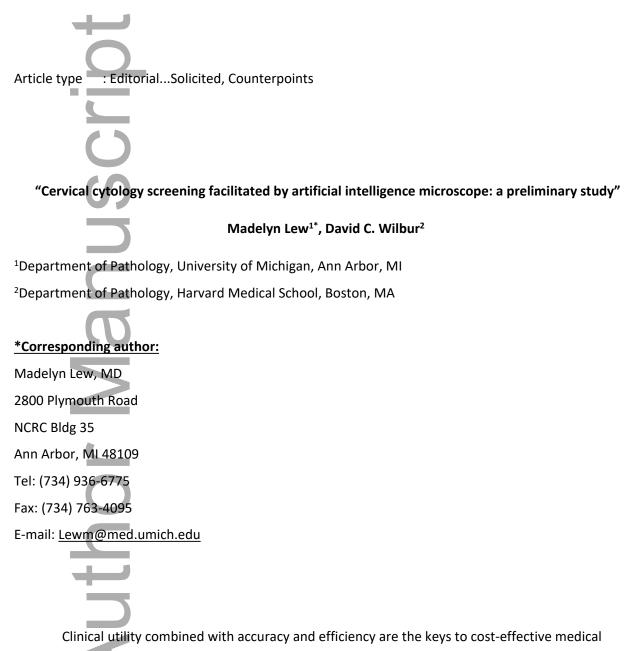
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procedures. The Pap test is a prime example of one such test; found to be highly useful but plagued by

problems in accuracy and work intensity. This combination of need and difficulty led to intense

investigation in the 1950s and 60s into computerization to enhance the diagnostic accuracy of This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the <u>Version of Record</u>. Please cite this article as <u>doi:</u> 10.1002/CNCY.22424

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gynecologic cytology and to enhance workflow efficiency. Since these initial investigations, computerbased technology has advanced such that morphologic features in cells can be translated into data points for algorithmic analysis and subsequent identification of squamous abnormalities, leading to the popularization of technology-based platforms such as Hologic's ThinPrep Imaging System (TIS). Continued research in the past decade has further enhanced image analysis algorithms to bring better performance of artificial intelligence (AI) in cytology screening.¹ The benefits of integrating AI into clinical practice include its capacity to increase detection sensitivity and decrease subjectivity and diagnostic "grey-zones" by providing quantitative data and analysis in real-time during morphologic assessment of specimens. Despite these documented improvements, AI has not been widely implemented into clinical practice. The most significant obstacles to its popularization include higher up-front costs of investment, disruption of historical workflows, a perceived negative impact on job security, and the regulatory burden (and hence cost) of bringing such products to market. However, as technology and AI algorithms further develop, more avenues are being explored to minimize these and other concerns.

In the corresponding article by Tang, et al., the authors beautifully highlight a practical example of how innovative AI applications can be implemented to leverage the advantages of technology in resource-limited regions while bypassing the need for large, expensive hardware, or an overhaul of workflow. Addressing the lack of experienced practitioners for optimal manual review of cervical cytology specimens and for training, the authors introduce a novel AI microscope that combines the conventional features of microscopy with augmented reality and an AI-empowered computer unit. The results yield a real-time visualization of the AI analysis into the optical path of evaluated slides for immediate user feedback. This application pivots from the foundation of previous AI systems, which have largely focused on whole slide imaging with subsequent "post-evaluation" guidance to selected fields/cells of interest or whole slide classification/scoring. Instead, the authors created an opportunity for real-time AI assistance. The utility of the authors' AI algorithm was demonstrated in the two-round reader study of the publication, in which 4 masked cytopathologists looked at a total of 486 Pap specimens twice - once without AI assistance and the second with AI assistance 15 days later. Use of the AI microscope enhanced the sensitivity of detection of squamous abnormalities designated as LSIL and above and also increased diagnostic agreement amongst cytopathologists. These promising results showcase how AI can not only enhance workflow efficiency but can also enhance quality improvement by reducing interobserver variability. Additionally, this work highlights how in areas lacking experts in cytology, AI can take the form of a trainer or educator by "marking" abnormalities that may otherwise

have been overlooked, or by confirming concerns of less experienced evaluators. However, one unanswered question in the study is the effect, with less experienced practitioners, of the AI result influencing the practitioner toward an incorrect, but reproducible, final diagnosis. Remembering that precision measures not the accuracy, but the reproducibility of the result, further investigation should focus on matching the clinical result with a "ground-truth" assessment. Despite this methodologic issue, the results of the AI-assisted approach are very promising for the intended uses of the device.

While this article explores an AI system's capacity to enhance healthcare delivery to populations with limited resources, it also challenges us to think how AI can be implemented into other existing workflows to provide quality improvement and educational tools at all levels of healthcare delivery in pathology. Given the projected future shortages of pathologists, AI can contribute to mitigating the increased work demands of growing case volumes while maintaining standards for consistent and accurate diagnoses. This principle of AI can extend beyond the article's focus on cervical cytology screening to include applications in quality assurance measures, such as the 5-year look back requirement for newly diagnosed HSIL cases in gynecologic cytology, or extension to other cytologic specimens, such as urine and effusion fluids, or to other subspecialties of surgical pathology. Such applications can expand laboratory capabilities in high-volume institutions and resource-limited regions alike. An early focus has been in the evaluation of AI algorithms and neural networks in prostate cancer detection and Gleason scoring. In this example, AI can help provide more consistent diagnoses and, through the integration of molecular and morphologic data points, can lead to predictive personalized reports ²⁻³. Although these developments may spark pathologists' concern for being deskilled or even replaced, AI is better viewed as a tool that augments diagnostic accuracy and efficiency in the pathologists' toolkit, no different than the previous emergence of other ancillary studies such as immunohistochemistry and molecular testing. Such advances all require pathologist oversight to ensure that they are applied, interpreted, and managed in appropriate systems that serve to enhance diagnostic pathology as we shift further into the realm of personalized medicine.

As this article highlights, technology can be leveraged in ways that do not require a massive disruption of the current state workflow. However, studies implementing new technology models will need to be tested on large and diverse datasets to optimize their use-cases and explore their utility across the wide variety of practices and specimen preparation techniques. Additionally, a systematized approach to regulatory approval and cost-benefit analyses must be developed in order to promote more widespread acceptance of AI-enhanced practice. Once all these pieces are in place, the developing story

of technological advancement that AI brings to practice will have the potential to enhance patient care and workflow efficiency, and to assist in the training of future practitioners.

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