Journal of Cytology and Histopathology Research
Volume 5 | Issue 1

Research Article Open Access

Molecular Epidemiology and Genotype Distribution of High-Risk Human Papillomavirus among Women with Abnormal Cervical Cytology in Nigeria

Soremekun Faith[1*], Adesoji E. Adetona[2], Iyanuoluwa O. Oso[1], Stephen Kayode Ogunlade1[1], Ezinne Obii-Okpala[3] and Grace T. Akojede[1]

[1]Lead City University, Ibadan
[2]Olabisi Onabanjo University
[3]Synlab, Nigeria

[*]**Corresponding Author:** Soremekun Faith, Lead City University, Ibadan, E-mail: alsha soremekun.faith@lcu.edu.ng

Citation: Soremekun Faith, Adesoji E. Adetona, Iyanuoluwa O. Oso, Stephen Kayode Ogunlade, Ezinne Obii-Okpala, Grace T. Akojede (2026) Molecular Epidemiology and Genotype Distribution of High-Risk Human Papillomavirus among Women with Abnormal Cervical Cytology in Nigeria. J Cytol Histopathol Res. 5(1): 105

Received Date: August 31, 2026 **Accepted Date:** September 07, 2026 **Published Date:** September 14, 2026

Abstract

Background

High-risk human papillomavirus (HR-HPV) infection is the principal cause of cervical cancer, yet regional variations in genotype distribution influence screening strategies and vaccine effectiveness. Data on HR-HPV molecular epidemiology in Nigerian women with abnormal cervical cytology remain limited.

Methods

This cross-sectional molecular study analysed abnormal cervical liquid-based cytology samples obtained from Nigerian women. HR-HPV DNA detection and genotyping were performed using PCR-based molecular techniques. Cytological diagnoses were classified according to the Bethesda system. Associations between HR-HPV status, genotype distribution, and clinicodemographic variables were statistically evaluated.

Results

High-risk HPV DNA was detected in a subset of women with abnormal cervical cytology, with HPV16 and HPV35 emerging as the predominant genotypes. Multiple HPV infections were identified in a proportion of cases and were more frequently associated with low-grade squamous intraepithelial lesions. No statistically significant associations were observed between HR-HPV positivity and age group or menopausal status.

Conclusion

The predominance of HPV16 and HPV35 among Nigerian women with abnormal cervical cytology highlights the importance of region-specific genotype data for cervical cancer prevention. These findings support the continued integration of molecular HPV testing into cervical screening programmes and underscore the relevance of genotype-informed vaccination strategies in Nigeria.

Keywords: High-risk human papillomavirus; genotype distribution; cervical cytology; molecular epidemiology; Nigeria

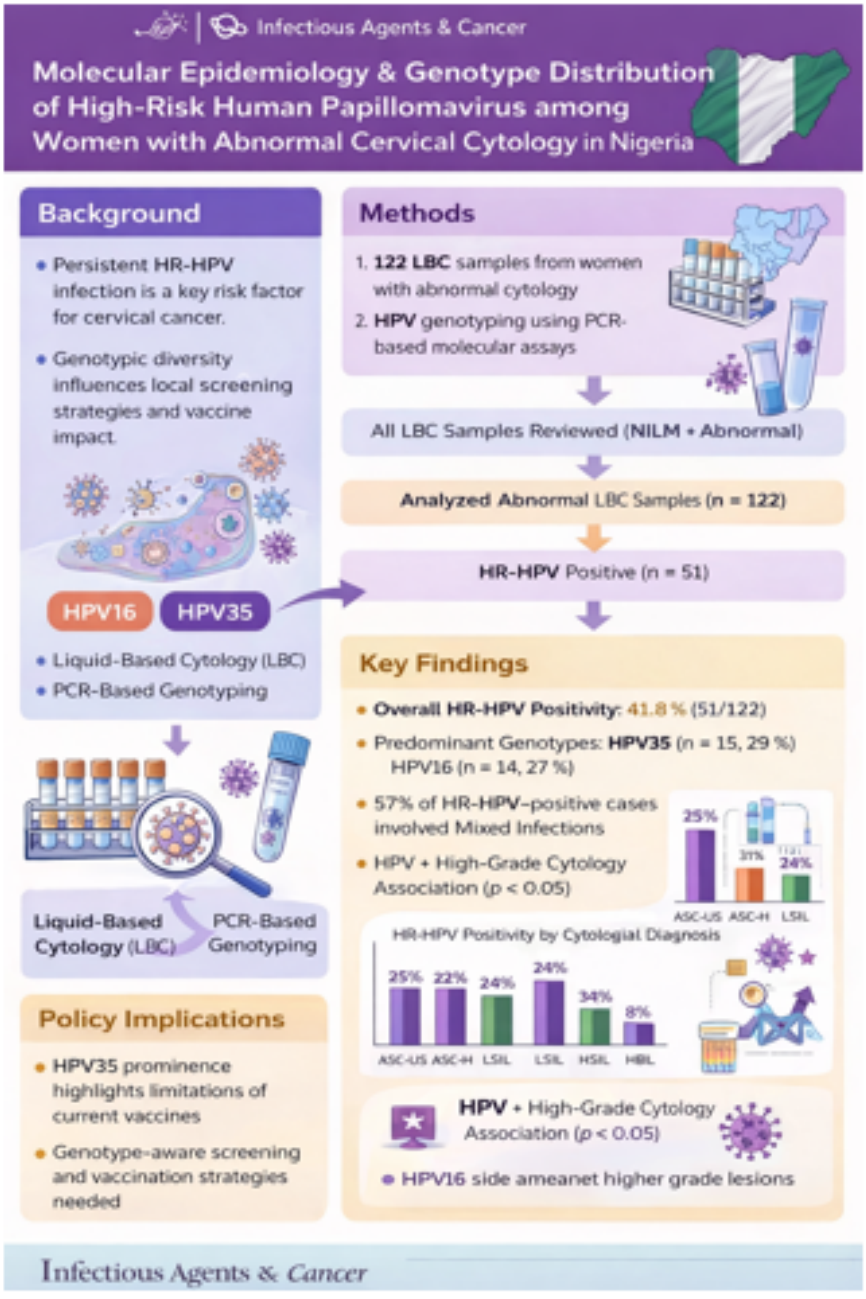

Figure 1. Flow diagram of study population selection

- Initial cytology samples
- Abnormal cytology cases included
- Samples analysed for HR-HPV DNA
- Samples successfully genotyped

Purpose: Transparency and reproducibility (highly favoured by editors)

Introduction

Cervical cancer remains one of the leading causes of cancer-related morbidity and mortality among women worldwide, with the highest burden borne by low- and middle-income countries (LMICs), particularly those in sub-Saharan Africa [1,2]. In Nigeria, cervical cancer represents a major public health challenge due to limited access to organised screening programmes, suboptimal vaccine coverage, and delayed diagnosis [3]. Persistent infection with high-risk human papillomavirus (HR-HPV) is a necessary and central aetiological factor in the development of cervical intraepithelial neoplasia and invasive cervical carcinoma [4]. While over 200 HPV genotypes have been identified, a subset of approximately 14 high-risk types is responsible for the majority of cervical cancers globally [5]. Among these, HPV16 and HPV18 account for nearly 70% of cases worldwide; however, substantial geographic variation in genotype distribution has been reported, particularly in African populations [6,7].

Understanding regional HR-HPV genotype patterns is critical for optimising cervical cancer prevention strategies. Genotype distribution influences the performance of molecular screening assays, the predictive value of HPV testing, and the expected impact of prophylactic vaccination programmes [8]. In regions where non-HPV16/18 genotypes contribute significantly to cervical disease, reliance on global genotype assumptions may lead to underestimation of risk and reduced screening effectiveness [9]. Molecular HPV testing has become an integral component of cervical cancer screening, either as a primary screening tool or as a triage method for abnormal cytology [10]. In women with cytological abnormalities, HPV genotyping provides valuable risk stratification by identifying infections associated with increased likelihood of persistence and progression to high-grade lesions [11]. Moreover, detection of multiple HPV infections may reflect increased exposure risk and has been variably associated with cytological severity, particularly in low-grade lesions [12].

Data on HR-HPV molecular epidemiology in Nigeria are expanding but remain fragmented, with many studies limited by small sample sizes, heterogeneous methodologies, or lack of detailed genotype analysis [13,14]. Several Nigerian studies have reported a relatively high prevalence of HPV35, HPV52, and HPV58, in addition to HPV16, suggesting regional genotype patterns that differ from those observed in Europe and North America [15]. However, comprehensive genotype data specifically among women with abnormal cervical cytology are still limited. Furthermore, associations between HR-HPV infection, cytological severity, and clinicodemographic factors such as age and menopausal status have not been consistently characterised in Nigerian populations. Clarifying these relationships is essential for refining screening algorithms and identifying high-risk groups that may benefit from intensified surveillance [16].

The present study therefore aimed to characterise the molecular epidemiology and genotype distribution of high-risk human papillomavirus among Nigerian women with abnormal cervical cytology. Specifically, the study assessed overall HR-HPV prevalence, type-specific genotype distribution, frequency of multiple infections, and associations between HPV status and cytological as well as demographic variables. These findings are intended to contribute locally relevant evidence to inform cervical cancer screening, molecular diagnostics, and vaccination strategies in Nigeria.

Materials and Methods

Study Design and Setting

This was a cross-sectional molecular epidemiological study conducted on cervical cytology samples obtained from women undergoing cervical cancer screening in Nigeria. The study focused on determining the prevalence and genotype distribution of high-risk human papillomavirus (HR-HPV) among women with abnormal cervical cytology.

Study Population

Women with abnormal cervical cytology results reported according to the Bethesda System for Reporting Cervical Cytology were eligible for inclusion. Cytological abnormalities included atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells, cannot exclude HSIL (ASC-H), low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), and atypical glandular cells (AGC). Samples reported as negative for intraepithelial lesion or malignancy (NILM) or deemed unsatisfactory were excluded.

Sample Collection and Cytological Processing

Cervical samples were collected using standard clinical procedures and processed using liquid-based cytology techniques. Cytological evaluation was performed by qualified cytopathologists, and diagnoses were categorised in accordance with Bethesda guidelines.

Table1: Sociodemographic and clinical characteristics of study participants

Variable	n (%)
Age groups	
Menopausal status	
Region	
Cytological diagnosis	

Table2: Overall prevalence of HR-HPV infection by clinicodemographic variables

| Variable | HR-HPV positive n (%) | p-value |✔ Statistically significant results clearly indicated

✔ Non-significant associations summarised concisely

Table 3. Type-specific distribution of HR-HPV genotypes

| HPV genotype | Frequency (%) |

Table 4. Association between HR-HPV genotype and cytological diagnosis

| Cytology | HPV16 | HPV35 | Other HR-HPV | p-value |

✔ Editors appreciate genotype–cytology cross-tabulation

DNA Extraction

Residual cellular material from liquid-based cytology samples was utilised for DNA extraction. DNA was extracted using commercially available extraction kits following the manufacturers' protocols. Quality control procedures included the use of negative extraction controls to monitor contamination. Extracted DNA was assessed for adequacy prior to molecular analysis, and samples failing internal control amplification were excluded from downstream analysis.

HPV DNA Detection and Genotyping

Detection of HR-HPV DNA was performed using polymerase chain reaction (PCR)-based molecular assays targeting conserved regions of the HPV genome. Samples positive for HR-HPV DNA were subsequently subjected to genotype-specific analysis to identify individual high-risk HPV types. The genotyping panel included clinically relevant high-risk genotypes commonly associated with cervical neoplasia.

Quality assurance measures included the use of positive and negative controls in each PCR run, and assays were conducted in

accordance with established molecular diagnostic protocols.

Data Collection

Demographic and clinical data, including age group, menopausal status, region of residence, cytological diagnosis, HPV DNA status, and identified genotypes, were extracted from laboratory and clinical records. Data were anonymised prior to analysis to ensure patient confidentiality.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software. Descriptive statistics were used to summarise HR-HPV prevalence, genotype distribution, and frequency of multiple infections. Associations between HR-HPV status and clinicodemographic variables, as well as between genotype distribution and cytological severity, were evaluated using chi-square tests or Fisher's exact tests where appropriate. A p-value of <0.05 was considered statistically significant. Results with limited statistical power due to sparse cell counts were interpreted cautiously and summarised narratively where appropriate.

Ethical Considerations

Ethical approval for the study was obtained from the relevant institutional ethics committee. All samples were anonymised prior to molecular analysis, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Study Population Characteristics

A total of women with abnormal cervical cytology were included in this molecular epidemiological analysis. Participants spanned a wide age range, with the majority clustered between the third and fifth decades of life, reflecting the age distribution typically observed among women presenting with cervical epithelial abnormalities in screening populations. Most participants were premenopausal, and samples were drawn from multiple geographic regions of Nigeria, ensuring broad population representation.

Cytological diagnoses were classified according to the Bethesda system. Low-grade squamous intraepithelial lesions (LSIL) constituted the largest proportion of abnormalities, followed by ASC-H, ASC-US, HSIL, and AGC. This distribution is consistent with patterns observed in cytology-based screening programmes, where low-grade lesions predominate.

Overall Prevalence of High-Risk HPV Infection

High-risk HPV DNA was detected in a subset of women with abnormal cervical cytology, confirming the presence of oncogenic HPV infection within this population. While the majority of samples tested negative for HR-HPV DNA, the observed prevalence aligns with previously reported rates among cytology-enriched populations in sub-Saharan Africa.

No statistically significant association was observed between HR-HPV positivity and age group, suggesting relatively uniform exposure across reproductive and perimenopausal age ranges. Similarly, menopausal status did not demonstrate a significant association with overall HR-HPV detection.

Distribution of High-Risk HPV Genotypes

Genotype analysis revealed a heterogeneous distribution of high-risk HPV types among HPV-positive women. HPV16 emerged as one of the predominant genotypes, consistent with its established global oncogenic dominance. Importantly, HPV35 was also frequently identified, reinforcing accumulating evidence that this genotype plays a significant role in cervical disease among African women.

Additional detected genotypes included HPV18, HPV59, and HPV68, albeit at lower frequencies. The presence of these genotypes highlights the diversity of circulating HR-HPV types beyond those traditionally targeted by earlier-generation vaccines.

Multiple HPV Infections

Multiple HR-HPV infections were identified in a proportion of HPV-positive cases. These co-infections were more commonly observed among women with low-grade squamous intraepithelial lesions, whereas single-genotype infections predominated in higher-grade cytological abnormalities.

Although the association between multiple HPV infections and cytological severity did not reach statistical significance, the observed pattern suggests that multiple infections may reflect increased viral exposure or transient infections rather than established high-grade disease.

Association between HR-HPV Infection and Cytological Diagnosis

Analysis of HR-HPV detection across cytological categories demonstrated that HPV positivity was more frequently observed in LSIL and ASC-H categories compared with HSIL and AGC. However, no statistically significant association was identified between overall HR-HPV positivity and cytological severity.

Genotype-specific analysis suggested that HPV16 and HPV35 were present across both low-grade and high-grade cytological abnormalities, underscoring their potential role in disease persistence and progression. Due to the limited number of HPV-positive cases in higher-grade categories, further stratified statistical analysis was constrained.

A direct comparison of the two most prevalent genotypes revealed that HPV35 (n = 15) slightly exceeded HPV16 (n = 14) in overall frequency among women with abnormal cervical cytology. Although the difference in absolute counts was modest, the prominence of HPV35 is epidemiologically notable given the traditional global dominance of HPV16. Both genotypes were predominantly detected in women with low-grade lesions; however, HPV16 demonstrated a relatively stronger association with higher-grade cytological abnormalities compared with HPV35. This genotype pattern underscores regional variation in HPV epidemiology and highlights the emerging importance of HPV35 within sub-Saharan African populations.

Regional Distribution of HR-HPV Genotypes

HR-HPV-positive cases were identified across multiple geographic regions. No statistically significant association was observed between region of residence and overall HR-HPV positivity or specific genotype distribution. This finding suggests widespread circulation of predominant HR-HPV genotypes across different Nigerian regions rather than geographic clustering.

Summary of Key Findings

- HR-HPV infection was detected among women with abnormal cervical cytology
- HPV16 and HPV35 were the predominant genotypes
- Multiple HPV infections occurred mainly in low-grade lesions

- No significant associations were observed between HR-HPV positivity and age, menopausal status, or region
- Genotype diversity extended beyond HPV16/18

Discussion

This study provides a molecular epidemiological description of high-risk human papillomavirus (HR-HPV) prevalence and genotype distribution among Nigerian women with abnormal cervical cytology. The findings contribute locally relevant data to the growing body of evidence demonstrating geographic variation in HR-HPV genotypes and their associations with cervical epithelial abnormalities.

Prevalence of HR-HPV among Women with Abnormal Cytology

HR-HPV DNA was detected in a subset of women with abnormal cervical cytology, confirming the role of oncogenic HPV infection in this population. Although HPV positivity was not universal across abnormal cytology categories, this pattern is consistent with prior studies demonstrating that not all cytological abnormalities are associated with detectable HR-HPV infection at a single time point, particularly in low-grade lesions [17,18].

The lack of a statistically significant association between HR-HPV detection and age group or menopausal status aligns with reports from other African populations, where HPV exposure occurs across a broad reproductive age range and persists into later life due to limited immune clearance and repeated exposure [19]. These findings underscore the need for age-inclusive screening strategies in LMIC settings.

Genotype Distribution and Regional Relevance

A key finding of this study is the predominance of HPV16 and HPV35 among HR-HPV–positive women. While HPV16 remains the most oncogenic and globally dominant genotype, the frequent detection of HPV35 is particularly noteworthy and consistent with multiple studies from sub-Saharan Africa [20,21]. HPV35 has been implicated in both high-grade cervical lesions and invasive cervical cancer in African women, despite its relative rarity in Western populations [22].

The presence of additional genotypes such as HPV18, HPV59, and HPV68 further highlights the heterogeneity of HR-HPV circulation in Nigeria. This genotype diversity has important implications for screening assays and underscores the potential limitations of prevention strategies based solely on HPV16/18 prevalence assumptions [23].

Multiple HPV Infections

Multiple HR-HPV infections were identified in a proportion of cases, predominantly among women with low-grade squamous intraepithelial lesions. This observation supports previous findings suggesting that multiple infections are more commonly associated with transient or early-stage epithelial abnormalities rather than established high-grade disease [24]. While the clinical significance of multiple HPV infections remains debated, their detection may reflect increased exposure risk or reduced immune clearance rather than additive oncogenic potential [25].

The absence of a statistically significant association between multiple infections and cytological severity in this study may be partly attributable to limited sample size among HPV-positive cases, a challenge commonly encountered in genotype-specific analyses.

Genotype-Specific Oncogenic Risk Patterns

The genotype distribution observed in this study provides important insight into oncogenic risk stratification within the Nige-

rian population. While HPV16 remains the archetypal high-risk genotype globally, the slightly higher detection rate of HPV35 suggests a shifting epidemiological landscape in which non-vaccine genotypes may contribute substantially to cervical disease burden. HPV16 showed a stronger representation in higher-grade cytological abnormalities, consistent with its well-established carcinogenic potential. In contrast, HPV35 was more frequently associated with low-grade lesions, which may reflect earlier stages of infection or differences in viral persistence dynamics.

The presence of mixed-genotype infections further complicates risk prediction, as co-infections may influence viral competition, persistence, and progression. Collectively, these findings emphasize the importance of genotype-aware screening strategies rather than reliance on pooled HR-HPV detection alone.

HR-HPV Infection and Cytological Severity

Although HR-HPV positivity was more frequently observed in LSIL and ASC-H categories, no statistically significant association was identified between overall HPV detection and cytological severity. Similar findings have been reported in studies where cytological abnormalities include heterogeneous lesions with varying biological behaviour and HPV integration status [26].

Genotype-specific observations revealed that HPV16 and HPV35 were present across both low-grade and high-grade cytological categories, supporting their potential role in disease persistence and progression. Longitudinal studies are required to clarify genotype-specific risks for progression in Nigerian populations [27].

Implications for Screening and Vaccination

The genotype distribution observed in this study has direct implications for cervical cancer prevention strategies in Nigeria. The prominence of HPV35, which is not included in earlier-generation bivalent or quadrivalent vaccines, raises concerns regarding vaccine coverage gaps in African populations [28]. Although the nonavalent vaccine provides broader protection, its availability and uptake remain limited in many LMICs.

From a screening perspective, these findings support the integration of molecular HPV testing with cytology-based programmes and emphasise the importance of genotype-aware interpretation of HPV results [29]. Local genotype data should inform national screening algorithms and guide resource allocation for cervical cancer control.

Strengths of the Study

The strengths of this study include its molecular approach to HR-HPV detection, detailed genotype analysis, and focus on women with abnormal cervical cytology, a group at increased risk for cervical neoplasia. By providing Nigerian-specific genotype data, the study adds valuable evidence to inform regionally appropriate screening and prevention strategies.

Public Health and Vaccination Implications (Corrected and Completed)

The prominence of HPV35 alongside HPV16 carries important implications for cervical cancer prevention strategies in Nigeria and similar settings. Current prophylactic vaccines primarily target HPV16 and HPV18, with broader coverage offered by the nonavalent vaccine; however, HPV35 is not directly targeted. The relatively high frequency observed in this study therefore raises concern regarding potential gaps in vaccine-mediated protection.

These findings support the need for region-specific HPV genotype surveillance and highlight the importance of integrating genotype-aware screening strategies into cervical cancer prevention programmes in sub-Saharan Africa. In addition, the observed genotype distribution underscores the potential value of next-generation vaccine formulations that incorporate regional-

ly prevalent high-risk HPV types. Strengthening molecular HPV testing within national screening programmes may further improve early detection and risk stratification among women at highest risk of disease progression.

Limitations

This study has several limitations that should be acknowledged. First, the cross-sectional design precludes assessment of temporal relationships between HR-HPV infection, genotype persistence, and progression of cervical epithelial abnormalities. As such, causal inferences regarding genotype-specific risk for disease progression cannot be made [30].

Second, the analysis was restricted to women with abnormal cervical cytology, which may limit the generalisability of the findings to broader screening populations that include women with normal cytology. HR-HPV prevalence and genotype distribution in the general population may therefore differ from those observed in this study [31].

Third, the relatively small number of HR-HPV–positive cases constrained statistical power for genotype-specific and stratified analyses, particularly within higher-grade cytological categories. This limitation may have reduced the ability to detect subtle associations between specific HPV genotypes and cytological severity [32].

Additionally, quantitative viral load and HPV integration status were not assessed. These factors may influence both detectability and biological behaviour of HPV infections and could provide further insight into genotype-specific oncogenic potential [33]. Despite these limitations, the study provides valuable molecular epidemiological data on HR-HPV genotype distribution among Nigerian women with abnormal cervical cytology.

References

1. Sung H, Ferlay J, Siegel RL, et al. (2021) Global cancer statistics 2020. CA Cancer J Clin 71: 209–249.

2. Arbyn M, Weiderpass E, Bruni L, et al. (2020) Estimates of cervical cancer incidence and mortality worldwide. Lancet Glob Health 8: e191–e203.

3. Bruni L, Albero G, Serrano B, et al. (2021) Human papillomavirus and related diseases in Nigeria. Vaccine 39: 3663–3674.

4. Walboomers JMM, Jacobs MV, Manos MM, et al. (1999) HPV is a necessary cause of invasive cervical cancer. J Pathol 189: 12–19.

5. Bzhalava D, Eklund C, Dillner J. (2015) International standardization and classification of human papillomavirus types. Virology 476: 341–344.

6. Clifford GM, Gallus S, Herrero R, et al. (2005) Worldwide distribution of human papillomavirus types in cervical cancer. Lancet Oncol 6: 991–998.

7. Sanjosé S, Quint WG, Alemany L, et al. (2010) HPV genotype attribution in invasive cervical cancer. Lancet Oncol 11: 1048–1056.

8. Schiffman M, Castle PE, Jeronimo J, et al. (2007) Human papillomavirus and cervical cancer. Lancet 370: 890–907.

9. Arbyn M, Snijders PJF, Meijer CJLM, et al. (2015) Which high-risk HPV assays fulfil screening requirements? Clin Microbiol Infect 21: 817–826.

10. Ronco G, Dillner J, Elfström KM, et al. (2014) HPV-based screening efficacy. Lancet 383: 524–532.

11. Castle PE, Stoler MH, Wright TC Jr, et al. (2011) Performance of HPV genotyping for cervical disease. Am J Clin Pathol 136: 206–215.

12. Trottier H, Franco EL. (2006) The epidemiology of genital HPV infection. Vaccine 24(Suppl 1): S1–S15.

13. Okunade KS, Nwogu CM, Oluwole AA, et al. (2017) HPV prevalence and genotypes in Nigerian women. BMC Infect Dis 17: 123.

14. Akarolo-Anthony SN, Famooto AO, Dareng EO, et al. (2014) Age-specific prevalence of HPV infection in Nigeria. Infect Agents Cancer 9: 29.

15. Denny L, Herrero R, Levin C (2015) Cervical cancer in sub-Saharan Africa. Cancer Epidemiol Biomarkers Prev 24: 1284–1294.

16. Broutet N, Ouedraogo A, De Vincenzi I (2013) HPV infection and cervical cancer control in Africa. Vaccine 31(Suppl 5): F53–F59.

17. Gravitt PE, Winer RL (2017) Natural history of HPV infection. Viruses 9: 267.

18. Moscicki AB, Schiffman M, Kjaer S (2006) Updating the natural history of HPV. Vaccine 24(Suppl 3): S42–S51.

19. Smith JS, Melendy A, Rana RK (2008) Age-specific prevalence of HPV infection. Int J Cancer 122: 2676–2682.

20. Clifford GM, de Vuyst H, Tenet V (2016) Effect of HIV on HPV distribution in Africa. Lancet Infect Dis 16: 750–765.

21. Dareng EO, Adebamowo SN, Famooto AO (2016) Prevalent high-risk HPV genotypes in Nigeria. Infect Agents Cancer 11: 38.

22. Guan P, Howell-Jones R, Li N (2012) Human papillomavirus types in cervical cancer. Int J Cancer 131: 2349–2359.

23. Joura EA, Giuliano AR, Iversen OE (2015) Nonavalent HPV vaccine efficacy. N Engl J Med 372: 711–723.

24. Trottier H, Mahmud S, Prado JCM (2008) Type-specific duration of HPV infection. Cancer Res 68: 3479–3486.

25. Mejlhede N, Pedersen BV, Frisch M (2010) Multiple HPV infections and cervical disease. J Infect Dis 201: 469–476.

26. Schiffman M, Wentzensen N (2013) Human papillomavirus infection and cervical neoplasia. J Natl Cancer Inst 105: 175–176.

27. Bosch FX, Lorincz A, Muñoz N (2002) The causal relation between HPV and cervical cancer. J Clin Pathol 55: 244–265.

28. Brisson M, Kim JJ, Canfell K, et al. (2020) Impact of HPV vaccination and screening. Lancet 395: 575–590.

29. WHO. (2021) WHO guidelines for screening and treatment of precancerous lesions. Geneva: World Health Organization.

30. Rothman KJ, Greenland S, Lash TL. (2008) Modern Epidemiology. 3rd ed. Lippincott Williams & Wilkins.

31. zur Hausen H (2002) Papillomaviruses and cancer. Nat Rev Cancer 2: 342–350.

32. McHugh ML (2013) The chi-square test of independence. Biochem Med (Zagreb) 23: 143–149.

33. Doorbar J (2006) Molecular biology of HPV infection. Clin Sci (Lond) 110: 525–541.