Response to Peer-Review Reports

Dear Editor and Reviewers,

We sincerely thank the reviewers for their thoughtful, constructive, and highly valuable comments regarding our Letter to the Editor. We have carefully revised the manuscript to address all the issues raised. We believe these revisions have significantly improved the clarity, balance, and scientific rigor of our letter.

Below, please find our point-by-point responses to each reviewer's comments.

Reviewer #1

Specific Comments to Authors:

This letter to the editor provides a thoughtful and well-articulated critique of the study by Hopley et al... The manuscript is suitable for publication pending minor revisions to improve clarity and address a few factual/editorial inconsistencies.

Response: We sincerely thank the reviewer for the positive appraisal of our manuscript and for the highly constructive suggestions.

Comment (1): *The authors argue that early resections may reflect "discovery bias" rather than true early malignancy. This is a valid point, but the letter would benefit from a brief explanation of why discovery bias matters for surveillance de-escalation. For example, if many early resections were performed because of incidental findings that triggered immediate workup (rather than true progression), then excluding those cases from long-term surveillance analysis could artificially inflate the safety of early discharge. A single sentence clarifying this mechanism would strengthen the argument.*

Response: We fully agree with this important point. To clarify why discovery bias is relevant in the context of surveillance de-escalation, we have added a sentence explaining that when early resections are prompted by the immediate workup of incidentally detected lesions rather than true rapid biological progression, excluding these patients from the long-term surveillance denominator may artificially overestimate the perceived safety of early discharge.

Line 65-68,

Specifically, if early resections result from the immediate evaluation of incidentally detected lesions rather than true rapid biological progression, excluding these patients from long-term follow-up analyses may lead to an overestimation of the safety of earl

y surveillance discontinuation.

Comment (2): *The letter is persuasive, but it does not acknowledge that Hopley et al. may have intentionally chosen a pragmatic "real-world" approach that includes discovery-phase events. Some guideline developers might argue that discovery bias is irrelevant because surveillance decisions must account for real-world clinical presentation, not just biological natural history. The authors could briefly acknowledge this perspective while reiterating their call for caution.*

Response: "This is an excellent point. We have added a brief acknowledgment that Hopley et al. likely adopted a pragmatic, "real-world" approach that inherently reflects actual clinical presentations and practice patterns. We balance this by reiterating that while this perspective is highly valuable for real-world application, interpreting it as a reflection of purely biological natural history still warrants caution."

Line 70-76,

We acknowledge that Hopley et al. may have adopted a pragmatic, "real-world" approach that includes discovery-phase events, reflecting actual clinical presentations encountered in routine practice. While this perspective is highly valuable for informing clinical policy, interpreting these pragmatic findings as definitive evidence of the underlying biological course of the disease still warrants caution, particularly because such observations may not fully capture the long-term natural history of low-risk cysts that progress slowly over decades [3, 4].

Comment (3): *The authors advocate that "complete discharge remains a highly individualized decision." It would be helpful to suggest what criteria might justify complete discharge (e.g., life expectancy < 5 years, severe frailty, patient preference). Without such examples, the recommendation remains somewhat abstract.*

Response: We appreciate this important suggestion. We have revised this section to provide more concrete clinical examples. The text now explicitly states that complete discharge may be justified in selected patients with severe frailty, limited life expectancy (e.g., less than 10 years), or a strong preference against future surgical intervention.

Line 121-125

We advocate for a stratified approach in which surveillance de-escalation may be appropriate for many patients, whereas complete discharge remains a hig

hly individualized decision that may be justified in selected patients with sever e frailty, limited life expectancy (e.g., less than 10 years), or a strong preferenc e against future surgical intervention.

Comment (4): *Page 3, paragraph 1: "the benefit of continued surveillance diminishes after 2 years requires caution" – This sentence would read better as: "...concluding t hat the benefit of continued surveillance diminishes after 2 years requires caution, as it may not reflect..."*

Response: We appreciate this helpful suggestion. In response, we revised this sentenc e to improve readability and further clarify our intended meaning. The revised text n ow emphasizes that while Hopley et al.'s pragmatic, real-world findings are highly val uable for informing clinical policy, caution is still warranted when interpreting these o bservations as definitive evidence of the long-term biological course of low-risk cyst progression.

Line 70-76,

We acknowledge that Hopley et al. may have adopted a pragmatic, "real-world" appr oach that includes discovery-phase events, reflecting actual clinical presentations enco untered in routine practice. While this perspective is highly valuable for informing clin ical policy, interpreting these pragmatic findings as definitive evidence of the underlyi ng biological course of the disease still warrants caution, particularly because such o bservations may not fully capture the long-term natural history of low-risk cysts that progress slowly over decades [3, 4].

Comment (5): *Page 4, paragraph 1: "discharging patients at 5 years may result in mi ssed opportunities" – This is clear; no change needed.*

Response: Thank you. We have retained this phrasing.

Reviewer #2

Specific Comments to Authors:

The manuscript provides a timely and thoughtful commentary on the de-escalation of surveillance... I recommend minor revision, primarily to improve conciseness, soften s everal strongly worded statements, and more clearly emphasize that de-escalation an d complete discontinuation are related but distinct clinical decisions.

Response: We greatly appreciate the reviewer's insightful feedback. We have revised t

he manuscript to adopt a more balanced tone and to ensure our clinical distinctions are precise.

Comment (1): *One of the main strengths of this letter is its discussion of "front-loaded" surgery... However, I suggest that the authors express this argument with slightly more caution. The current wording may imply that the original study's findings are largely explained by bias, whereas they may still provide valuable real-world information about surveillance practice. A more balanced phrasing would strengthen the constructive tone of the letter.*

Response: We appreciate this helpful feedback and agree that our previous wording may have unintentionally conveyed an overly critical interpretation. We have revised this section to adopt a more balanced and constructive tone. The revised text now clarifies that although discovery bias is an important consideration, the findings by Hopley et al. nonetheless provide valuable pragmatic insights into real-world surveillance practice.

Line 70-76,

We acknowledge that Hopley et al. may have adopted a pragmatic, "real-world" approach that includes discovery-phase events, reflecting actual clinical presentations encountered in routine practice. While this perspective is highly valuable for informing clinical policy, interpreting these pragmatic findings as definitive evidence of the underlying biological course of the disease still warrants caution, particularly because such observations may not fully capture the long-term natural history of low-risk cysts that progress slowly over decades [3, 4].

Comment (2): *The discussion of cyst-size stratification is also relevant and well supported... Nevertheless, this section is relatively long for a Letter to the Editor and could be condensed. In particular, some expressions, such as "monolithic < 30-mm classification" and "threatens an untimely withdrawal of surveillance," may sound overly strong. I recommend revising these phrases to more neutral language, such as "a single < 30-mm category may obscure risk heterogeneity" or "may lead to premature discontinuation in selected patients."*

Response: We appreciate this helpful suggestion. We have shortened this section to improve conciseness and better align with the format of a Letter to the Editor. In addition, we replaced the previously strong wording with more neutral phrasing, incorpor

ating the reviewer's suggested expressions. The revised text now emphasizes that a si ngle <30-mm category may obscure risk heterogeneity and may lead to premature d iscontinuation in selected patients.

Line 77-85

Hopley et al. adopted a single 30-mm threshold for stepwise surveillance de-escalatio n. However, more granular size-based stratification may provide a more nuanced fram ework. Recent evidence, including the 2024 International Kyoto Guidelines, suggests t hat biological behavior differs significantly across size strata [5]. For example, BD-IPM Ns <20 mm generally exhibit indolent behavior, whereas cysts measuring 20–29 mm demonstrate a higher cumulative incidence of progression within a shorter timeframe [6, 7]. Consequently, a single <30-mm category may obscure risk heterogeneity and lead to premature discontinuation of surveillance in selected patients. Incorporating th ese established size strata may enhance the precision of surveillance de-escalation str ategies.

Comment (3): *The authors' emphasis on the dual oncologic purpose of BD-IPMN sur veillance is another strength... However, the authors may consider clarifying that surve illance de-escalation is still reasonable in carefully selected low-risk patients, while co mplete discontinuation should be approached more cautiously in patients with preser ved life expectancy and acceptable surgical candidacy.*

Response: We appreciate this important suggestion. We have added clarifying text to better distinguish surveillance de-escalation from complete discontinuation. The revis ed manuscript now explicitly states that while de-escalating surveillance (i.e., extendin g imaging intervals) may be appropriate for carefully selected low-risk patients, compl ete discontinuation is a separate decision that warrants substantially greater caution i n patients with preserved life expectancy and acceptable surgical candidacy.

Line 96-99

While surveillance de-escalation (i.e., lengthening the intervals between imaging) repre sents a reasonable strategy for carefully selected low-risk patients, complete discontin uation is a distinct decision that warrants substantially greater caution in individuals with preserved life expectancy and acceptable surgical candidacy.

Comment (4): *The section on aging and surgical fitness is clinically meaningful... This*

paragraph could be better integrated with the preceding discussion by emphasizing that the decision to discontinue surveillance should combine cyst biology, competing cancer risk, and patient-level operative fitness.

Response: We appreciate this important observation. To better integrate this section with the preceding discussion, we revised the paragraph to emphasize that decisions regarding surveillance discontinuation should not rely on chronological age alone, but instead require a more holistic assessment incorporating cyst biology, competing cancer risks, and patient-level operative fitness.

Line 109-111

Consequently, rather than relying on chronological age alone, the decision to discontinue surveillance should be based on a comprehensive assessment integrating cyst biology, competing cancer risks, and patient-level surgical fitness.