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# HPV and Cardiovascular Risk: Unpacking a Novel Link Between Viral Infection and Heart Disease

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***Abstract***

*Human papillomavirus (HPV) is best known for its oncogenic potential, yet a growing body of evidence suggests that persistent HPV infection may also contribute to cardiovascular disease (CVD). In 2025, pooled analyses and conference reports galvanized attention by estimating that HPV-positive individuals have ~40% higher risk of CVD and approximately double the risk of coronary artery disease (CAD) compared with HPV-negative peers, even after adjustment for traditional risk factors. These findings build on earlier cohorts linking high-risk HPV (hrHPV) to incident CVD and, more recently, to CVD mortality in population studies. Mechanistic hypotheses include chronic low-grade inflammation, endothelial dysfunction, immune and metabolic reprogramming driven by HPV oncoproteins (E6/E7), and even more provocatively possible direct vascular involvement, with small studies detecting HPV DNA and proteins within atherosclerotic plaques. Although causality is not proven, the totality of data positions HPV as a candidate "non-traditional" risk factor that may help explain residual CVD risk beyond smoking, hypertension, dyslipidemia, and diabetes. This review synthesizes epidemiologic signals, pathophysiologic plausibility, and early translational observations connecting HPV to atherosclerotic disease and stroke. It also considers the emerging question of whether HPV vaccination might confer cardiometabolic spillover benefits. This paper highlights knowledge gaps (temporal dynamics, genotype specificity, sex differences, and confounding by sexual health and socioeconomic determinants), outline practical, low-regret clinical responses (opportunistic vaccination, vigilant risk factor control in hrHPV-positive adults), and propose a research agenda spanning prospective cohorts, plaque viromics, and randomized vaccine-outcome trials. While definitive causality awaits, clinicians and public health teams should recognize HPV as a potential contributor to CVD risk and leverage existing prevention tools particularly vaccination and aggressive management of modifiable risks while the science matures.*

**Keywords:** Human papillomavirus, cardiovascular disease, atherosclerosis, endothelial dysfunction, inflammation, coronary artery disease, HPV vaccination, residual risk

## INTRODUCTION: WHY AN STI BELONGS IN A CARDIOLOGY CONVERSATION

For decades, the CVD playbook has emphasized "the usual suspects": smoking, blood pressure, lipids, glycemia, and physical inactivity. Yet even perfect control of these factors leaves a sizable proportion of events unexplained; an uncomfortable reminder that residual risk is real. Viral infections are increasingly implicated as contributors to atherogenesis. Cytomegalovirus, herpesviruses, HIV, and influenza have each been associated with vascular injury or atherosclerotic acceleration. In this context, the proposition that HPV a ubiquitous, often silent infection – may also shape vascular risk is no longer far-fetched [1].

Recent pooled analyses and conference presentations in 2025 crystallized the signal: HPV-

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positive adults show roughly 40% higher odds of developing CVD and about twice the risk of CAD vs. HPV-negative peers, with associations persisting after adjustment for age, metabolic profile, lifestyle, and family history. These updates catalyze an interdisciplinary discussion at the crossroads of infectious disease, cardiology, and women's health.

This review walks through the epidemiology, mechanisms, and clinical implications of the HPV CVD connection, and frames concrete priorities for research and practice [2].

## EPIDEMIOLOGIC SIGNAL: WHAT DO THE HUMAN DATA SHOW?

### Incident CVD in Population Cohorts

A landmark Korean cohort (n ≈ 63,000 women) found that hrHPV positivity was associated with higher incident CVD over follow-up. The association strengthened among those with obesity or metabolic syndrome suggesting biological interaction between viral factors and adverse metabolic milieu.

### Cardiovascular Mortality

Building on incidence data, a 2024 cohort of young and middle-aged Korean women reported higher cardiovascular mortality (particularly atherosclerotic and ischemic heart disease deaths) among hrHPV-positive individuals, with stronger gradients in participants with obesity consistent with earlier incident CVD findings.

### Cross-Sectional Associations and Special Populations

Among climacteric (perimenopausal/menopausal) women, hrHPV infection is correlated with prevalent CAD, independent of standard risk factors. In head and neck cancer cohorts, HPV status has been linked to cerebrovascular events after radiation, underscoring the need to disentangle tumor, treatment, and viral effects.

### 2025 Pooled/Consensus Updates

A 2025 aggregation (presented at the American College of Cardiology Scientific Session) reported that HPV-positive individuals had ~40% higher risk of CVD and a twofold increase in CAD risk; adjusted estimates still indicated ≈33% excess risk. While derived from observational data, consistency across continents and study designs lends weight to a real association.

- *Take-Home:* Across multiple lines of epidemiologic evidence incident events, mortality, and prevalence hrHPV tracks with higher cardiovascular risk, particularly in the presence of adverse metabolic profiles [3].

## PATHOPHYSIOLOGIC PLAUSIBILITY: HOW COULD HPV INFLUENCE ATHEROGENESIS?

### Chronic Inflammation and Immune Activation

Persistent HPV infection is characterized by local immune evasion and low-grade inflammation. Systemically, such inflammation can amplify endothelial activation, increase leukocyte adhesion, and promote foam cell formation canonical steps in atheroma development and progression [4].

### Endothelial Dysfunction

Endothelial dysfunction reduced nitric oxide bioavailability, oxidative stress, and pro-thrombotic shifts sit at the nexus of infection and atherosclerosis. Viral triggers can perturb endothelial signaling pathways, upregulate adhesion molecules, and shift the balance toward vasoconstriction and thrombosis. Although direct endothelial infection by HPV remains debated, the inflammatory milieu and extracellular vesicle signaling plausibly injure the endothelium [5].

### Oncoprotein Biology: E6/E7 Beyond Cancer

HPV E6 and E7 oncoproteins degrade p53 and disrupt Rb pathways well-known in oncogenesis. But these axis disruptions also influence vascular smooth muscle proliferation, apoptosis, and lipid

 

metabolism, all relevant to plaque biology. Experimental and review data suggest that E6/E7 activity can, in principle, accelerate atherosclerosis by promoting SMC proliferation and altering repair responses [6].

**Direct Vascular Involvement?**

Provocative small studies have detected HPV DNA and proteins (e.g., E7) within atherosclerotic coronary plaques. While sample sizes are limited and contamination cannot be entirely excluded, these observations raise the possibility of direct or paracrine viral participation in plaque evolution or instability. Rigorous plaque viromics using contamination-aware methods is an urgent research need [7].

**The Infection–Metabolism Intersection**

Epidemiologic effect modification by obesity and metabolic syndrome mirrors mechanistic hypotheses: adipose inflammation, insulin resistance, and dyslipidemia may amplify HPV's vascular impact. Whether hrHPV alters host lipid handling or intersects with metabolic pathways through p53 dysfunction remains an open but testable question.

- *Synthesis:* HPV plausibly contributes to atherogenesis via inflammation, endothelial dysfunction, smooth-muscle proliferation, and perhaps direct vascular presence especially in metabolically unhealthy hosts [8].

**Beyond Coronaries: Cerebrovascular and Peripheral Vascular Clues**

Stroke and transient ischemic events have been reported more frequently in HPV-positive subgroups after head-and-neck cancer treatment. In general populations, cerebrovascular mortality signals are less consistent and require larger prospective cohorts. Microvascular dysfunction endothelial and autonomic could be a unifying thread across vascular beds.

**Vaccination: Could Cancer Prevention Spill Over to the Heart?**

While HPV vaccines were designed to prevent hrHPV-related cancers and anogenital warts, 2025 retrospective data from a large health-records network reported lower risks of new-onset cardiovascular and cerebrovascular diseases among vaccinated adults, with stronger associations in women and in those aged 30–40. Observational design and residual confounding preclude causal claims, but the signal is intriguing: preventing persistent hrHPV might reduce cardiometabolic events over the long term.

Public health messaging has begun to reflect this possibility: if the infection itself tracks with higher CVD risk, vaccination could in theory mitigate a sliver of residual risk, joining influenza and COVID-19 vaccines as plausible, indirect cardiovascular protectants. Formal trials and target trial emulations are needed.

## CLINICAL IMPLICATIONS: WHAT TO DO NOW (WHILE WE WAIT FOR DEFINITIVE PROOF)

- *Recognize hrHPV as a Candidate "Non-Traditional" Risk Factor:* For patients known to be hrHPV-positive especially women with persistent infection, individuals with obesity/metabolic syndrome, and those with additional inflammatory conditions adopt a lower threshold for aggressive risk-factor control (LDL-C reduction, BP targets <130/80 mmHg where appropriate, smoking cessation, exercise, and glucose control). This is a low-regret strategy that addresses multiple pathophysiologic pathways [9].
- *Leverage Vaccination Opportunities:* Adhere to national recommendations for routine and catch-up HPV vaccination, which already deliver unambiguous cancer prevention benefits and may, yield cardiovascular spillovers, though stronger evidence is pending. The 2025 data are hypothesis-generating but encouraging [10].
- *Integrate Sexual and Cardiovascular Health:* Discuss HPV status in the context of holistic risk. For example, a patient with persistent hrHPV and metabolic syndrome might merit more vigilant lipid

 

management or earlier coronary risk imaging, depending on local guidelines and shared decision-making [11].
- *Avoid Overreach:* Do not order HPV testing to "risk-stratify" the heart in isolation; current evidence does not support screening for CVD based on HPV alone. Use HPV information as one input among many [12].

## METHODOLOGICAL CAVEATS AND SOURCES OF BIAS

- *Confounding & Shared Determinants:* Sexual health, socioeconomic position, tobacco use, and healthcare access can correlate with both HPV status and CVD risk. Even well-adjusted cohorts cannot fully purge confounding.
- *Reverse Causality & Detection Bias:* Individuals in oncology follow-up may undergo more intensive cardiovascular surveillance.
- *Heterogeneity Across Genotypes and Sex:* Many studies pool hrHPV types; genotype-specific risks (e.g., 16, 18 vs. others) and male risks remain underexplored.
- *Outcome Definitions:* Some studies use composite CVD; others isolate CAD or stroke; ascertainment methods vary.
- *Laboratory Concerns:* Plaque studies face contamination risks; rigorous negative controls and orthogonal assays are essential [13].

## RESEARCH AGENDA: WHAT WILL MOVE THE FIELD

- *Prospective, Adjudicated Cohorts:* With repeated HPV genotyping (including viral load), inflammatory panels, and careful CVD phenotyping to define temporality and dose response.
- *Plaque and Vascular-Tissue Viromics:* With contamination-aware pipelines to confirm or refute in-plaque HPV and map cellular tropism (endothelium vs. SMC vs. macrophages).
- *Mechanistic Studies:* E6/E7 in vascular cells (SMC proliferation, endothelial barrier integrity, mitochondrial function, lipid handling).
- *Target-Trial Emulations and Randomized Trials:* Testing whether HPV vaccination reduces hard CVD endpoints (or validated surrogates like coronary calcium progression or inflammatory biomarkers).
- *Intersectional Analyses:* Obesity, metabolic syndrome, autoimmune disease, and sex hormones as effect modifiers [14].

## A PRACTICAL FRAMEWORK FOR CLINICIANS

- *Step 1: Ask and Educate:* If a patient discloses persistent hrHPV, normalize the conversation: HPV is common, often silent, and primarily a cancer prevention issue but it may also relate to heart health.
- *Step 2: Optimize Fundamentals:* Use HPV positivity as a behavioral nudge to close care gaps: statin initiation/intensification where indicated, BP and glycemic control, tobacco cessation, diet quality, and physical activity counseling.
- *Step 3: Vaccinate When Eligible:* Offer or reinforce guideline-concordant HPV vaccination; discuss its proven cancer benefits and the possibility (not guarantee) of cardiovascular benefit.
- *Step 4: Tailor Follow-Up:* In hrHPV-positive adults with accumulating risks (e.g., obesity, metabolic syndrome, family history), consider earlier or more intensive ASCVD risk assessment within existing guideline frameworks [15].

## CONCLUSIONS

The emerging picture is coherent: persistent hrHPV infection associates with higher risk of incident CVD, CAD, and in some cohorts cardiovascular mortality. The signal appears stronger in metabolically unhealthy individuals, aligning with biologically plausible mechanisms involving inflammation, endothelial dysfunction, and smooth-muscle proliferation driven (directly or indirectly) by viral oncoproteins. While residual confounding cannot be dismissed and causality is unproven, the convergence of epidemiologic and mechanistic clues justifies pragmatic action now: vaccinate

 

according to guidelines and close traditional risk-factor gaps, especially for patients living with hrHPV. The next wave of studies genotype-resolved cohorts, contamination-aware plaque viromics, and, ideally, randomized vaccine-outcome trials should tell us whether HPV is merely a traveler in the cardiovascular journey or an actual driver of disease.

## REFERENCES

1. Joo EJ, Chang Y, Kwon MJ, Cho A, Cheong HS, Ryu S. High-risk human papillomavirus infection and the risk of cardiovascular disease in Korean women: A cohort study. Circ Res. 2019;124(5):747–56.
2. Kim M, Chang Y, Kwon MJ, Cho A, Cheong HS, Ryu S, et al. Human papillomavirus infection and cardiovascular mortality in young and middle-aged Korean women. Eur Heart J. 2024;45(12):1072–82. doi: 10.1093/eurheartj/ehae020.
3. Chan NC, Lawson JS, Hirsh J. Human papilloma virus and atherosclerotic cardiovascular disease. Eur Heart J. 2024;45(12):1083–5.
4. Tonhajzerova I, Olexova LB, Jurko A Jr, Spronck B, Jurko T, Sekaninova N, et al. Novel biomarkers of early atherosclerotic changes for personalised prevention of cardiovascular disease in cervical cancer and HPV infection. Int J Mol Sci. 2019;20(15):3720.
5. Silva VM, et al. Human papillomavirus and coronary artery disease in climacteric women. Obstet Gynecol Int. 2019;2019:1872536.
6. Lawson JS, Khanna R, Al-Ahdal MN, et al. Multiple infectious agents and the origins of atherosclerotic coronary artery disease. Front Cardiovasc Med. 2016;3:30.
7. Reis F, et al. HPV infection as a risk factor for atherosclerosis: A connecting hypothesis. Med Hypotheses. 2020;144:110021.
8. Zhang Y, et al. Human papillomavirus as a non-traditional cardiovascular risk factor: Mechanisms and evidence. Am J Med. 2024.
9. American College of Cardiology (ACC). Colorectal cancer and HPV pose increased CV risk: ACC.25 update. ACC.org News. 2025 Mar 25.
10. CIDRAP. Meta-analysis adds to emerging evidence tying HPV to cardiovascular disease. CIDRAP News. 2025 Mar 25.
11. Reuters Health. Health Rounds: HPV infection linked to higher heart risk (ACC.25). Reuters. 2025 Mar 26.
12. ScienceDaily. Growing body of evidence links HPV with heart disease. ScienceDaily. 2025 Mar 25.
13. News-Medical. New evidence suggests HPV could increase risk of coronary artery disease (ACC.25). News-Medical. 2025 Mar 25.
14. Feng A, et al. The association between HPV vaccination and new-onset cardiovascular and cerebrovascular diseases: Retrospective cohort. J Health Popul Nutr. 2025.
15. Kuo HK, et al. Human papillomavirus and cardiovascular disease among U.S. Women (NHANES). J Am Coll Cardiol. 2011;58(17):2001–6.

 