

High-Risk Human Papillomavirus Genotypes in a Private Healthcare Cohort in El Salvador

AARON ISAAC CORNEJO RODRIGUEZ

aaronicornejor@gmail.com

Escuela Americana

Article

Keywords:

Posted Date: October 6th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11013179/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Cervical cancer remains a significant health burden in El Salvador and Latin America. While national screening programs have traditionally focused on public health sectors using conventional cytology, there is no published literature regarding populations with access to private or high-complexity healthcare systems. Most screening data comes from vulnerable populations with limited healthcare access. However, evaluating a middle-to-high socioeconomic cohort where molecular testing is readily available allows us to observe the true viral prevalence and build a more accurate national epidemiological profile. Globally, the persistence of high-risk genotypes (HR-HPV) represents a serious challenge despite vaccination efforts. Using a retrospective consecutive sampling scheme, this is the first study in El Salvador that uses molecular techniques to evaluate the prevalence of 14 high-risk genotypes among 3,245 women undergoing routine gynecological screening (predominantly estimated between 30 and 65 years of age) over a three-year period. By moving beyond traditional screening methods, this research aims to provide a new baseline for personalized preventive medicine in El Salvador, including the identification of unique viral patterns that may vary from general information typically available in previous public health assessments.

Introduction

Cervical cancer is a leading cause of morbidity and mortality among women in Latin America [1]. In El Salvador, it remains the second most frequent cancer among women, with recent estimates showing an age-standardized mortality rate of 7.4 per 100,000 women [2]. Furthermore, regarding viral prevalence, recent epidemiological data from large-scale public cervical screening cohorts in El Salvador indicates an HPV positivity rate of approximately 11.5% among the general screening population [1, 2]. Despite the global efforts by the World Health Organization (WHO) to eliminate cervical cancer, achieving the necessary screening and vaccination targets remains a profound challenge in low- and middle-income countries (LMICs) [3].

Historically, El Salvador's national cervical cancer prevention program relied on conventional cytology (Pap smears) [4]. However, following successful pilot implementations, the Ministry of Health (MINSAL) has shifted its national guidelines. Current public health protocols now utilize primary molecular HPV testing (detecting 14 high-risk genotypes) combined with a "screen-and-treat" algorithm [4, 5]. While this represents a monumental public health advancement, the vast majority of published data regarding these molecular genotypes in El Salvador is exclusively derived from public-sector interventions [5].

Despite these advancements, cervical cancer screening in El Salvador still faces significant psychosocial and systemic barriers. Studies in the region demonstrate that lack of education regarding HPV, fear of the screening procedure, discomfort with providers, and the profound social stigma associating HPV strictly with promiscuity or sexually transmitted infections (STIs) severely limit screening adherence [6, 7]. Consequently, HPV and cervical cancer disproportionately affect lower socioeconomic groups who continue to bear the impact of these systemic and educational barriers.

Because the existing epidemiological data—such as the findings from the public-sector Cervical Cancer Prevention in El Salvador (CAPE) initiative—is derived from vulnerable populations facing these profound access barriers [4], there is a critical gap in our understanding of the broader virological landscape. There is currently no published literature evaluating the specific distribution of high-risk HPV genotypes among Salvadoran populations utilizing high-complexity private healthcare. This study aims to fill that knowledge gap. By evaluating a middle-to-high socioeconomic cohort where molecular testing (PCR-based genotyping) is readily available and cultural barriers to preventative healthcare are minimized, we can observe the baseline viral ecology of high-risk HPV without the confounding variable of healthcare inaccessibility. Notably, our cohort revealed a distinct overall high-risk HPV positivity rate of 34.18%, highlighting critical differences when compared to public-sector data. Ultimately, this research responds to the clinical need for a comprehensive national epidemiological profile, establishing a new baseline for personalized, genotype-specific preventative medicine in El Salvador.

Results

A total of 3,245 cervical samples from reproductive-age women were analyzed. The overall prevalence of HR-HPV in this cohort was 34.18% (n = 1,109), leaving a negative population of 65.82% (n = 2,136). Among the positive cases, a high rate of multiple concurrent infections (≥ 2 genotypes) was observed, representing 31.83% of the infected patients (Table 1).

Table 1
General Cohort Characteristics

Clinical Parameter	Number of Patients	Percentage
Total Patients Analyzed	3,245	100%
Negative Patients (No infection)	2,136	65.82%
Positive Patients (Infected)	1,109	34.18%
Patients with Co-infections (≥ 2 genotypes)	353	31.83%*

*Co-infection percentage calculated based on the positive population (n = 1,109).

Table 1: **General Cohort Characteristics**

Regarding the specific genotype distribution among the positive population, HPV-16 was the most prevalent at 18.30% (n = 203). This was closely followed by HPV-39 (16.86%) and HPV-58 (12.71%). Most notably, HPV-18 ranked significantly lower than anticipated by international models, appearing in tenth place with only 8.93% of the positive samples (Table 2).

Table 2
Prevalence Ranking of High-Risk HPV Genotypes

Ranking	Genotype	Detected Cases	Prevalence (Positive Population)
1	16	203	18.30%
2	39	187	16.86%
3	58	141	12.71%
4	51	135	12.17%
5	31	128	11.54%
6	66	127	11.45%
7	68	113	10.19%
8	59	108	9.74%
9	52	107	9.65%
10	18	99	8.93%
11	56	94	8.48%
12	45	67	6.04%
13	35	63	5.68%
14	33	42	3.79%
Note: Percentages calculated based on the positive population (n = 1,109).			

Table 2: **Prevalence Ranking of High-Risk HPV Genotypes**

Viral load intensity was estimated qualitatively through the multiplex PCR fluorescent signal. Genotypes 16, 39, and 58 not only dominated in overall prevalence but also exhibited the highest absolute frequencies of high viral load signals (+++) (Table 3, Fig. 1).

Table 3
Viral Load Distribution (Signal Intensity) by Genotype

Genotype	Total Cases	High (+++)	Moderate (++)	Mild (+)	Unreported
16	203	37	91	71	4
39	187	57	70	57	3
58	141	40	54	43	4
51	135	23	69	42	1
31	128	9	61	57	1
66	127	16	57	54	0
68	113	14	45	52	2
59	108	12	38	56	2
52	107	12	41	54	0
18	99	18	42	37	2
56	94	9	38	43	4
45	67	8	31	27	1
35	63	21	37	5	0
33	42	5	26	10	1

Discussion

In comparison to historical data describing the predominance of HPV-16 and HPV-18 in the Americas [1,2], as well as in other regions globally [2,3], the unique genotype distribution observed in this cohort suggests that there are distinct epidemiologic characteristics influencing HR-HPV within El Salvador's private healthcare sector. Historical data collected locally, nationally, and regionally [2] described traditional genotype-based prevalence hierarchies; however, emerging data suggested that alternative high-risk genotypes were increasingly becoming part of a broader virologic community [1]. The current analysis provides definitive molecular evidence that a shift in this virology is underway. Similar to emerging data from Mexico, where extensive epidemiologic studies have shown significant deviations from traditional genotype hierarchies [8,9,10], the prevalence rates observed in this cohort mirror similar trends observed in Latin America. For example, as previously reported [9,10], there is considerable prevalence of HPV-58 and HPV-59 in certain lesion types in Mexico. Also, atypical distributions, including unexpected associations between HPV-33 and neoplastic lesions, have been previously reported [8,9]. Additionally, recent comprehensive analyses have demonstrated that HPV-18 has fallen far behind other genotypes in terms of prevalence; specifically, they reported that HPV-18 represented only 2.9% prevalence and was surpassed by genotypes 51, 52, and 53, alongside direct correlations between

changing patterns and demographic and clinical variables in Mexican women [10]. South American cohorts also exhibit identical changes in their virology, supporting HPV-58 as the second-most commonly occurring genotype overall, which is consistent with our data [11]. Their findings build upon earlier Colombian epidemiologic benchmarks [12] which indicated a very diverse viral distribution. Additionally, comprehensive data from unvaccinated adolescent cohorts in southern regions of the continent clearly indicate that genotypes 52, 56, 51, and 58 represent a dominant force behind the epidemiological landscape immediately below HPV-16 [13]. Similarly, aggressive profiles associated with HPV-58 have been correlated with invasive cervical cancer cases [14]; also, long-term surveillance projects in more developed areas and unimmunized pre-screening studies have consistently demonstrated a high level of regional burden attributable to these non-16/18 variant viruses [15,16]. The displacement of HPV-18 can largely be attributed to ecological niche replacement [17]. As first-generation prophylactic vaccines continue to exert sustained immunological pressure against genotypes 16 and 18 [17], a biological space is inadvertently opened for non-vaccine targeted genotypes to thrive [17]. Additional large-scale US studies have provided quantitative documentation demonstrating declines in vaccine-targeted types in cervical precancerous lesions [18-19], simultaneously demonstrating that genotypes 52 and 51 are replacing HPV-18 in high-grade cervical lesions nationwide [20]. It is worth considering that the remarkably high prevalence of HPV-39 (16.86%) and HPV-58 (12.71%) in our Salvadoran cohort may reflect underlying variations in the Major Histocompatibility Complex (MHC/HLA) endemic to Latin American populations, which could dictate a localized susceptibility to these specific strains. Furthermore, our data revealed a significant proportion of multiple HPV genotype infections within this cohort. We categorized these patterns based on infection complexity, observing that the majority were dual infections (two concurrent genotypes), while a notable subset exhibited moderate to complex profiles involving three or more concurrent high-risk genotypes. Regarding viral intensity—as determined by the Anyplex™ II HPV HR assay's signal strength—we observed that genotypes HPV-16 and HPV-58 frequently presented with **high-intensity signals**, suggesting higher viral loads and greater replicative activity. In contrast, genotypes such as HPV-51 and HPV-53 were more commonly associated with **moderate-to-low intensity signals**, potentially reflecting either latent infections or lower viral replication states. The prevalence of these mixed-genotype infections suggests a complex viral interaction dynamic; the high frequency of such patterns—particularly complex profiles involving three or more non-16/18 variants—warrants further investigation, as simultaneous exposure to multiple HR-HPV types may modulate the immune response and alter the natural history of the infection compared to single-type infections. **Future clinical implications and screening strategies.** The shifting virological landscape observed in our study underscores the need for more comprehensive preventative strategies in the Salvadoran healthcare system. While current public health protocols represent a monumental advancement, the high prevalence of non-16/18 genotypes found in our cohort suggests that future screening programs should move toward extended genotype-based molecular surveillance. To overcome the systemic and psychosocial barriers traditionally associated with cervical cancer screening in our region, future initiatives should consider the implementation of alternative testing pathways, such as HPV self-sampling, which has demonstrated high acceptability in developed countries. Furthermore, adopting extended genotyping panels that cover a broader spectrum of HR-HPV variants—rather than

focusing solely on traditional high-risk markers—may be necessary to maintain clinical efficacy as the viral ecology continues to evolve in response to vaccination efforts.

Several limitations must be acknowledged. First, the retrospective nature of this study, utilizing data from private healthcare settings, may not fully represent the general population's virologic landscape in El Salvador, potentially introducing a selection bias toward middle-to-high socioeconomic groups. Second, while the use of multiplex PCR provides robust qualitative evidence of viral genotypes and signal intensity, it does not quantify absolute viral load, which could offer deeper insights into clinical progression. Future prospective, nationwide studies are necessary to confirm these findings and to evaluate the long-term impact of current vaccination strategies on this specific viral distribution.

Conclusions

In conclusion, this study provides the first molecular mapping of HR-HPV genotypes within a private healthcare cohort in El Salvador. The remarkably high prevalence of non-16/18 genotypes, particularly HPV-39 and HPV-58, highlights a distinct virological profile compared to historical public-sector data. These findings emphasize the necessity of transitioning toward broader, genotype-specific molecular surveillance. Adopting extended genotyping panels will be crucial to inform personalized preventative medicine, adapt to ecological niche replacement, and guide future public health policies in the region.

Materials & Methods

Study design and clinical setting A retrospective cross-sectional analysis was conducted utilizing de-identified historical laboratory records. Data extraction and statistical analysis were performed from January 2026 onwards, analyzing virological results from women who underwent routine gynecological HPV testing **over a three-year period**, between January 2023 and December 2025. All laboratory processing and data aggregation were conducted at GeneX Laboratory, a molecular diagnostic reference center in San Salvador, El Salvador. GeneX Laboratory does not perform direct patient recruitment; rather, it receives clinical specimens from various private gynecological clinics and hospitals nationwide.

Ethical Considerations. Due to the retrospective, observational nature of this study, which utilized existing de-identified laboratory records from GeneX Laboratory, the requirement for formal informed consent from individual participants was waived. This study did not involve active patient recruitment, clinical interventions, or the collection of identifiable biological samples; it was strictly a secondary analysis of anonymized diagnostic data. In accordance with institutional policy, the study protocol was reviewed and formally authorized by the Laboratory Directorate, confirming that the research adheres to the ethical principles of the Declaration of Helsinki regarding the use of historical diagnostic data. Data were accessed for research purposes from January 7, 2026, onwards, and all patient identifiers were irreversibly removed prior to analysis to ensure strict data confidentiality and compliance with privacy standards. **The inclusion criteria comprised:**

1. Cervical swab samples submitted specifically for molecular HPV genotyping.

2. Samples originating from women undergoing routine clinical screening in private specialized healthcare settings in El Salvador between 2023 and 2025.
3. Patients predominantly estimated to be between 30 and 65 years of age, based on the established clinical screening protocols of the referring primary gynecologists.

Exclusion criteria included:

1. Samples with inadequate cellular material that failed the endogenous internal control (beta-globin) amplification.
2. Records with completely missing clinical indication or basic requisition data.

Demographic Data Justification Because this study utilized secondary data from a molecular reference laboratory, extended demographic characteristics—such as exact numerical age, race, socioeconomic status, employment, and insurance status—were not systematically provided by referring physicians on the laboratory requisition forms. Therefore, the dataset is restricted to virological outcomes and basic clinical indications. This limitation accurately reflects the real-world operational constraints of reference laboratories, prioritizing virological mapping in a cohort known to have unhindered access to high-complexity private healthcare. **Specimen collection and laboratory processing.** While the present research study is a retrospective analysis of a database, the physical samples were prospectively processed by GeneX Laboratory personnel at the time of collection. Cervical specimens were collected by gynecologists during routine clinical examinations across various private clinics. Swabs were immediately placed in specialized viral transport medium (eNAT Copan®) by the referring providers to ensure nucleic acid integrity. Transport personnel ensured the secure and timely delivery of the specimens to our reference facility. Total genomic DNA was isolated using the ReliaPrep™ Blood gDNA Miniprep System (Promega). This manual extraction process isolates total cellular DNA—and subsequently, intracellular viral DNA—from cervical epithelial cell pellet lysates. The efficacy of this process was evaluated through the systematic validation of both lysis and DNA isolation by the successful amplification of the human beta-globin endogenous internal control (IC), contained within the Anyplex™ II HPV HR Detection (Seegene) multiplex assay. The targeted amplification of all 14 HR-HPV genotypes was performed on a Bio-Rad CFX Opus thermal cycler [8,9]. **Data management and Statistical Analysis** De-identified laboratory results were collated into a unified database. Data tabulation, cleaning, and statistical analyses were performed using Microsoft office LTSC Standard 2021. Given the descriptive nature of the study, data analysis focused on virological distribution. Categorical variables, including overall HPV positivity, specific high-risk genotype frequencies, and viral load intensity levels, were calculated and are expressed as absolute frequencies and percentages.

Declarations

Acknowledgments

The authors would like to thank the clinical staff and gynecologists at the participating private clinics and hospitals for their collaboration in sample collection and clinical coordination. We also extend our gratitude to the logistics and transport personnel at GeneX Laboratory for ensuring the secure and timely delivery of specimens, which was essential to maintaining nucleic acid integrity throughout the study period. Finally, we appreciate the technical staff at GeneX Laboratory for their diligent laboratory processing and data management support. Their meticulous and tireless efforts in DNA extraction, sample processing, and genotyping analysis were fundamental to the successful execution of this project.

Author Contributions

Conceptualization: Aaron Isaac Cornejo-Rodriguez

Data curation: Aaron Isaac Cornejo-Rodriguez

Formal analysis: Aaron Isaac Cornejo-Rodriguez.

Investigation: Aaron Isaac Cornejo-Rodriguez

Methodology: Aaron Isaac Cornejo-Rodriguez

Project administration: Aaron Isaac Cornejo-Rodriguez

Resources: Aaron Isaac Cornejo-Rodriguez

Writing – original draft: Aaron Isaac Cornejo-Rodriguez.

Writing – review & editing: Aaron Isaac Cornejo-Rodriguez.

Additional Information

Funding: This research received no external funding from any public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that they have no competing interests.

Data Availability Statement: Due to ethical restrictions regarding patient privacy and the nature of de-identified clinical laboratory records, the raw data cannot be made publicly available. However, the aggregated data that support the findings of this study are available from the corresponding author upon reasonable request, provided that such requests comply with local data protection regulations.

Ethical Statement: Due to the retrospective, observational nature of this study, which utilized existing de-identified laboratory records from GeneX Laboratory, the requirement for formal informed consent from individual participants was waived by the **Institutional Ethics Committee of GeneX Laboratory**. This study did not involve active patient recruitment, clinical interventions, or the collection of identifiable

biological samples; it was strictly a secondary analysis of anonymized diagnostic data. In accordance with institutional policy, the study protocol was reviewed and formally authorized by the **Institutional Ethics Committee of GeneX Laboratory (San Salvador, El Salvador)**, confirming that the research adheres to the ethical principles of the Declaration of Helsinki regarding the use of historical diagnostic data. Data were accessed for research purposes from January 7, 2026, onwards, and all patient identifiers were irreversibly removed prior to analysis to ensure strict data confidentiality and compliance with privacy standards.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-249. doi: 10.3322/caac.21660.
2. Bruni L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases Report: El Salvador. Geneva: ICO/IARC; 2023.
3. World Health Organization. Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020.
4. Maza M, Melendez M, Masch R, et al. Outcomes for Step-Wise Implementation of a Human Papillomavirus Testing–Based Cervical Screen-and-Treat Program in El Salvador. *JCO Glob Oncol*. 2020;6:340-349. doi: 10.1200/GO.19.00350.
5. Alfaro K, Maza M, Cremer M, et al. Long-term outcomes after cervical cancer screening in El Salvador: primary human papillomavirus screen-and-treat compared with cytology. *BMJ Glob Health*. 2024;9:e014389. doi: 10.1136/bmjgh-2023-014389.
6. Maza M, Melendez M, Peralta D, et al. High Acceptability of Human Papillomavirus Self-Sampling Among Nonattenders of a Public Cervical Cancer Screening Program in El Salvador. *JCO Glob Oncol*. 2018;4:1-9. doi: 10.1200/JGO.17.00192.
7. Agurto I, Bishop A, Sanchez G, Betancourt Z, Brodie A. Perceived barriers and benefits to cervical cancer screening in Latin America. *Prev Med*. 2004;39(1):91-98. doi: 10.1016/j.ypmed.2004.03.017.
8. DelaRosa-Martínez R, Sánchez-Garza M, López-Revilla R. HPV genotype distribution and anomalous association of HPV33 to cervical neoplastic lesions in San Luis Potosí, Mexico. *Infect Agent Cancer*. 2016;11:16. doi: 10.1186/s13027-016-0063-z.
9. Velázquez-Márquez N, Jaime Jiménez-Aranda L, Sánchez-Alonso P, et al. Human papillomavirus infection in women from Tlaxcala, Mexico. *Braz J Microbiol*. 2010;41:749-56. doi: 10.1590/S1517-83822010000300026.
10. López Rivera MG, Flores MO, Villalba Magdaleno JD, et al. Prevalence of human papillomavirus in women from Mexico City. *Infect Dis Obstet Gynecol*. 2012;2012:384758. doi: 10.1155/2012/384758.
11. Trujillo E, Morales N, Buitrago O, et al. Distribución de los genotipos del virus del papiloma humano en mujeres de Bogotá con anomalías en la citología cervicouterina. *Rev Colomb Cancerol*.

- 2016;20:3-9. doi: 10.1016/j.rccan.2015.11.003.
12. Molano M, Posso H, Weiderpass E, et al. Prevalence and determinants of HPV infection among Colombian women with normal cytology. *Br J Cancer*. 2002;87:324-33. doi: 10.1038/sj.bjc.6600442.
 13. González JV, Deluca GD, Liotta DJ, et al. Baseline prevalence and type distribution of Human papillomavirus in sexually active non-vaccinated adolescent girls from Argentina. *Rev Argent Microbiol*. 2021;53:11-19. doi: 10.1016/j.ram.2020.06.004.
 14. García Muentes GD, Abdul Latif F, Beltrán Rodríguez CC, et al. High frequency of HPV high-risk preventable genotypes in Ecuadorian women with invasive cervical cancer. *Rev Panam Salud Publica*. 2024;48:128. doi: 10.26633/RPSP.2024.128.
 15. Ramírez VE, Bruneau N, Balanda M, et al. Tendencias y Genotipos del VPH en Mujeres Chilenas e Inmigrantes: Estudio de Vigilancia de 10 Años (2014-2023). *Rev Med Chil*. 2026;154. doi: 10.4067/s0034-98872026000300339.
 16. de Almeida LM, Martins LFL, Pontes VB, et al. Human Papillomavirus Genotype Distribution among Cervical Cancer Patients prior to Brazilian National HPV Immunization Program. *J Environ Public Health*. 2017;2017:1645074. doi: 10.1155/2017/1645074.
 17. Adcock R, Wheeler CM, Hunt WC, et al. HPV vaccine impact: genotype-specific changes in cervical pre-cancer share similarities with changes in cervical screening cytology. *J Natl Cancer Inst*. 2025;117:1377-1386. doi: 10.1093/jnci/djaf055.
 18. Centers for Disease Control and Prevention. Trends in Cervical Precancers Identified Through Population-Based Surveillance – Human Papillomavirus Vaccine Impact Monitoring Project, Five Sites, United States, 2008-2022. *MMWR Morb Mortal Wkly Rep*. 2025;74:155-161. doi: 10.15585/mmwr.mm7406a4.
 19. McClung NM, Gargano JW, Bennett NM, et al. Trends in Human Papillomavirus Vaccine Types 16 and 18 in Cervical Precancers, 2008-2014. *Cancer Epidemiol Biomarkers Prev*. 2019;28:602-609. doi: 10.1158/1055-9965.EPI-18-0885.
 20. Hariri S, Unger ER, Powell SE, et al. Human papillomavirus genotypes in high-grade cervical lesions in the United States. *J Infect Dis*. 2012;206:1878-86. doi: 10.1093/infdis/jis627.

Figures

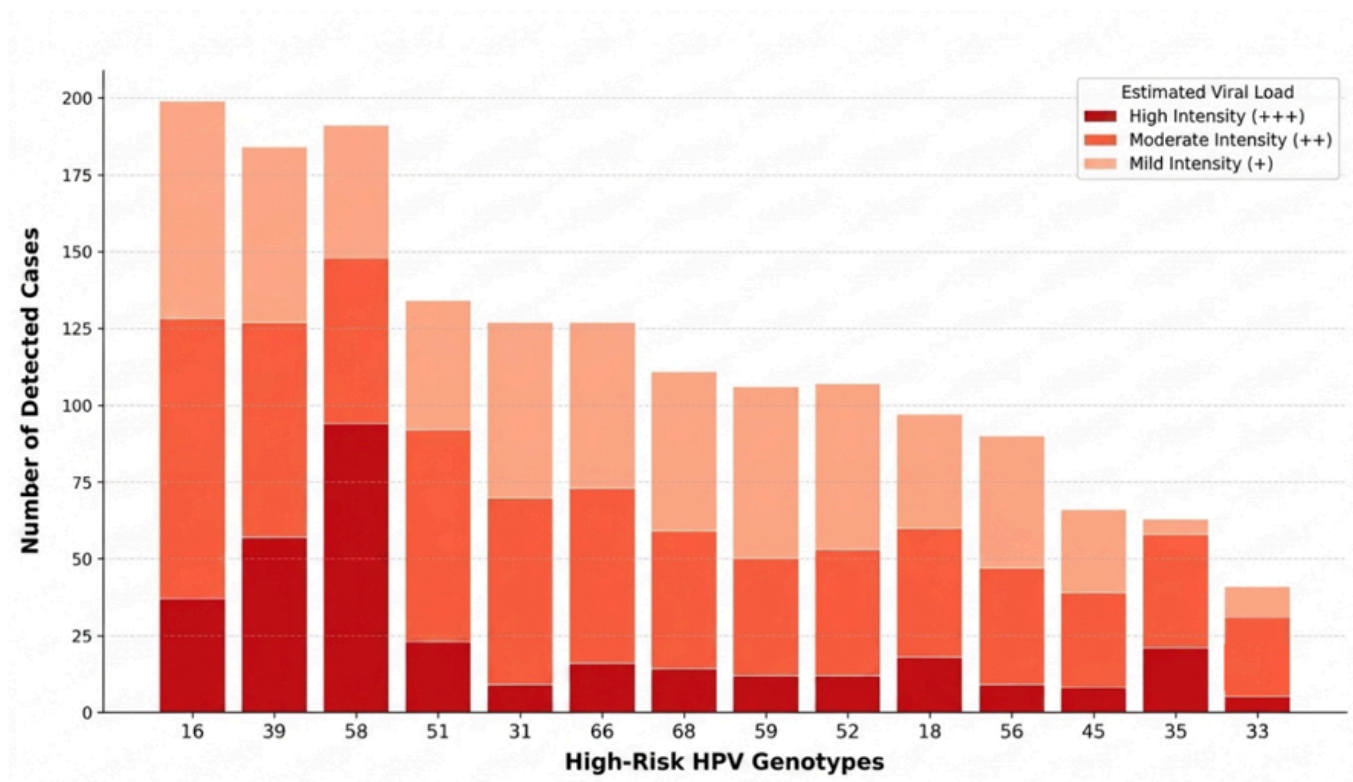


Figure 1

Prevalence and viral load stratification of 14 high-risk HPV genotypes

Figure legend. The vertical axis represents the absolute number of positive cases detected (n=1,109). Bars are ordered descending by total frequency. Colors within each bar illustrate the proportion of qualitative viral load estimated by multiplex PCR: dark red for high intensity (+++), orange for moderate intensity (++), and salmon for mild intensity (+)