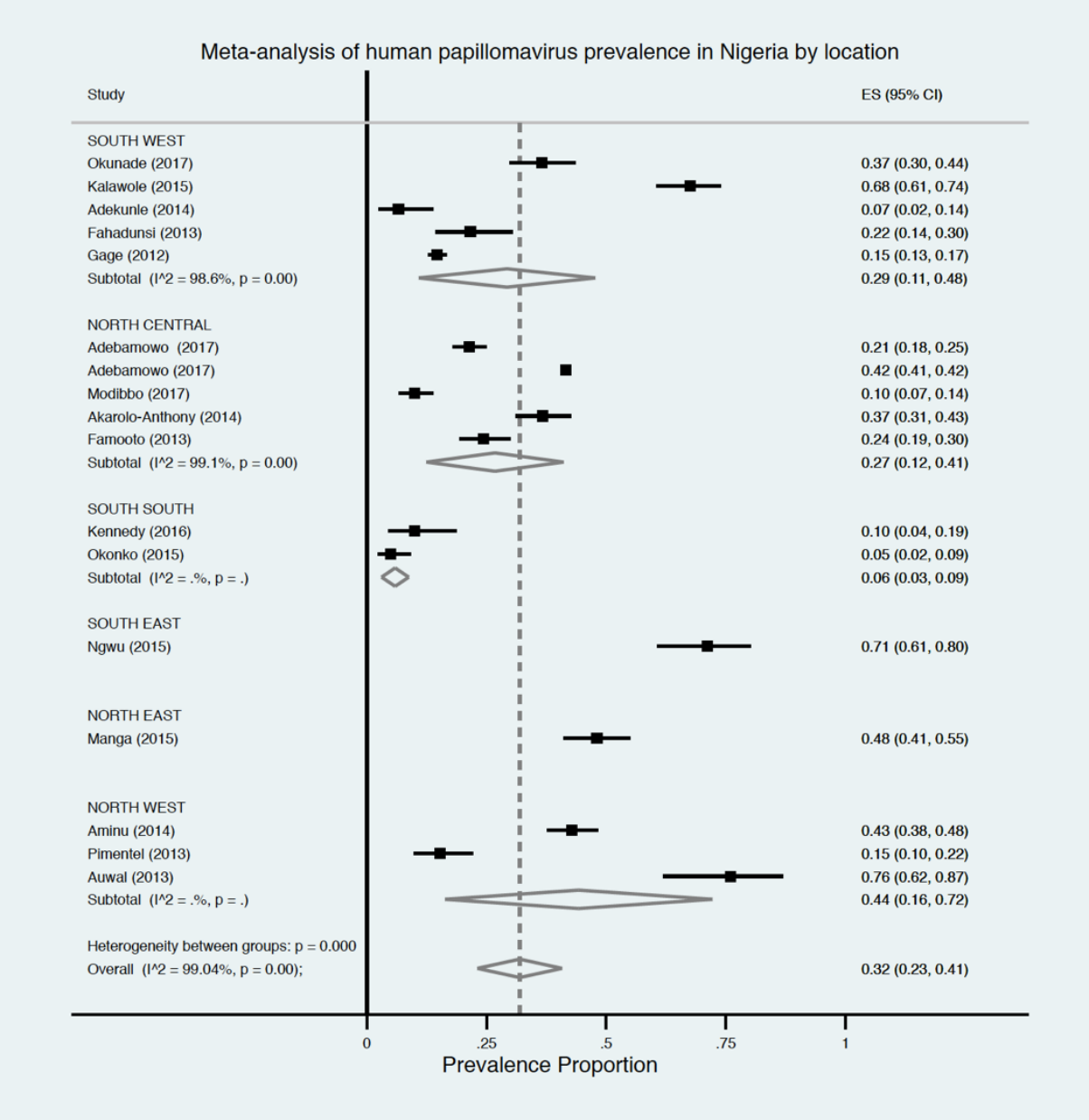

Figure 3: Meta-analysis of human papillomavirus prevalence in Nigeria by location

susceptible to cervical cancer and other HPV-related cancers. This underscores the significance of establishing initiatives for HPV and cervical cancer surveillance.

The greatest limitation in our analysis was the low number of studies that represented the SE and NE geopolitical zones, where PP of HPV may differ significantly from the small studies used in this analysis. Stratification by geopolitical zones showed significant heterogeneity. It is possible that stratification by the six geopolitical zones yielded either too many strata or strata that were too dissimilar, with specific regard to the SE and NE geopolitical zone strata. Additional studies particularly in these two regions would contribute to a more representative analysis, and possibly reduce the observed heterogeneity. Additionally, our analysis excluded the study of HPV in men, with the intent to further elucidate the association between HPV prevalence and cervical cancer prevalence. However, this does not minimize the significance of HPV infection in men and its influence on the prevalence of non-cervical cancers such as anal, penile, and throat cancers.

In summary, we completed a systematic review and meta-analysis on the prevalence of HPV in women residing in Nigeria. The prevalence of infection was high, leaving a high proportion of women at risk for cervical cancer. Our pooled estimate presents an illustrative impression of the HPV disease burden for women living in Nigeria. This information may serve to inform future strategies for epidemiologic surveillance and future design of HPV and cervical cancer prevention initiatives.

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