used in Gerami et al,[2] which was selected to understand the true NPV (above 99%) in the clinical setting and not simply in a research validation setting. Again, by way of comparison with the current histopathologic pathway using a 7% prevalence, the calculated NPV from Elmore et al[5] for early-stage melanoma based on the sensitivity described herein is well below 83%.[1,4,5] It is also important to note that 708 PLA-evaluated real-world lesions have now been followed up for over a year, and no missed melanomas have been identified (D.M.S. and Laura K. Ferris, MD, PhD, unpublished observations), further supporting the high NPV of the PLA.

We agree that it is important to carefully test new technologies such as the PLA. To date, the performance of the PLA has been established and corroborated by over 40 investigators, and findings have been summarized in over 10 peer-reviewed publications including the references found in Gerami et al,[2] Ferris et al,[3] Hornberger and Siegel,[1] and Rivers et al.[4] Additional corroborating data sets come from over 1350 clinicians in 40 US states who have used the PLA on over 20 000 patients. If used as intended, the PLA improves the current diagnostic paradigm of ruling out melanoma by reducing the number needed to biopsy about 10-fold from about 25[6] to 2.7,[4] while significantly increasing the NPV to 99%. This in turn drives cost savings for the health care system (−47% at the PLA selling price reference point of $500) and demonstrates that the PLA is a new technology that can deliver better care at a lower cost.[1-4]

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Conflict of Interest Disclosures: Dr Siegel is a member of DermTech's Scientific Advisory Board and a stockholder in DermTech; Dr Hornberger is a consultant to DermTech.

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Mohs Appropriate Use Criteria for Superficial Basal Cell Carcinoma

To the Editor We read with interest the Viewpoint by Steinman and colleagues[1] suggesting a reevaluation of appropriate use criteria for Mohs micrographic surgery (MMS) with respect to primary superficial basal cell carcinoma (sBCC). We must note that MMS is only 1 means of margin control of skin cancers, and perhaps the Viewpoint title would more accurately read "Reevaluation of Excisional Surgery for Primary Basal Cell Carcinoma."

The authors assert that "studies of sBCCs treated with curettage followed by topical imiquimod found recurrence rates of 4% or less."[1(p756)] We note the lack of reference for this statement.

While we found noncited studies claiming that twice-daily application of imiquimod has demonstrated 100% clearance at 6 weeks after therapy, other studies have not been as positive, demonstrating clearance rates of 77.9% to 80.4% at 5-year follow-up—a stark contrast with the 1% recurrence rate for primary BCC managed with MMS.[2] The majority of tumors evaluated by Steinman and colleagues[1] were located on the trunk and extremities. Moreover, imiquimod treatment of nodular BCC and sBCC has demonstrated 82.5% success compared with 97.7% success with surgical excision (with 4-mm margins) at 5-year follow-up in a randomized clinical trial of 401 participants.[3]

With respect to the cure rates stated by Steinman and colleagues,[1] it should be noted that imiquimod cream is approved by the US Food and Drug Administration (FDA) for treatment of primary sBCC with a maximum diameter of 2 cm on the trunk, neck, or extremities (excluding hands and feet). The head is excluded from FDA-approved use.

Hair follicle density on the face is an order of magnitude higher than other body sites (292 hair follicles/cm^2 on the forehead compared with 29/cm^2 on the back and 18/cm^2 on the forearm[4]), and BCCs preferentially arise from stem cells within hair follicle niches. While Steinman and colleagues[1] mention that sBCCs seldom penetrate more than 1 mm down hair follicles, tumors measuring greater than only 0.4 mm have a significantly higher risk of treatment failure with imiquimod, associated with a recurrence rate of 58%.[5] Limiting the use of excisional surgery with pathologic margin control (MMS or otherwise) could greatly hinder patient care and successful outcomes.

Clearly stated in the Methods section of the "2012 Appropriate Use Criteria for Mohs Micrographic Surgery" is that "the development of the [appropriate use criteria] was supported by an evidence review and analysis of surgical and disease outcomes related to the practice of MMS within the United States."[6(p533)] Four of the 6 references cited by Steinman and colleagues[1] cannot be considered for the development of the appropriate use criteria under current methodology because they reported outcomes occurring outside and were published outside of the United States.

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To the Editor I read with great interest the Viewpoint by Steinman and colleagues[1] on treating superficial basal cell carcinoma (sBCC) with Mohs surgery. The authors rightly point to the paucity of evidence regarding sBCC management, though this limitation applies not just to sBCC but to most other nonmelanoma skin cancers as well.[2]

While I laud the authors' attempt to highlight the importance of responsible stewardship of the health care system, their underlying argument—that sBCC tumors are indolent and easily amenable to alternate treatment options—is undermined by the fact that in a recent study more than one-third of all sBCC were ultimately upgraded to deeper or more aggressive BCC subtypes.[3] While a true sBCC may be treated topically, treating an underdiagnosed infiltrative BCC using topical therapy may result in masking the tumor, leading to an ultimately disfiguring outcome for the patient.[3]

The authors allude to this concern in noting that "more than 50% [of tumors] diagnosed as sBCC show[ed] foci of more aggressive BCC subtypes."[1(p755)] They argue, however, that even such tumors are amenable to topical therapy owing to their "very low" risk of progression, though this assertion is uncited, and the article referenced earlier studied curettage coupled with cryosurgery, a technique rarely practiced in the United States.[4] Moreover, in nonrandomized studies, confounding by indication would represent a serious drawback, as more clinically suspicious sBCCs, or those in particularly high-risk areas, are likely preferentially treated with Mohs surgery—as seen in the study cited by the authors, which excluded high-risk tumor locations.[4]

Increased utilization is not synonymous with overutilization, and the global increase in Mohs microsurgery utilization may be owing to other secular trends such as the increase in nonmelanoma skin cancer diagnosis more broadly, as well as the increased accessibility of Mohs surgery for patients.[5]

The authors are correct that sBCC has not specifically been studied for Mohs surgery, though this shortcoming is a reason to advocate for further study, not to restrict clinician and patient choice a priori. The authors advocate reconsideration (rather than wholesale rejection) of Mohs surgery for sBCC, but given that sBCC diagnosed based on a superficial shave biopsy specimen frequently masks more aggressive BCC, it may be more responsible to retain substantial clinician flexibility in the face of uncertainty.

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To the Editor Appropriate patient care relies on many factors, including data and judgment. Steinman and colleagues[1] contend that the biological behavior of superficial basal cell carcinomas (sBCCs) should lead to their reclassification by the Mohs surgery appropriate use criteria (MAUC) as "uncertain" or "inappropriate" for Mohs surgery (MS).[1] This type of discussion of hypotheses is essential to optimizing patient care. At its inception, the MAUC were intended to evolve as increasing empirical evidence became available.[2]

However, the data identified by Steinman et al[1] seem to support conclusions contrary to what they claim. Many biopsies initially interpreted as sBBCs in fact contain evidence of more aggressive tumor subtypes on deeper sectioning or definitive excision. The authors themselves note that this phenomenon may occur in 50% of specimens. Thus, initial biopsies will frequently fail to detect concurrent, more aggressive tumor subtypes. Disallowing MS for sBCCs (based on the initial biopsy) would mean excluding an appropriate treatment

for the approximately 50% of sBCC tumors that actually include more aggressive subtypes.

Steinman et al[1] also cite a study of 158 sBCC treated with MS.[3] The study showed that an average of 2.6 stages were required for clearance. Based on this fact, it would seem that sBCCs should be especially well suited to MS treatment; clinical impressions of margins rarely match histological realities. Furthermore, a close reading of the study[3] reveals that almost 16% of sBCCs treated with MS on the head and neck had been previously treated with imiquimod, fluorouracil, cryotherapy, or MS. This underscores the challenges of treating sBCCs in these locations.

Steinman and colleagues[1] focus on biological behavior and cure rate, but they overlook other significant treatment considerations. Mohs surgery provides important advantages in tissue sparing and cosmesis. Additionally, MS requires only a single treatment session and may be the most convenient and cost-effective modality in many situations.[4]

While Steinman et al[1] acknowledge that the MAUC are not intended to draw comparisons with alternative treatments, they seem to miss the point that MAUC identify cases where MS may be appropriate—although MS is far from mandated for all of these situations. All would agree that MS is not the right choice for a small, well-defined sBCC on the face of an infirm individual's preauricular cheek. However, advocating that the MAUC reclassify sBCCs as "uncertain" or "inappropriate" removes an important technique that is wholly appropriate for certain patients. Consider, for example, the younger healthy patient with an ill-defined, indurated sBCC located on the nasal tip.

Optimizing patient care requires an accurate understanding of published data as well as reasoned judgment. Narrowing MAUC for sBCCs restricts physician judgment and creates more barriers to providing our patients with appropriate care. Rising health care costs and potential overutilization of MS are important concerns for all dermatologists. To this end, the American College of Mohs Surgery (ACMS) (https://www.mohscollege.org/) has developed the Improving Wisely program, in collaboration with the Robert Wood Johnson Foundation and Johns Hopkins University School of Medicine, as well as the Mohs Advancing and Improving Quality (MohsAIQ) national registry. These programs will help ensure that we continue to provide the best treatments for patients in an appropriate and cost-effective manner. It is the position of the ACMS Scientific Advisory Committee that Mohs surgery for superficial BCC of the face is appropriate.

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1. Steinman HK, Dixon A, Zachary CB. Reevaluating Mohs surgery appropriate use criteria for primary superficial basal cell carcinoma. *JAMA Dermatol*. 2018; 154(7):755-756. doi:10.1001/jamadermatol.2018.0111

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In Reply We thank Drs Montuno and Coldiron, Kantor, and MacFarlane and Perlis for their comments on our Viewpoint.[1] As our colleagues understand, the Mohs appropriate use criteria (MAUC) were created to limit use of Mohs surgery (MS) when simpler treatments would be more appropriate. Our Viewpoint was written with this in mind, reinforcing the importance of MS for more complex tumors, while emphasizing that primary superficial basal cell carcinoma (sBCC) can generally be treated more efficiently and less expensively with simple excision and curettage alone or combined with other modalities.[1]

Drs Kantor and MacFarlane and Perlis suggest that high reported cure rates with non-MS treatments are undermined by several studies showing that up to 50% of sBCCs contained foci of more aggressive, deeper BCC tumor subtypes.[2] We note this fact,[1] which would apply to any BCC study.[3] The very high cure rates we cite for alternative surgical treatments, despite the presence of other BCC subtypes, support our conclusion about MS for most sBCCs.

Drs Montuno and Coldiron comment about lower cure rates for sBCC using imiquimod. We agree, and have documented this, stating that imiquimod had "potentially acceptable cure rates, particularly in aged or infirm populations."[1(p756)] While not approved by the US Food and Drug Administration for use in areas H (forehead, temples, central face, ears, postauricular, hands, feet, areola, and genitalia) and M (scalp, posterior aspect of the cheeks, neck, and anterior aspect of the legs), except the neck, many studies have evaluated off-label imiquimod use in these areas.

Dr Kantor incorrectly states that "sBCC has not specifically been studied for Mohs surgery." We cited several studies demonstrating that MS for sBCC results in significantly larger surgical wounds, requires more stages to clear margins, and has higher recurrence rates than for all other subtypes.[4,5] Yet, MacFarlane and Perlis suggest that these findings are justification for MS use. We noted that cure rates for excision with 4-mm margins (96.8%), curettage plus cryotherapy (C&C) (98.1%),[6] and curettage and imiquimod (96%)[7] are equivalent to MS (97.4%).[4] Dr Kantor faults the study of C&C for excluding tumors in high-risk areas. The study referenced BCCs on the face and scalp, including tumors on the nose, ears, and eyelids.[6]

MacFarlane and Perlis suggest we "miss the point" that MAUC identify cases appropriate for, but not mandated for, MS, and that reclassification creates barriers to appropriate care. They cite the example of a younger healthy patient with an ill-

defined, indurated nasal tip sBCC. In practice, none of us will rely only on a pathology report to determine optimal treatment; the clinical features, including location, appearance (including induration), response to curettage, and other clues will guide appropriate treatment.

We cite data suggesting that MS for essentially all sBCCs does not merit a MAUC score of "appropriate," and we note that this conclusion is supported by a majority of national comparative treatment guidelines. MAUC uses "uncertain" for scenarios where insufficient data are available for definitive categorization or there is varying agreement regarding MS appropriateness. Current data supporting MS for sBCC are at best uncertain.

The MAUC indicate that an appropriate treatment method is one in which the anticipated clinical advantage combined with clinical judgment outweighs the potential negative sequelae for a specific indication. Because MS for sBCC creates significantly larger defects, requires more stages than for other BCC subtypes, and offers cure rates no better than simple excision, C&C, and curettage and imiquimod, we maintain that the MAUC for sBCC merit reevaluation.

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CORRECTION

Data Errors in Tables 1 and 2: In the Original Investigation titled "Safety and Efficacy of Methotrexate for Chinese Adults With Psoriasis With and Without Psoriatic Arthritis" by Yan et al,[1] published online January 30, 2019, in Table 1, the *P* value for smoking was corrected, and in Table 2, the percentage of patients without psoriatic arthritis who achieved 90% reduction from baseline Psoriasis Area Severity Index score was corrected. This article has been corrected online.

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