

Cervical Cancer Screening and Prevention

Precursor biology • Cytology • HPV-based screening
Colposcopy • Prevention

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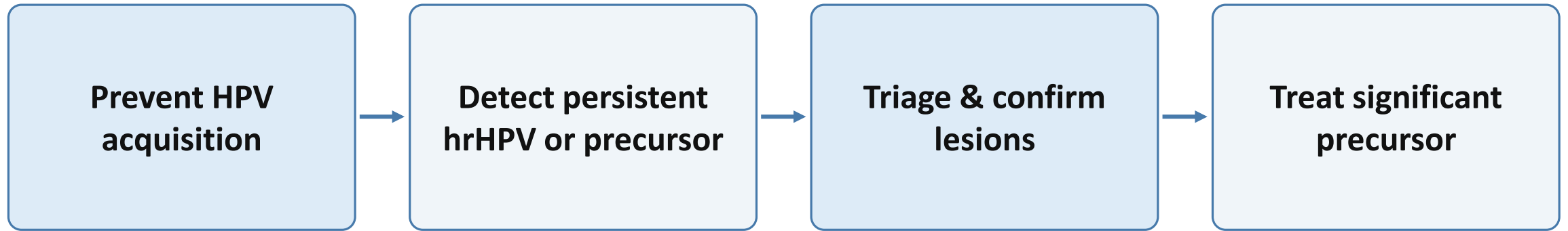
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Learning objectives

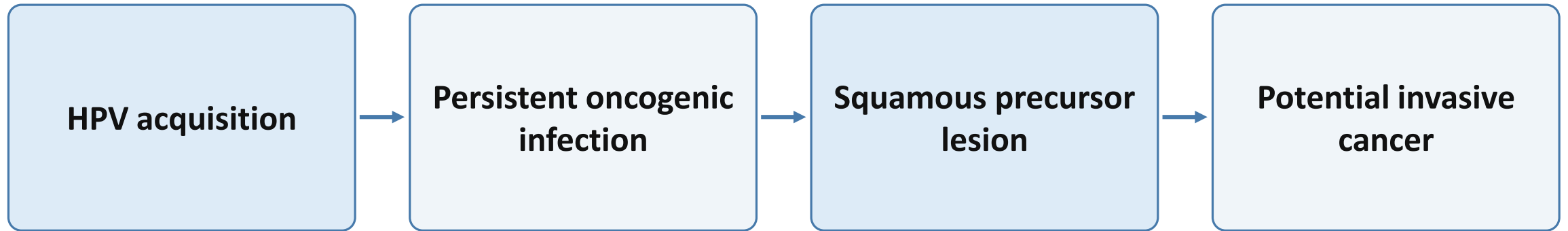
- Explain why the natural history of HPV-associated cervical neoplasia makes screening effective.
- Interpret the biological meaning of Pap cytology, high-risk HPV tests, and colposcopic biopsy.
- Connect LSIL and HSIL findings to appropriate surveillance or treatment concepts.
- Distinguish screening recommendations from risk-based management and primary prevention.

Three linked opportunities for prevention



Vaccination and effective screening are complementary, not interchangeable.

The biological window that makes screening possible

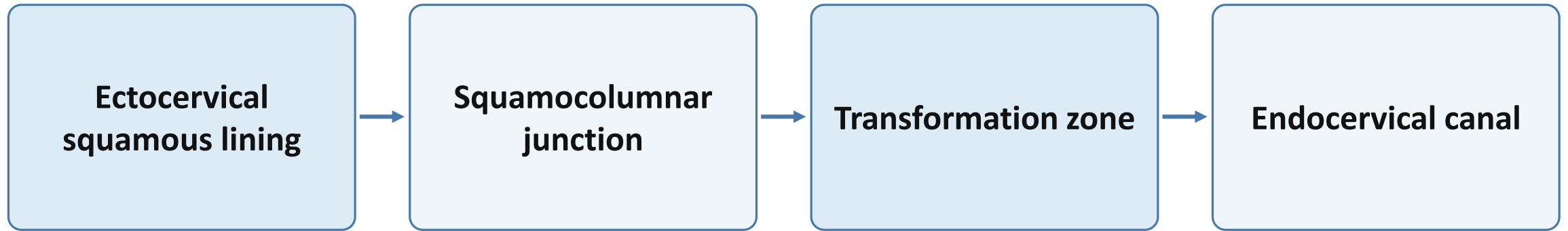


Progression generally unfolds over years; Surveillance can interrupt the pathway before invasion.

Screening targets a preinvasive disease phase

- Cytologic abnormalities can be detected because precursor lesions exfoliate cells.
- Histologic progression can remain confined to the epithelium before stromal invasion.
- Precursor detection enables treatment before an invasive mass or symptoms develop.
- An HPV-positive result identifies infection/risk, not a diagnosis of cancer.

Transformation zone: The sampling target

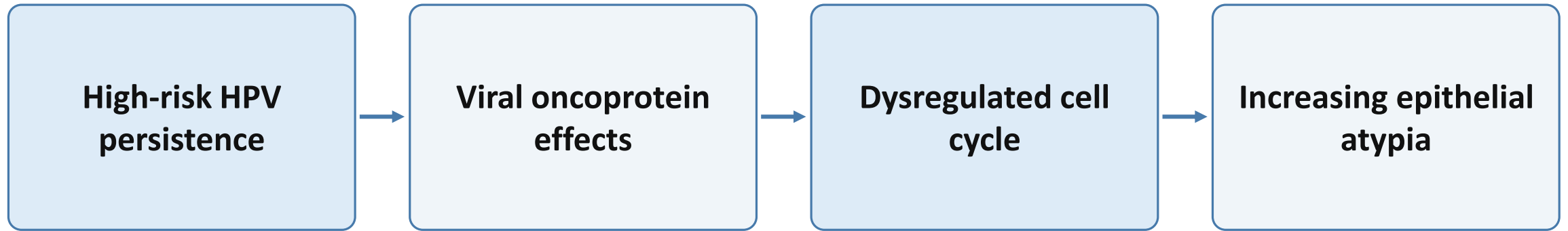


Adequate sampling depends on obtaining representative cells from the relevant cervical epithelium.

Why the transformation zone matters

- Squamous metaplasia develops at the squamocolumnar junction.
- The transformation zone is the characteristic site of HPV-associated cervical SIL.
- Cytology specimens are collected with brushes or spatulas designed to sample this region.
- The location and visibility of the transformation zone vary across individuals.

HPV-associated carcinogenesis: Causal sequence



Persistent transforming infection—not merely transient HPV detection—underlies precursor risk.

Productive infection versus transforming infection

LSIL: Productive infection

- Viral replication is prominent.
- Koilocytic atypia reflects viral cytopathic change.
- Squamous maturation is partly preserved.
- Most lesions regress rather than progress.

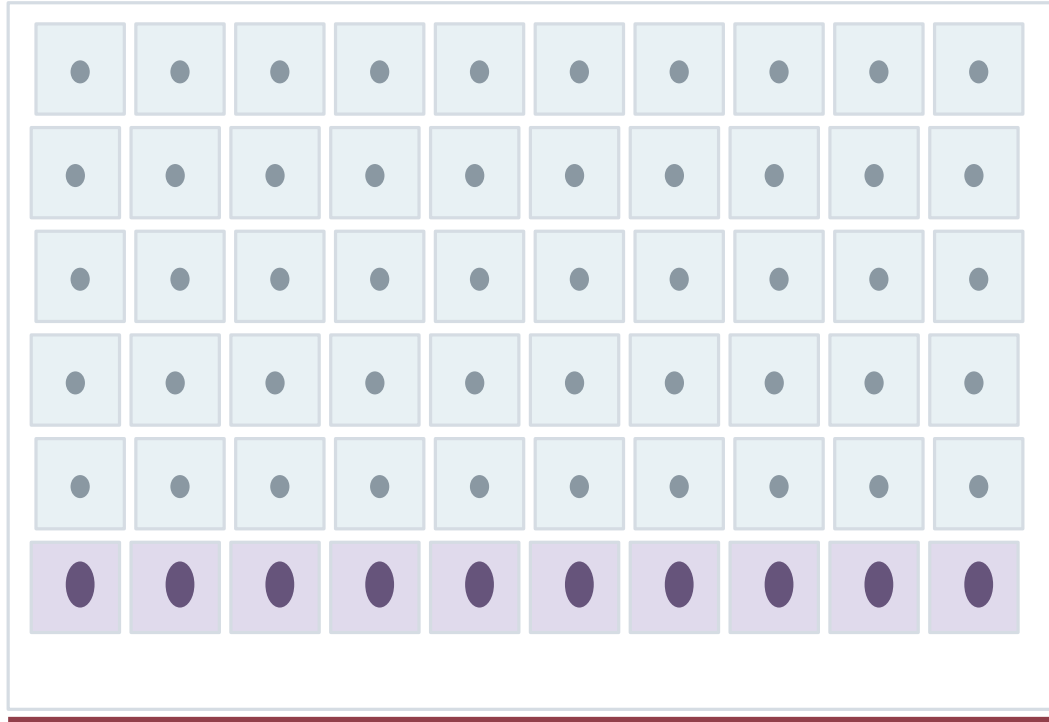
HSIL: Transforming infection

- Cell-cycle deregulation predominates.
- Proliferation extends above the basal layer.
- Maturation is reduced or arrested.
- Substantial precursor risk warrants close evaluation.

Terminology across classification systems

Older terms	CIN system	Two-tier terminology
Mild dysplasia	CIN 1	LSIL
Moderate dysplasia	CIN 2	HSIL
Severe dysplasia / carcinoma in situ	CIN 3	HSIL

Normal cervical squamous maturation

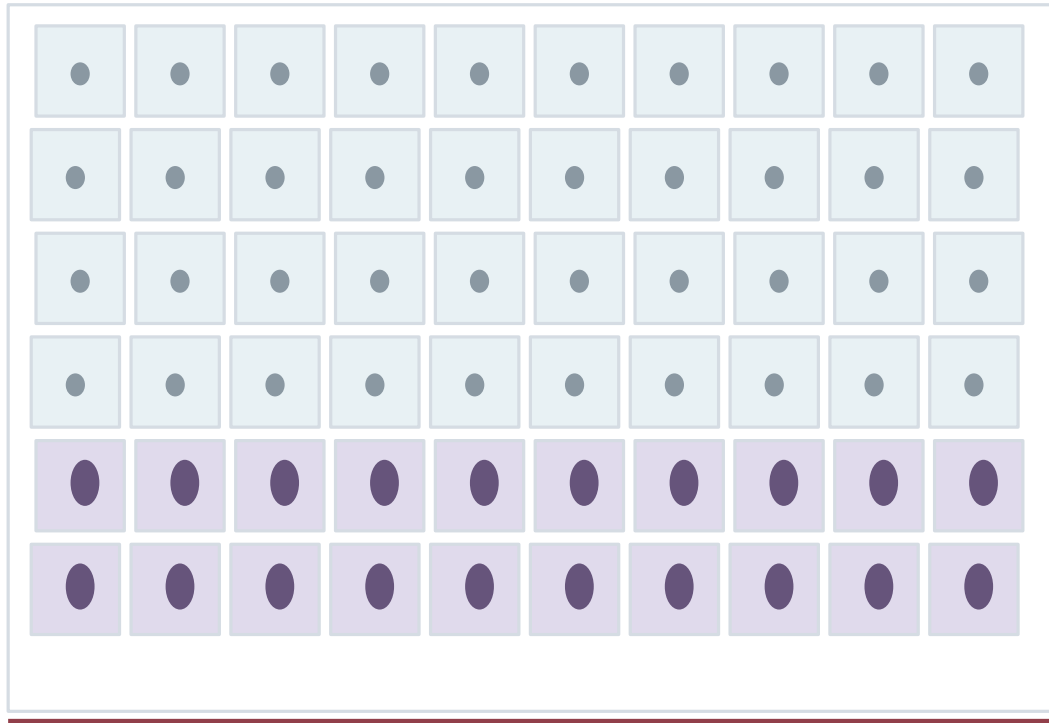


Basement membrane

Mature squamous cells occupy the superficial layers; Proliferation is concentrated basally.

Original schematic — not a histology image

LSIL: Limited atypia with retained maturation

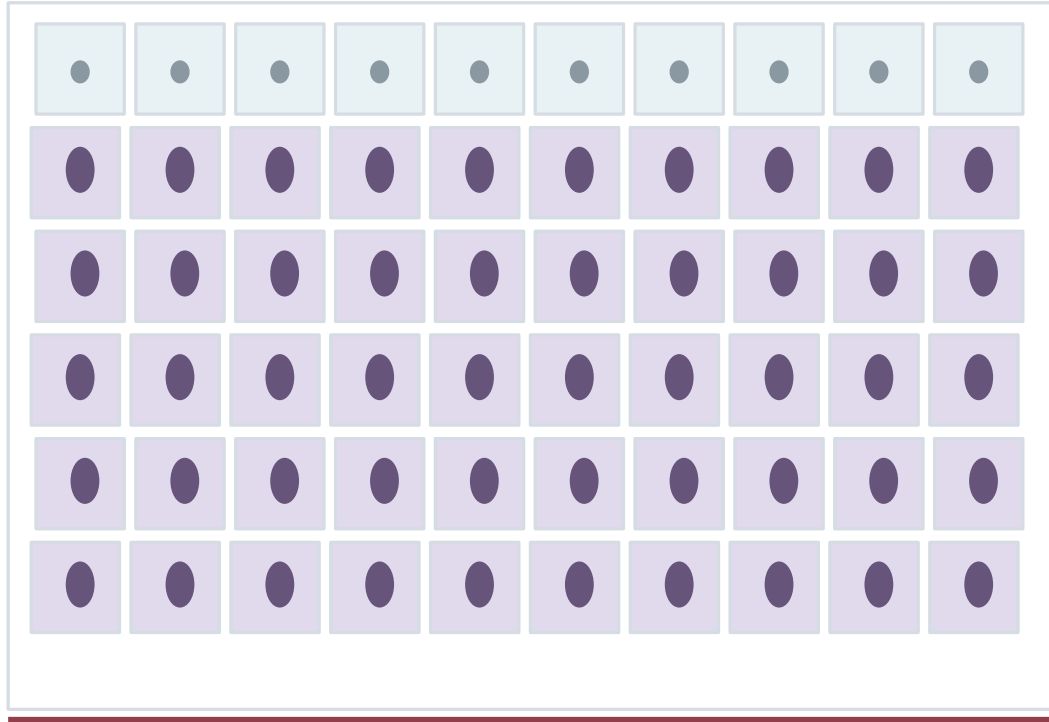


Basement membrane

Low-grade alteration predominates in basal and parabasal regions; Koilocytosis is evident in maturing cells.

Original schematic — not a histology image

HSIL: Expansion of immature atypical cells



Basement membrane

Atypical immature cells extend upward; Marked loss of maturation reflects increased proliferative activity.

Original schematic — not a histology image

Morphologic basis of a squamous intraepithelial lesion

- Nuclei become enlarged, hyperchromatic, irregular, and variable in size or shape.
- Increasing histologic grade corresponds to reduced epithelial maturation.
- Perinuclear halos with nuclear atypia are characteristic of koilocytic change.
- The basement membrane remains intact in an intraepithelial lesion.

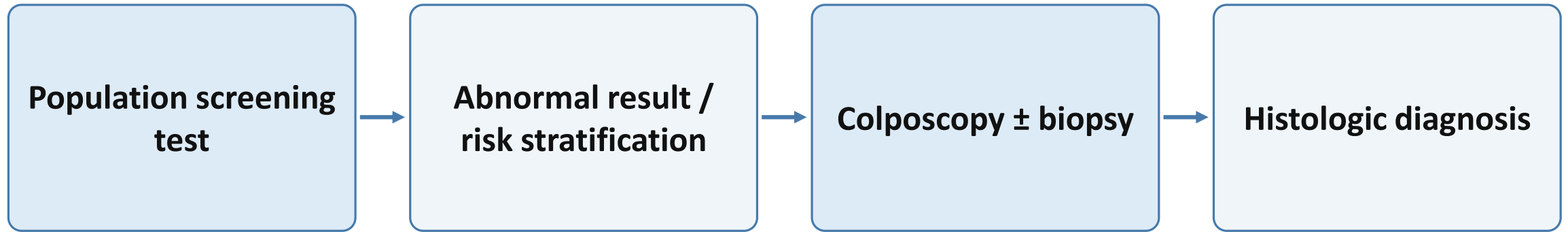
Koilocytosis links morphology to HPV infection

- Koilocytes show a perinuclear cytoplasmic halo with an atypical enlarged nucleus.
- This cytopathic pattern is especially prominent in productive HPV infection.
- A clear halo alone is insufficient without accompanying nuclear atypia.
- Koilocytic changes support LSIL but are not a substitute for the complete morphologic assessment.

Why HSIL cells differ from normal surface cells

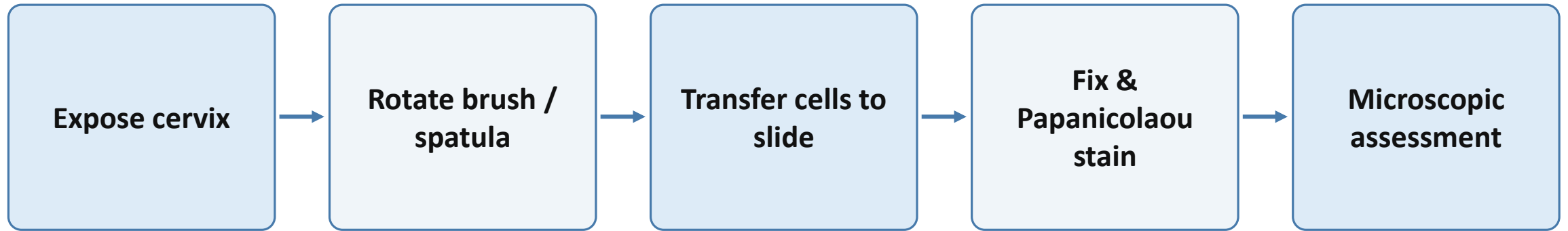
- High-risk HPV-driven cycle deregulation expands immature epithelial populations.
- Less terminal differentiation produces exfoliated cells with scant cytoplasm.
- Nuclear enlargement raises the nucleus-to-cytoplasm ratio.
- Pap cytology uses these changes to identify high-grade precancer risk.

Screening and diagnostic confirmation are different



A screening result triggers further assessment; Biopsy establishes tissue architecture when indicated.

How a conventional Pap smear is produced



The method assesses exfoliated cells, not full epithelial thickness.

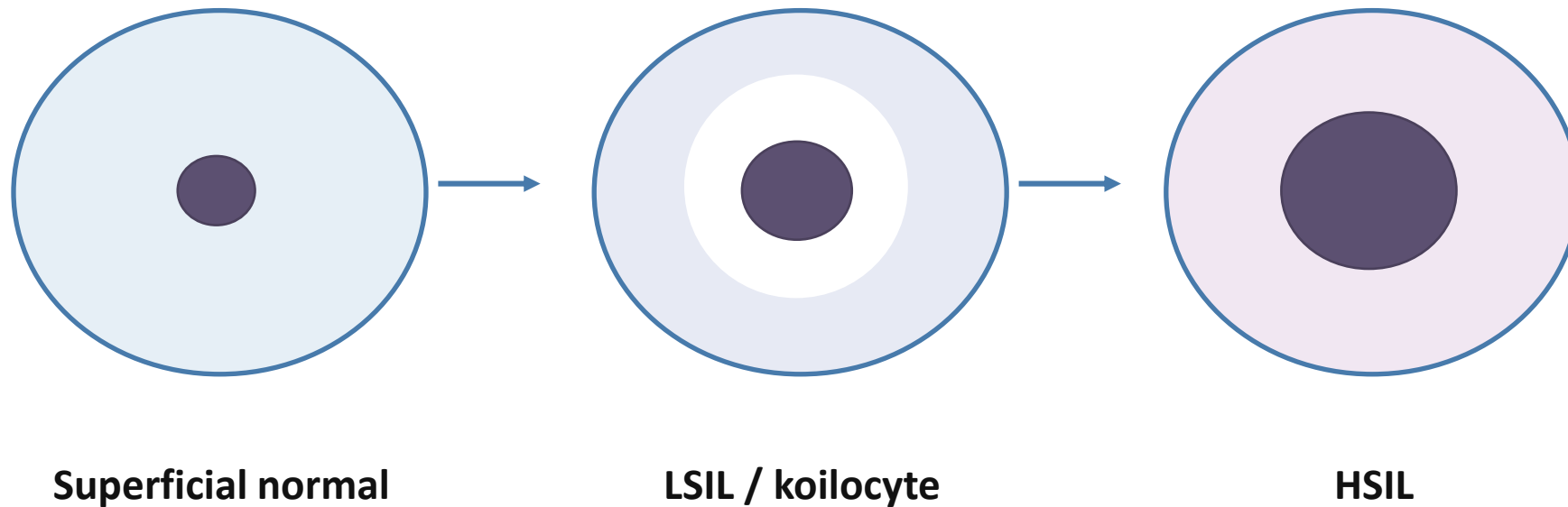
Conventional and liquid-based cervical cytology

- Conventional cytology spreads the collected cells directly on a glass slide.
- Liquid-based cytology places collected material into a preservative for processing.
- Both approaches are assessed for cellular abnormalities and specimen adequacy.
- Sample quality and appropriate cervical sampling affect clinical performance.

Specimen adequacy is a preanalytic safeguard

- Identification, sampling, fixation, and transport influence result reliability.
- Excess obscuring blood, inflammation, or scant cellularity may limit interpretation.
- The cytology report should identify unsatisfactory material rather than imply normality.
- Follow-up after an unsatisfactory result differs from follow-up after a valid negative result.

Pap cytology: Progressive nuclear dominance



Schematic cell silhouettes — not source cytology

Higher nuclear-to-cytoplasmic ratio correlates with impaired squamous differentiation.

Normal superficial squamous cells on a Pap test

- A mature cell has abundant, often polygonal cytoplasm.
- Its nucleus is comparatively small and compact.
- Organized maturation produces a low nucleus-to-cytoplasm ratio.
- These features provide a comparator for dysplastic cells.

LSIL cytology: Koilocytes and mild nuclear atypia

- Typical koilocytes show a perinuclear halo and a thickened cytoplasmic rim.
- Nuclei are enlarged and may be irregular or hyperchromatic.
- Cytoplasm often remains more abundant than in HSIL.
- Cytologic LSIL indicates a low-grade epithelial abnormality, not invasive carcinoma.

HSIL cytology: Immature high-N:C cells

- Cells frequently have less cytoplasm and more conspicuous nuclear atypia.
- Irregular nuclear contours and coarse chromatin support a high-grade interpretation.
- These abnormalities reflect dysregulated epithelial proliferation.
- HSIL cytology requires risk-appropriate evaluation; It is not automatically proof of invasion.

Cytology and histology answer different questions

Pap cytology

- Examines exfoliated individual cells.
- Recognizes atypia and cytomorphologic grade.
- Cannot directly show epithelial thickness or stromal invasion.

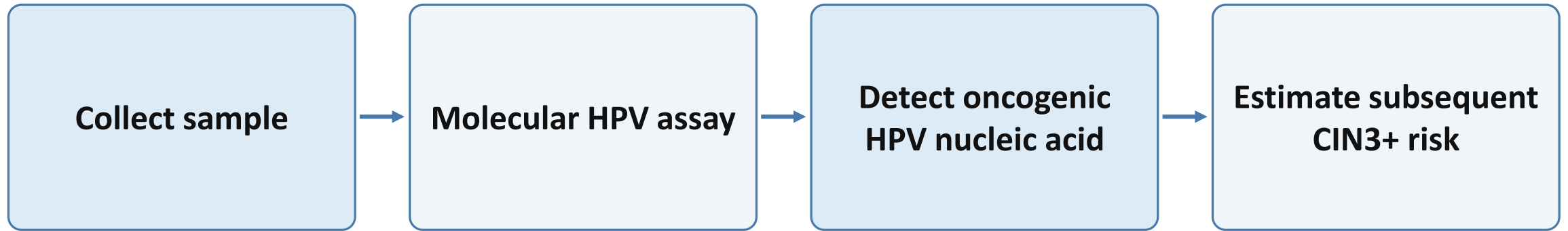
Cervical biopsy

- Preserves epithelial architecture.
- Estimates the depth of immature atypical cells.
- Assesses the basement membrane and stromal invasion.

Limits of morphology-only screening

- Abnormal cells may be missed because lesions were not sampled or shed sparsely.
- Reactive or inflammatory changes can complicate cytologic interpretation.
- A negative Pap result does not exclude all clinically significant disease.
- A positive result requires management guided by risk and relevant history.

High-risk HPV testing changes the screening question



HPV testing identifies etiologic risk upstream of overt cytologic dysplasia.

What a high-risk HPV result actually means

- A positive assay detects one or more carcinogenic HPV types covered by that test.
- It does not establish the duration of infection or the presence of HSIL.
- Most HPV infections clear; Persistent high-risk infection is the concern.
- Interpretation depends on HPV genotype, cytology, prior screening, and clinical context.

Why HPV tests can be more sensitive than cytology

- Viral DNA may be detected before exfoliated dysplastic cells appear.
- Testing is less dependent on an observer identifying cell morphology.
- Greater sensitivity can also detect transient, clinically nonprogressive infections.
- Thus specificity for prevalent high-grade lesions is often lower than Pap cytology.

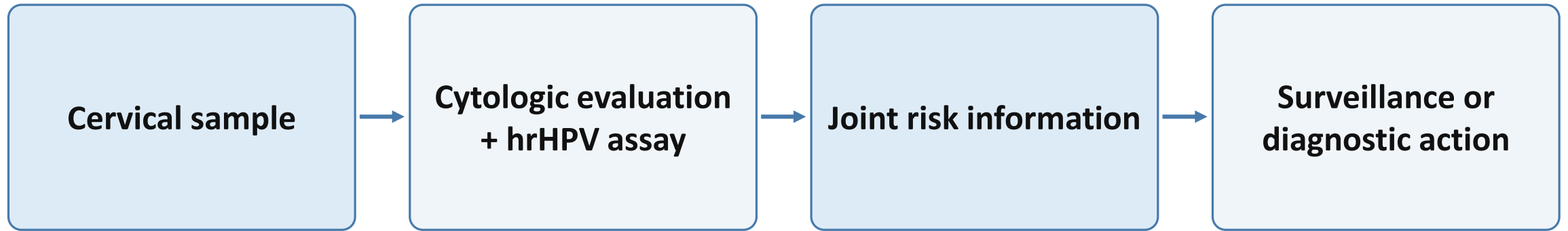
Pap cytology compared with hrHPV DNA testing

Dimension	Cytology	High-risk HPV test
Primary target	Morphologic atypia	Oncogenic infection
Typical strength	Morphologic specificity	Higher sensitivity for precancer
Common limitation	Sampling/reader dependence	Transient infections reduce specificity
Clinical meaning	Abnormal cells identified	Higher future precursor risk

Why patient age affects HPV test specificity

- Transient HPV detection is common after sexual debut.
- Testing a population with frequent transient infection increases false-positive referrals for significant precancer.
- Age and local guideline frameworks therefore influence screening strategy.
- Do not generalize a single age threshold across ACS, USPSTF, and WHO policies.

Cotesting: Complementary observations



Cotesting is one accepted screening option, but is not interchangeable with management of an abnormal result.

Screening eligibility is defined before test selection

- Routine population screening applies to asymptomatic persons with a cervix at average risk.
- Abnormal bleeding, a visible lesion, or other symptoms require diagnostic assessment—not routine screening alone.
- Prior CIN2+, treatment, immunosuppression, and other factors can change surveillance.
- Screening policies must be applied within the named health system.

Contemporary screening recommendations are not uniform

Organization / scope	Starting age	Preferred strategy
ACS (US; 2025 update)	25 years	Clinician-collected primary HPV every 5 years
WHO (general population; 2021)	30 years	HPV DNA every 5–10 years
WHO (women with HIV; 2021)	25 years	HPV DNA every 3–5 years

ACS: Routine screening begins at age 25

- The ACS guideline applies to asymptomatic individuals with a cervix at average risk.
- Routine screening begins at age 25 and generally continues through age 65.
- The preferred screening method is primary hrHPV testing on a clinician-collected cervical specimen.
- A prior abnormal result or relevant clinical risk can require a separate management pathway.

ACS: Clinician-collected primary HPV testing

- The provider samples the cervix during a speculum examination.
- A negative result permits a five-year screening interval at average risk.
- A positive specimen can support additional triage testing from collected cervical material.
- Test intervals assume validated assays and appropriate follow-up systems.

ACS 2025: Self-collected HPV specimens are an option

- Self-collected vaginal specimens may be used with approved tests and devices.
- The clinician-collected cervical specimen remains the preferred approach.
- After a negative self-collected HPV result, repeat screening in three years.
- A positive self-collected result requires clinician evaluation and cervical sampling.

Self-collection versus clinician collection

Self-collected vaginal sample

- Potentially improves access and autonomy.
- HPV testing only, using validated device/assay.
- ACS negative-result interval: 3 years.
- Positive results require clinical follow-up.

Provider-collected cervical sample

- Directly targets cervical epithelial cells.
- Allows reflex or additional cervical tests.
- ACS preferred primary HPV strategy.
- ACS negative-result interval: 5 years.

ACS: Alternative screening modalities

- Clinician-collected HPV/Pap cotesting every five years remains acceptable.
- Pap cytology alone every three years is an alternative when HPV strategies are unavailable.
- Choice of pathway does not remove the need for proper abnormal-result follow-up.
- Do not apply average-risk intervals to those requiring surveillance after precancer.

ACS 2025: Prerequisites for screening exit

- Average-risk patients may stop at age 65 when adequate recent negative screening is documented.
- Examples: Last two provider-collected HPV tests or cotests normal, or last three Pap tests normal.
- A history of CIN2+ within the preceding 25 years precludes routine exit.
- Unknown screening history generally calls for continued screening until exit criteria are met.

Who does not follow the average-risk algorithm?

- Previous cervical precancer or cancer may require prolonged surveillance.
- Immunosuppressed individuals, including those living with HIV, need tailored regimens.
- Prenatal diethylstilbestrol exposure is another higher-risk circumstance.
- Symptomatic patients require diagnostic work-up independent of their screening interval.

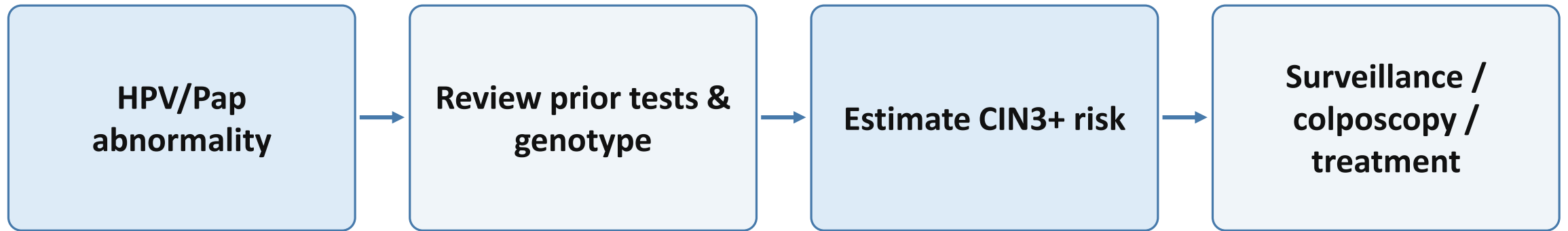
WHO: Primary HPV testing supports elimination programmes

- WHO 2021 suggests primary HPV DNA testing beginning at age 30 in the general population.
- A regular five- to ten-year interval can be used in screen-and-treat or triage pathways.
- National programme design depends on access, capacity, treatment linkage, and quality assurance.
- The goal is a functioning screening-to-treatment system, not HPV testing in isolation.

WHO: Women living with HIV need a distinct strategy

- WHO 2021 suggests beginning HPV DNA-based screening at age 25.
- Regular three- to five-year screening is advised in a screen–triage–treat approach.
- Higher vulnerability to persistent HPV infection justifies differentiated prevention.
- Programme recommendations should not be substituted for individual specialist management.

An abnormal screening result initiates triage

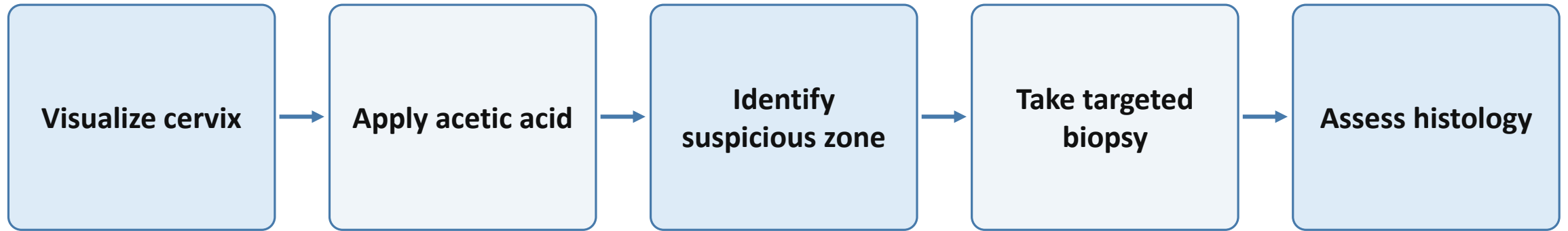


The next action is determined by risk, not simply whether a test was “positive.”

What colposcopy contributes after abnormal screening

- A magnified cervical examination seeks abnormal epithelial regions.
- Dilute acetic acid can accentuate an abnormal surface as an acetowhite area.
- The examination directs targeted biopsy of suspicious tissue.
- Colposcopy findings require histologic correlation when biopsy is indicated.

Colposcopic biopsy: Sampling-to-diagnosis



Acetowhite appearance is a localization clue—not an independently definitive diagnosis.

Why colposcopy is not the same as biopsy

- Visual patterns can suggest lesion distribution and severity.
- They do not demonstrate the epithelial full-thickness or stromal interface microscopically.
- Biopsy distinguishes LSIL from HSIL and assesses possible invasion.
- Sampling error remains possible if the most relevant region is missed.

Histologic LSIL usually favours conservative care

- LSIL as a productive infection with high spontaneous regression.
- A biopsy diagnosis must be interpreted with the cytology/HPV and screening history.
- Observation is often appropriate when risk and reliable follow-up permit.
- Ablation may be considered in selected settings, but is not a blanket default for all LSIL.

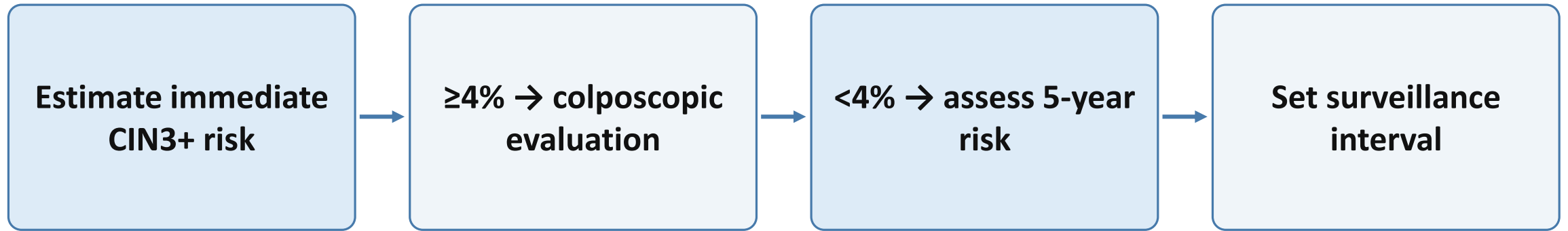
Histologic HSIL is a clinically meaningful precursor

- CIN2/CIN3 changes show more extensive atypia and less maturation.
- HSIL is associated with appreciably greater progression risk than LSIL.
- The pathology finding may require excisional or otherwise guideline-directed treatment.
- Age, pregnancy, reproductive considerations, and confidence in follow-up influence choices.

ASCCP: A risk-based approach replaces simple result rules

- The 2019 ASCCP framework uses current HPV/cytology plus prior screening and clinical history.
- Management thresholds are based on estimated immediate and five-year CIN3+ risk.
- The same mild abnormality may be followed or referred depending on prior negative HPV-based screening.
- Later ASCCP updates should be checked for applicable scenarios.

ASCCP risk thresholds: Principal branch



The 4% referral threshold is specific to the ASCCP risk framework, not an isolated test-result rule.

High-risk genotype can change colposcopy decisions

- HPV16 and HPV18 carry higher oncogenic risk than many other detected types.
- ASCCP recommends colposcopy for HPV16- or HPV18-positive results even with NILM cytology.
- A positive high-risk HPV test without genotype information is not managed identically in all contexts.
- HPV results need cytologic and historical interpretation.

Risk-based surveillance is not routine rescreening

- After abnormal tests or treatment, return intervals are calculated from CIN3+ risk and prior findings.
- One-year surveillance may be appropriate for selected minor abnormalities below the colposcopy threshold.
- Post-treatment HSIL surveillance can extend long beyond initial excision.
- Do not insert an average-risk five-year interval without establishing eligibility.

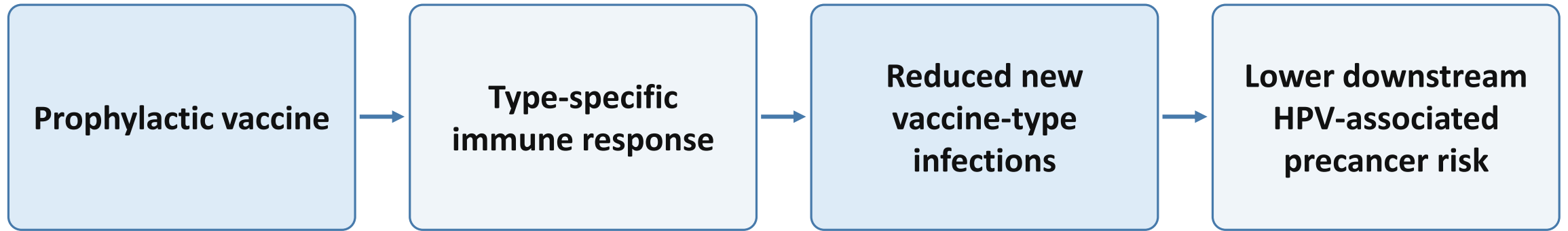
Excision and ablation have different pathology implications

- Excision removes tissue that can be evaluated for lesion extent and margin status.
- Ablation destroys tissue and yields no intact specimen for microscopic review.
- Conization or loop excision may be required for suitable high-grade lesions.
- Choice requires histologic, colposcopic, and patient-specific assessment.

Why preventing overtreatment matters

- Many low-grade lesions regress without intervention.
- Unnecessary excision exposes patients to procedural and reproductive harms.
- Conversely, under-recognizing HSIL delays prevention of invasive disease.
- Risk-based triage aims to balance sensitivity, referral burden, and harm.

HPV vaccination provides primary prevention



Prophylactic vaccination prevents infection; It is not a treatment for existing CIN or persistent HPV.

Nine-valent HPV vaccine: Included types

- Oncogenic targets: HPV 16, 18, 31, 33, 45, 52, and 58.
- Non-oncogenic wart-associated targets: HPV 6 and 11.
- Coverage does not include every carcinogenic HPV genotype.
- Consequently vaccination is not a reason to stop recommended cervical screening.

CDC HPV vaccination: Initiation age determines series

Clinical group	Recommended series	Key qualification
Routine, age 11–12 (may start at 9)	2 doses if begun before 15	Second dose 6–12 months later
Initiated at age 15–26	3 doses	0, 1–2 and 6 months
Immunocompromised, age 9–26	3 doses	Regardless of age at initiation
Unvaccinated age 27–45	Shared decision-making	Not routine catch-up for all

Why vaccination is recommended for all genders

- Transmission of HPV involves sexual networks of all genders.
- Vaccination can reduce infections that cause cervical cancer.
- It also addresses other HPV-associated anogenital and oropharyngeal cancers.
- Pre-exposure immunization provides the greatest preventive benefit.

Aged 27–45 years: Shared clinical decision-making

- CDC does not recommend universal catch-up vaccination beyond age 26.
- Some previously unvaccinated adults aged 27–45 may benefit.
- Prior HPV exposure reduces expected population-level benefit.
- Decisions consider future exposure risk and patient preferences.

Vaccinated people still require cervical screening

- Vaccination does not treat an infection already acquired.
- Not every oncogenic HPV type is included in the vaccine.
- Individual vaccine histories and timing vary.
- Current ACS screening recommendations still apply to vaccinated average-risk patients.

Two preventive strategies protect at different points

Primary prevention

- Vaccinate before HPV exposure.
- Reduce acquisition of vaccine-targeted types.
- Offer population-wide prevention for all genders.

Secondary prevention

- Detect persistent hrHPV or abnormal cytology.
- Confirm and treat relevant precancer.
- Maintain repeat testing and follow-up systems.

Population impact depends on screening completion

- A screening test alone cannot prevent cancer if a positive result is never evaluated.
- Barriers include access, cost, acceptability, recall, and pathology capacity.
- Self-collection may remove some barriers but cannot substitute for needed cervical follow-up.
- Organized programmes require tracking of results, referrals, and treatment completion.

Why under-screened populations carry more disease burden

- Absent or limited cytology programmes with continued cervical cancer mortality.
- Cancer prevention requires early identification and management of precancer.
- Screening participation and follow-up inequities can undermine test efficacy.
- Improving programme continuity is as important as selecting a sensitive assay.

Case 1: Asymptomatic 26-year-old, average risk

A 26-year-old with a cervix has no symptoms, no history of cervical precancer, and asks which U.S. Screening method is preferred.

Reasoning

- Identify the guideline framework: ACS average-risk screening begins at age 25.
- Choose clinician-collected primary HPV as the preferred ACS strategy.
- If negative, the ACS interval is five years.

Apply ACS recommendations; Other organizations may use different age thresholds.

Case 2: HPV-positive result with negative cytology

A 33-year-old has a positive high-risk HPV test and NILM cytology; HPV genotype and prior testing are not yet available.

Reasoning

- A positive HPV assay is not a cancer diagnosis.
- Genotype and prior HPV-based testing alter immediate CIN3+ risk.
- Complete risk stratification before assigning colposcopy or surveillance.

Avoid the outdated rule that every HPV-positive/NILM result automatically receives a fixed cytology interval.

Case 3: Biopsy reports LSIL / CIN1

A patient has biopsy-confirmed cervical LSIL and reliable access to repeat testing; No separate high-grade features are stated.

Reasoning

- LSIL is typically associated with productive HPV infection.
- Most lesions regress; Initial conservative management is often suitable.
- Use current screening history and risk to specify follow-up.

Do not automatically equate LSIL biopsy with an indication for cone excision.

Case 4: HSIL cytology and suspicious lesion

A 37-year-old has HSIL cytology and a visually suspicious cervical region at colposcopy.

Reasoning

- Cytology raises concern but does not show stromal invasion.
- Obtain indicated tissue for histologic assessment and manage per risk.
- Biopsy/excision is needed to establish epithelial grade and exclude invasion.

Invasive carcinoma cannot be diagnosed from cytology alone.

Case 5: Vaccinated individual asks to stop screening

A vaccinated 31-year-old with a cervix has normal previous testing and assumes vaccination removes screening needs.

Reasoning

- Prophylactic vaccine protection is type-specific and not therapeutic.
- Average-risk ACS screening continues irrespective of HPV vaccination.
- Use an age-appropriate approved screening strategy.

Vaccination and screening work together rather than replace each other.

Integrating screening and pathology in practice

- Precursor lesions are detectable because cervical carcinogenesis generally has a prolonged preinvasive phase.
- Pap cytology identifies cellular atypia; HPV assays identify etiologic risk; Biopsy defines tissue architecture.
- Current management is history- and risk-dependent: A positive screen is not a treatment decision.
- Vaccination and reliable screening–follow-up systems remain complementary.

Five diagnostic and preventive distinctions to retain

- Screening is for asymptomatic populations; Suspicious symptoms require diagnostic assessment.
- HPV positive $\neq$ HSIL; HSIL cytology $\neq$ invasive carcinoma.
- LSIL and HSIL have different natural histories and management implications.
- High-risk genotype and prior test history may change management after an abnormal result.
- Vaccinated individuals continue guideline-based screening.

Primary textbook and contemporary guideline references

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