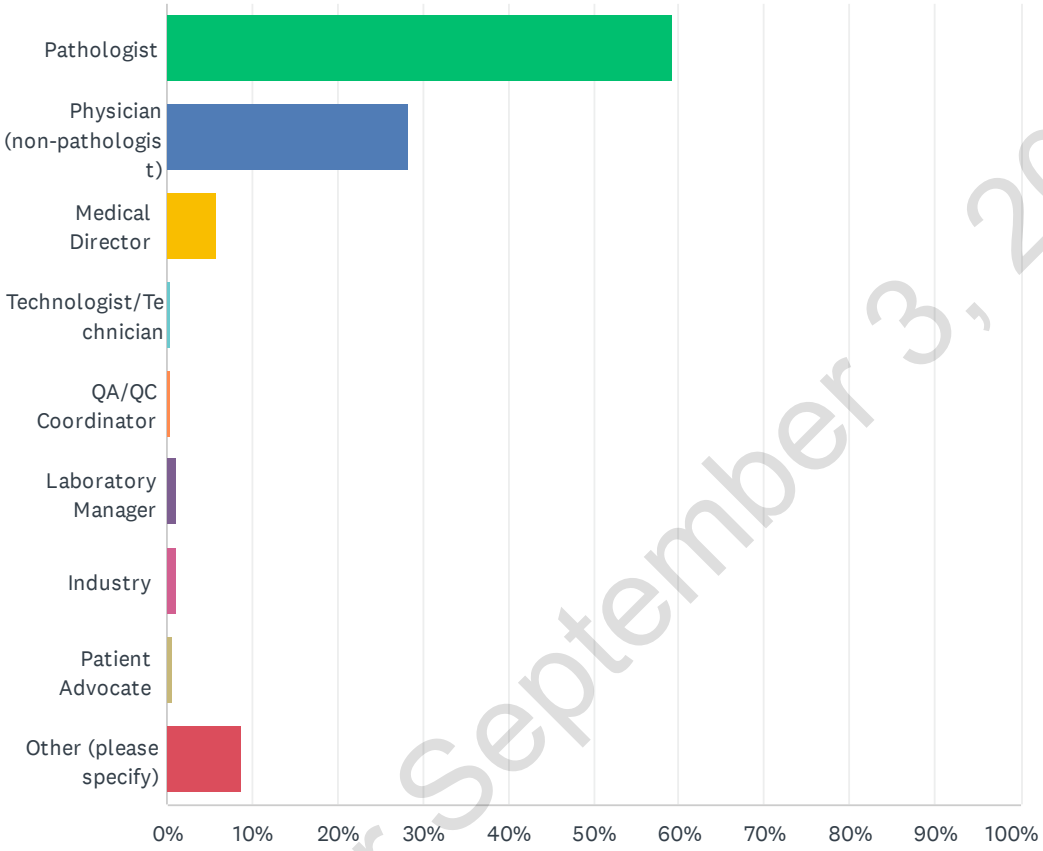
Q1 What is your occupation/role? (select all that apply)

Answered: 297 Skipped: 0



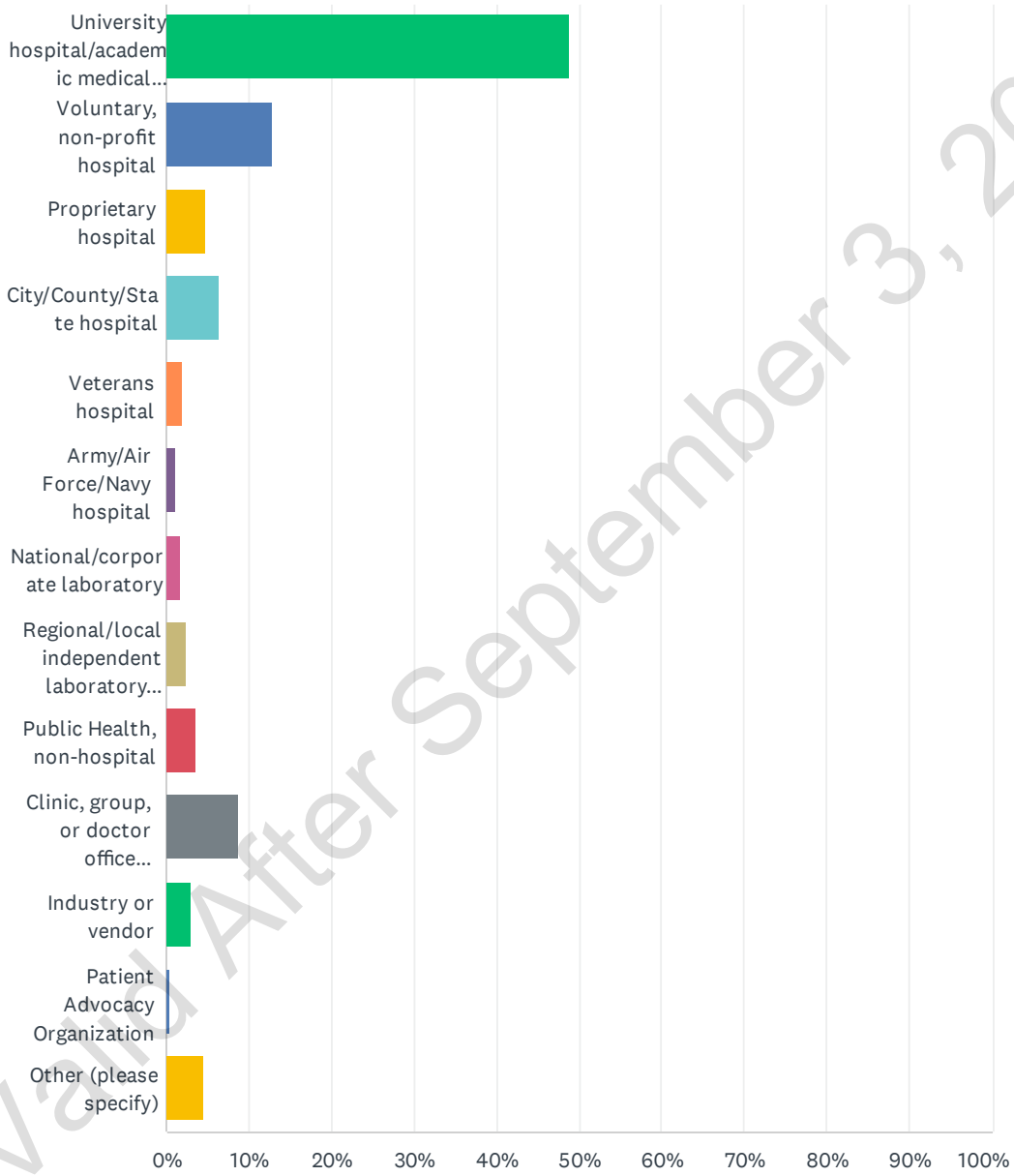
ANSWER CHOICES	RESPONSES	
Pathologist	59.26%	176
Physician (non-pathologist)	28.28%	84
Medical Director	5.72%	17
Technologist/Technician	0.34%	1
QA/QC Coordinator	0.34%	1
Laboratory Manager	1.01%	3
Industry	1.01%	3
Patient Advocate	0.67%	2
Other (please specify)	8.75%	26
Total Respondents: 297		

#	OTHER (PLEASE SPECIFY)	DATE
1	women's health nurse practitioner	8/26/2025 7:04 AM

2	Registered Nurse- Pap Navigator	8/25/2025 4:33 PM
3	Nurse practitioner	8/25/2025 12:34 PM
4	Nurse Practitioner	8/25/2025 7:01 AM
5	Gynecological Oncologist	8/23/2025 10:32 AM
6	Professor Em.	8/23/2025 4:05 AM
7	Medical virologist	8/23/2025 1:24 AM
8	Physician's Assistant	8/22/2025 5:56 PM
9	Nurse Practitioner	8/22/2025 2:30 PM
10	Certified Nurse-Midwife	8/22/2025 12:32 PM
11	APRN	8/22/2025 12:22 PM
12	Nurse Practitioner	8/22/2025 12:03 PM
13	Nurse practitioner	8/22/2025 11:48 AM
14	Family Nurse Practitioner/Business Owner	8/22/2025 10:17 AM
15	Nurse practitioner	8/22/2025 9:32 AM
16	FNP working primarily Women's Health	8/22/2025 9:20 AM
17	Nurse Practitioner	8/22/2025 9:18 AM
18	Nurse practitioner	8/22/2025 8:46 AM
19	Nurse practitioner	8/22/2025 8:14 AM
20	Nurse Practitioner	8/22/2025 7:17 AM
21	Nurse Practitioner	8/22/2025 7:03 AM
22	Physician associate	8/22/2025 6:53 AM
23	Genecologist	8/19/2025 12:19 AM
24	Professor, nurse practitioner, clinician scientist	8/14/2025 5:38 PM
25	Pathology Resident PHysician	8/14/2025 5:27 PM
26	Research Director	8/14/2025 11:57 AM

Q2 Which of the following best describes your practice setting? (select one)

Answered: 297 Skipped: 0

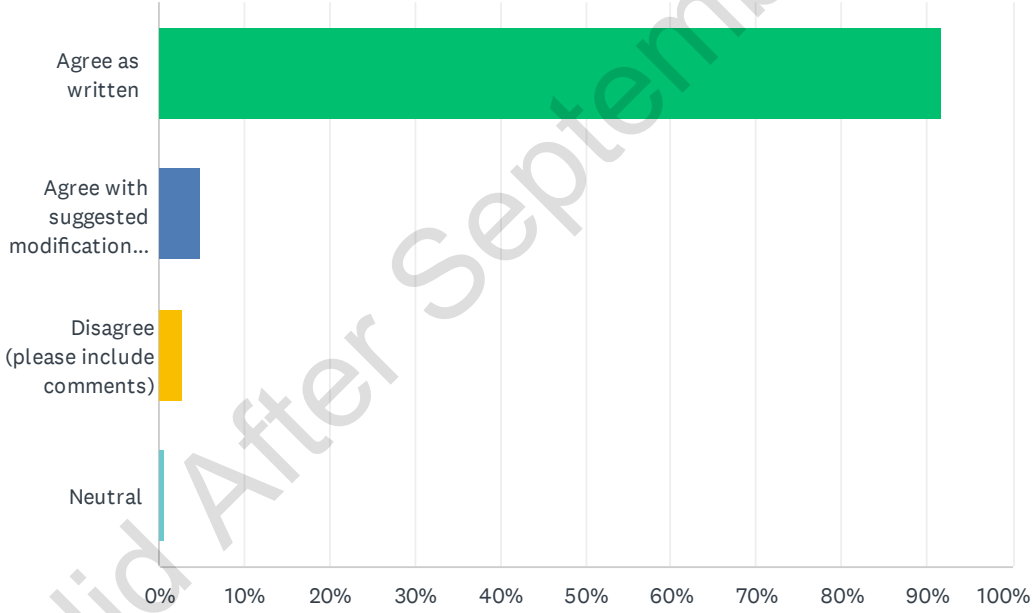


ANSWER CHOICES	RESPONSES	
University hospital/academic medical center	48.82%	145
Voluntary, non-profit hospital	12.79%	38
Proprietary hospital	4.71%	14
City/County/State hospital	6.40%	19
Veterans hospital	2.02%	6
Army/Air Force/Navy hospital	1.01%	3
National/corporate laboratory	1.68%	5
Regional/local independent laboratory (except clinic or group practice and not owned by a national corporation(s))	2.36%	7
Public Health, non-hospital	3.70%	11
Clinic, group, or doctor office laboratory	8.75%	26
Industry or vendor	3.03%	9
Patient Advocacy Organization	0.34%	1
Other (please specify)	4.38%	13
TOTAL		297

#	OTHER (PLEASE SPECIFY)	DATE
1	Prison	8/25/2025 7:50 AM
2	Private Hospital	8/23/2025 10:32 AM
3	Research	8/23/2025 4:05 AM
4	Retired	8/22/2025 9:39 PM
5	Prv	8/22/2025 3:17 PM
6	College Health Clinic	8/22/2025 3:06 PM
7	College Health	8/22/2025 1:25 PM
8	University Student Health Center	8/22/2025 7:10 AM
9	Freelancer	8/21/2025 9:32 AM
10	Group practice	8/14/2025 2:08 PM
11	Federal Goverment	8/14/2025 10:14 AM
12	Retired pathologist	8/14/2025 9:31 AM
13	Retired	8/14/2025 8:39 AM

Q3 Draft Statement 1 Pathologists should perform p16 when the H&E morphologic differential diagnosis is between high-grade squamous intraepithelial lesion (HSIL, –IN 2 or –IN 3) and a mimic of HSIL (eg, processes unrelated to neoplastic risk such as immature squamous metaplasia, atrophy, reparative epithelial changes, tangential cutting).1Note: Strong and diffuse block-positive p16 results support a categorization of HSIL (–IN 2 or –IN 3) in this context.(Conditional Recommendation)Abbreviations: H&E, hematoxylin and eosin stain; HSIL, high-grade squamous intraepithelial lesion; -IN, intraepithelial neoplasia; p16, CDK4 inhibitor p16-INK41 Reaffirmed recommendation statement from 2012 guideline

Answered: 180 Skipped: 117



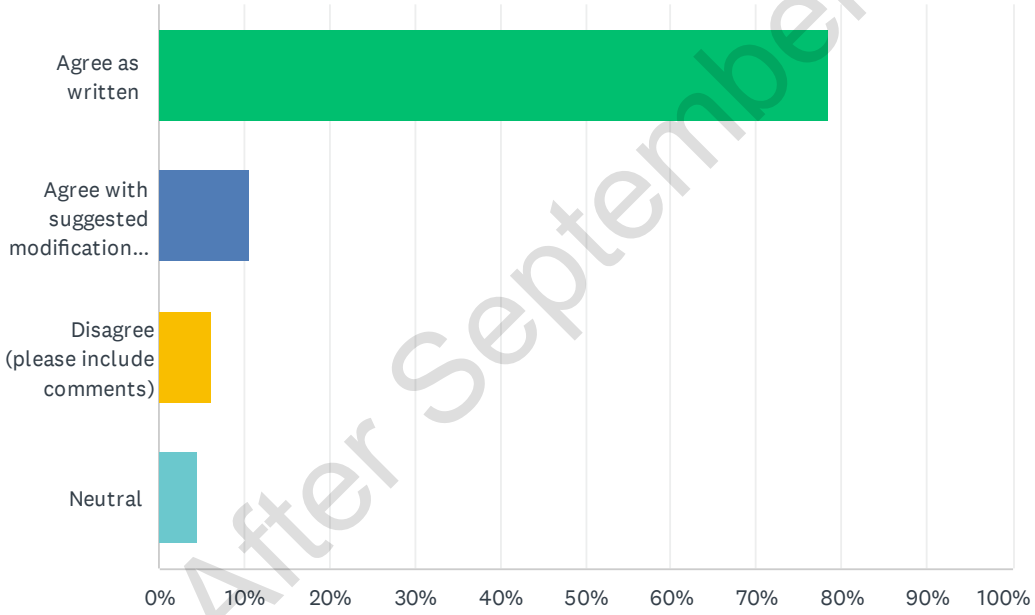
ANSWER CHOICES	RESPONSES	
Agree as written	91.67%	165
Agree with suggested modifications (please include comments)	5.00%	9
Disagree (please include comments)	2.78%	5
Neutral	0.56%	1
TOTAL		180

#	COMMENTS	DATE
1	CIN 2 that is p16 (+) is classified as HSIL & CIN 2 that is p16 (-) is classified as LSIL.	8/23/2025 12:24 PM

2	No need I think	8/22/2025 10:17 PM
3	cytology should only be used for triage after positive 12 Hr hpv screening. Then p16 can be used on that cytology as stated.	8/21/2025 9:20 AM
4	Tangential cutting is a maybe for me. I do levels first and do not default to p16. Otherwise agree	8/19/2025 7:37 AM
5	p16 block positivity does not define high grade, false negatives are frequent, false positives are also seen.	8/17/2025 1:46 PM
6	Agree with statement. I include nuclear and/or cytoplasmic staining within the area of block positivity.	8/15/2025 7:32 PM
7	An H&E corresponding to the level that is stained should always be available (either by the stain being performed on a pre-cut unstained or, if performed off a new block shave, by cutting a concomitant H&E stained section). Also, as far as the note is concerned, the opposite is not true: in cases with p16 negative and high suspicion of HSIL, HPV in situ should be obtained, since a small albeit real and sizeable proportion of HSIL may be p16-negative (Arch Pathol Lab Med (2023) 147 (3): 323–330.)	8/15/2025 1:39 PM
8	… when the remaining tissue of interest is sufficient for p16 IHC	8/15/2025 7:53 AM
9	Shouldn't we add "more than 1/3 of the epithelial thickness"? To my knowledge >1/3 is sufficient for CIN2	8/14/2025 4:45 PM
10	Should say "p16 iHC" to match the wording in statements 2, 3 and 6.	8/14/2025 11:47 AM
11	For HSIL with classic morphology, there is no need to perform p16.	8/14/2025 10:29 AM
12	May be Ki67 should accompanied as well.	8/14/2025 8:43 AM
13	Reflex HPV-ISH testing to be included in the guidelines.	8/14/2025 8:38 AM

Q4 Draft Statement 2Pathologists should perform p16 IHC to secure a diagnosis for HSIL (-IN 2) for cases with a morphologic differential for LSIL (-IN 1).1Note: A negative or non–block-positive staining strongly favors an interpretation of LSIL (-IN 1) in this context.(Conditional Recommendation)Abbreviations: HSIL, high-grade squamous intraepithelial lesion; IHC, immunohistochemistry; -IN, intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesion; p16, CDK4 inhibitor p16-INK41 Updated recommendation statement from 2012 guideline

Answered: 177 Skipped: 120



ANSWER CHOICES	RESPONSES	
Agree as written	78.53%	139
Agree with suggested modifications (please include comments)	10.73%	19
Disagree (please include comments)	6.21%	11
Neutral	4.52%	8
TOTAL		177

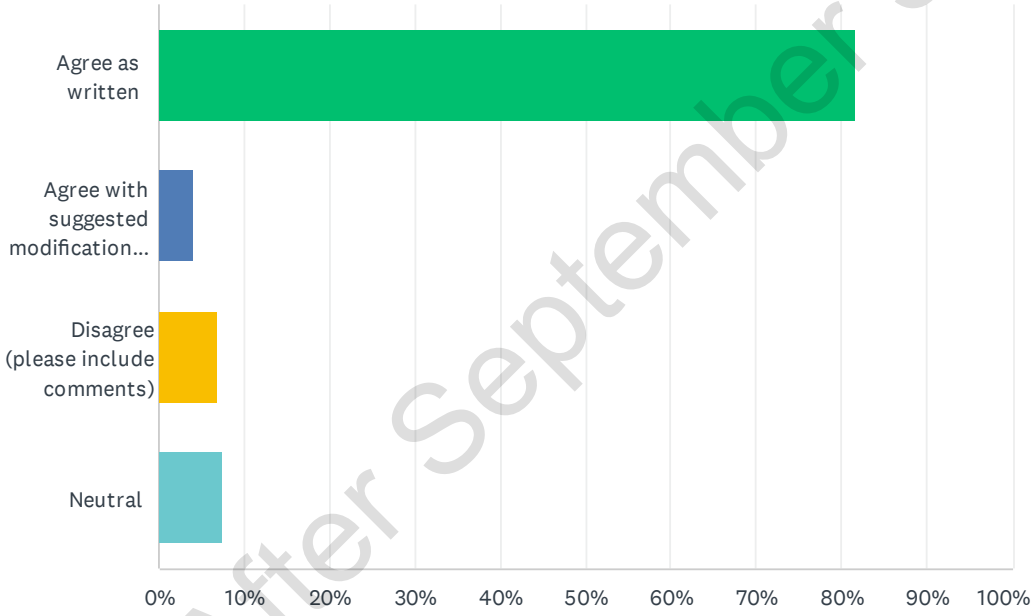
#	COMMENTS	DATE
1	The wording needs to be clarified as to what this exactly means. Do you mean a case where low grade is definitively present but there are features that make HG in the differential? or that if LSIL is possible (may or may not be LSIL), still do p16??????	8/25/2025 1:31 PM
2	CIN 2 that is p16 (+) is classified as HSIL & CIN 2 that is p16 (-) is classified as LSIL.	8/23/2025 12:24 PM

3	Only when Colposcopy findings suggest major grade abnormality	8/23/2025 10:37 AM
4	However, since LSIL may be block positive for p16, positive staining does not confirm that a lesion represents HSIL	8/22/2025 4:51 PM
5	I worry this will lead to a lot of upgrading of lsil to Hsil and unnecessary treatment	8/22/2025 2:56 PM
6	Are we now totally disregarding the existence of p16-positive LSIL?	8/21/2025 3:25 PM
7	Given that a fairly high number of LSIL may stain with p16 this feels like over-use that could potentially lead to over-treatment if a biologic LSIL is called CIN 2 due to more than expected p16 staining (let's be real, many that practice general surgical pathology will just call everything that is p16 positive HSIL). Its not that p16 can't occasionally be helpful here, but blanket application sounds too much	8/19/2025 7:37 AM
8	Should read "Pathologists may" or more details should be listed to better define "a morphologic differential"	8/18/2025 8:37 AM
9	I wouldn't say p16 positivity strongly favors HSIL, I would say favors only.	8/17/2025 1:46 PM
10	p16staining just for being distinguished some Cin2from Lsil，once Lsil could be determined clearly，p16shining should not be overdone.	8/16/2025 9:56 PM
11	Focal intense and strong block staining may suggest focal high risk HPV caused high grade dysplasia	8/16/2025 8:00 AM
12	I agree with the statement, but in the commentary, I would recommend mentioning that about half of LSILs can stain positive for p16, and thus with a positive p16 in this scenario, the pathologist must rely on the H&E for final classification of LSIL vs HSIL.	8/15/2025 7:32 PM
13	I would want to know if in this case the p16 IHC trumps morphology. And if not, then I would disagree with the recommendation. If so, then that's fine, but then I don't understand why you would not also use p16 for -IN1 vs -IN3 which is also a LSIL vs. HSIL diagnosis.	8/15/2025 2:11 PM
14	A small albeit real and sizeable proportion of HSIL may be p16-negative (Arch Pathol Lab Med (2023) 147 (3): 323–330.). The opposite (a block-positive p16 IHC strongly favors an interpretation of HSIL) is also not necessarily true, but will be assumed with this recommendation... HPV in situ (ISH) would be more reliable, when available, in cases with either strong p16 and suspect LSIL and negative p16 and suspect HSIL (-IN2)	8/15/2025 1:39 PM
15	Only if you're uncertain on H&E.	8/14/2025 5:30 PM
16	Please clarify that the differential is between HSIL and LSIL and not just LSIL. I would not use p16 for a straight up LSIL.	8/14/2025 5:11 PM
17	Lgsil should not be mistaken for hgsil	8/14/2025 5:08 PM
18	The phrase "secure a diagnosis" is unconventional and may easily be misinterpreted. Shouldn't this be "support a diagnosis"?	8/14/2025 11:47 AM
19	This only applies if HSIL/CIN2 is in the morphologic differential.	8/14/2025 10:50 AM
20	LSIL can have block-positive p16 stain.	8/14/2025 10:29 AM
21	Low grade can show diffuse p16 positivity in certain cases and must be correlated with KI67 and morphology.	8/14/2025 9:52 AM
22	pathologist should consider additional workup (p16 and levels).	8/14/2025 9:46 AM
23	I think that p16 can be considered in this context, but not use the word "should" in the statement. I think saying "should" may result in overuse of p16.	8/14/2025 9:31 AM
24	Not required in most cases. Would accept this recommendation with "may" rather than "should". Too much unneeded IHC otherwise.	8/14/2025 9:10 AM
25	The use of Ki67 may help in some cases. Keating JT, Cviko A, Riethdorf S, Riethdorf L, Quade BJ, Sun D, Duensing S, Sheets EE, Munger K, Crum CP. Ki-67, cyclin E, and p16INK4 are complimentary surrogate biomarkers for human papilloma virus-related cervical neoplasia. Am J Surg Pathol. 2001 Jul;25(7):884-91. doi: 10.1097/00000478-200107000-00006. PMID: 11420459.	8/14/2025 8:49 AM
26	Use caution using co-use Ki-67 immunustain. Reflex HPV-ISH testing to be included in the	8/14/2025 8:38 AM

	guidelines.	
27	does this mean performing p16 is recommended when the pathologist cannot decide between LSIL and HSIL? as written the statement is a bit unclear.	8/14/2025 8:12 AM

Q5 Draft Statement 3Pathologists should NOT use p16 IHC as a routine adjunct to histologic assessment of biopsy specimens with unequivocal morphologic differential diagnosis of negative, LSIL (–IN 1) and HSIL (–IN 3).1(Conditional Recommendation)Abbreviations: HSIL, high-grade squamous intraepithelial lesion; IHC, immunohistochemistry; -IN, intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesion; p16, CDK4 inhibitor p16-INK41 Reaffirmed recommendation statement from 2012 guideline

Answered: 174 Skipped: 123



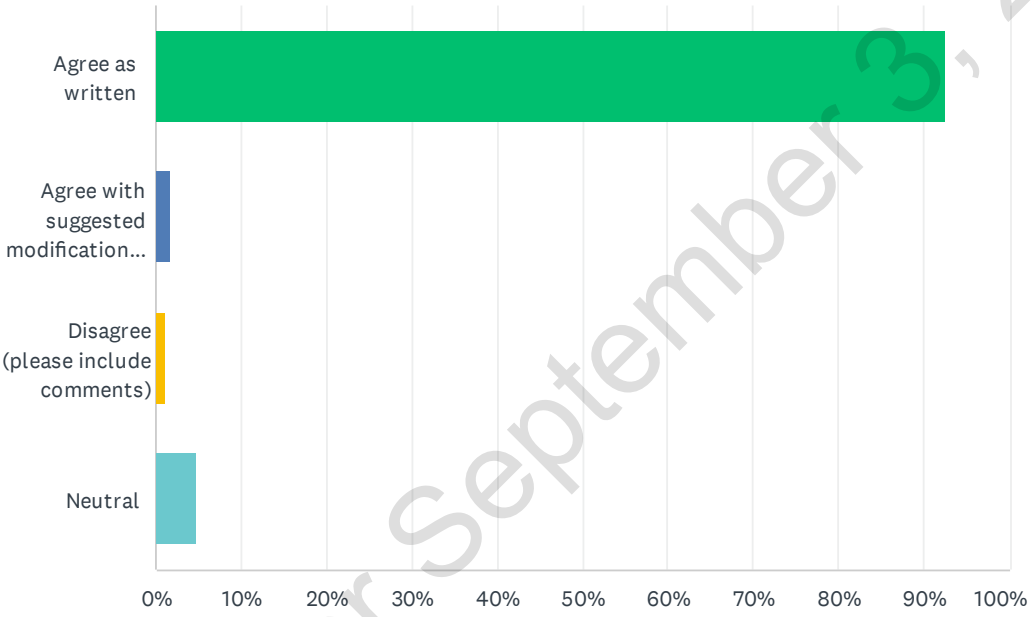
ANSWER CHOICES	RESPONSES	
Agree as written	81.61%	142
Agree with suggested modifications (please include comments)	4.02%	7
Disagree (please include comments)	6.90%	12
Neutral	7.47%	13
TOTAL		174

#	COMMENTS	DATE
1	p16 is a strong differentiator, histology review is sometimes subjective and therefore a clear and objective verification helps us clinicians to be secure and comfortable in our recommendations to our patients. I suggest that all specimens undergo confirmation of grade of SIL by p16 and Ki67 staining	8/26/2025 9:55 AM
2	p16 is overexpressed when HPV E7 oncoprotein disrupts the retinoblastoma (pRb) pathway and is a good choice for unequivocal diagnostic tools	8/23/2025 1:59 AM

3	unless in doubt.	8/22/2025 9:52 PM
4	P16 is crucial	8/22/2025 2:05 PM
5	p16 IHC is low cost but on clear pathologies, overkill. However, with the "unequivocal" being somewhat subjective, is there a way to clarify it in an objective manner to reduce the risk of a missed diagnoses.	8/22/2025 10:25 AM
6	General pathologists struggle making this distinction and reflex p16 can be helpful	8/21/2025 4:14 PM
7	we must clarify whether the tissue is undergoing oncogenic transformation, therefore, since a visual diagnosis of CIN2 vs 3 is not possible, p16 immunohistochemistry is necessary.	8/21/2025 9:20 AM
8	agree but can be used in selected cases (clinical request, uncertainty about whether squamous cell carcinoma in situ is HPV related or not, for example if it is unclear from available information whether the biopsy location is anogenital)	8/20/2025 5:34 PM
9	In my opinion, p16 should be done in all cases regardless of the morphological changes to keep it as a baseline for future biopsies and interval between biopsies. Pathologists of course needs to add a disclaimer for each positivity without morphological changes.	8/18/2025 4:18 PM
10	Some oncologists still seem to ask for p16 to assess the patient's HPV status for any -IN. Therefore statement should not be written in such a definitive manner.	8/18/2025 8:37 AM
11	In my institution they ask me to secure a LSIL diagnosis either an accompanying p16, either positive or negative	8/18/2025 1:18 AM
12	I'm not sure what that statement actually means.	8/17/2025 1:46 PM
13	Pathologists should NOT use p16 IHC as a routine adjunct to histologic assessment of biopsy specimens with unequivocal morphologic diagnosis on H&E section[s] of negative, LSIL (–IN 1) and HSIL (–IN 3). or Pathologists should NOT use p16 IHC as a routine adjunct to histologic assessment of biopsy specimens when confident of morphologic diagnosis on H&E section[s] of negative, LSIL (–IN 1) and HSIL (–IN 3).1	8/17/2025 11:52 AM
14	Confirm HSIL (-IN3) with HR-HPV ISH	8/14/2025 10:15 AM
15	Suggest p16 even in definitely morphologically diagnostic of High Grade. Clinicians may ask to be done anyway. If p16 equivocal but morphology definite, a comment would help.	8/14/2025 9:32 AM
16	Use caution while using Ki-67 immunostain.	8/14/2025 8:38 AM

Q6 Draft Statement 4The use of a unified histopathological nomenclature with a single set of diagnostic terms is recommended for all HPV-associated preinvasive squamous lesions of the LAT.1(Good Practice Statement)Abbreviations: HPV, human papilloma virus; LAT, lower anogenital tract1 Reaffirmed recommendation statement from 2012 guideline

Answered: 174 Skipped: 123



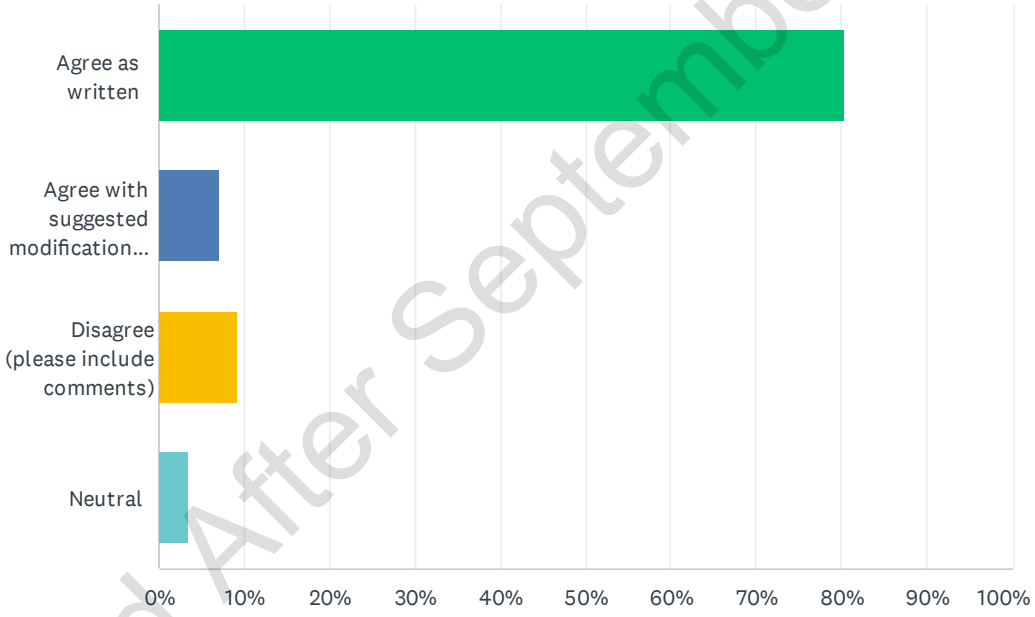
ANSWER CHOICES	RESPONSES	
Agree as written	92.53%	161
Agree with suggested modifications (please include comments)	1.72%	3
Disagree (please include comments)	1.15%	2
Neutral	4.60%	8
TOTAL		174

#	COMMENTS	DATE
1	We cannot have the cytology and histology use the same terms. The terms must reflect a screening diagnosis versus a tissue diagnosis.	8/21/2025 9:20 AM
2	I agree, but many gastroenterologists (sadly) only recognize "condyloma acuminatum". So we include that in the diagnosis along with LSIL/AIN1).	8/17/2025 1:46 PM
3	Such set of diagnostic terms has to be agreed upon by the physicians/clinicians who will be using them for subsequent management or comments are likely to be needed in the first phase of implementation of such single set of diagnostic terms to guide clinical interpretation (and subsequent management)	8/15/2025 1:39 PM

4	as long as it's not exclusive. It is still useful to use LAST terminology along with equivalent older terms (eg. mild, moderate, severe) to aid clinicians with the transition	8/15/2025 7:53 AM

Q7 Draft Statement 5The use of a 2-tiered nomenclature is recommended for noninvasive HPV-associated squamous proliferations of the LAT, which should routinely be further qualified with the appropriate –IN terminology.1Note: –IN refers to the generic intraepithelial lesion terminology, without specifying the location. For a specific location, the appropriate complete term should be used eg, –IN 3 lesions: cervix = CIN 3, vagina = VaIN 3, vulva = VIN 3, anus = AIN 3, perianus = PAIN 3, and penis = PeIN 3 (Good Practice Statement)Abbreviations: HPV, human papilloma virus; -IN, intraepithelial neoplasia; LAT, lower anogenital tract1 Updated recommendation statement from 2012 guideline

Answered: 173 Skipped: 124



ANSWER CHOICES	RESPONSES	
Agree as written	80.35%	139
Agree with suggested modifications (please include comments)	6.94%	12
Disagree (please include comments)	9.25%	16
Neutral	3.47%	6
TOTAL		173

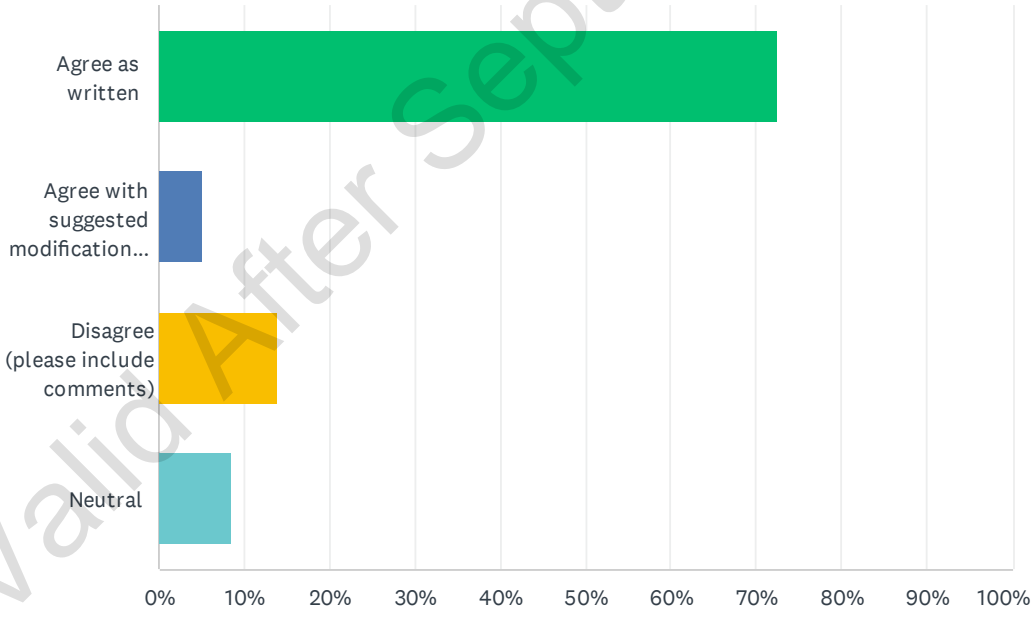
#	COMMENTS	DATE
1	I believe the numeric grading system is a problem. Its continuation encourages people to persist with using VIN1/PAIN1/AIN1, which are unhelpful in sites that instead have condyloma and flat LSIL. In addition, I often see cases of pathologists using VIN2 to describe lesions that	8/25/2025 7:17 PM

	are actually HPV-independent (HPVi) VIN (eg differentiated VIN).\ The WHO and ISSVD are both working on updates to nomenclature for vulvar squamous precursors. This will likely reflect etiology, not morphology. It would be nice for HSIL vulva to be the accepted name for HPV-associated (HPVa) precursors, as this is obviously different to HPV-i VIN.	
2	There has been movement in the vulvar health sphere to identify VIN 3 as d-VIN or vulvar HSIL to indicate underlying etiology related to HPV or vulvar dermatosis AND the progression to cancer is higher risk in d-VIN population	8/22/2025 5:07 PM
3	Please give an example	8/22/2025 4:51 PM
4	I don't think we should go back to 2/3 ie this promotes 1-3 stages again as opposed to All hsil. Problematic and not good reasons to go back	8/22/2025 2:56 PM
5	2-tier nomenclature is enough. No need to further qualify with the -IN terminology.	8/22/2025 1:07 PM
6	I would say "may" instead of "should". The LAST system has been around long enough now that labs should have more discretion as to whether to include the outdated -IN terminology.	8/22/2025 12:16 PM
7	Consider clarifying /emphasizing that the IN terminology is not for cytology, only for histopathologic lesion terminology	8/22/2025 6:19 AM
8	Duplicative and not needed for management decisions to include both.	8/21/2025 3:18 PM
9	Recommend -IN designation only for cervix.	8/21/2025 12:39 PM
10	We cannot have the cytology and histology use the same terms. The terms must reflect a screening diagnosis versus a tissue diagnosis. If you use a 2 tiered system, then p16 on the cytology and p16 on the histology are required	8/21/2025 9:20 AM
11	should clarify that further qualification with for high grade lesions can use -IN(2-3), not necessary to separate into -IN 2 or -IN3)	8/20/2025 5:34 PM
12	Please include HSIL [-IN 2/3] and LSIL [condyloma] as options. Grading of high-grade SIL as -IN 2 or -IN3 is very subjective with significant interobserver variation and may have significant management implications. An interpretation of HSIL [-IN 2/3] indicates that the lesion is histologically high-grade on sections [whether or not p16 done or levels, consultation, expert review used. Since currently it is not possible to predict behavior of a specific HSIL lesion, if left untreated, it is important for management decisions to include additional clinical information. Size of lesion is not incorporated into current clinical management recommendations for cervical HSIL. Some pathologists do not use the term -IN3 if there is 'any' maturation at the surface, even when significant basal atypia, atypical mitotic figures, etc -- when most 'experts' would clearly call the lesion HSIL. Calling such lesions as HSIL[-IN2] can lead to overuse of p16 to confirm high-grade impression and/or undertreatment of potential pre-cancer is some clinical settings. For example, a circumferential cervical lesion that spans most of the active transformation zone that is called HSIL[CIN 2] on biopsy could, per ASCCP management recommendations, be managed 'conservatively' in a women concerned about future fertility; however, the management recommendation is treatment for a small HSIL[CIN3] lesion that may have be removed by the the biopsy and subsequent healing process. Given what we know about the natural history of cervical HSIL [based in large part on the "Unfortunate Experiment" in New Zealand], an observed large CIN2 lesion most likely has more malignant potential that the small CIN3 lesion mainly removed by biopsy. See also: Richart RM. A modified terminology for cervical intraepithelial neoplasia. Obstet Gynecol. 1990 Jan;75(1):131-3. PMID: 2296409.	8/17/2025 11:52 AM
13	sometimes IN could be found in cervix and vain at the same time , marked clearly all?the IN location could prevent some missed lessons.	8/16/2025 9:56 PM
14	The site is already provided, e.g., Cervix, biopsy- Low grade squamous intraepithelial lesion. It will be redundant to include the corresponding -IN. It only prolongs retention of obsolete terms. Waste of time and it doesn't contribute anything.	8/16/2025 3:07 PM
15	Anus is a special organ that needs more specific and clear grading for clinical patient care	8/16/2025 8:00 AM
16	if we should (must?) use the -IN terminology after the LSIL/HSIL, why don't we stick to the -IN terminology only? Are we simplifying or creating room for mistakes/errors?	8/15/2025 1:39 PM
17	This is incredibly confusing as written. If using a two-tiered nomenclature is the proposal to list as either -IN1 versus -IN3 (and remove -IN2)? I'm not sure this will be clear to most clinicians.	8/15/2025 1:10 PM

18	I prefer the word "may" instead of "should"	8/15/2025 7:53 AM
19	If we are committing to the two-tier system we should not be holding onto the prior three-tier terminology. This would obviate the need for the former in the first place. It has been more than 10 years since the LAST guidelines and it's time to transition away from the -IN terminology.	8/15/2025 7:43 AM
20	This should be 2-3 for all categories if we are using HSIL/LSIL, you are still encouraging a 3 tier system this way	8/14/2025 4:26 PM
21	-IN terminology may be included	8/14/2025 2:32 PM
22	It is confusing to use dual terminology. We either do 2 or 3 tiered approach.	8/14/2025 11:16 AM
23	Where necessary mild , moderate and severe dysplasia may be used	8/14/2025 9:21 AM
24	Rather than "should" I suggest "may". The distinction between 2 & 3 is not always clear or needed. And LSIL is 1 by definition, so follow up of CIN-1 for example is redundant	8/14/2025 9:10 AM
25	The CIN 2 category is still useful, to reflect cases where it is difficult to distinguish between LSIL and HSIL based on extent (thickness) of dysplasia in well oriented sections of biopsy specimens.	8/14/2025 9:04 AM
26	Include both: eg: High-grade SIL (AIN2 or AIN3) eg: Low-grade SIL (AIN1)	8/14/2025 8:38 AM

Q8 Draft Statement 6Performing p16 IHC is recommended as an adjunct to morphologic assessment for specimens interpreted as ≤ –IN 1 that are at high risk for missed high-grade disease, which is defined as HPV16, 18, or 18/45+; a prior cytologic interpretation of HSIL, ASC-H, AGC*, or AEC *; or a prior histologic diagnosis of HSIL.1Note: Any identified p16-positive area must meet H&E morphologic criteria for HSIL to be reinterpreted as such.*AGC and AEC: including NOS and favor neoplastic(Good Practice Statement)Abbreviations: ASC-H, Atypical Squamous Cells, cannot exclude HSIL; AGC, Atypical Glandular Cells; AEC, Atypical Endocervical Cells; H&E, hematoxylin and eosin stain; HPV, human papilloma virus; HSIL, high-grade squamous intraepithelial lesion; IHC, immunohistochemistry; -IN, intraepithelial neoplasia; LAT, lower anogenital tract; NOS, not otherwise specified; p16, CDK4 inhibitor p16-INK41 Reaffirmed recommendation statement from 2012 guideline

Answered: 174 Skipped: 123



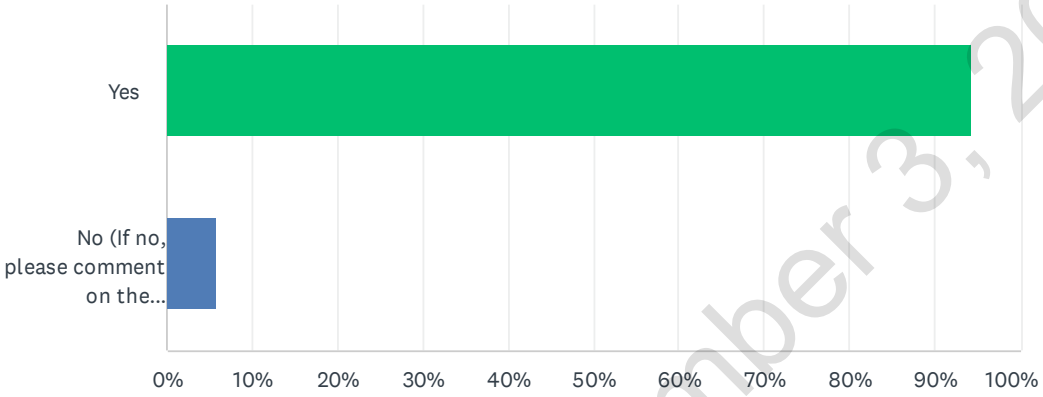
ANSWER CHOICES	RESPONSES	
Agree as written	72.41%	126
Agree with suggested modifications (please include comments)	5.17%	9
Disagree (please include comments)	13.79%	24
Neutral	8.62%	15
TOTAL		174

#	COMMENTS	DATE
1	CIN 2 that is p16 (+) is classified as HSIL & CIN 2 that is p16 (-) is classified as LSIL.	8/23/2025 12:24 PM
2	Only for cervical specimens	8/23/2025 3:50 AM
3	Run-on sentence makes it difficult to read. Consider splitting into two sentences. Performing p16 IHC is recommended as an adjunct to morphologic assessment for specimens interpreted as ≤ –IN 1 that are at high risk for missed high-grade disease. High-risk for missed high-grade disease is defined as HPV16, 18, or 18/45+; a prior cytologic interpretation of HSIL, ASC-H, AGC*, or AEC *; or a prior histologic diagnosis of HSIL.	8/22/2025 6:35 PM
4	Should not run p16 if morphologically negative. Levels would be a better use of resources for missed lesions.	8/22/2025 2:48 PM
5	What about cases in which f/u sampling is clearly inadequate? p16 doesn't seem needed in these situations, despite the risk for missed high grade disease	8/21/2025 3:18 PM
6	If not morphologically suspicious or suggestive then p16 is not necessary based on HPV status alone.	8/21/2025 12:39 PM
7	We cannot have the cytology and histology use the same terms. The terms must reflect a screening diagnosis versus a tissue diagnosis. If Draft 6 refers only to histology, then agree.	8/21/2025 9:20 AM
8	Given that we see TONS of negative specimen from patients with HRHPV in our practice I have to assume other see at least some. It is incredibly common to see tiny fragments of tissue that are p16 "positive" yet aren't dysplastic and aren't readily identifiable on H&E (too small to tell, cut through, etc.) This could lead to over-treatment as a lot of pathologist will likely note "positive" p16 as "atypical"	8/19/2025 7:37 AM
9	I agree with this wording, however this wording seems to conflict with Draft Statement 3, resulting in my suggestion above.	8/18/2025 8:37 AM
10	Pathologist should review slide again if it's high risk or there is hesitation in the low grade diagnosis. If upon review he finds something that raises concern for HGSIL then p16 needs to be performed since it is in the differential diagnosis. Routine use of p16 without morphologic support will result in overdiagnosis.	8/16/2025 3:07 PM
11	Is there a way to make this recommendation for sites where prior specimens may be available but protect sites where we may not have that information? Working at a safety net hospital our EMR is cobbled together and information is often incomplete.	8/15/2025 2:11 PM
12	As long as H&E levels corresponding to the stained sections are obtained/available (see comment for draft statement 1). In other words, I believe that obtaining the stain might also mean looking at more levels and perhaps increasing the diagnostic yield of the sample.	8/15/2025 1:39 PM
13	I would favor deeper levels first, and add p16 if higher grade lesion is discovered. The practice as defined above assumes that in the practice of ordering the p16, such a focus is serendipitously discovered. A deeper level may obviate the need for p16.	8/15/2025 7:53 AM
14	If there is no morphologic evidence of high grade disease, then how can you interpret a positive p16 as HSIL? This should be up to the individual pathologist to decide if a p16 is useful to them.	8/14/2025 8:19 PM
15	I would not use p16 staining unless there is H&E support first. This is setting up pathologists for failure through overuse of p16 to prevent getting sued.	8/14/2025 5:11 PM

16	Given the risk for CIN3 is no less than a genotype positive for HPV 16, 18 or 18/45 if CINTec Plus is positive. Why is a positive CINTec Plus cytology results preceding a biopsy not included?	8/14/2025 12:04 PM
17	Given that a high proportion of LSIL/CIN1 lesions are p16+ (>20% in some studies), p16 should only be performed on lesions that are morphologically suspicious for -IN2. By doing p16 on all HPV16,18,18/45+ lesions there will be a lot of cases of LSIL with +p16 expression that will be erroneously upgraded to -IN2	8/14/2025 11:53 AM
18	This should be left to the judgment of the pathologist.	8/14/2025 11:16 AM
19	This applies if morphology is suspect. If no fragments contain dysplastic mucosa, there is no need to stain.	8/14/2025 10:50 AM
20	This can cause false positive interpretation.	8/14/2025 10:29 AM
21	Confirm with HR-HPV RNA ISH	8/14/2025 10:15 AM
22	"screening" p16 is not a good idea. An better idea would be "additional workup" which should include deepers, consideration of review of the pap smear, and consideration of p16 IHC. This statement would also suggest that workup NEEDS to occur on EVERY specimen in an otherwise negative case (including scant ECC, clearly ectocervical mucosa with no transition zone, etc). The specific definition of high-risk HPV can also be challenging when a patient comes with an outside pap smear and a reported HPV+ status, but the specific subtypes are not available (which is not uncommon in community practice). Similarly, this is problematic recommendation for cases in which the pap smear is not reviewable.	8/14/2025 9:46 AM
23	Similar to draft statement 2, I think it would be better to say that p16 could be considered, but not necessarily recommended.	8/14/2025 9:31 AM
24	If morphological criteria meets then they should never be missed. If this guideline is implemented p16 will be performed on all anal biopsies regardless - risk of over diagnosis.	8/14/2025 9:21 AM
25	If there is nothing suspicious for a higher grade lesion, p16 should not be performed. The note above is the reason why. If it doesn't look like HSIL, I am not going to call it HSIL despite staining.	8/14/2025 9:16 AM
26	It needs to be emphasized that this recommendation should apply only to specimens with histologic evidence of dysplasia, and not in all biopsies with the prior cytologic interpretations listed. We wouldn't want the cytologic interpretations to become self-fulfilling prophecies.	8/14/2025 9:04 AM
27	p16 should be done only when IN 2 or 3 are suspected on H&E.	8/14/2025 8:42 AM
28	Reflex HPV testing to be included in the guidelines.	8/14/2025 8:38 AM
29	should we really be required to do p16 on a morphologically negative biopsy? is that what the statement recommends?	8/14/2025 8:12 AM

Q9 Does the following definition of CIN3 align with your diagnostic practice? “CIN3 should be diagnosed when high-grade high-risk HPV-associated squamous epithelial changes are nearly indistinguishable from surface to base, with minimal to absent surface koilocytosis.”

Answered: 158 Skipped: 139

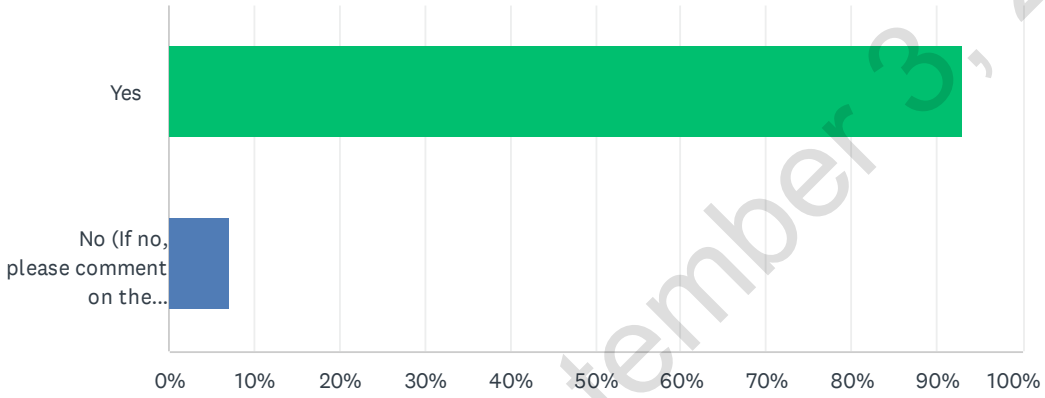


ANSWER CHOICES	RESPONSES	
Yes	94.30%	149
No (If no, please comment on the morphologic criteria you enlist to diagnose CIN3).	5.70%	9
TOTAL		158

#	COMMENT	DATE
1	more than nearly indistinguishable from surface to base - more like a third	8/21/2025 9:22 AM
2	This description applies to the classic one for Carcinoma in Situ which does not include other patterns of HSIL[CIN3].]	8/17/2025 11:59 AM
3	CIN 3 also includes severe dysplasia wherein the base can still be distinguished from the surface of the epithelium.	8/16/2025 3:14 PM
4	Presence or absence of koilocytes does not define low grade vs. high grade	8/16/2025 1:42 PM
5	We moved to using HSIL versus LSIL. HSIL is as described above plus p16 positive -IN2s.	8/15/2025 1:11 PM
6	A comment describing CIS should be added	8/14/2025 4:50 PM
7	Why if we are using a 2-tier system, defining a 3-tier system	8/14/2025 4:27 PM
8	I don't use CIN3 terminology, just HSIL	8/14/2025 11:19 AM
9	I would think that koilocytosis refers to the typical changes in LG. I would rather use the word dysplasia	8/14/2025 9:37 AM
10	I mostly agree with the definition but I allow surface koilocytosis in CIN 3 as long as the basal layer hyperplasia involves greater than two-thirds of the mucosal thickness.	8/14/2025 8:40 AM

Q10 Does the following statement about CIN2 align with your diagnostic practice? “CIN2 should be considered for high-risk HPV-associated squamous lesions that fall short of diagnostic criteria CIN3, but exceed what is typical of CIN1 (for example: lesions that retain some koilocytosis, but demonstrate basaloid atypia and mitotic figures extending into the upper half the epithelium).”

Answered: 157 Skipped: 140



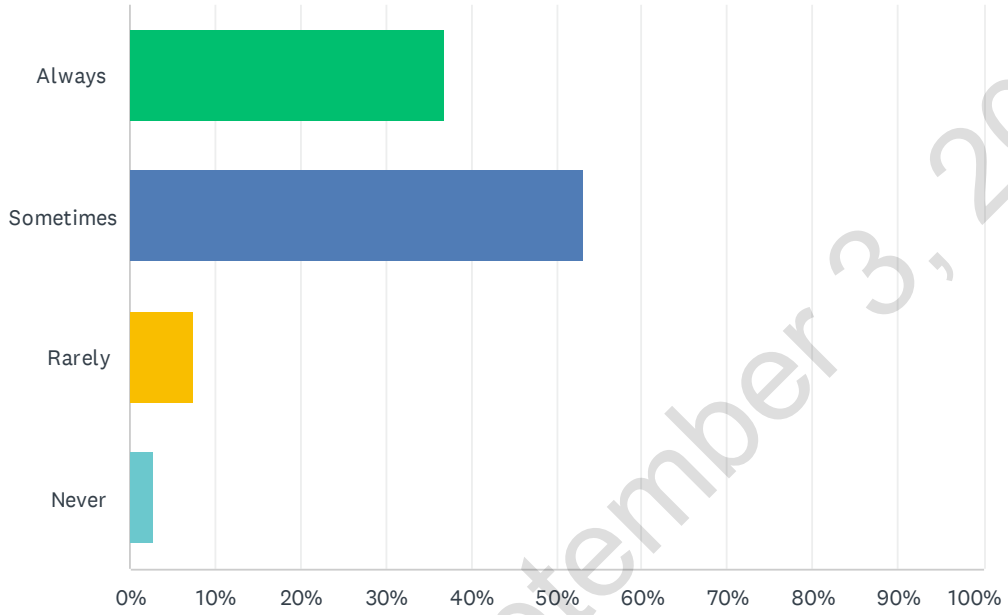
ANSWER CHOICES	RESPONSES	
Yes	92.99%	146
No (If no, please comment on the morphologic criteria that prompt you to consider a diagnosis of CIN2).	7.01%	11
TOTAL		157

#	COMMENT	DATE
1	Remove High risk	8/23/2025 3:54 AM
2	and consider additional slide prep or biopsy	8/22/2025 5:08 PM
3	I do not use the 3-tier system	8/22/2025 1:11 PM
4	we use the lower third for CIn 1 - middle third for CIN 2	8/21/2025 9:22 AM
5	I do not use this term. For example: massive koilocytosis is not that typical of CIN1 but is not at all high grade lesion	8/18/2025 1:22 AM
6	See other comments. Also HPV data not always available in US. Primary HPV testing for screening has poor uptake, unfortunately.	8/17/2025 11:59 AM
7	Same reason; Presence or absence of koilocytes does not define low grade vs. high grade	8/16/2025 1:42 PM
8	We moved to using HSIL versus LSIL.	8/15/2025 1:11 PM
9	Although this fits with what we'd consider -IN2 we no longer use this diagnostic term and have transitioned over to using HSIL and LSIL. I do not render a diagnosis of -IN2.	8/15/2025 7:46 AM
10	I use 1/3 instead of 50% for CIN2	8/14/2025 4:50 PM
11	see above	8/14/2025 4:27 PM

12	I don't use CIN terminology, only LSIL or HSIL	8/14/2025 11:19 AM
13	My criteria are very similar but I use basaloid atypia extending into the middle third of the epithelium (so some CIN 2 cases may not have basaloid atypia extending into the upper half).	8/14/2025 8:40 AM

Q11 In your practice, do you perform p16 immunostaining prior to rendering a diagnosis of CIN2?

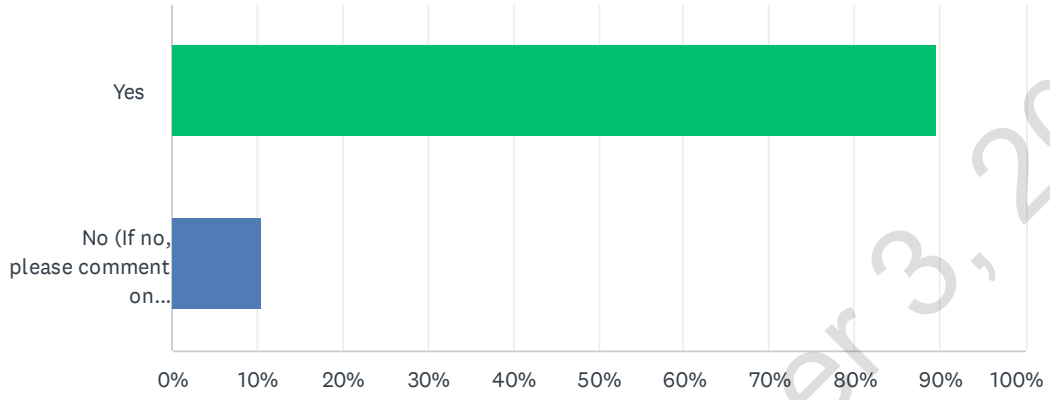
Answered: 149 Skipped: 148



ANSWER CHOICES	RESPONSES	
Always	36.91%	55
Sometimes	53.02%	79
Rarely	7.38%	11
Never	2.68%	4
TOTAL		149

Q12 If you perform a p16 immunostain prior to rendering a diagnosis of CIN2, do you require block-positivity to confirm a CIN2 diagnosis?

Answered: 145 Skipped: 152



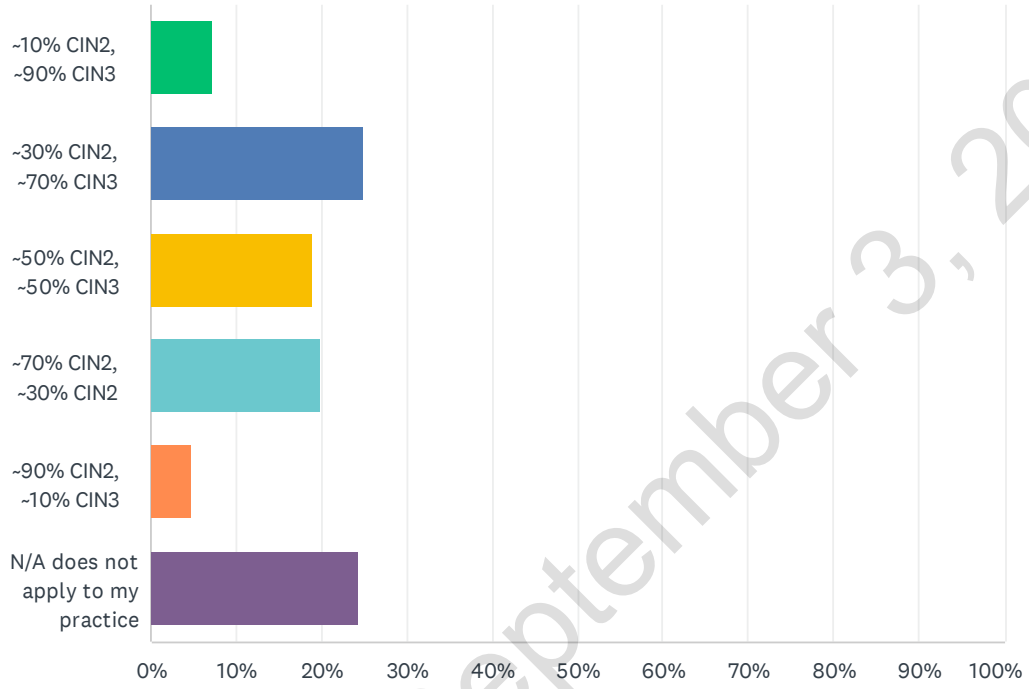
ANSWER CHOICES	RESPONSES	
Yes	89.66%	130
No (If no, please comment on circumstances in which you would diagnose CIN2 with a negative p16).	10.34%	15
TOTAL		145

#	COMMENT	DATE
1	unsure	8/24/2025 9:54 AM
2	i don't do this testing; I am not a pathologist	8/22/2025 6:00 PM
3	I do not give CIN-2 diagnosis	8/22/2025 1:11 PM
4	Associated with ki-67	8/19/2025 12:28 AM
5	I diagnose CIN2 without p16 staining frequently.	8/18/2025 8:39 AM
6	If the histologic features are those of -IN 2, the diagnosis will be made even if not confirmed by p16	8/17/2025 1:48 PM
7	And I use the term -IN2 only when I have diagnostic uncertainty with the DDX being HSIL vs benign/reactive or HSIL[-IN2] vs LSIL [-IN1]	8/17/2025 11:59 AM
8	I do not practice cervical pathology any longer. In the past we would be asked to do p16. Nowadays, I would suggest HPV-HR in situ (also because it is now available as in house test and a bit faster than it was once)	8/15/2025 1:44 PM
9	Yes, but it doesn't have to be full thickness. Can be lower 50%.	8/15/2025 10:45 AM
10	I almost always use p16 if I'm trying to differentiate CIN1 and CIN2. If the p16 is not diffuse but atypical mitotic figures are present, I will favor HSIL/CIN 2.	8/15/2025 8:41 AM
11	I do not render a diagnosis of -IN2.	8/15/2025 7:46 AM
12	If the H&E looks like cin2 I will comment that the p16 favors LSIL but HSIL cannot be excluded or it is approaching cin2	8/14/2025 5:15 PM
13	Sometimes p16 staining can be patchy but atypia extending more than 1/2 the thickness, increased KI67 and mitosis higher up in the epithelium favor diagnosis of ASIL/CIN-2	8/14/2025 9:54 AM

14	I also look at patterns with p53	8/14/2025 9:01 AM
15	Block like positivity will make it 3	8/14/2025 8:43 AM

Q13 In your practice, approximately what percentage of HSIL are diagnosed as CIN2 versus CIN3?

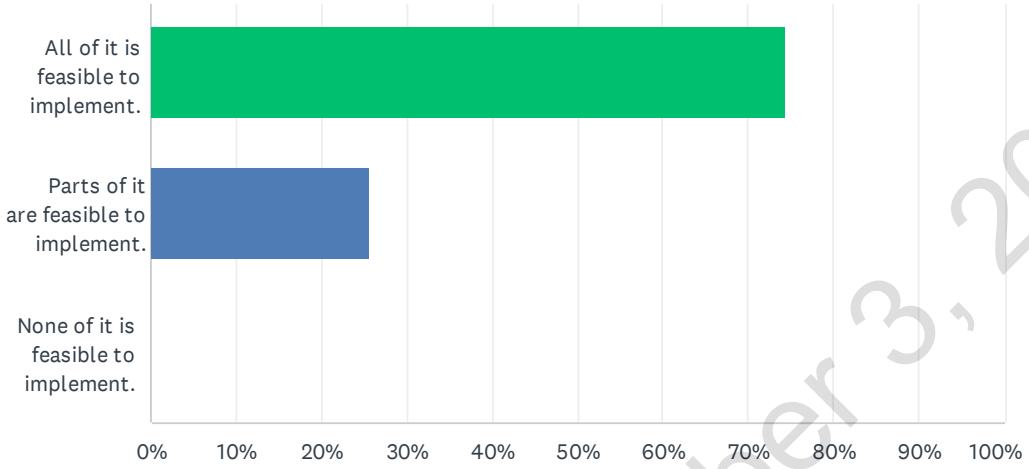
Answered: 152 Skipped: 145



ANSWER CHOICES	RESPONSES	
~10% CIN2, ~90% CIN3	7.24%	11
~30% CIN2, ~70% CIN3	25.00%	38
~50% CIN2, ~50% CIN3	19.08%	29
~70% CIN2, ~30% CIN2	19.74%	30
~90% CIN2, ~10% CIN3	4.61%	7
N/A does not apply to my practice	24.34%	37
TOTAL		152

Q14 How feasible is it to implement this guideline?

Answered: 148 Skipped: 149

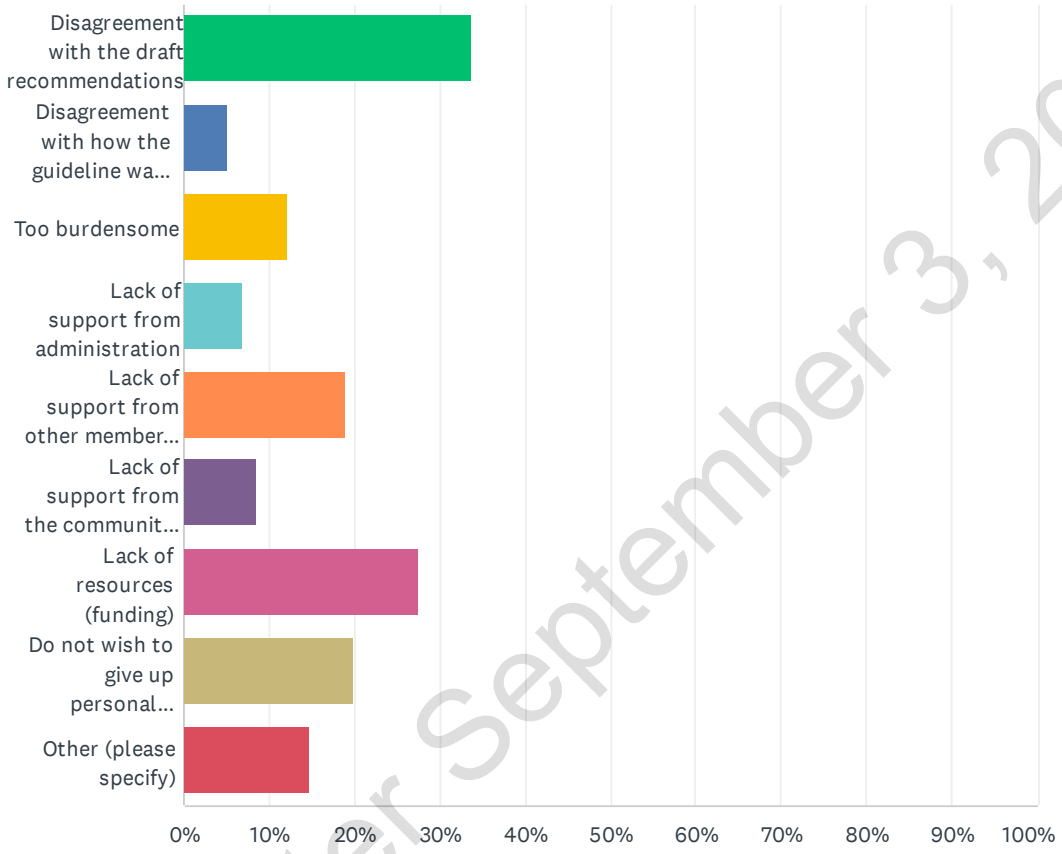


ANSWER CHOICES	RESPONSES	
All of it is feasible to implement.	74.32%	110
Parts of it are feasible to implement.	25.68%	38
None of it is feasible to implement.	0.00%	0
TOTAL		148

#	COMMENTS ABOUT THE FEASIBILITY OF IMPLEMENTING THE GUIDELINE:	DATE
1	My only concern is running p16 on morphologically negative cases.	8/22/2025 2:50 PM
2	how to translate to the clinicians who order the test and interpret the test. pathology is only a tool to get an answer for the clinician.	8/21/2025 9:24 AM
3	Feasibility and practical application are two different things. Most practices have p16, and some private groups in my region do not hesitate to abuse it	8/19/2025 7:43 AM
4	In present , some parhologist in china still use cin1-3 to diagnosis.	8/16/2025 10:00 PM
5	See sections disagreed	8/16/2025 3:17 PM
6	Running p16 is probably the easiest part for all labs: the H&E and stain interpretation, as well as the potential caveats, might be the limiting factor	8/15/2025 1:49 PM
7	I prefer the two-tier system to mimic to biological activity of the lesions (HSIL risk of CA, LSIL active productive infection of HPV). Going back to a three tier system seems to be moving us backward.	8/15/2025 1:14 PM
8	Good guidelines, with flexibility to allow for real-life exceptions is desirable	8/15/2025 7:59 AM
9	Different labs use different p16 antibodies, causing interpretation issues.	8/14/2025 10:33 AM
10	The absence of block like positivity should not be a criteria for differentiating LSIL vs HSIL as some of The LSIL cases can show diffuse positivity, in these cases KI67 is helpful.	8/14/2025 9:56 AM

Q15 What barriers might impede adoption of the final guideline? (Choose all that apply.)

Answered: 116 Skipped: 181



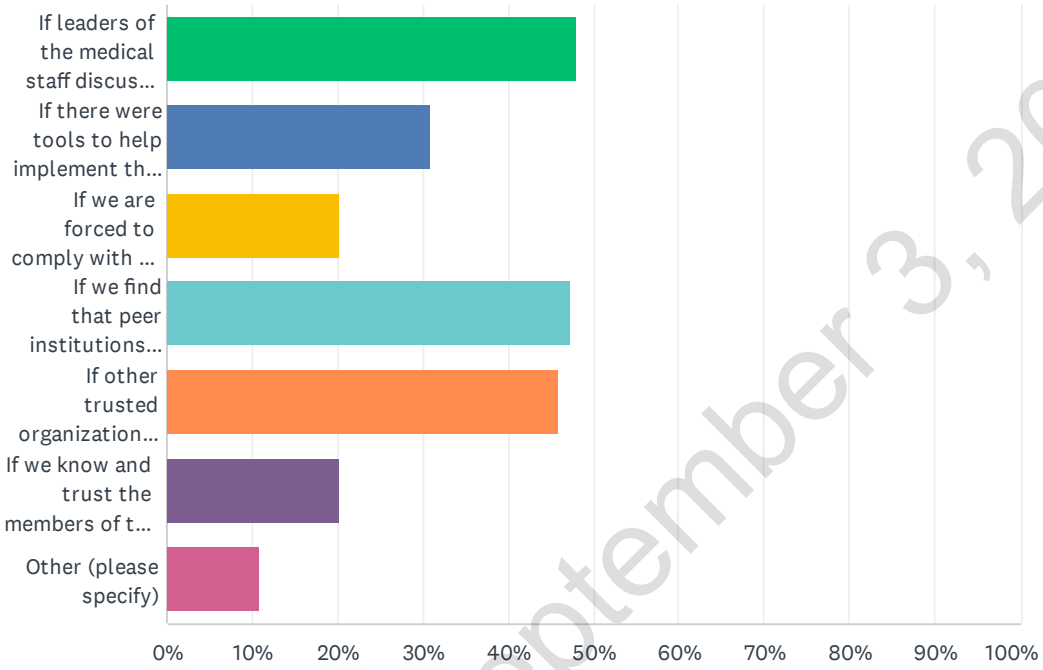
ANSWER CHOICES	RESPONSES	
Disagreement with the draft recommendations	33.62%	39
Disagreement with how the guideline was developed	5.17%	6
Too burdensome	12.07%	14
Lack of support from administration	6.90%	8
Lack of support from other members of the medical team	18.97%	22
Lack of support from the community (others outside your institution e.g., patients, industry)	8.62%	10
Lack of resources (funding)	27.59%	32
Do not wish to give up personal autonomy to follow the guideline	19.83%	23
Other (please specify)	14.66%	17
Total Respondents: 116		

#	OTHER (PLEASE SPECIFY)	DATE

1	None	8/25/2025 8:20 PM
2	Vulvar terminology needs to align with upcoming changes to WHO and ISSVD. A comment about the p53 appearance of HSIL may also be useful.	8/25/2025 7:19 PM
3	Resource limited	8/22/2025 10:21 PM
4	None	8/22/2025 1:58 AM
5	None	8/20/2025 9:19 AM
6	I do not use the 3-tier scheme, only LSIL/HSIL	8/18/2025 1:24 AM
7	p16 staining is helpful, but not reliable.	8/17/2025 1:49 PM
8	Implementation of change is slow! Continue educational efforts and collaboration with clinical colleagues to understand strengths/limitations of histopathological diagnoses.	8/17/2025 12:04 PM
9	Need more work	8/16/2025 8:03 AM
10	the bulk of recommendation (references) obviously comes from cervical pathology. More data on the use, validity and, ultimately, clinical significance of p16 in other sites are needed in my opinion	8/15/2025 1:49 PM
11	None really (no checkbox option for this)	8/15/2025 7:59 AM
12	none	8/15/2025 6:22 AM
13	No barriers. At our institution some pathologist routinely perform Ki-67 when they request p16	8/14/2025 4:54 PM
14	why are you defining a 3-tier system on a 2-tier recommendation	8/14/2025 4:29 PM
15	no barriers	8/14/2025 10:21 AM
16	Not applicable	8/14/2025 9:38 AM
17	NA	8/14/2025 8:40 AM

Q16 What facilitators might assist in your adoption of the final guideline? (Please select your top 3 facilitators.)

Answered: 129 Skipped: 168



ANSWER CHOICES	RESPONSES	
If leaders of the medical staff discussed adoption/adaption of the guideline for our practice setting	48.06%	62
If there were tools to help implement the guideline	31.01%	40
If we are forced to comply with the guideline by administration or an accreditation body	20.16%	26
If we find that peer institutions/practices adopt the guideline	47.29%	61
If other trusted organizations endorse the guideline	45.74%	59
If we know and trust the members of the panel members and/or organizations who developed the guideline	20.16%	26
Other (please specify)	10.85%	14
Total Respondents: 129		

#	OTHER (PLEASE SPECIFY)	DATE
1	None	8/25/2025 8:20 PM
2	see above	8/25/2025 7:19 PM
3	if pathology talked to family medicine, general internal medicine as they are the primary users of cervical cancer screening - how do they want to see the results reported to them?	8/21/2025 9:24 AM
4	If funding is guaranteed from governmental and non-governmental payors.	8/18/2025 8:40 AM
5	Change/updates to EMR, SNOMED, ICD codes	8/17/2025 12:04 PM

6	funding	8/17/2025 2:55 AM
7	availability of resources	8/15/2025 1:49 PM
8	none	8/15/2025 6:22 AM
9	It is always best to point to a written guideline or mandate as a fallback reference	8/14/2025 5:16 PM
10	I already agree with this guideline. No barriers	8/14/2025 4:54 PM
11	If the guidelines make things simpler, not more complicated	8/14/2025 11:22 AM
12	no need for facilitators	8/14/2025 10:21 AM
13	Retirement of a senior faculty member who only uses neoplasia terminology.	8/14/2025 9:15 AM
14	NA	8/14/2025 8:40 AM

Q17 Please provide any general comments or concerns:

Answered: 24 Skipped: 273

#	RESPONSES	DATE
1	None	8/25/2025 8:20 PM
2	note: question on page prior should have read 70% CIN-2, 30% CIN-3*** (typo)	8/24/2025 9:56 AM
3	The LAST guideline is an easy way to practice and standardize.	8/24/2025 4:38 AM
4	As gynecologist, routine categorization of HSIL as -IN2 vs -IN3 is critical and much needed.	8/23/2025 1:25 PM
5	Guidelines always guide the clinicians. It is often difficult to implement fully in resource limited areas.	8/23/2025 10:42 AM
6	Please don't go back to using or encoring 3 part staging. The data on inter rated reliability continues to be poor. I have national and international Colpo admin roles and am a very clinically busy colposcopist ie 1000 cases /year managing cervix vagina and vulvar dysplasia and I think last was a big improvement. Thanks	8/22/2025 3:01 PM
7	Thank you for your work on this. The LAST guidelines have been very helpful.	8/22/2025 12:18 PM
8	you must include your family medicine and general internal medicine clinical colleagues who do more than half of all cervical cancer screening and follow up. What do they want to see as a test result? what do they want to see as a biopsy result?	8/21/2025 9:24 AM
9	Overall most of this sounds okay and aligns with current practice where I am. A couple of the points noted could lead to issues with p16 over-use / misinterpretation and therefore over-treatment, especially in the south where CIN 2 is frequently treated with LEEP (essentially automatic in my setting).	8/19/2025 7:43 AM
10	The guideline should be concise,clear, and highly practical	8/19/2025 12:33 AM
11	Also need to update collection of data by cancer surveillance groups.	8/17/2025 12:04 PM
12	The economic conditions of each country or region are different, and the technical levels of each medical institution also vary, which may lead to different practices. Therefore, standardization is very necessary.	8/17/2025 5:31 AM
13	No additional cost to patients	8/17/2025 2:55 AM
14	The guidelines has some major errors that need to be corrected. Besides p16, what about ki67? What about HPV testing? Need to be more specific and practical.	8/16/2025 1:44 PM
15	There should be a lot more clarity on what terminology is to be used. This current recommendation as written will only confuse the picture even further.	8/15/2025 1:14 PM
16	Thanks for circling around on this topic	8/15/2025 7:59 AM
17	At our institution some pathologist routinely perform Ki-67 when they request p16.	8/14/2025 4:54 PM
18	Please stick to a 2 or 3 tired system. I personally prefer and like the 2- tired system. I have used for many years, and the clinicians seem to be happy with it. It took some education, initially.	8/14/2025 11:22 AM
19	In general i strongly agree with everyone except essentially coercing the use of p16 in some circumstances (IN-1 vs. IN-2, and negative biopsies with high risk pap/HPV status). Costs associated with this need to be considered, as well as understanding systems based practice and complexities of care. Rather, strongly recommending these cases are called out as sometimes requiring additional workup at the discretion of the pathologist, in the context of the patient and practice-specific factors, would be beneficial. While p16 IHC is routine, let us not forget that there are additional costs associated with it, both to the laboratory/health system, but also to patients. Many times this can be avoided simply by deeper levels and careful consideration of the case at hand.	8/14/2025 9:51 AM

20	I am against blindly using an immunization for among diagnosis. P16 is a great adjunct but its use should be guided by morphology. The tendency of using IHC first and morphing later can lead to a lot of overdiagnosis. And further add to the declining morphological skills	8/14/2025 9:24 AM
21	Could the panel members address use of the diagnosis “HSIL/CIN2-3” when the morphologic features show both CIN2 and CIN3? Should you only report the higher grade? No need for P16 in this scenario, correct?	8/14/2025 9:15 AM
22	Please send to the American Society of Dermatopathology for review and comment as some of these lesions are biopsied and sent to dermatopathology.	8/14/2025 9:02 AM
23	Reflex HPV testing to be included the first time diagnosis in all patients.	8/14/2025 8:40 AM
24	Having had to complete this survey at least 5 times because a pop-up tells me that the survey has been modified by its creators is, ironically enough, a [pain].	8/14/2025 8:25 AM