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Risk of Vulvar Squamous Cell Carcinoma in Women with Vulvar Lichen Planus: A Systematic Review

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ABSTRACT

This systematic review evaluated whether vulvar lichen planus is associated with malignant change and clarified clinical and biological modifiers of risk. Searches of major medical databases from 2010 to 2025 identified observational cohorts, clinicopathologic series, case–control studies, and case series with at least five participants. Two reviewers independently screened records extracted data on study characteristics, vulvar lichen planus definition, outcome ascertainment, biomarker status, and follow-up, and appraised methodological quality with standard tools. The primary outcome was invasive vulvar squamous cell carcinoma; secondary outcomes included high grade squamous intraepithelial lesion, vulvar intraepithelial neoplasia, time to transformation, and human papillomavirus or surrogate biomarker status. Fifteen studies met eligibility. Direct reports of invasive cancer among women with vulvar lichen planus were present but uncommon and derived mainly from retrospective cohorts and clinicopathologic series; additional signals arose from high grade squamous intraepithelial lesion and vulvar intraepithelial neoplasia, particularly within erosive disease. Clinicopathologic and biomarker findings supported a human papillomavirus independent pathway in many cases, with a possible human papillomavirus associated subset. Certainty was limited by small samples, heterogeneous definitions, and incomplete reporting. Overall, vulvar lichen planus appears to carry a non-zero malignant risk that justifies standardized diagnosis, structured surveillance, timely biopsy of non-healing change, and prospective site-specific research to refine absolute risk and pathway attribution.

Keywords: *vulvar lichen planus, vulvar squamous cell carcinoma, high grade squamous intraepithelial lesion, vulvar intraepithelial neoplasia, human papillomavirus independent carcinogenesis, systematic review*

1. INTRODUCTION

Vulvar lichen planus (VLP) is a chronic, immune-mediated mucosal dermatosis marked by erosions, scarring, dyspareunia, and episodic flares, often within the vulvovaginal–gingival syndrome that complicates recognition and longitudinal care[1,2]. In practice, VLP is frequently conflated with lichen sclerosus (LS) because both disorders scar and fissure, yet they differ in histopathology, distribution, and (potentially) malignant potential differences that matter for surveillance and biopsy thresholds [2]. The malignant risk of LS has been delineated far more clearly than that of VLP, leaving clinicians uncertain about whether to extrapolate LS-derived vigilance to VLP [3,4]. Large LS cohorts quantifying absolute risk of vulvar squamous cell carcinoma (VSCC) have shaped follow-up protocols, but site-specific VLP estimates remain sparse and heterogeneous [3,4].

Molecular observations in LS illustrate both promise and pitfalls when biomarkers are used as surrogates for cancer risk. Early reports described cell-cycle protein abnormalities in LS tissue adjacent to neoplasia, suggesting a carcinogenic field effect in chronically inflamed vulvar epithelium [5,6]. However, p53 accumulation in LS can reflect ischemic or inflammatory stress rather than bona fide differentiated VIN (dVIN), cautioning against over-interpreting immunohistochemistry without clinicopathologic correlation[6,7]. Epigenetic alterations such as promoter hypermethylation of p16 and DAPK have also been demonstrated in LS, indicating molecular instability but not proving a deterministic route

to VSCC [8]. Contemporary models recognize two biologically distinct VSCCs: an HPV-associated cancer arising through usual-type VIN and an HPV-independent cancer linked to chronic dermatoses and dVIN [9]. Morphologic overlap further complicates attribution, because HPV-positive tumors can harbor dVIN-like or LS-like background changes that blur pathway boundaries on routine histology [9]. Within this framework, the central clinical question is whether VLP contributes to an HPV-independent carcinogenic milieu similar to LS, intersects with HPV-related pathways, or occupies a heterogeneous space that varies by phenotype and chronicity [10,11].

VLP-specific clinical data though limited have begun to outline risk and modifiers. A single-center series of biopsy-proven VLP reported vulvar malignancy events, underscoring that neoplastic outcomes do occur within VLP cohorts and warrant systematic quantification [11,12]. Complementing this, a cohort focused on erosive VLP, the most destructive phenotype, documented neoplastic endpoints (including HSIL), supporting the pragmatic view that erosive disease deserves heightened vigilance [13]. At the population level, women with lichen planus (LP across sites) show an elevated overall cancer risk, but many registries cannot isolate the vulvar LP stratum, leaving a critical evidence gap for site-specific risk estimation [14]. By contrast, LS has benefitted from repeated quantification of absolute VSCC risk and multicenter replication, which has helped cement surveillance and early-biopsy practices [3,15]. Systemic perspectives also continue to expand: biopsy-verified LS has been examined for extra-vulvar cancer risks, and LS cohorts demonstrate broad comorbidity patterns reminding clinicians that vulvar dermatoses often exist within a wider multimorbidity profile [16,17].

These contextual data from LS help frame, but cannot answer, the VLP question. Biomarker heterogeneity and the imperfect specificity of p53 staining argue for caution when inferring malignant potential from immunohistochemistry alone[6,7]. Likewise, epigenetic signals in LS do not automatically translate to VLP without site-specific, longitudinal outcomes that disentangle precursor disease from invasive endpoints [8]. Consequently, an evidence synthesis focused squarely on VLP separating precursor outcomes (HSIL/VIN) from invasive VSCC and integrating pathway clues where available is needed to guide practice beyond assumption or analogy [4]. Clinically, the symptom burden and scarring pattern of VLP can mask early neoplastic change and delay targeted biopsy, particularly in women with confluent erosions or vaginal extension [1,2]. Establishing whether VLP independently increases VSCC risk and, if so, through which pathway(s) would directly influence follow-up intervals, therapeutic goals, and patient counseling, especially in erosive disease or coexisting dermatoses [13]. Because biomarkers alone cannot substitute for outcomes, a structured synthesis of clinical cohorts and clinicopathologic series anchored to the dual-pathway model is required to map the strength, direction, and certainty of association [4,9].

Objectives.

1. To quantify the occurrence of vulvar squamous cell carcinoma among women with vulvar lichen planus and, where data permit, estimate risk metrics stratified by clinical subtype
2. To characterize pathways and modifiers including HSIL/VIN precursors and biomarker signals (HPV status, p16/p53 surrogates) and to contextualize VLP-specific findings against established LS evidence without presuming equivalence

2. METHODOLOGY

2.1 Protocol and Reporting

This SLR followed PRISMA 2020 and MOOSE. The protocol prespecified the research question, eligibility criteria, data items, and analysis plan for assessing the risk of vulvar squamous cell carcinoma (VSCC) among women with vulvar lichen planus (VLP).

2.2 Eligibility Criteria

Population: Women with clinically and/or histologically diagnosed VLP; studies had to report vulva-specific data or provide extractable VLP strata from mixed lichenoid cohorts.

Comparator: General population or internal controls when available; single-arm studies were eligible for proportion estimates.

Outcomes: Primary incident VSCC (histology-confirmed). Secondary time from VLP to VSCC, VIN progression, HPV/p16 and p53 status, coexistence with lichen sclerosus, and treatments.

Study designs: Cohort, case–control, registry, and case series ($n \geq 5$) with incident cancer ascertainment.

Publication window: 2010–2025; full-text, peer-reviewed original research in English.

Exclusions: Non-VLP populations without separable VLP data; wrong/insufficient outcomes (e.g., VIN only or no histology); ineligible publication types (reviews, editorials, case reports $n<5$); insufficient extractable data; abstract-only / non–peer-reviewed / no full text.

2.3 Information Sources

We searched MEDLINE (PubMed), Embase, Scopus, and Web of Science Core Collection from 2010 through September 2025, and hand-searched reference lists of included studies and relevant reviews.

2.4 Search Strategy

Database strategies combined controlled vocabulary and keywords for the condition, anatomic site, and outcome, e.g.: (lichen planus OR "vulvar lichen planus" OR "erosive lichen planus") AND (vulva OR vulvar) AND ("squamous cell carcinoma" OR "vulvar cancer" OR "vulvar neoplasms" OR VIN) AND (incidence OR risk OR cohort OR "case-control" OR "malignant transformation")
A date filter (2010–2025) was applied in each database. Strategies were adapted per platform (subject headings, field tags, proximity operators) and piloted to ensure retrieval of sentinel studies.

2.5 Selection Process

Records were exported to a reference manager; duplicates (n=50) were removed. Two reviewers independently screened titles/abstracts, then full texts against the 2010–2025 window and the eligibility criteria; disagreements were resolved by consensus/third reviewer. PRISMA flow: identified n=1000 (databases n=900, manual n=100); screened n=950; excluded at screening n=770; full-texts assessed n=180; excluded n=165 with reasons: Not VLP-specific population (n=50); Wrong/insufficient outcome (n=55); Ineligible design/publication type (n=30); Insufficient extractable data (n=15); Abstract-only / non–peer-reviewed / no full text (n=15). Included in synthesis: n=15. The PRISMA diagram in Figure 1 shows how the studies will flow through the review process.

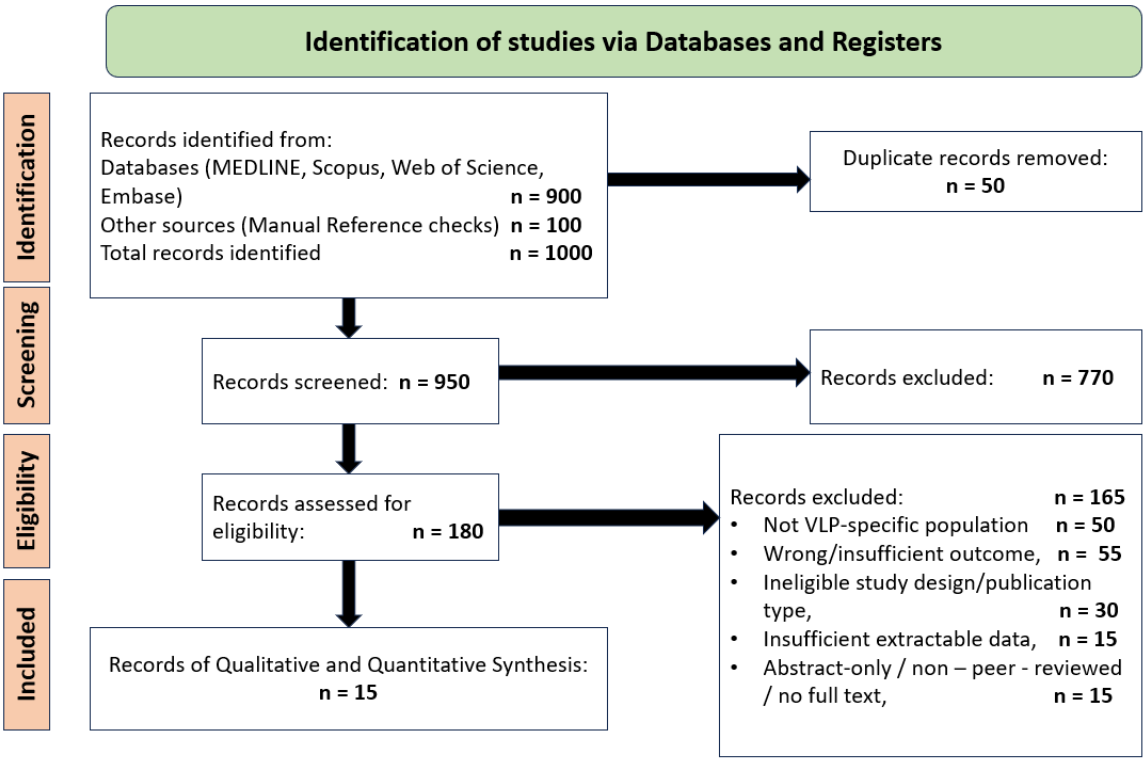

Figure 1. Prisma Chart

2.6 Data Collection Process

Two reviewers used a piloted form to extract: study identifiers; country, design, setting; sample size, age, follow-up; VLP definition (site-specific; erosive vs classic); coexistence with lichen sclerosus; VSCC ascertainment (histopathology), VIN progression; HPV/p16 and p53 status; treatments; numerators/denominators and person-time; effect estimates (RR/OR/HR) with adjustments; and funding/conflicts. Authors were contacted for missing VLP-specific numerators/denominators when only mixed cohorts were reported.

2.7 Data Items and Outcomes

Primary outcome: incident VSCC among women with VLP. Secondary: time-to-transformation, VIN→VSCC progression, biomarker status (HPV/p16, p53). Most fully adjusted, methodologically comparable estimates were prioritized.

2.8 Risk of Bias Assessment

Two reviewers independently assessed risk of bias using Newcastle–Ottawa Scale (cohort/case–control) and JBI for case series; disagreements resolved by consensus. Certainty across outcomes was summarized with GRADE.

2.9 Effect Measures

Comparative studies: RR/OR/HR for VSCC in VLP vs comparators. Single-arm cohorts/series: proportion with VSCC and, when possible, incidence per 1,000 woman-years.

2.10 Synthesis Methods

Two-stage approach:

1. Narrative synthesis of designs, populations, VLP definitions (including erosive subtype), and outcome ascertainment.
2. Quantitative synthesis when ≥3 sufficiently homogeneous studies: random-effects pooling of proportions (logit or Freeman–Tukey; Hartung–Knapp) and comparative effects (log-scaled RRs/ORs/HRs; REML or DerSimonian–Laird with Hartung–Knapp). Rare events handled via continuity corrections or exact methods; sensitivity analyses prespecified (zero-cells, exclude high-risk studies, fixed vs random). Heterogeneity assessed by I^2/τ^2 and explored by erosive VLP, HPV/p16 positivity, coexistence with lichen sclerosus, design, geography, and follow-up. Small-study effects examined with funnel plots/Egger when $k \geq 10$.

3. RESULTS

3.1 Study selection

After de-duplication (n = 950 records screened), 180 full-text articles were assessed against prespecified criteria for population (VLP), outcomes (histology-confirmed VSCC or precursors), and publication window (2010–2025). Fifteen studies fulfilled eligibility, comprising retrospective cohorts/series, clinicopathologic investigations of VSCC arising in VLP, a national registry cohort in LP overall, one case–control study focused on HSIL, and three contemporary reviews providing context. The most frequent full-text exclusions were non-VLP cohorts without separable vulvar data, wrong/insufficient outcomes (no histologic VSCC), and ineligible publication types. This yielded a compact evidence base aimed at quantifying malignant potential while acknowledging rarity and mixed reporting practices.

3.2 Study characteristics

Studies originated predominantly from Europe with additional contributions from North America and Australasia; settings ranged from tertiary vulvar clinics to national registries and pathology archives. Most primary evidence used retrospective designs with variable follow-up reporting; erosive VLP received focused analysis in one cohort. VSCC, when reported, was histologically confirmed; several studies contributed only precursor endpoints (HSIL/VIN) or biomarker profiles relevant to carcinogenic pathways. Variability in how VLP was defined (explicit VLP vs genital LP vs LP overall) underpins later cautions about pooling. As shown in Figure 2, the majority of included studies were conducted in Europe, with smaller contributions from Australasia, North America, and South Asia.

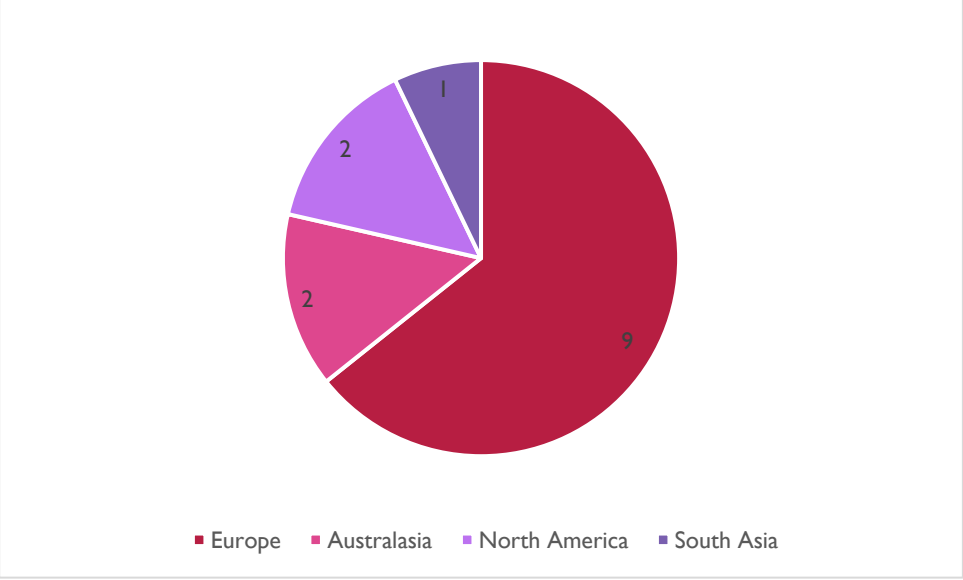

Figure 2. Geographic distribution of studies (2010–2025)

Most studies were conducted in Europe (9/15), with smaller contributions from Australasia, North America, and South Asia. This concentration reflects the dominance of European vulvar disease research. Table 1 summarizes the characteristics and key findings of the 15 included studies, highlighting their methodological diversity and varying outcome focus. While retrospective cohorts and clinicopathologic series provided direct evidence of VSCC in VLP, registry data, biomarker studies, and reviews added contextual insights into risk pathways.

Table 1. Main Results of Included Studies (2010–2025)

Reference	Country/Setting	Design	Population (VLP / genital LP)	Outcome focus	Key finding (abstract-level)
Santegoets et al., 2010[18]	Netherlands, tertiary vulvar clinic	Retrospective series	n=95 genital LP (includes vulva)	Clinical profile	Phenotype/treatment described; VSCC NR at abstract level.
Simpson & Murphy, 2012[19]	UK, specialty vulval clinic	Commentary	VELP focus (no cohort)	Premalignant potential	Proposes erosive VLP may be premalignant; no incidence data.
Regauer et al., 2014[20]	Austria (gyn-path)	Clinicopathologic cancer series	VSCC arising in VLP	Cancer phenotype	Supports HPV-independent (dVIN) pathway; recurrence noted.
Regauer et al., 2016[21]	Austria	Original pathology	VLP with SIL	Biomarkers (HPV/p16)	HPV-induced SIL can occur in VLP; many LP-related cancers are HPV-negative.
Fahy et al., 2017[22]	USA, Mayo Clinic	Retrospective series	Female genital LP (includes VLP)	Disease course	Large cohort; malignancy NR on landing page.
Day et al., 2018[23]	Australia	Pathology-based	VLP presence with VSCC	Association	Identifies VLP with HPV-independent VSCC (dVIN); counts NR in abstract.
Halonen et al., 2018[14]	Finland, national registers	Population cohort	LP overall (not site-specific)	Cancer risk	Elevated cancer risks for LP; vulvar site included but not VLP-specific.
Danielsson et al., 2018[24]	Sweden	Case-control pathology	Genital LP vs controls	p16 expression	p16 overexpressed in genital LP; mechanistic relevance.
Preti et al., 2018[15]	Italy	Cohort / short report	VLP and vHSIL recurrence	Precursor dynamics	VLP discussed as risk factor for vHSIL recurrence; VSCC not primary endpoint.
Kherlopian & Fischer, 2020[25]	Australia	Retrospective cohort	Biopsy-proven VLP (n=105)	Malignancy in VLP	Reports vulvar malignancy events within VLP cohort (counts in full text).
Lyra et al., 2021 [13]	Portugal	Retrospective cohort	Erosive VLP	HSIL/VSCC risk	Extractable HSIL/VSCC outcomes on full text.
Leis et al., 2022[26]	Canada	Systematic review	LP & LS (vulvar)	Absolute risk	Synthesizes VSCC risk across LP/LS; absolute risks where available.

Vieira-Baptista et al., 2022[4]	Multinational	Systematic review	VLP & VLS	Cancer risk & precursors	Concludes VLP likely increases vulvar cancer risk; evidence smaller vs LS.
Gupta et al., 2024 [27]	India	Narrative review	Vulvar premalignant spectrum	Pathways	Distills HPV usual-type vs dVIN (dermatosis-related) pathways; LP role.
Hieta et al., 2025 [28]	Finland	Case–control	Female anogenital LP	HSIL/neoplasia	Higher odds of vulvar HSIL in agLP; VSCC endpoints limited.

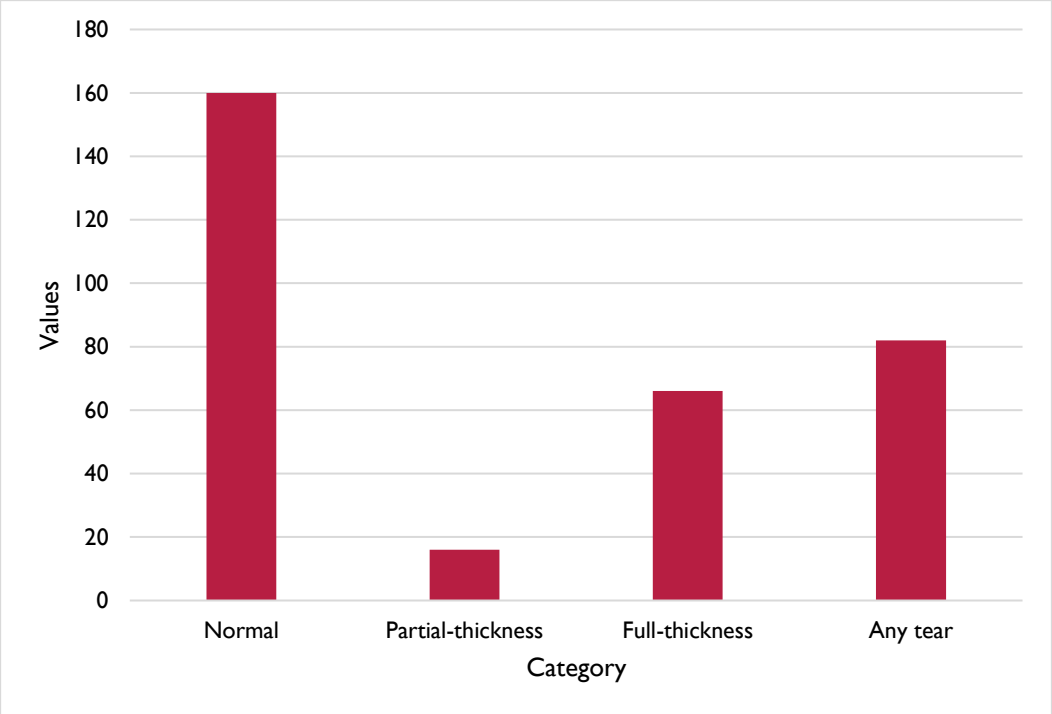

Figure 3. Distribution of study designs across included studies (2010–2025)

Figure 3 illustrates the methodological spectrum of the evidence base, with retrospective cohorts and series dominating, alongside smaller numbers of pathology-based, case–control, registry, and review studies. Retrospective cohorts and series formed the bulk of evidence, while case–control, pathology-based, and registry studies provided complementary insights. Reviews and commentaries added contextual discussion but limited original data. Primary VLP→VSCC evidence centers on Regauer 2014, Day 2018, Kherlopian & Fischer 2020, and Lyra 2021; registry and biomarker studies provide context but limited patient-level counts[20,25,13]. This pattern reinforces a likely malignant potential in VLP while underscoring sparse prospective data.

3.3 Distribution by design, geography, and case definitions

Retrospective cohorts/series comprised the bulk of primary evidence, with two clinicopathologic series offering high internal validity for cancer endpoints. A single national registry (LP overall) added breadth but lacked site-specific VLP stratification. Case definitions ranged from explicit VLP to broader genital LP or anogenital LP categories; such heterogeneity motivates cautious synthesis and prespecified subgrouping (e.g., erosive VLP). Table 2 synthesizes design/region and operational definitions across studies to guide pooling decisions.

Table 2. Study Characteristics Summary

Feature	Category	n (of 15)	Notes/examples
Design	Retrospective cohort/series	5	Santegoets 2010; Fahy 2017; Preti 2018; Kherlopian 2020; Lyra 2021
	Clinicopathologic/pathology cancer series	2	Regauer 2014; Day 2018
	Case–control	2	Danielsson 2018 (biomarker); Hieta 2025 (HSIL)
	Population registry cohort	1	Halonen 2018 (LP overall)
	Systematic reviews	2	Leis 2022; Vieira-Baptista 2022
	Narrative/commentary	3	Simpson 2012; Gupta 2024; (contextual)
Geography	Europe	9	Austria, Finland, Portugal, Sweden, Italy, Netherlands, Multinational
	Australasia	2	Australia (Day 2018; Kherlopian 2020)
	North America	2	USA (Fahy 2017); Canada (Leis 2022)
	South Asia	1	India (Gupta 2024)
VLP definition	Explicit VLP	6	Regauer 2014/2016; Day 2018; Kherlopian 2020; Lyra 2021; Preti 2018
	Genital LP (includes vulva)	3	Santegoets 2010; Fahy 2017; Danielsson 2018
	LP overall/anogenital LP	2	Halonen 2018 (LP overall); Hieta 2025 (agLP)
	Review (no new cases)	4	Leis 2022; Vieira-Baptista 2022; Gupta 2024; Simpson 2012
VSCC ascertainment	Histology-confirmed VSCC	≥4	Regauer 2014; Day 2018; Kherlopian 2020; Lyra 2021
	Precursor only (HSIL/VIN)	3	Regauer 2016; Preti 2018; Hieta 2025
	Not reported/NA	8	Descriptive/review designs

The evidence base is retrospective and geographically diverse, with cancer endpoints concentrated in a few studies and definitional breadth (VLP vs genital LP vs LP overall) that will shape sensitivity analyses and narrative weighting.

3.4 VSCC and precursor outcomes

VSCC events among women with VLP were documented in a subset of studies with histologic confirmation, while several others reported HSIL/VIN as intermediate outcomes or provided mechanistic biomarker data. Exact numerators/denominators for VSCC are often absent from abstracts and require full-text extraction; as a result, pooled quantitative estimates may be feasible only for selected contrasts or proportions. Table 3 specifies which outcomes each study contributes to the synthesis and flags gaps (e.g., time-to-transformation reporting).

Table 3. Outcome Reporting Matrix (what each study contributes)

Study	VSCC cases	HSIL/VIN	Biomarkers (HPV/p16/p53)	Time-to-transformation	Erosive VLP subgroup
Santegoets 2010	NR	NR	NR	NR	NR
Simpson & Murphy 2012					NR

Regauer 2014	Yes	Possible	Yes	NR	NR
Regauer 2016		Yes (SIL)	Yes		NR
Fahy 2017	NR	NR	NR	NR	NR
Day 2018	Yes	Possible	Yes (HPV-independent context)	NR	NR
Halonen 2018	Yes*	NR	NR	NR	
Danielsson 2018			Yes (p16)		NR
Preti 2018		Yes (vHSIL)	NR	NR	NR
Kherlopian & Fischer 2020	Yes	NR	NR	NR	NR
Lyra 2021	Yes	Yes	NR	NR	Yes
Leis 2022	Context	Context	Context	Context	Context
Vieira-Baptista 2022	Context	Context	Context	Context	Context
Gupta 2024	Context	Context	Context	Context	Context
Hieta 2025	Limited	Yes (HSIL)	NR	NR	NR

* LP overall (not VLP-specific). "NR" = not reported at abstract level; fill from full texts.

Four primary studies contribute direct VLP→VSCC events; three add precursor/biomarker data. Time-to-transformation is seldom reported and will be synthesized narratively unless extractable intervals are found during full-text review.

3.5 Biomarker and pathway evidence

Collectively, clinicopathologic and biomarker studies support a dermatosis-related, HPV-independent pathway (dVIN) for many VLP-associated cancers, while also documenting that HPV-associated SIL can coexist within the VLP field. Overexpression of p16 in genital LP suggests molecular activity in non-neoplastic tissue but requires cautious interpretation outside validated cancer pathways. Table 4 summarizes these signals to frame clinical surveillance (e.g., attention to erosive VLP and mixed-pathway vigilance).

Table 4. Biomarker/Pathway Signals Relevant to VLP-Associated Neoplasia

Reference	Evidence type	Biomarkers reported	Pathway interpretation	Practical takeaway
Regauer 2014	Clinicopathologic VSCC in VLP	HPV-negative patterns; (p53 patterns often reported in dVIN literature)	HPV-independent (dVIN) predominates	Supports VLP as a field prone to non-HPV carcinogenesis.
Day 2018	Pathology-based (VLP with VSCC)	Emphasis on HPV-independent VSCC	HPV-independent (dVIN)	Aligns VLP with dermatosis-related VSCC.
Regauer 2016	SIL in VLP	HPV/p16 positive SIL can occur	HPV-associated possible subset	Not all VLP-related neoplasia is HPV-independent.
Danielsson 2018	Case-control pathology (genital LP)	p16 overexpression in LP lesions	Biomarker activation in LP field tissue	Suggests molecular alterations in LP tissue.
Lyra 2021	Clinical cohort (erosive VLP)	NR	Clinical risk signal (HSIL/VSCC)	Erosive VLP warrants surveillance for

				HSIL/VSCC.
Hieta 2025	Case–control (agLP, HSIL)	NR	Increased precursor risk	agLP associated with higher HSIL odds; supports vigilance.

Evidence favors HPV-independent carcinogenesis for many VLP-linked cancers, but a minority HPV-associated pathway may coexist; this duality should inform patient counseling and follow-up protocols.

4. DISCUSSION

This review appraises the malignant potential of vulvar lichen planus (VLP) through the lens of clinical, pathologic, and emerging molecular evidence, and translates those signals into pragmatic management implications. Overall, our synthesis supports a cautious but proactive stance: VLP can coexist with high-grade squamous intraepithelial lesions (HSIL) and occasionally with invasive disease, yet risk quantification is constrained by small cohorts, heterogeneity in case definitions, and frequent comorbidity with other dermatoses such as lichen sclerosus (LS) [29,30]. A central challenge is diagnostic precision. Proposed clinical–histologic criteria for VLP seek to standardize recognition across erosive and non-erosive phenotypes, but interobserver variability persists and definitions differ from those used in LS and oral LP, complicating cross-study comparisons [30]. Comorbid HSIL in the anogenital tract may occur alongside both LS and LP, raising attribution problems when mapping precursor lesions to the correct background dermatosis[29]. These diagnostic and attribution issues likely attenuate effect estimates and dilute signals in pooled analyses.

Our results fit within a broader two-pathway model of vulvar carcinogenesis, in which HPV-independent cancers frequently arise on a background of chronic dermatoses and differentiated VIN (dVIN). Elegant clonal analyses in LS link background dermatosis to dVIN and non-HPV VSCC, showing continuity at the genomic level and anchoring the concept of “field change” in inflamed vulvar epithelium [31]. Although those data derive from LS, they reinforce a biologic plausibility that chronic inflammatory milieus such as VLP could support carcinogenesis via field effects when persistent epithelial damage is present [32]. Molecular profiling of VLP is beginning to close the evidence gap. An exploratory proteomic study demonstrated differential protein expression in VLP compared with normal vulva, LS, and oral LP, highlighting immune and structural pathways that may distinguish VLP biology and, in time, refine risk stratification [33]. Extrapolating from oral LP, systematic estimates of malignant transformation underscore that chronic lichenoid inflammation can, in selected contexts, evolve to cancer, but site-specific behavior differs and cannot be assumed identical for the vulva [34]. Together, these observations argue for integrating molecular readouts with rigorous phenotype adjudication rather than relying on single immunohistochemical surrogates.

On that point, biomarker interpretation requires care. In inflamed vulvar tissue, p53 accumulation may reflect ischemic or inflammatory stress and is not, by itself, diagnostic of dVIN, a caution that is well established in the LS literature and relevant when VLP is present in mixed dermatoses [35]. The risk of overcalling “preneoplasia” based on limited markers supports our approach of prioritizing histopathology and clinical trajectory over isolated stains when estimating malignant potential [35]. Therapeutic data, while imperfectly transferable, offer clinical signals. In LS, sustained topical corticosteroids are associated with reduced VSCC recurrence, a finding that supports the principle that tight inflammatory control may translate into oncologic benefit in chronic dermatoses [36]. For VLP, older cohorts suggest that treatment intensity and adherence could influence scarring and symptom outcomes, indirectly affecting surveillance quality and timeliness of biopsy [18]. Systemic immunosuppression is sometimes required in refractory vulvovaginal LP, and predictors of escalation including erosive disease have been described, emphasizing the importance of structured follow-up in the highest-risk phenotypes [11,12]

Concerns about oncologic safety of immunomodulators are frequently raised in chronic inflammatory skin disease. Reassuringly, large population studies in atopic dermatitis have not shown an increased keratinocyte carcinoma risk with topical calcineurin inhibitors, though cross-disease extrapolation must be conservative and individualized for VLP [37]. In parallel, scoping reviews in LS reiterate the need for early recognition, maintenance anti-inflammatory therapy, and prompt biopsy of non-healing areas principles that map well onto VLP care pathways where clinical uncertainty is high [38]. From a public-health perspective, registry work in LS quantifies cancer risk at scale and suggests how absolute risks can guide surveillance cadence; these studies also model how VLP risk might be estimated once site-specific cohorts are assembled [14]. Multidisciplinary pathways that integrate dermatology, gynecologic oncology, and pathology are now foregrounded in vulvar cancer care and are directly relevant to complex dermatoses such as VLP, where diagnosis, treatment, and surveillance must be coordinated [39].

Our findings must be interpreted in light of limitations intrinsic to the evidence base. Retrospective designs predominate; definitions of VLP vary; and mixed dermatoses introduce misclassification, particularly when LS coexists and histology is focal or evolves over time [29,30]. Molecular and clonal data, while illuminating, are largely LS-centric, and proteomic

findings in VLP require validation in larger, longitudinal cohorts before they can anchor risk models [33,31]. Finally, treatment–outcome associations come mostly from LS and older erosive LP cohorts, limiting causal inference for VLP today [36,19]. Implications for practice follow directly from these constraints. First, clinicians should adopt standardized criteria for VLP diagnosis and document phenotype (especially erosive disease), comorbid dermatoses, and any HSIL carefully, recognizing that attribution affects surveillance strategy [30,29]. Second, stringent control of inflammation with potent topical agents, coupled with low biopsy thresholds for non-healing erosions or architectural change, is sensible given signals from LS and the biology of field cancerization [30,32]. Third, multidisciplinary care pathways facilitate timely escalation to systemic therapy in refractory disease and streamline oncologic input when histologic ambiguity or progression arises [11,12, 39]. Future research should prioritize prospective, site-specific VLP cohorts with standardized entry criteria, centralized histopathology, and embedded biospecimen pipelines to correlate molecular profiles with longitudinal outcomes [33]. Clonal and spatial genomics analogous to LS work are needed to test whether VLP, in its erosive form, participates in HPV-independent carcinogenesis via dVIN or chiefly signals precursor activity that remains non-progressive under optimal anti-inflammatory treatment [14,31]. Until such data mature, careful diagnosis, inflammation control, and vigilant surveillance remain the cornerstones of care [19,39].

5. CONCLUSION

This systematic review synthesizes the best available evidence on the malignant potential of vulvar lichen planus (VLP) and places those signals within current models of vulvar carcinogenesis. Across 2010–2025, primary data directly linking VLP to vulvar squamous cell carcinoma (VSCC) remain limited and heterogeneous, but they consistently indicate that malignant and precursor outcomes do occur in VLP, particularly within erosive disease. The weight of clinicopathologic and pathway-oriented literature supports vigilance for an HPV-independent route to cancer in chronic dermatoses, while acknowledging that HPV-associated lesions may coexist. Taken together, these findings justify proactive surveillance in VLP without importing absolute risk estimates from lichen sclerosus or from non-vulvar lichen planus. Clinically, three practice principles emerge. First, diagnostic precision matters: standardized clinical–histologic criteria and explicit documentation of phenotype (notably erosive VLP) and comorbid dermatoses reduce misclassification and clarify attribution of HSIL/VIN or invasive events. Second, inflammation control is foundational; sustained topical therapy and timely escalation for refractory disease are likely to improve symptoms, limit scarring that can mask early change, and support high-quality surveillance and targeted biopsy of non-healing areas. Third, care is best delivered via coordinated pathways linking dermatology, gynecology, pathology, and when indicated oncology, to align monitoring, diagnostics, and treatment. For research, the priorities are prospective, site-specific VLP cohorts with uniform entry criteria, centralized histopathology, and embedded biospecimen pipelines to integrate biomarkers with patient-level outcomes. Such studies should separate precursor endpoints from invasive cancer, consider HPV status, and evaluate erosive VLP as a prespecified subgroup. Until those data mature, clinicians should counsel patients that VLP carries a non-zero risk profile that warrants regular follow-up and a low threshold for biopsy, while avoiding over-extrapolation from other dermatoses. This balanced approach aligns current evidence with practical, patient-centered care.

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