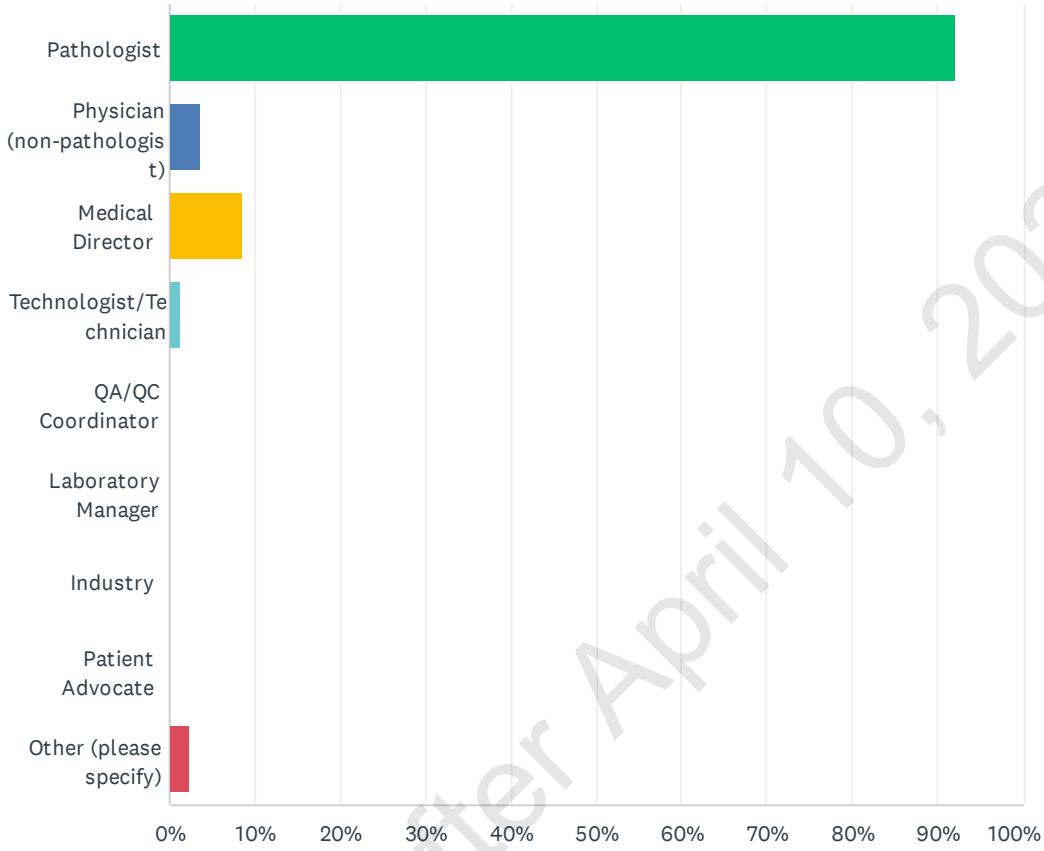
Q1 What is your occupation/role? (select all that apply)

Answered: 164 Skipped: 0



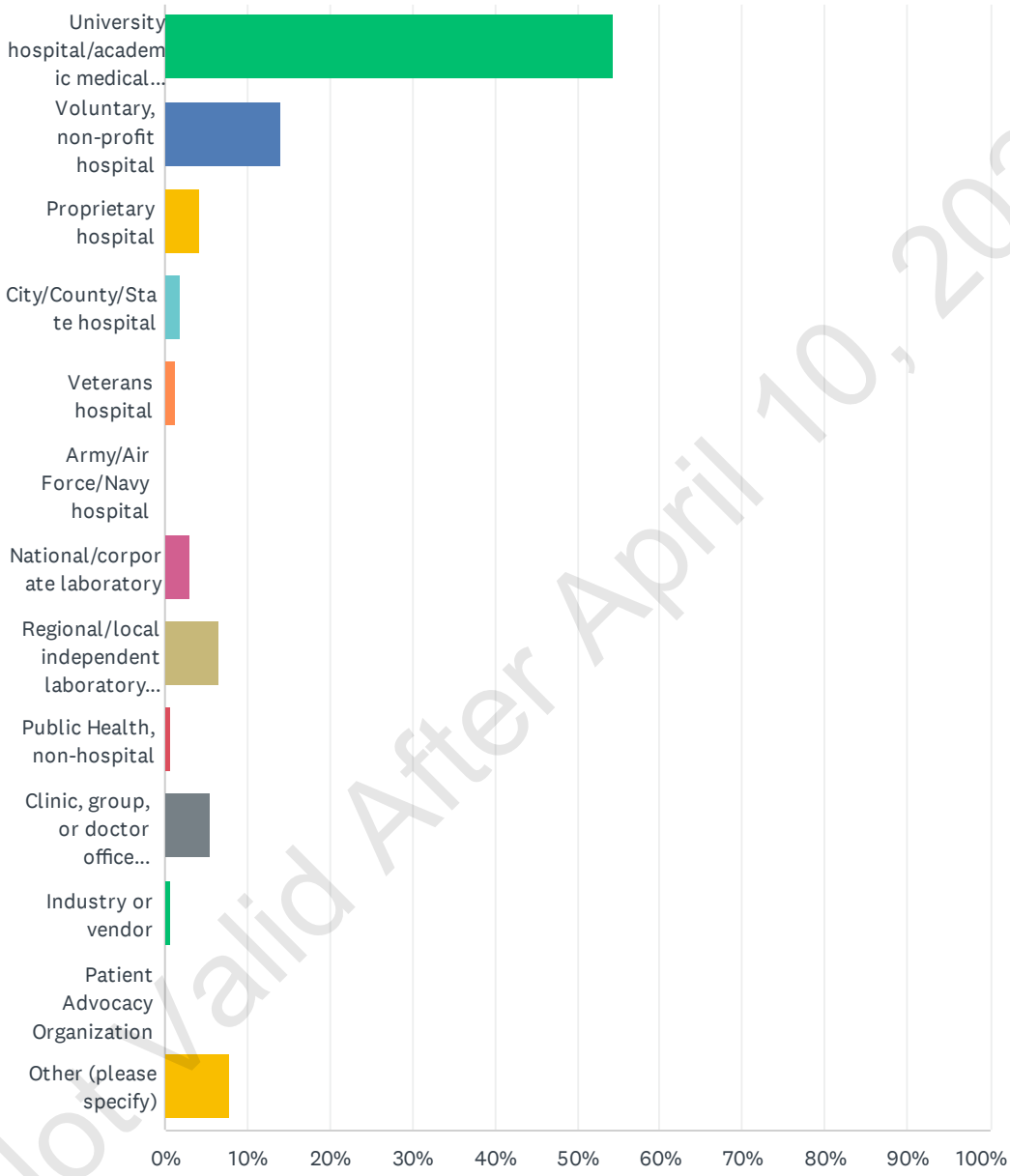
ANSWER CHOICES	RESPONSES	
Pathologist	92.07%	151
Physician (non-pathologist)	3.66%	6
Medical Director	8.54%	14
Technologist/Technician	1.22%	2
QA/QC Coordinator	0.00%	0
Laboratory Manager	0.00%	0
Industry	0.00%	0
Patient Advocate	0.00%	0
Other (please specify)	2.44%	4
Total Respondents: 164		

#	OTHER (PLEASE SPECIFY)	DATE
1	CAP employee	3/18/2025 9:10 AM

2	CAP Staff	3/18/2025 8:42 AM
3	Senior Director - Gastrointestinal Pathology	3/17/2025 2:02 PM
4	media	3/17/2025 1:35 PM

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

Answered: 164 Skipped: 0

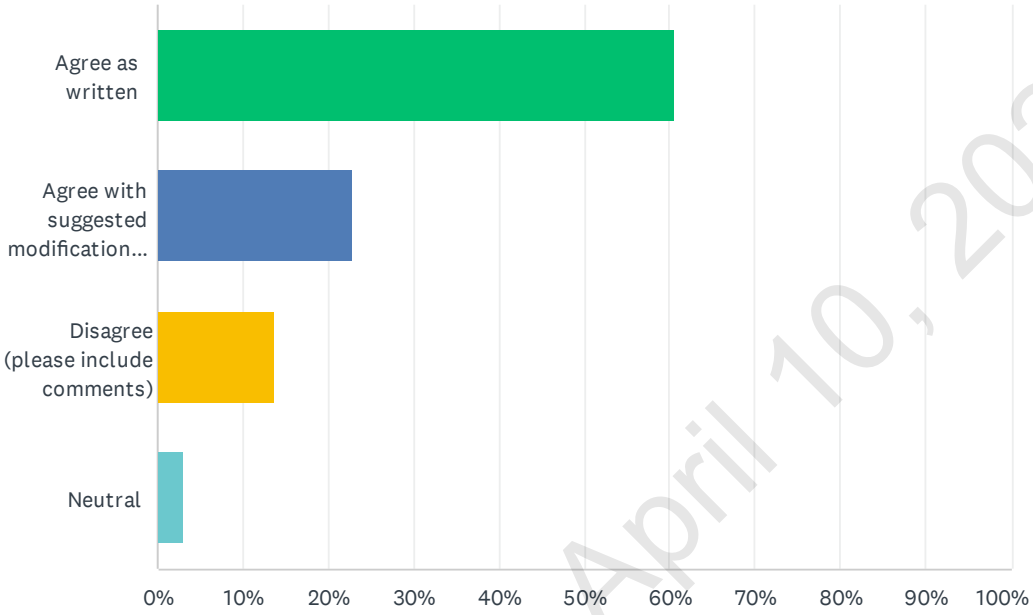


ANSWER CHOICES	RESPONSES	
University hospital/academic medical center	54.27%	89
Voluntary, non-profit hospital	14.02%	23
Proprietary hospital	4.27%	7
City/County/State hospital	1.83%	3
Veterans hospital	1.22%	2
Army/Air Force/Navy hospital	0.00%	0
National/corporate laboratory	3.05%	5
Regional/local independent laboratory (except clinic or group practice and not owned by a national corporation(s))	6.71%	11
Public Health, non-hospital	0.61%	1
Clinic, group, or doctor office laboratory	5.49%	9
Industry or vendor	0.61%	1
Patient Advocacy Organization	0.00%	0
Other (please specify)	7.93%	13
TOTAL		164

#	OTHER (PLEASE SPECIFY)	DATE
1	for profit hospital	3/28/2025 12:50 PM
2	Retired pediatric pathologist	3/27/2025 9:25 PM
3	independent pahologist	3/27/2025 8:38 PM
4	CRO	3/20/2025 1:55 PM
5	CRO	3/18/2025 9:27 AM
6	Association	3/18/2025 9:10 AM
7	CAP LAP Department	3/18/2025 8:42 AM
8	Whatever	3/18/2025 7:09 AM
9	DHA reference lab	3/17/2025 8:16 PM
10	Private Lab	3/17/2025 3:03 PM
11	Private lab	3/17/2025 2:11 PM
12	retired	3/17/2025 2:08 PM
13	media	3/17/2025 1:35 PM

Q3 Draft Statement 1 – When scoring GEP-NETs, pathologists must perform Ki67 grading on FNA/FNB or endoscopic biopsy.(Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



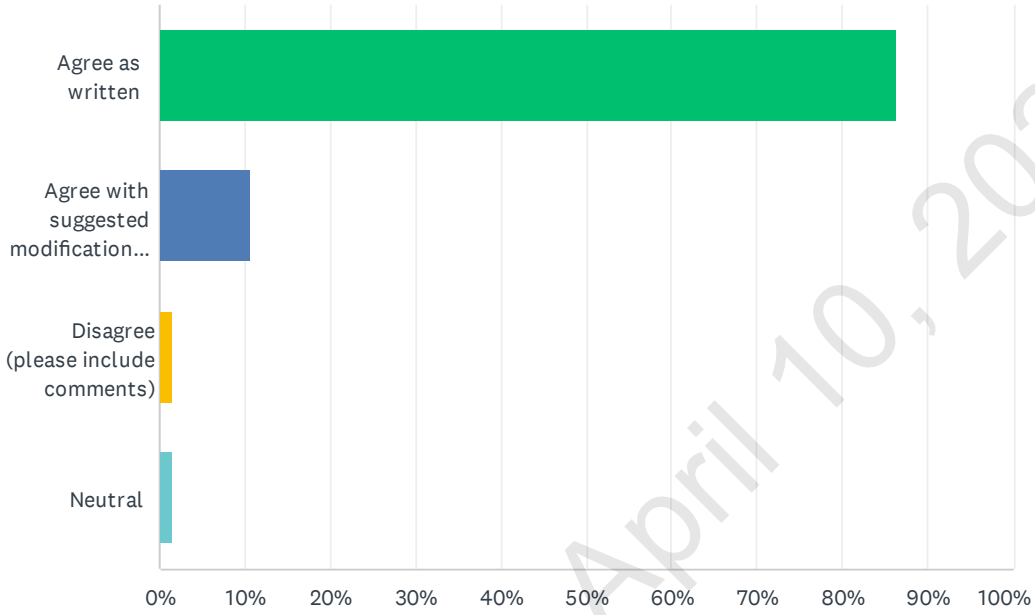
ANSWER CHOICES	RESPONSES	
Agree as written	60.61%	40
Agree with suggested modifications (please include comments)	22.73%	15
Disagree (please include comments)	13.64%	9
Neutral	3.03%	2
TOTAL		66

#	COMMENTS	DATE
1	Does not account for potential "hot spots"	4/3/2025 3:54 PM
2	Making a "STRONG RECOMMENDATION" that can include "MUST" or "SHOULD" needs to be supported by "high or moderate quality of evidence". Since NONE of these statements are supported by HIGH or even MODERATE CERTAINTY evidence, I cannot agree to any strong recommendations.	4/2/2025 6:51 PM
3	Is there a minimum tumor cell count needed?	3/29/2025 9:03 AM
4	Utilizing FNA/FNB as well as biopsy for Ki67 it should be taken to the account that the "hot" spot might not be present in the sample provided.	3/28/2025 12:15 PM
5	The low certainty of evidence argues against requiring such a practice. In addition intratumoral heterogeneity may be present and unsampled, potentially changing treatment plans.	3/28/2025 8:07 AM
6	may not be accurate on small tissue	3/28/2025 6:49 AM

7	for low income or resources "must" should be replaced with " recommended"	3/27/2025 10:03 PM
8	The tumor is fragmented or crushed in a lot of biopsies which make counting mitosis and ki67 difficult. In sone of the case there might not be enough cells. It might be a good idea to add “when possible”	3/27/2025 6:23 PM
9	Provided there are sufficient tumor cells. Some aspirations very hypocellular, may not allow for an accurate estimation/extrapolation of ki67	3/27/2025 3:41 PM
10	Ki67 grading is time-consuming and more costly than mitotic counts. While preliminary grading is important in biopsy specimens, treatment and prognosis will be determined by the grade as determined on the resection specimen.	3/27/2025 2:12 PM
11	Cytology cases perhaps should have a minimum number of cells present or a decent core for evaluation.	3/27/2025 1:51 PM
12	Make certain that issues with alcohol fixation and ki-67 are discussed in the text	3/27/2025 1:36 PM
13	Ki67 may be more difficult to evaluate in FNA specimens due to disaggregation of lesional cells.	3/22/2025 1:08 PM
14	If there is sufficient material (>100 cells)	3/20/2025 8:30 AM
15	Validation of KI67 in varying fixation conditions has not been adequately done and pilot studies on my part have shown deceraesed performance.	3/20/2025 8:29 AM
16	Always put a comment that Ki-67 grading may not be accurately representative of the entire tumor.	3/18/2025 12:57 PM
17	Should (not must)	3/18/2025 12:18 PM
18	Because some samples may be too scant to accurately assess for Ki-67, I would recommend making this a suggestion and not a requirement.	3/18/2025 7:32 AM
19	Depends on the number of tumor cells present in the cell block or biopsy, therefore should be worded as 'should' rather than must. Also should have a caveat allowing for inadequate cellularity for meaningful result, i.e. along the lines of 'provided that there are sufficient number of tumor cells'.	3/17/2025 10:05 PM
20	If a sufficient number of tumor cells are present	3/17/2025 9:30 PM
21	provided cellularity is adequate	3/17/2025 4:24 PM
22	Small biopsies might give false reading.	3/17/2025 4:01 PM
23	Most important and applicable to all: Please define and carefully introduce "scoring." WHO considers grading a combination of mitotic count and Ki67 proliferation index. Sounds like you want to use "grade" for Ki67 and "score" for what WHO calls "grade." I find that risky and unnecessarily confusing.	3/17/2025 3:05 PM
24	On a limited material, comment may be included in the report that proliferative index may not be representative of the entire lesion.	3/17/2025 2:15 PM
25	with comment that the grade is limited by sample size	3/17/2025 2:09 PM

Q4 Draft Statement 2 – When surgical resection is available, pathologists must repeat Ki67 grading on the resection.(Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



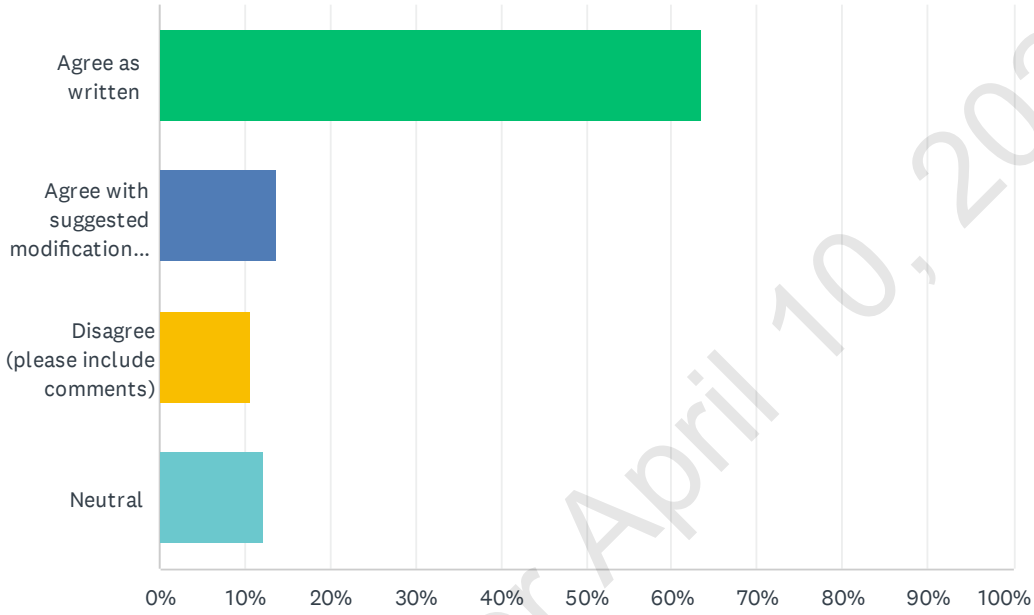
ANSWER CHOICES	RESPONSES	
Agree as written	86.36%	57
Agree with suggested modifications (please include comments)	10.61%	7
Disagree (please include comments)	1.52%	1
Neutral	1.52%	1
TOTAL		66

#	COMMENTS	DATE
1	Making a "STRONG RECOMMENDATION" that can include "MUST" or "SHOULD" needs to be supported by "high or moderate quality of evidence". Since NONE of these statements are supported by HIGH or even MODERATE CERTAINTY evidence, I cannot agree to any strong recommendations.	4/2/2025 6:51 PM
2	must repeat Ki67 grading or mitotic figure count	3/28/2025 8:07 AM
3	for low income or resources "must" should be replaced with " recommended"	3/27/2025 10:03 PM
4	The word "must" is a strong obligatory statement. It would be better to say "it is strongly recommended" to mitigate medicolegal risk. Furthermore, Ki67 may not have been performed on the biopsy specimen (see statement 1 above).	3/27/2025 2:12 PM
5	"pathologists must perform Ki67 grading on the resection" "repeat" only is applicable if there is a previous biopsy	3/19/2025 11:49 AM
6	If the biopsy was grade 2, Ki-67 may not need to be repeated on the resection if the mitotic	3/18/2025 2:50 PM

	rate is not close to grade 3.	
7	Should (not must)	3/18/2025 12:18 PM
8	If grade 3 on FNA/FNB or endo bx, no repeat scoring needed -- you're not going to downgrade it.	3/17/2025 2:10 PM

Q5 Draft Statement 3 – In patients with multiple primaries undergoing resection, pathologists should perform Ki67 grading on all primary tumors if possible. Note: The largest tumors should be tested for Ki67. (Conditional Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



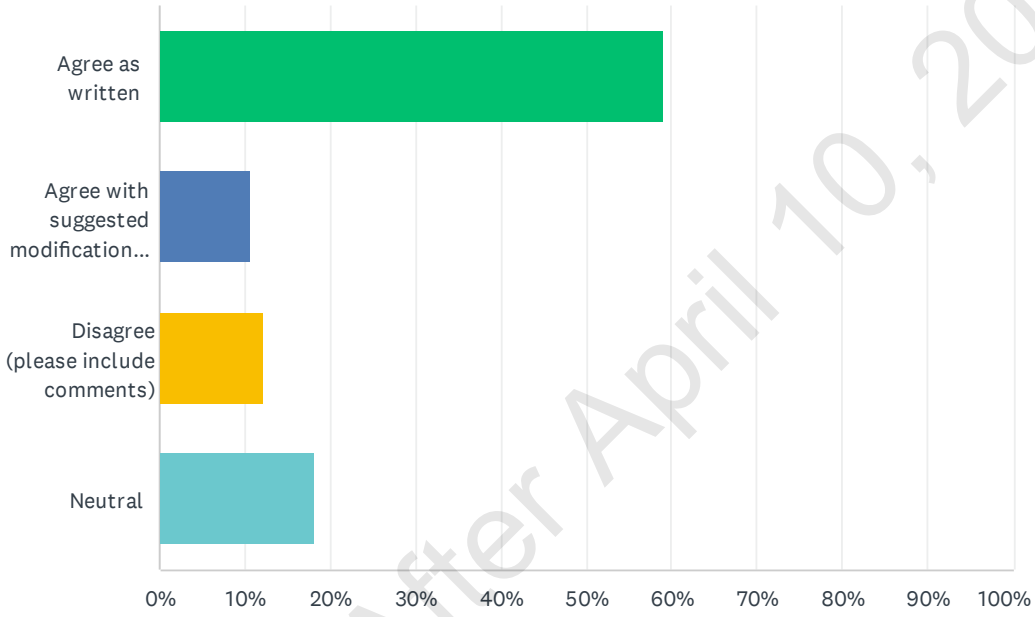
ANSWER CHOICES	RESPONSES	
Agree as written	63.64%	42
Agree with suggested modifications (please include comments)	13.64%	9
Disagree (please include comments)	10.61%	7
Neutral	12.12%	8
TOTAL		66

#	COMMENTS	DATE
1	I am not sure how applicable this will be in practice. It may be difficult or impossible to distinguish multiple primaries from metastatic foci. Because this is just a a "conditional" recommendation, I cannot categorically disagree, but I would reconsider the practicality of this recommendation.	4/2/2025 6:51 PM
2	Strong recommendation	4/2/2025 2:34 PM
3	The language is self-contradictory, all vs. largest, and is not specific. Suggest "Up to 3 largest primary tumors should be tested for Ki67"	3/30/2025 9:25 AM
4	This statement should be edited to comport better with the "conditional recommendation" status. Without the parenthetical information, this statement reads as a strong recommendation.	3/28/2025 8:07 AM
5	Largest tumors (is there a maximum number of tumors to stain)	3/28/2025 6:49 AM

6	for low income or resources "must" should be replaced with " recommended"	3/27/2025 10:03 PM
7	Perform on largest tumor, others at discretion of pathologist.	3/27/2025 2:17 PM
8	If Ki67 grading is the preferred method of grading, it should be performed on the most mitotically active tumor which may or may not be the largest tumor.	3/27/2025 2:12 PM
9	This is going to cause massive confusion in regard to how many tumors should be evaluated if they are all of similar size. More granularity would be useful here.	3/27/2025 1:36 PM
10	One synoptic report should be made and should reflect the tumor with the highest grade.	3/20/2025 8:30 AM
11	The largest tumor is not always the one with the highest Ki67	3/19/2025 11:49 AM
12	No need to perform Ki-67 on all primary tumors. Not cost effective. Do Ki-67 either on the largest tumor and/or on the one with highest mitotic activity.	3/18/2025 12:57 PM
13	This recommendation is vague regarding which tumor should be tested as there is no size cutoff for "largest." Also, in practical terms, this requirement may be particularly onerous for those without a digital automated counting system.	3/18/2025 7:32 AM
14	Seems to be an inconsistency between 'all primary tumors' and 'Note: The largest tumor should be tested...'	3/17/2025 10:05 PM
15	The largest tumors from each presumed primary site should be tested for Ki67	3/17/2025 3:15 PM
16	In patients with multiple primaries undergoing resection, pathologists should perform Ki67 grading on the largest tumor and on the tumor with the highest mitotic activity if the tumor with the highest mitotic activity is not the largest tumor.	3/17/2025 3:05 PM
17	Suggestion to do Ki-67 on the largest lesion, any mesenteric deposit greater than or equal to 2.0 cm and/or any other focus which may appear to be higher histological grade, necrosis, apoptosis or higher mitotic activity on H&E staining.	3/17/2025 2:15 PM
18	If primary tumor is very small, it may not be necessary. Large metastatic deposits may have higher Ki67.	3/17/2025 2:09 PM

Q6 Draft Statement 4 – Pathologists must perform Ki67 grading on lymph node metastases and/or mesenteric mass (in small intestinal NET) in addition to primary resections, provided that there are sufficient number of tumor cells. Note: In cases with multiple lymph node and/or mesenteric masses, the largest tumor should be tested for Ki67.(Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



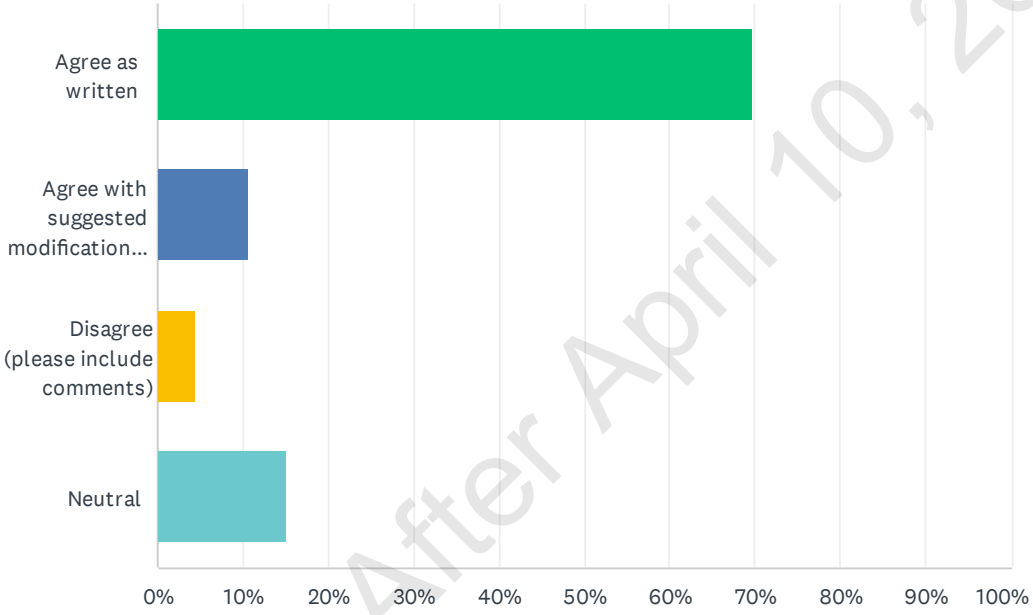
ANSWER CHOICES	RESPONSES	
Agree as written	59.09%	39
Agree with suggested modifications (please include comments)	10.61%	7
Disagree (please include comments)	12.12%	8
Neutral	18.18%	12
TOTAL		66

#	COMMENTS	DATE
1	Do not see the prognostic benefit in that…it's already metastatic, so it's aggressive	4/3/2025 3:54 PM
2	Making a "STRONG RECOMMENDATION" that can include "MUST" or "SHOULD" needs to be supported by "high or moderate quality of evidence". Since NONE of these statements are supported by HIGH or even MODERATE CERTAINTY evidence, I cannot agree to any strong recommendations.	4/2/2025 6:51 PM
3	Suggest up to 3 largest tumors	3/30/2025 9:25 AM
4	Presence of lymph node metastasis and mesenteric masses already means that it is an aggressive tumor.	3/28/2025 12:15 PM

5	for low income or resources "must" should be replaced with " recommended"	3/27/2025 10:03 PM
6	One metastatic site (largest).	3/27/2025 2:17 PM
7	Due to tumor heterogeneity, it is necessary to grade metastases and/or mesenteric tumors. If Ki67 is performed, it should be performed on the most mitotically active metastasis.	3/27/2025 2:12 PM
8	Insufficient data to support this recommendation.	3/27/2025 1:52 PM
9	If the Ki67 grading guides whether we consider lesions to be aggressive, the presence of lymph node metastases basically confirms aggressiveness. If there's no strong evidence that scoring both primary and metastatic sites guides treatment or predicts outcome, why are we spending time and money on this?	3/27/2025 1:51 PM
10	Testing thre primary and regional disease is in adequate. The distant disease site (usually liver) must also be included since there are alot of cases where the highest WHO grade is in the liver, and that is the one that will drive prognosis	3/27/2025 1:13 PM
11	I agree with performing on as many sites as possible because there is marked tumor heterogeneity. However I do not agree that only the largest should be tested.	3/19/2025 11:49 AM
12	Is there data showing regional lymph node metastases having significant differences of Ki67 from primary tumor?	3/18/2025 12:57 PM
13	Perform ki-67 on the largest one and/or on the one with the highest mitotic activity	3/18/2025 12:57 PM
14	testing Ki67 in primary tumour only.	3/18/2025 9:22 AM
15	In practical terms, this requirement may be particularly onerous for those without a digital automated counting system.	3/18/2025 7:32 AM
16	Ki67 is a measure of behavior, not sure what evidence is for staining LN and primary, when the biology is already known to be metastatic. In such case, staining LN OR mesenteric (not LN AND Mesenteric) mass. I would remove "and/or" and leave just "or"	3/17/2025 3:15 PM
17	In this context, please provide discussion what the biological meaning of a higher Ki67 proliferation index in a metastasis would mean. Maybe the word "grade" is not appropriate anymore because traditionally grading was only done on the primary tumor and not the met (not everyone using this is a GI pathologist). The concept of primary tumor(s) and met(s) being considered a single neoplastic entity that has a grade (no matter where that grade is highest) would have to be discussed in the guideline. The WHO is not very good at it. All this also pertains to Draft Statement 5.	3/17/2025 3:05 PM
18	Would favor more to get Ki-67 on mesenteric mass but not on smaller isolated nodal metastasis.	3/17/2025 2:15 PM

Q7 Draft Statement 5 – In patients with metastatic GEP-NETs, pathologists must report tumor grade for both primary and metastatic tumors for clinical management. Note: The final reported grade must be based on the higher grade of the primary or metastatic tumor if resected simultaneously. Note: In multiple metastatic samples, the largest metastasis per site should be tested for Ki67. (Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



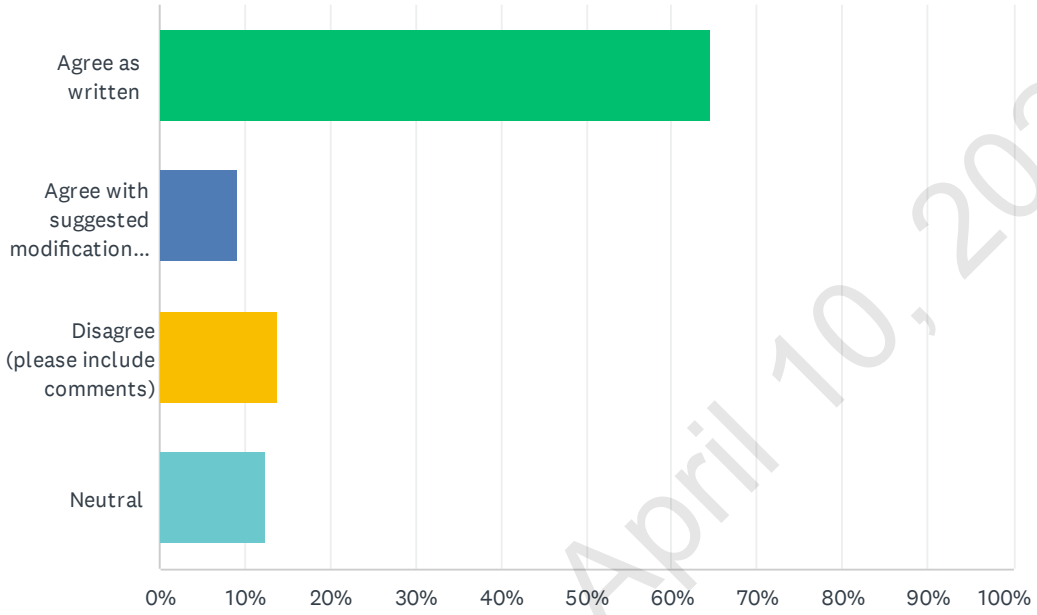
ANSWER CHOICES	RESPONSES	
Agree as written	69.70%	46
Agree with suggested modifications (please include comments)	10.61%	7
Disagree (please include comments)	4.55%	3
Neutral	15.15%	10
TOTAL		66

#	COMMENTS	DATE
1	Making a "STRONG RECOMMENDATION" that can include "MUST" or "SHOULD" needs to be supported by "high or moderate quality of evidence". Since NONE of these statements are supported by HIGH or even MODERATE CERTAINTY evidence, I cannot agree to any strong recommendations. I agree with the notion of the final grade being based on the highest grade area. I would not report multiple grades in the same specimen - it will lead to confusion. And again, you are violating the rules you set for yourself in making a strong recommendation on low certainty evidence.	4/2/2025 6:51 PM
2	Suggest up to 3 largest.	3/30/2025 9:25 AM

3	This is a lot of work for low certainty of evidence. The costs to time will likely outweigh the perceived benefit to patients without supporting evidence. Changing this behavior could be quite difficult in practice.	3/28/2025 8:07 AM
4	How would pathologists/clinicians handle a scenario where the largest same-site (eg: liver) metastatic focus was not the highest ki67? Or hypothetical scenario where you do not run Ki67 on a smaller metastatic focus yet that would have resulted in a higher grade tumor.	3/27/2025 3:41 PM
5	Report higher grade	3/27/2025 2:17 PM
6	If Ki67 is performed, it should be performed on the most mitotically active metastatic tumor. If they have similar mitotic counts, the largest should be chosen.	3/27/2025 2:12 PM
7	If the Ki67 grading guides whether we consider lesions to be aggressive, the presence of lymph node metastases basically confirms aggressiveness. If there's no strong evidence that scoring both primary and metastatic sites guides treatment or predicts outcome, why are we spending time and money on this?	3/27/2025 1:51 PM
8	Agree with the concept but disagree that the largest metastasis per site should be tested - as many as can be should be tested	3/19/2025 11:49 AM
9	Perform ki-67 on the largest metastatic site and/or the one with the highest mitotic activity.	3/18/2025 12:57 PM
10	Grade of primary tumour represents metastatic tumour.	3/18/2025 9:22 AM
11	Some metastases have differing levels of differentiation or presence of aggressive features such as an “invasive” growth pattern, desmoplasia, or PNI, LVI. Some large tumors have indolent histology such as hyalinized stoma, endocrine type nuclear atypia etc. The most aggressive lesion should be tested which may be necessarily be the largest.	3/17/2025 3:31 PM

Q8 Draft Statement 6 – For scoring of GEP-NETs, pathologists may use mitotic count in addition to the Ki67 grading.(Conditional Recommendation, Low Certainty of Evidence)

Answered: 65 Skipped: 99



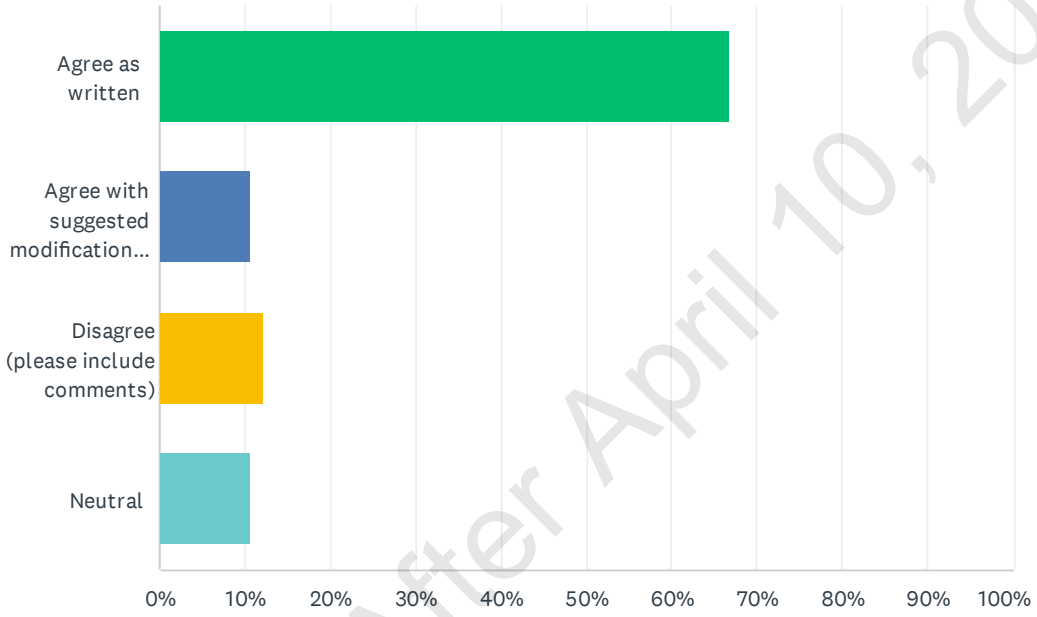
ANSWER CHOICES	RESPONSES	
Agree as written	64.62%	42
Agree with suggested modifications (please include comments)	9.23%	6
Disagree (please include comments)	13.85%	9
Neutral	12.31%	8
TOTAL		65

#	COMMENTS	DATE
1	I've always been told that the Ki67 and mitotic count don't correlate well.	4/3/2025 3:54 PM
2	The way I read this, you are contradicting some of your other statements that say you MUST use Ki-67 grading. This recommendation is more consistent with the rules for recommendations you are supposed to be following, though.	4/2/2025 6:51 PM
3	Strong recommendation	4/2/2025 2:34 PM
4	Ki67 is considered superior to mitotic count.	3/28/2025 12:15 PM
5	The key word is "may"	3/27/2025 9:26 PM
6	Counting both mitosis and ki67 is very time consuming especially in GI services that are very busy. Ki67 seems to be enough.	3/27/2025 6:23 PM
7	KI-67 is a much better estimate of prognosis than mitosis	3/27/2025 6:16 PM
8	I wouldn't make extra work if there is low certainty of evidence	3/27/2025 3:53 PM

9	At pathologist's discretion, if visibly discordant with ki67	3/27/2025 2:17 PM
10	Ki67 should be primary method of assessment of proliferation.	3/22/2025 1:08 PM
11	these counts may vary depending on time prior to fixation	3/20/2025 8:29 AM
12	The higher grade should be used if there is discrepancy between mitotic count and ki67 count.	3/18/2025 12:57 PM
13	Pathologists must use mitotic count	3/17/2025 9:30 PM
14	mitotic count suffers from lower reproducibility and not as reliable as ki67. This creates more confusion when these parameters conflict. best to stick with Ki67	3/17/2025 3:15 PM
15	Please define and carefully introduce "scoring." WHO considers grading a combination of mitotic count and Ki67 proliferation index. Sounds like you want to use "grade" for Ki67 and "score" for what WHO calls "grade." I find that risky and unnecessarily confusing.	3/17/2025 3:05 PM
16	Needs to be standardized across the board and eliminate confusion, Ki-67 is the best way to do so.	3/17/2025 2:10 PM

Q9 Draft Statement 7 – When scoring GEP-NETs, pathologists should calculate Ki67 proliferation index using a manual count. Note: A printed camera captured image is preferred, although if a camera captured image is not available, a manual count may be performed under a microscope.Note: Eyeball estimation is not recommended. (Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



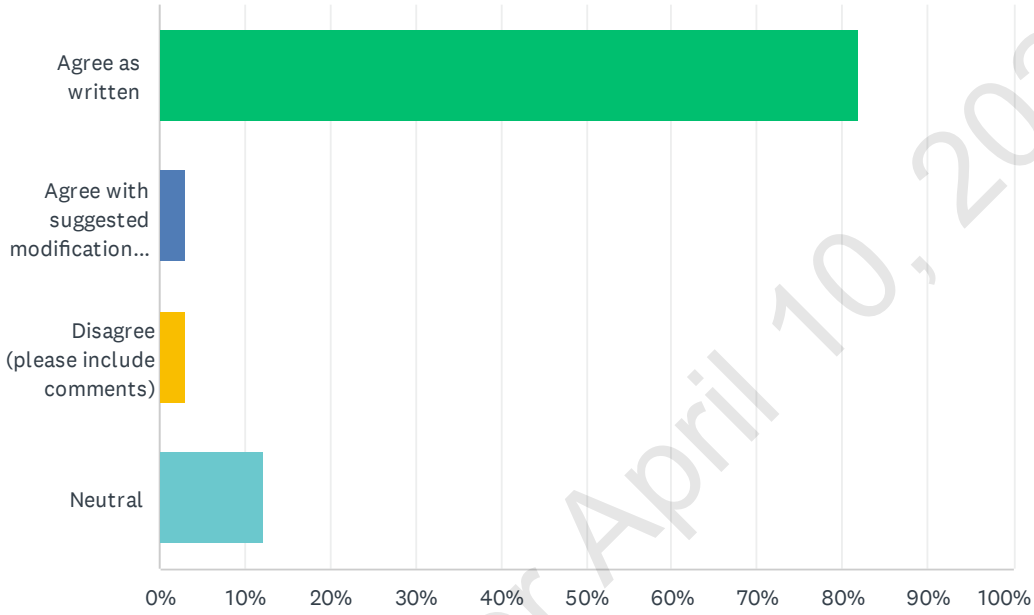
ANSWER CHOICES	RESPONSES	
Agree as written	66.67%	44
Agree with suggested modifications (please include comments)	10.61%	7
Disagree (please include comments)	12.12%	8
Neutral	10.61%	7
TOTAL		66

#	COMMENTS	DATE
1	While I agree with the statement that 'eyeball estimation is not recommended', and that a proper count is more precise, you are again making a "strong" recommendation on "low certainty of evidence", which I disagree with.	4/2/2025 6:51 PM
2	"Eyeball" estimation is often sufficient unless the values are close to cut points.	3/30/2025 9:25 AM
3	Quite a few programs are available to perform the count.	3/28/2025 12:15 PM
4	Low certainty of evidence for a much more cumbersome process. I agree with the idea, but there has to be a better way to risk stratify these patients.	3/28/2025 8:07 AM

5	Ki67 should be automated	3/27/2025 9:26 PM
6	Keep language as “should” ultimately should still be at pathologist’s discretion.	3/27/2025 2:17 PM
7	Agree that a manual count is preferred over eyeball estimation, however, mitotic counts may be used in place of Ki67 scoring (see statement 6)	3/27/2025 2:12 PM
8	Manual count if not obviously <3%, or obviously > 20%	3/27/2025 2:11 PM
9	If the Ki-67 proliferative index is virtually zero, eyeballing should be acceptable. It does not serve our patients well to waste time on such a count.	3/27/2025 1:50 PM
10	add "or an automated count that can be verified as accurate"	3/19/2025 11:49 AM
11	If we make a computer assisted count undergo validation, shouldn't we also require human counting to be validated? We know there is significant interobserver variability.	3/18/2025 2:50 PM
12	Pathology is going to digital and we should allow high tech like image analysis and AI to assist this counting	3/18/2025 12:57 PM
13	May (not should)	3/18/2025 12:18 PM
14	Strongly agree with the two notes.	3/17/2025 10:05 PM
15	I would recommend using digital automated counting rather than manual. Website-based tool can be developed to help pathologist without app.	3/17/2025 4:27 PM
16	Far too labor intensive method for routine practice.	3/17/2025 3:31 PM
17	Personally no one should be using either eyeball of manual counts these days of WSI	3/17/2025 3:15 PM

Q10 Draft Statement 8 – When scoring GEP-NETS, pathologists may use digital automated counting of Ki67 as an alternative to manual counting if properly validated.(Conditional Recommendation, Very Low Certainty of Evidence)

Answered: 66 Skipped: 98



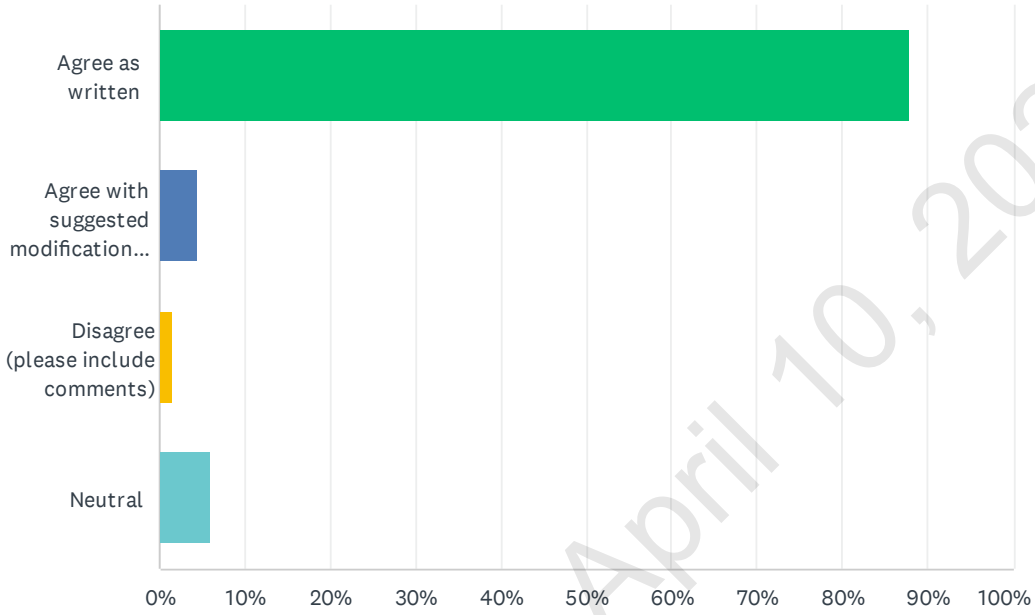
ANSWER CHOICES	RESPONSES	
Agree as written	81.82%	54
Agree with suggested modifications (please include comments)	3.03%	2
Disagree (please include comments)	3.03%	2
Neutral	12.12%	8
TOTAL		66

#	COMMENTS	DATE
1	I do not have access to digital automated counting and am abstaining from the vote in this one, but this seems reasonable thing to suggest.	4/2/2025 6:51 PM
2	While very promising, the automated counting programs that I have seen in the last 6 months have not been robust enough to codify this recommendation. The big players in medicine may be able to properly validate and maintain such systems, but may leave many smaller practices doing things much more slowly than the competition or cutting corners on validation. There is the potential for harm here.	3/28/2025 8:07 AM
3	More reproducible and less time consuming but not all laboratories will have digital automated counter.	3/27/2025 2:12 PM
4	Needs validation.	3/20/2025 8:29 AM
5	Proper validation and routine interval validations must be done for any digital software based	3/17/2025 2:15 PM

analysis. Note for moderators: We have noted that the image may be enhanced and automated reading may be affected. The digital software must have mechanism to lock the image enhancement by the user.

Q11 Draft Statement 9 – When scoring GEP-NETs, pathologists must grade Ki67 on hotspots.(Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



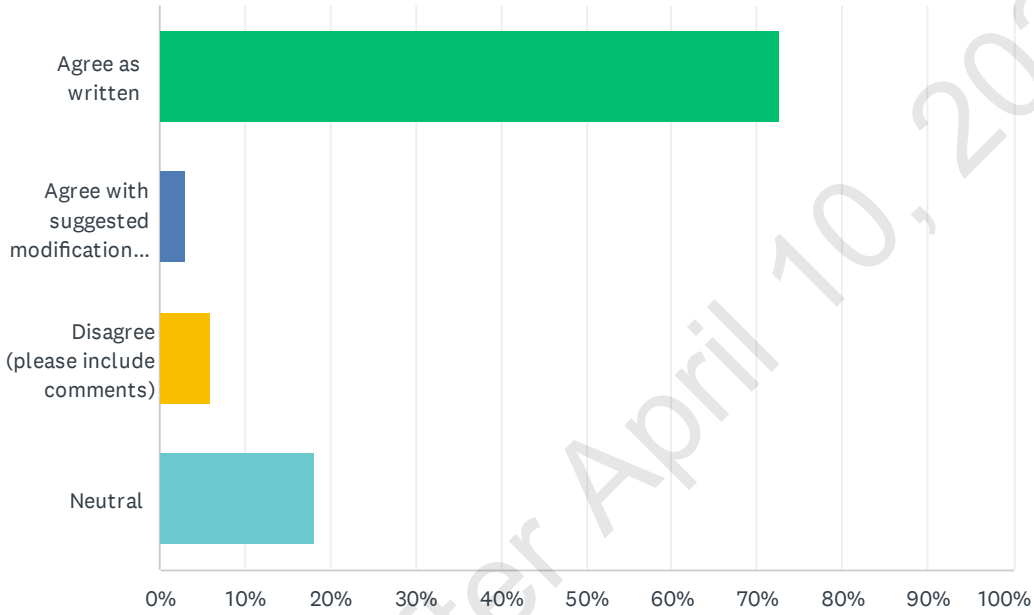
ANSWER CHOICES	RESPONSES	
Agree as written	87.88%	58
Agree with suggested modifications (please include comments)	4.55%	3
Disagree (please include comments)	1.52%	1
Neutral	6.06%	4
TOTAL		66

#	COMMENTS	DATE
1	Making a "STRONG RECOMMENDATION" that can include "MUST" or "SHOULD" needs to be supported by "high or moderate quality of evidence". Since NONE of these statements are supported by HIGH or even MODERATE CERTAINTY evidence, I cannot agree to any strong recommendations. I think that this is pretty standard practice. Unfortunately, selection of the 'hot spots' is almost certainly done on the basis of an 'eyeball estimate'. (Another inconsistency...)	4/2/2025 6:51 PM
2	Provided it is within a 20x field.	3/20/2025 8:30 AM
3	I think there needs to be recommendations around standardizing Ki-67 methodologies in general. We know there is significant variability in Ki-67 from lab to lab and from pathologist to pathologist. We are putting a lot of faith in a test that we all know is fundamentally poorly reproducible in the current state. All Ki-67 counts by any method should be validated against a standard.	3/18/2025 2:50 PM
4	Can we standardize? How many hot spots?	3/18/2025 12:57 PM

5	When grading GEP-NETs, pathologist must assess the Ki67 proliferation index in hotspots.	3/17/2025 3:05 PM

Q12 Draft Statement 10 – In mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs), pathologists should perform Ki67 grading in the NEN component. Note: The non-neuroendocrine component should be categorized based on the WHO tumor classification.(Strong Recommendation, Low Certainty of Evidence)

Answered: 66 Skipped: 98



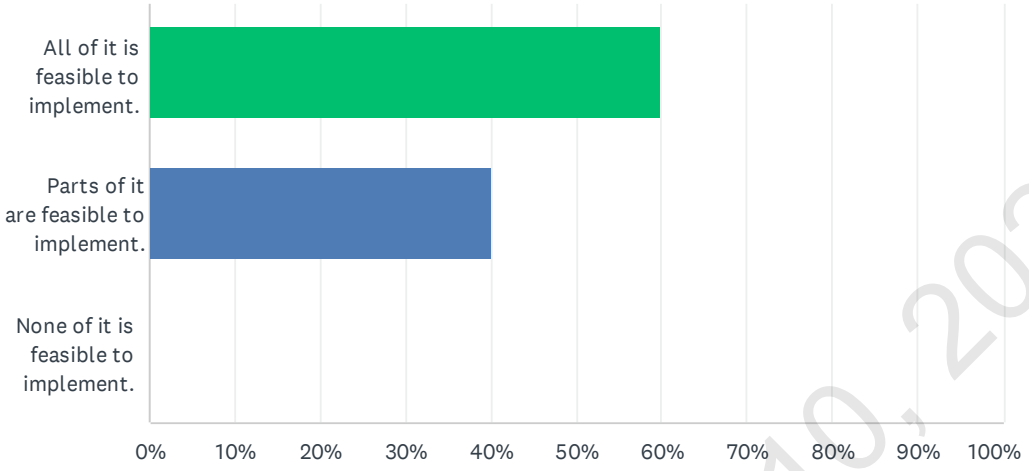
ANSWER CHOICES	RESPONSES	
Agree as written	72.73%	48
Agree with suggested modifications (please include comments)	3.03%	2
Disagree (please include comments)	6.06%	4
Neutral	18.18%	12
TOTAL		66

#	COMMENTS	DATE
1	Making a "STRONG RECOMMENDATION" that can include "MUST" or "SHOULD" needs to be supported by "high or moderate quality of evidence". Since NONE of these statements are supported by HIGH or even MODERATE CERTAINTY evidence, I cannot agree to any strong recommendations. If there is a carcinoma component that is most likely to drive the prognosis. I am not sure what value Ki-67 grading will add in the majority of cases. Making a "strong recommendation" seems like a stretch just in principle (let alone the low certainty of evidence).	4/2/2025 6:51 PM
2	Is there a minimum tumor cell count needed?	3/29/2025 9:03 AM
3	I am not certain how it is going to change the management. The grade of NEN component can be determined without Ki 67 count.	3/28/2025 12:15 PM
4	These tumors tend to behave like their non-neuroendocrine component and more aggressive	3/27/2025 2:12 PM

	than pure well-differentiated neuroendocrine tumors, hence grade of NEN is less important in determining behavior. With mixed tumors containing a poorly differentiated neuroendocrine component, these are all high grade and Ki67 grading is unnecessary.	
5	Most of GI MiNEN will be treated based on the nonneuroendocrine component. Proving Ki-67 might be confusing for clinical colleagues. Some of the cases might be interpreted as neuroendocrine carcinomas. It is better to provide on request after discussion with the clinician.	3/27/2025 1:48 PM

Q13 How feasible is it to implement this guideline?

Answered: 65 Skipped: 99

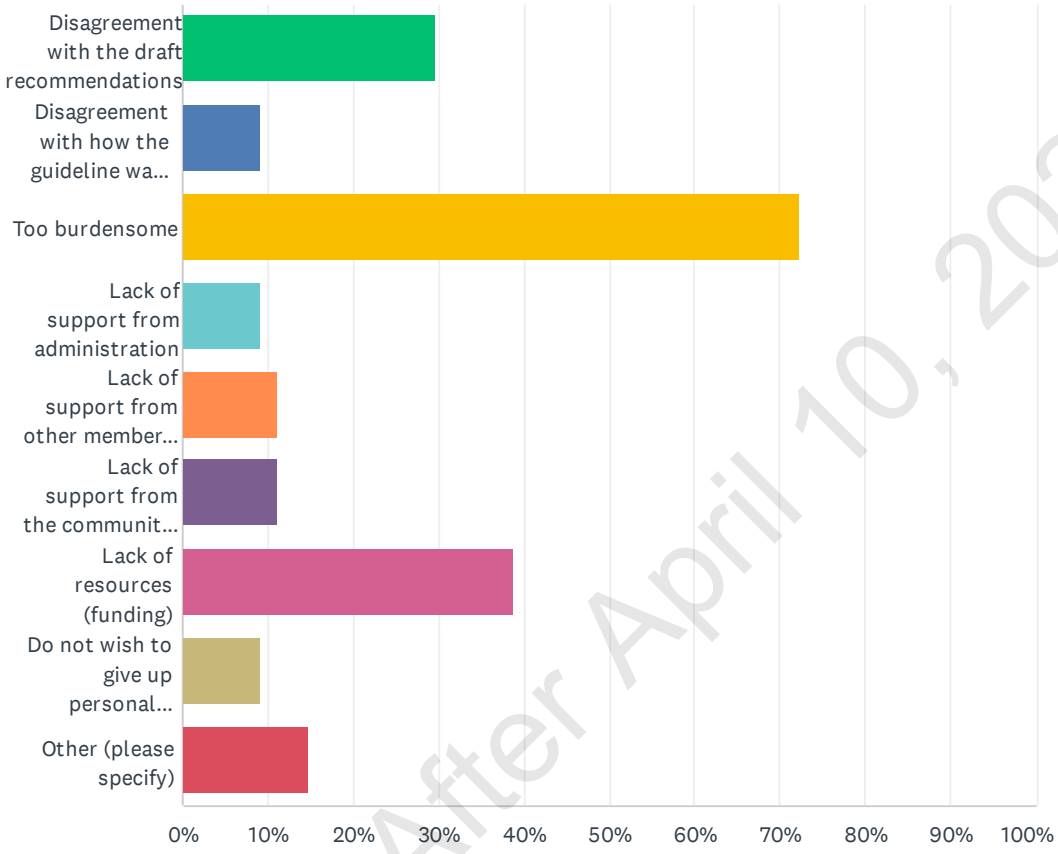


ANSWER CHOICES	RESPONSES	
All of it is feasible to implement.	60.00%	39
Parts of it are feasible to implement.	40.00%	26
None of it is feasible to implement.	0.00%	0
TOTAL		65

#	COMMENTS ABOUT THE FEASIBILITY OF IMPLEMENTING THE GUIDELINE:	DATE
1	I do not WANT to implement any of it because I think that all of the strong recommendations are not allowed given the low certainty of evidence.	4/2/2025 6:57 PM
2	It will increase time per case depending on number of mets/primaries.	3/29/2025 9:11 AM
3	requiring pathologists to do Ki67 on primary and LNs mets is impractical	3/27/2025 9:29 PM
4	All of it's feasible but the aim is to make things less rather than more burdensome	3/27/2025 3:55 PM
5	Generally grading of well-differentiated NETs by performing mitotic counts agree with Ki67 scoring. Unless there is strong evidence to the contrary, mitotic counts should be the preferred method, especially as a preliminary grade on non-resections specimens. Ki67 scoring is more costly and time-consuming, especially if utilizing more advanced methods like scoring a printed microscopic image.	3/27/2025 2:31 PM
6	Feasible but manual counts are time intensive for the pathologist or resident.	3/17/2025 10:06 PM
7	I don't think staining multiple blocks is going to be widely adopted so you probably shouldn't mandate something that isn't feasible. I also think that these recommendations should make it clear that this classification is only for first presentations of disease. The classification has not been validated in tumors that have significant treatment effects or multiple recurrences status post therapy. This is meant to predict behavior of the first presentation. We are seeing patient being treated with multiples different modalities including radio-pharmaceuticals such as lutathera. I don't think it is wise to grade these tumor stays post therapy using this system.	3/17/2025 3:44 PM
8	In cases with many tumor or metastases these recommendations could be burdensome	3/17/2025 2:15 PM

Q14 What barriers might impede adoption of the final guideline? (Choose all that apply.)

Answered: 54 Skipped: 110



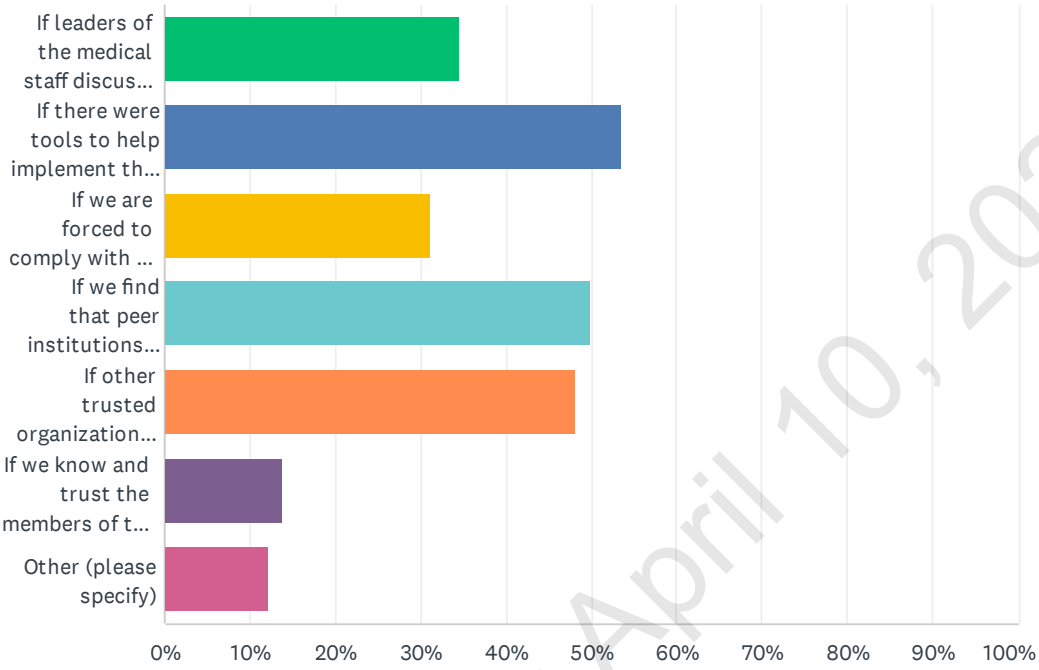
ANSWER CHOICES	RESPONSES	
Disagreement with the draft recommendations	29.63%	16
Disagreement with how the guideline was developed	9.26%	5
Too burdensome	72.22%	39
Lack of support from administration	9.26%	5
Lack of support from other members of the medical team	11.11%	6
Lack of support from the community (others outside your institution e.g., patients, industry)	11.11%	6
Lack of resources (funding)	38.89%	21
Do not wish to give up personal autonomy to follow the guideline	9.26%	5
Other (please specify)	14.81%	8
Total Respondents: 54		

#	OTHER (PLEASE SPECIFY)	DATE

1	often low certainty of evidence limits the incentive to make the changes proposed.	3/28/2025 8:09 AM
2	Too many "strong recommendations" with "low level" evidence pair ups.	3/27/2025 1:38 PM
3	If made a requirement for accreditation, it will be feasible!	3/19/2025 11:50 AM
4	Performing multiple Ki-67's on the same case might not be covered by some payors.	3/18/2025 2:57 PM
5	My main concern is that some draft recommendations would be too burdensome for those in busy practices without a digital automated counting system.	3/18/2025 7:35 AM
6	See above	3/17/2025 3:44 PM
7	The scoring/grading terminology will be confusing	3/17/2025 3:07 PM
8	Digitization and automation may work in institutional systems but may be burdensome for smaller laboratories.	3/17/2025 2:20 PM

Q15 What facilitators might assist in your adoption of the final guideline? (Please select your top 3 facilitators.)

Answered: 58 Skipped: 106



ANSWER CHOICES	RESPONSES	
If leaders of the medical staff discussed adoption/adaption of the guideline for our practice setting	34.48%	20
If there were tools to help implement the guideline	53.45%	31
If we are forced to comply with the guideline by administration or an accreditation body	31.03%	18
If we find that peer institutions/practices adopt the guideline	50.00%	29
If other trusted organizations endorse the guideline	48.28%	28
If we know and trust the members of the panel members and/or organizations who developed the guideline	13.79%	8
Other (please specify)	12.07%	7
Total Respondents: 58		

#	OTHER (PLEASE SPECIFY)	DATE
1	Some of the panel members should work to develop stronger evidence to support making guidelines/recommendations.	4/2/2025 6:57 PM
2	Pier-reviewed evidence based scientific evidence.	3/27/2025 2:31 PM
3	This is time consuming and most places are short staffed. Are we going to be paid extra for printing a camera image and calculating the ki-67---there needs to be a billing code for this.	3/27/2025 1:38 PM
4	If clinicians agree that the tumor with highest Ki67 (whether it be in multiple primaries, lymph nodes, metastases), are actionable over the primary.	3/20/2025 8:32 AM

5	If there was a clear discussion of the evidence supporting the guideline.	3/18/2025 2:57 PM
6	Reimbursement for multiple Ki67 stains on a single specimen by CMS	3/18/2025 8:00 AM
7	Increased reimbursement for 88360 or automated counting code.	3/17/2025 9:31 PM

Q16 Please provide any general comments or concerns:

Answered: 9 Skipped: 155

#	RESPONSES	DATE
1	I have already made clear my opposition to these guidelines. The problem is that making and publishing a guideline like this leads to the supposition that the guidelines were based on sound evidence. As you stated for EACH draft statement, you have low (or even very low) quality of evidence. Eventually guidelines have a way of becoming accepted as fact, and when that happens the impetus to produce higher quality evidence disappears.	4/2/2025 6:57 PM
2	I think the guidelines should clearly state the minimum tumor cells needed for manual Ki-67 count. And allow for a statement if FNA, biopsy, or Ki-67 level does not contain minimum number of tumor cells,	3/29/2025 9:11 AM
3	I think the diagnostic term and clinical implication of "large cell neuroendocrine carcinoma" need to be addressed. The morphologic criteria for LCNEC are poorly defined with significant inter-observer variability. There is non-specific NE marker positive staining in these tumors if NE markers are performed routinely. Can this category be eliminated so there will be neuroendocrine tumors, small cell carcinomas, or poorly differentiated adenocarcinoma/squamous cell carcinomas (with NE marker expressions).	3/28/2025 5:27 PM
4	The current recommendation listed in the CAP protocol of using either mitotic counts or Ki67 scoring for grading of NETs is the preferred option. It is less restrictive and gives more flexibility to requiring Ki67 scoring. Furthermore, it is much easier to count mitotic figures per 40-50 high power fields than evaluating 500+ tumor cells for Ki67 staining. The grade cutoffs for the two methods should be adjusted to allow greater concordance between the two methods of grading.	3/27/2025 2:31 PM
5	Mitotic count may be performed with an automated system, if properly validated.	3/17/2025 9:31 PM
6	The guideline should INCLUDE what kinds of Ki-67 positive cells should be counted: weakly stained vs strongly stained vs both. This is very IMPORTANT for getting the Ki-67 proliferation index.	3/17/2025 5:30 PM
7	See above comments regarding suitability of classification for first presentations of disease and not for tumor with recurrent subsequent to treatment.	3/17/2025 3:44 PM
8	I think it would be perfectly fine to add a phase 0 checklist question asking whether the lab reports NET grade (or score) using this guideline.	3/17/2025 3:07 PM
9	Ki-67 proliferation index is better and relatively more objective as compared to mitotic count. It should be a preferred way for grading of GEP-NETs.	3/17/2025 2:20 PM