

## INCIDENCE, RISK FACTORS, AND PREVENTION OF VULVAR CANCER IN WOMEN

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**Abstract.** Vulvar cancer is a relatively uncommon malignancy, yet it carries substantial morbidity because it affects a sensitive anatomical site, is frequently diagnosed at later stages, and often requires treatment that can be physically and psychologically burdensome. Epidemiologic evidence suggests that vulvar cancer incidence varies widely across regions and age groups, reflecting differences in population aging, human papillomavirus (HPV) exposure, screening practices for precursor lesions, and the prevalence of chronic vulvar inflammatory conditions. Contemporary understanding recognizes two major etiologic pathways: (1) HPV-associated disease, often preceded by usual-type vulvar intraepithelial neoplasia (uVIN/HSIL) and more common in younger women; and (2) HPV-independent disease, frequently linked to chronic dermatoses such as lichen sclerosus and preceded by differentiated VIN, typically occurring in older women and associated with poorer outcomes. Prevention therefore requires a dual strategy: primary prevention by HPV vaccination and risk-reduction behaviors, and secondary prevention through early recognition and treatment of precursor lesions and prompt evaluation of persistent vulvar symptoms. This article synthesizes current evidence on global incidence patterns, established and emerging risk factors, and practical prevention frameworks. Emphasis is placed on integrating HPV immunization, targeted education, clinician vigilance for chronic vulvar symptoms, and proactive management of vulvar dermatoses to reduce disease burden and improve women's health outcomes.

**Keywords:** vulvar cancer, incidence, risk factors, prevention, HPV, vulvar intraepithelial neoplasia, lichen sclerosus, women's health.

**INTRODUCTION**

Vulvar cancer accounts for a small fraction of female cancers, but its public health importance is disproportionately high for three reasons. First, the disease primarily affects older women, a demographic expanding in many countries due to population aging. Second, diagnosis is often delayed because early symptoms—pruritus, burning, irritation, dyspareunia, or a small lesion—may be mistaken for benign dermatologic or infectious conditions. Third, treatment frequently involves surgical excision with potential impacts on sexual function, body image, urinary function, and quality of life, and advanced disease may require multimodality therapy. These realities make vulvar cancer a useful model for prevention-oriented oncology: the disease has recognizable precursor lesions, identifiable risk factors, and feasible points of intervention at both community and clinical levels.

Epidemiologically, vulvar cancer incidence is not uniform. Global cancer surveillance resources report marked geographic variability in age-standardized incidence rates, implying that population structure, HPV prevalence, access to gynecologic care, diagnostic intensity, and background rates of chronic vulvar dermatoses all shape the observed burden. The Global Cancer Observatory's vulva fact sheet illustrates wide ranges in age-standardized incidence rates across regions. While overall rates remain low compared with cervical or breast cancer, the burden becomes clinically meaningful

at the level of health systems because cases cluster in older age groups, where comorbidities may complicate care.

Modern prevention efforts require an understanding of vulvar cancer's dual-pathway biology. HPV-associated vulvar squamous cell carcinoma (SCC) is often linked to oncogenic HPV types and may be preventable through vaccination programs and interventions targeting HPV transmission and persistence. HPV-independent vulvar SCC, by contrast, is commonly associated with chronic inflammatory conditions—especially lichen sclerosus—and is less directly affected by HPV vaccination. Evidence indicates that HPV-independent disease tends to occur in older women and may carry worse outcomes, reinforcing the need for clinical vigilance and long-term follow-up of high-risk vulvar dermatoses [1].

### **MATERIALS AND METHODS**

**Global burden and regional variation.** Vulvar cancer is uncommon, but global cancer surveillance demonstrates notable variability in age-standardized incidence rates across regions. The Global Cancer Observatory provides country- and region-level estimates and presents broad incidence rate ranges, highlighting the importance of local epidemiology rather than assuming uniform risk. Such variation may reflect differences in HPV prevalence, sexual behavior patterns, smoking rates, immunosuppression prevalence, and—critically—differences in clinical recognition and diagnostic coding of vulvar lesions.

**Age distribution.** Vulvar SCC most often presents in older women, particularly in HPV-independent cases. HPV-associated disease is more likely to be diagnosed at younger ages, consistent with an etiologic pathway driven by oncogenic HPV infection and precursor HSIL/uVIN. HPV-independent vulvar SCC is more frequent in older women, often on a background of chronic dermatoses and differentiated VIN, and is associated with a more aggressive clinical course in multiple series. The age gradient has prevention implications: HPV vaccination primarily targets future HPV-associated disease burden, while immediate risk reduction in older women depends heavily on clinical surveillance and management of vulvar dermatoses and premalignant changes [2].

**Histology.** The majority of vulvar cancers are squamous cell carcinomas. Other histologies (melanoma, Bartholin gland carcinoma, adenocarcinoma, sarcoma) are rarer but clinically significant due to distinct behaviors and management. From a prevention standpoint, however, the SCC pathways dominate because of their links to modifiable or monitorable risk factors (HPV, smoking, immunosuppression, lichen sclerosus, VIN).

**Trends over time.** While precise trend directions differ by region, several countries have reported changes consistent with population aging and shifting prevalence of HPV-related disease and precursor lesions. Interpreting trends requires caution: increased clinician awareness and improved biopsy practices can “inflate” incidence by capturing earlier or previously missed cases. Conversely, regions with limited access to gynecologic services may undercount disease burden.

### **RESULTS AND DISCUSSION**

A practical framework divides vulvar SCC into two broad pathways:

#### **A. HPV-associated pathway.**

This pathway is linked to persistent infection with oncogenic HPV types and is often preceded by high-grade squamous intraepithelial lesion of the vulva (HSIL), historically termed usual-type VIN. Clinical risk factors overlap with those for other HPV-related anogenital cancers: early sexual debut, multiple sexual partners, smoking (which impairs immune clearance), and immunosuppression. HPV-

associated vulvar cancers tend to occur at younger ages than HPV-independent cancers, and prevention is strongly tied to HPV vaccination and control of HPV persistence. Reputable clinical summaries emphasize that a substantial fraction of vulvar cancers are HPV-associated, often involving HPV types such as 16.

#### B. HPV-independent pathway.

HPV-independent vulvar SCC is commonly linked to chronic vulvar inflammatory conditions, especially lichen sclerosus, and is often preceded by differentiated VIN. This pathway is more frequent in older women and is associated with a higher likelihood of aggressive behavior and worse outcomes, even when controlling for age and stage in some studies. The prevention implications are profound: HPV vaccination has limited direct impact on HPV-independent disease, so early detection relies on recognizing chronic vulvar symptoms and monitoring high-risk dermatoses over time [3]. These pathways are not merely academic categories; they shape clinical prevention logic. HPV-associated disease is best prevented at the population level (vaccination + behavioral risk reduction). HPV-independent disease is best prevented through strengthened clinical pathways (early biopsy of persistent lesions, accurate diagnosis and treatment of lichen sclerosus, structured follow-up, and patient education about alarm symptoms).

#### Major risk factors in women

1. Persistent high-risk HPV infection and HPV-related precursor lesions. Persistent oncogenic HPV infection is a central risk factor for HPV-associated vulvar SCC. Women with vulvar HSIL/uVIN have elevated risk of progression to invasive disease, particularly if immunosuppressed or if lesions are untreated or recurrent. Prevention therefore includes both primary prevention (vaccination) and secondary prevention (detection and treatment of vulvar HSIL). The American Cancer Society's clinical resource highlights HPV as a major driver for a substantial portion of vulvar cancers [4].

2. Lichen sclerosus and chronic vulvar dermatoses. Lichen sclerosus is strongly associated with HPV-independent vulvar SCC. Chronic inflammation, epithelial injury, and altered local immune responses likely contribute to malignant transformation in susceptible individuals. The association underpins an important prevention message: women with chronic vulvar pruritus or persistent vulvar skin changes require careful evaluation, often including biopsy, and long-term follow-up. The clinical literature notes that HPV-independent vulvar SCCs are associated with worse outcomes and higher nodal metastasis risk, making early detection especially valuable.

3. Age and menopausal status.

Age is a consistent risk marker, reflecting cumulative exposure to chronic inflammatory conditions, immune senescence, and the predominance of HPV-independent carcinogenesis in older women. Aging populations may therefore face increasing vulvar cancer case counts even if age-standardized rates remain stable.

4. Smoking.

Smoking is associated with HPV persistence and impaired immune clearance, contributing to HPV-associated vulvar neoplasia. It also correlates with lower health service utilization and other risk behaviors, potentially compounding risk. Smoking cessation is therefore an actionable prevention lever, especially in younger women at risk of HPV-associated disease [5].

5. Immunosuppression (HIV, transplant, immunosuppressive therapy). Immunosuppressed women have higher risk of persistent HPV infection and HPV-related neoplasia, including vulvar HSIL and invasive SCC. This group benefits from intensified clinical surveillance and timely treatment of premalignant lesions.

6. History of HPV-related cervical/vaginal disease.

Women with cervical HSIL or other HPV-related genital tract neoplasias may share persistent HPV risk and field cancerization phenomena, increasing the need for comprehensive anogenital evaluation.

7. Socioeconomic and access-related factors.

Delayed diagnosis is often rooted in access barriers, stigma, low symptom awareness, and fragmented referral pathways. Because vulvar cancer can present with nonspecific symptoms, systems that support prompt biopsy of persistent lesions are essential to reduce diagnostic delay.

Prevention of vulvar cancer should be conceptualized across three levels: primary prevention (prevent disease initiation), secondary prevention (detect and treat precursor lesions or early cancer), and tertiary prevention (reduce recurrence and complications after treatment).

A) Primary prevention

HPV vaccination.

The strongest population-level prevention tool for HPV-associated vulvar cancer is HPV vaccination. The CDC describes HPV vaccination as cancer prevention and provides evidence that vaccination reduces HPV infections and related precancer outcomes in women. While direct long-latency endpoints (invasive vulvar cancer reduction) take years to mature, intermediate endpoints—reduction in HPV infection and HPV-related precancers—support a preventive effect. A 2010 review also emphasizes the role of HPV vaccines in preventing HPV-related vulvar and vaginal cancers, while noting that screening and clinical vigilance remain necessary.

Risk-reduction counseling and behavior change.

Because HPV is sexually transmitted, behavioral strategies that reduce HPV exposure and increase clearance (safer sex practices, smoking cessation, and prompt treatment of sexually transmitted infections) have theoretical and practical value. Importantly, messaging should avoid stigma and focus on empowerment: HPV is common, and prevention is achievable through vaccination and health-seeking behaviors.

Smoking cessation.

Smoking cessation is a high-yield intervention not only for vulvar neoplasia risk reduction but also for broader cancer and cardiovascular risk reduction. In the context of HPV-associated vulvar disease, cessation supports immune competence and HPV clearance.

B) Secondary prevention

Unlike cervical cancer, vulvar cancer does not have a universally adopted population screening test. Prevention therefore depends on symptom recognition and timely clinical evaluation [6].

Early recognition of symptoms and low threshold for biopsy. Persistent vulvar itching, burning, pain, bleeding, dyspareunia, skin color change, thickening, ulceration, or a mass should prompt clinical assessment. A key prevention principle is the “time threshold”: symptoms that persist despite basic treatment warrant further evaluation, often including biopsy. Delays can allow progression from VIN to invasive disease or allow early invasive lesions to enlarge and metastasize.

Detection and treatment of precursor lesions (VIN).

Treating vulvar HSIL/uVIN reduces the pool of lesions that can progress to invasive cancer. Clinical strategies include excision, ablation, or topical therapies in selected cases. Follow-up is essential because recurrence can occur, especially in smokers and immunosuppressed women.

Management of lichen sclerosus and differentiated VIN.

For HPV-independent disease prevention, proactive management of lichen sclerosus is central. Although treatment choices are clinical decisions, prevention logic is straightforward: reduce chronic inflammation, monitor tissue changes, and biopsy suspicious or changing lesions. Given evidence of worse outcomes for HPV-independent vulvar SCC, earlier detection in this pathway may be especially consequential.

Clinical guideline frameworks.

NCCN guideline publications and summaries for vulvar cancer management emphasize structured evaluation, staging, and follow-up—resources that can be adapted into local clinical pathways for early detection and rapid referral.

C) Tertiary prevention

After treatment, prevention focuses on reducing recurrence, managing treatment sequelae, and supporting quality of life. This includes structured follow-up, management of chronic dermatoses, counseling regarding sexual function and vulvar care, and coordinated survivorship services.

A coherent prevention framework for vulvar cancer in women can be built around four pillars:

Vaccinate early, vaccinate broadly. Implement HPV vaccination programs with high coverage to reduce HPV-associated vulvar HSIL and future cancers.

Educate to reduce diagnostic delay. Public and clinician education should emphasize that persistent vulvar symptoms are not “normal,” especially in older women, and warrant evaluation.

Create a rapid pathway for biopsy and specialist referral. Secondary prevention hinges on shortening time-to-biopsy for persistent lesions and ensuring access to gynecologic oncology when needed.

Manage chronic vulvar dermatoses long-term. For lichen sclerosus and suspected differentiated VIN, implement structured follow-up plans and clear criteria for re-biopsy.

## **CONCLUSION**

Vulvar cancer in women is uncommon but clinically significant due to delayed diagnosis, treatment-related morbidity, and its strong association with identifiable risk factors and precursor lesions. Incidence varies across regions, underscoring the importance of local surveillance and tailored prevention strategies. Two etiologic pathways—HPV-associated and HPV-independent—provide a useful clinical framework. HPV-associated vulvar cancer is best addressed through primary prevention with HPV vaccination and risk-reduction behaviors, supported by evidence that vaccination reduces HPV infection and related precancer outcomes. HPV-independent disease, often associated with lichen sclerosus and differentiated VIN, requires a prevention strategy centered on clinical vigilance, long-term management of chronic vulvar dermatoses, and a low threshold for biopsy of persistent or changing lesions.

Because no universal population screening test exists for vulvar cancer, prevention success depends on a systems approach: high HPV vaccine coverage, strong symptom-awareness messaging, clinician education, and streamlined referral and biopsy pathways. Investments in these areas are likely to yield benefits that exceed vulvar cancer alone, improving broader anogenital health and strengthening women’s preventive care more generally.

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