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2019 ASCCP Risk-Based Management Consensus Guidelines: Updates Through 2023

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Abstract: This Research Letter summarizes all updates to the 2019 Guidelines through September 2023, including: endorsement of the 2021 Opportunistic Infections guidelines for HIV+ or immunosuppressed patients; clarification of use of human papillomavirus testing alone for patients undergoing observation for cervical intraepithelial neoplasia 2; revision of unsatisfactory cytology management; clarification that 2012 guidelines should be followed for patients aged 25 years and older screened with cytology only; management of patients for whom colposcopy was recommended but not completed; clarification that after treatment for cervical intraepithelial neoplasia 2+, 3 negative human papillomavirus tests or cotests at 6, 18, and 30 months are recommended before the patient can return to a 3-year testing interval; and clarification of postcolposcopy management of minimally abnormal results.

Key Words: cervical cancer screening and management, 2019 ASCCP guidelines, updates

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This report summarizes all updates and corrections to the 2019 ASCCP Risk-Based Management Consensus Guidelines (hereafter abbreviated as 2019 Guidelines) since publication in April 2020 through September 2023.[1] All changes and corrections to the 2019 Guidelines included here are expected to represent the final report directly linked to the original publication.[1] The updates are summarized in Box 1.

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The following listed authors have conflicts of interest:

- A-B. M.: Merck and GSK, advisory board member
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Future updates, including guidelines for use of new technologies and updated recommendations related to new risk estimates for established technologies, will be developed by the Enduring Consensus Cervical Cancer Screening and Management Guidelines (hereafter abbreviated as Enduring Guidelines).[2] The Enduring Guidelines process is an extension of the 2019 Guidelines consensus process, and represents a consensus group representing 20 national organizations, nearly all of which participated in the 2019 Guidelines process. Enduring Guidelines updates will be disseminated through full guidelines articles.[5]

Since the publication of the 2019 Guidelines, 2 types of updates have been required: updates that change recommendations and updates related to typographical errors or minor wording clarifications. Updates that involve a change in recommendations or a new recommendation were put to a formal vote of the original 2019 Guidelines Committee, which required a two-thirds majority to pass. Minor wording clarifications and typographical errors were corrected and reviewed by coauthors, but not formally voted on. Between 2020 and 2021, 1 recommendation change and 1 minor clarification were published as Letters to the Editor and/or Errata that are linked to the original 2019 Guidelines article.[3,4] This report summarizes all substantive recommendation updates confirmed by vote (1 previously published, 3 new to this report and not published previously) and several cumulative minor clarifications and corrections.

Box 1 Summary of updates to 2019 Guidelines

Summary of updates to 2019 Guidelines

- Endorsement of the 2021 Opportunistic Infections guidelines for screening and management of HIV+ or immunosuppressed patients.[7]
- Guidelines were clarified for use of human papillomavirus (HPV) testing alone (primary HPV) for patients undergoing observation for cervical intraepithelial neoplasia (CIN) 2. Figure 8 was updated to reflect this change.
- Guidelines were revised for repeating an unsatisfactory cytology. ***Cytology should be repeated as soon as convenient and no later than 4 months.***
- Guidelines were clarified around cytology-only screening. ***For patients 25 and older who are still receiving cytology-only screening, 2012 guidelines should be followed.***[3]
- Guidelines were clarified for patients for whom colposcopy was recommended but not completed.[11]
- Figure 7 from the 2019 Guidelines was revised for clarity. ***After treatment for CIN2+, 3 negative HPV tests or cotests at 6, 18, and 30 months are recommended before the patient can return to a 3-year testing interval.***
- The legend of Figure 2 from the 2019 Guidelines was revised to clarify the algorithm for management after a minimally abnormal screening test result followed by a colposcopy at which high-grade histology was not found.[4]

2019 GUIDELINE SUBSTANTIVE RECOMMENDATIONS CHANGES AND UPDATES

1) **Endorsement of the 2021 Opportunistic Infections Guidelines:**

The 2019 Guidelines endorsed the 2018 "Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV" that were current at the time of publication.[6] The Opportunistic Infections Guidelines were subsequently updated in 2021.[7] The updated Opportunistic Infections Guidelines recommend beginning cervical cancer screening at age 21 years, a change from previous guidelines that recommended initiating screening 1 year after sexual debut.

2) **Clarification to recommendation statement for patients undergoing observation of CIN2:**

The recommendation statement has been updated to clarify that both HPV testing alone and cotesting are acceptable for patients undergoing observation of CIN2. The revised recommendation now states:

Guideline: For patients with a diagnosis of histologic HSIL (CIN 2) whose concerns about the effects of treatment on a future pregnancy outweigh their concerns about cancer, either observation or treatment is acceptable provided the squamocolumnar junction is fully visualized and CIN 2+ or ungraded CIN is not identified on endocervical sampling (CII) (see Figure 8). If the histologic HSIL cannot be specified as CIN 2, treatment is preferred, but observation is acceptable (CIII). For patients 25 years or older, observation includes colposcopy and HPV-based testing at 6-month intervals for up to 2 years (See Section K.1 of the 2019 Guidelines[1] for management of patients aged younger than 25 years). If during surveillance, all evaluations demonstrate less than CIN 2 histology and either less than ASC-H cytology if using cotesting or HPV negative if using HPV testing alone on 2 successive occasions, 6 months apart, subsequent surveillance should occur at 1 year after the second evaluation and use HPV-based testing. If negative on 3 consecutive annual surveillance tests, proceed to long-term surveillance (Section J.3 of the 2019 Guidelines[1]). If CIN 2 remains present for a 2-year period, treatment is recommended (CII). Note that the original Figure 8 from the 2019 Guidelines was updated. The revised Figure 8 in this report replaces the older version and should be used for clinical management.

3) **Update to interval for repeating unsatisfactory cytology:** The recommendation statement has been updated to reflect evidence that waiting 2 months before repeating the cytology test is not necessary.

Guideline: For patients with an unsatisfactory cytology result and no, unknown, or a negative HPV test result, repeat age-based screening (cytology, cotest, or primary HPV test) as soon as convenient and no later than 4 months is recommended (BIII).

Rationale: The 2- to 4-month waiting period was initially proposed due to early studies indicating differences in cytology results repeated over a short time interval. The recommendation was carried forward through several guideline iterations, but rereview of evidence supports revision of the 2-month waiting period. A seminal article in 2005 specifically addressed this question and found the concern of reduced cellularity with short interval repeat not to hold true.[8] In this study, the cytology interval ranged from 8 to 30 days in 763 women, 31 to 60 days in 2,317 women, 61 to 90 days in 1,090 women, 91 to 120 days in 491 women, and 121 to 184 days in 394 women. They found that repeat cytologic interpretations of unsatisfactory findings, atypical squamous cells of undetermined significance (ASC-US), and high-grade squamous intraepithelial lesion (HSIL) did not vary among the Pap interval groups. Most importantly, the approximate cellularity of the samples was slightly better in the interval group of 8 to 30 days (P trend = 0.04). In addition, higher rates of unsatisfactory results have been documented in patients with cancer compared with those with CIN3 or lower grade results.[9,10] Waiting to repeat an unsatisfactory cytology in the presence of cancer could lead to harm, specifically if other recommended workup for symptomatic patients is not performed. For this reason, the 2019 recommendations were updated.

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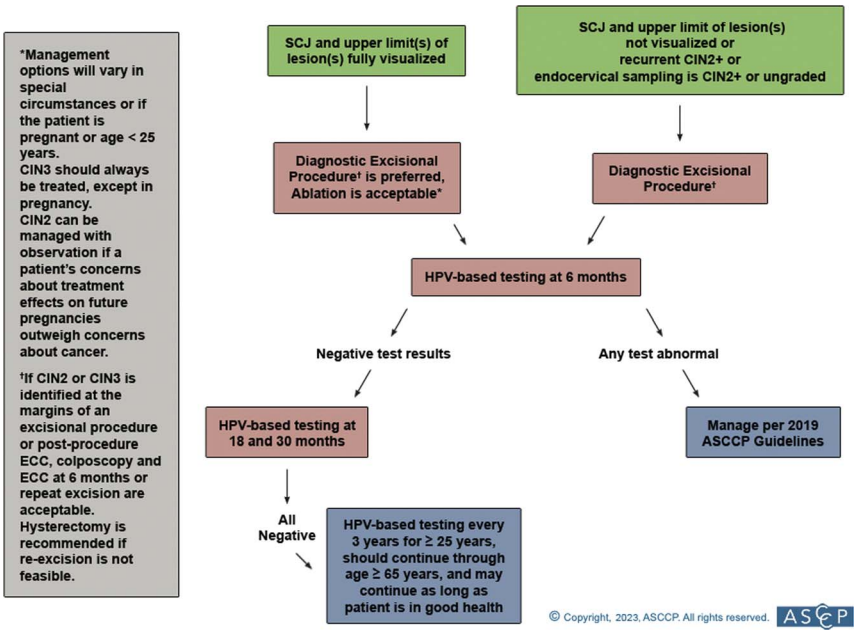

FIGURE 7. (of the originally published paper) Management of histologic HSIL (CIN2 or CIN3 or Not Further Specified)*. CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion.
Figures 7 and 8 originally published in Perkins et al.[1]

4) **Patient Scenarios Not Initially Addressed in the 2019 Guidelines:**

Additional guidance was developed to address scenarios for which the 2019 Guidelines did not initially provide management recommendations. This guidance was voted on in July 2021 and previously published.[3] To summarize, this guidance (1) outlined management guidelines for cytology results without HPV testing among individuals aged 25 years and older and (2) clarified management when previous guidelines had not been followed[3]:

(a) Guideline for individuals aged 25 and older screened with cytology alone: For individuals aged 25 years or older screened with cytology alone, the 2012 guidelines should be followed. In the 2012 guidelines, colposcopy is recommended for low-grade squamous intraepithelial lesion (LSIL) or a more severe cytologic interpretation.[11]

(b) Guideline for cases in which colposcopy was previously recommended but not completed: In cases in which a colposcopy was previously recommended but not completed, the recommendation is for colposcopy if the previous result was high-grade cytology [atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), atypical glandular cells (AGC), HSIL, or a more severe cytologic interpretation]. If the previous cytology result was not high grade, and the patient undergoes repeat testing with HPV

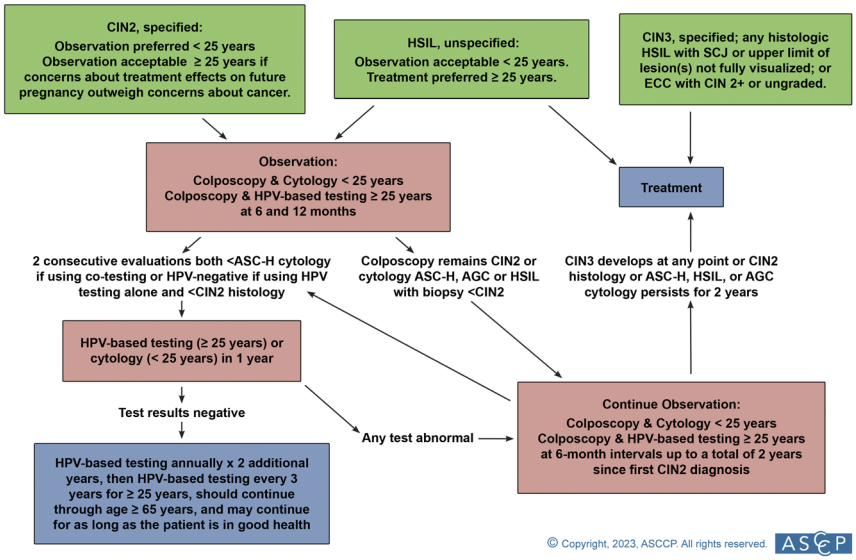

FIGURE 8. (of the originally published paper) Management of CIN2 at age younger than 25 years or for those concerned about the effects of treatment on future pregnancy.
Figures 7 and 8 originally published in Perkins et al.[1]

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testing or cotesting instead of colposcopy: colposcopy is recommended if the result on repeat testing indicates a second consecutive HPV-positive result and/or persistent cytologic abnormality (ASC-US or a more severe cytologic interpretation); repeat HPV testing or cotesting in 1 year is acceptable if the result on repeat testing is HPV negative or cotest negative.

MINOR 2019 GUIDELINE UPDATES TO CORRECT TYPOGRAPHICAL ERRORS OR CLARIFY WORDING

1) **Correction to Figure 7 clarifying that a total of 3 negative HPV-based tests are needed after treatment to return to a 3-year testing interval:** The original Figure 7 of the 2019 Guidelines was updated. The revised Figure 7 in this report replaces the original Figure 7 and should be used for clinical management. The revised Figure 7 matches the information included in Table 5b of Egemen et al[12] and the text of the guidelines article, which reads: "In patients treated for histologic or cytologic HSIL, after the initial HPV-based test at 6 months, annual HPV or cotesting is preferred until 3 consecutive negative tests have been obtained (AII)."[1] Risk estimates for the 2019 Guidelines indicate that, following excisional treatment for histologic HSIL/CIN2–3, three consecutive negative HPV tests or cotests are needed at 1-year intervals to identify a group of patients at sufficiently low risk that they can safely return to 3-year testing interval. The 2019 Guidelines recommend that the first test occur 6 months after the excisional procedure. Figure 7 erroneously recommended an HPV test or cotest at 6 months followed by 3 consecutive annual HPV or cotests (a total of 4 consecutive negative tests). This has been corrected to recommend the first HPV test or cotest at 6 months followed by additional HPV or cotests at 18 months and 30 months. The figure has also been modified to clarify that follow-up should continue at 3-year intervals for a minimum of 25 years and through at least age 65 years and may continue for as long as the patient is in good health.

2) **Prior Correction to Figure 2 Legend Published October 2020[4]:** The legend for Figure 2 of the original 2019 Guidelines article[1] was updated to clarify the algorithm for management after a minimally abnormal screening test result followed by a colposcopy at which high-grade histology was not found.[4] The figure legend is repeated here for clarity: "This figure demonstrates how a patient with a common minimally abnormal screening test result (HPV-positive ASC-US) would be managed based on risk estimates. The initial screening result would lead to colposcopy (immediate risk 4.45%). If colposcopy shows less than CIN 2, the 5-year risk is 2.9% (1-year return). At the 1-year return visit, a second HPV-positive ASC-US result has an immediate risk of 3.1% (1-year return). Note similar management would be recommended if the initial abnormality preceding colposcopy were any minimally abnormal test result (i.e., less severe than ASC-H). If the HPV-based test performed for the second postcolposcopy surveillance test is negative, return in 3 years is recommended. If the second postcolposcopy surveillance test results are either a positive HPV test with any cytology result or a negative HPV test result with a cytology result of ASC-H or higher, colposcopy is recommended. Return in 1 year is recommended for HPV-negative ASC-US or LSIL results."

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