Unraveling Women's Cancer Screening

New Cervical Cancer Screening Guidelines Raise Concerns Among the Laboratory Community

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The recently published American Cancer Society (ACS) cervical cancer screening guidelines are cause for concern to pathologists and cytotechnologists, and many question how the guidelines will negatively impact their ability to protect their patients' health.

The two most dramatic changes include:
(1) removing support for cervical cancer screening in women 21-24 years old, and (2) seeking to minimize the role of Pap testing, the most successful cancer screening tool in history.

Going further, the ACS outlines its intent to entirely remove Pap testing, both alone and as part of co-testing, from future guidelines.

For the first time in almost a decade, the ACS guidelines now diverge from the American College of Obstetricians and Gynecologists, the United States Preventive Services Task Force, and the Women's Preventative Services Initiative[1,2,3] guidelines—all of which endorse cytology, alone or in combination with HPV testing, as important cervical cancer screening options.

In response to the new ACS guidelines, many clinicians and women's health and patient advocacy organizations have spoken out publicly against these changes. In addition, the College of American Pathologists, the American Society of Clinical Pathology, and the American Society of Cytopathology have all released statements voicing their serious concerns with these changes, affirming that they "remain committed to retaining the use of co-testing and cytology for optimal cervical cancer screening and precancer detection."[4,5,6]

With so many different groups across the spectrum of women's healthcare raising concerns about ACS's unwarranted shift away from Pap testing and co-testing, one must ask:
Who, in fact, is driving these changes, and what is the underlying motivation?

A survey co-sponsored by the National Association of Nurse Practitioners in Women's Health and HealthyWomen, a women's health advocacy group, showed that over the past five years there has been an increase in the number of both healthcare providers and women who consider the use of Pap and HPV tests together as important to overall health. Additionally, 95% of healthcare providers and 90% of women find the Pap test valuable in screening for cervical cancer.[7] The survey also showed that an overwhelming 89% of healthcare providers believe co-testing is essential for women's health—yet the value of the voices of frontline providers and women has been minimized in the ACS's recent revision to their guidelines for cervical cancer screening.[7]

The specific concerns with the ACS guidelines are as follows:

Ignoring Pap Test's Positive Role

The historic value of the Pap test in protecting women's health is undeniable. There is a wealth of evidence showing the Pap test detects pre-cancer and cancer, whether alone or in combination with the HPV test.[8,9] Over the past 50 years, pathologists and cytotechnologists have used the Pap test to dramatically reduce the occurrence of this often-deadly form of cancer in women. The result has been a decrease in the incidence of cervical cancer by over 70 percent.[10]

Despite this decline, the ACS estimates that more than 4,200 women will still die from cervical cancer in 2020.[11] More alarming is that in the U.S. since 2013, the incidence of cervical cancer has been increasing in women under 50. A recent study from the New Mexico HPV Pap Registry offers some explanation of why we are seeing this trend. It was found that 64% of women diagnosed with cervical cancer during the study period were unscreened or not adequately screened prior to their diagnosis. Now is the time to be vigilant—to focus on increasing screening adherence and to address any disparities in access—in order to protect women's health.

Moreover, the benefit of the Pap to women's health overall is directly connected to the role pathologists and cytotechnologists play. In addition to identifying HPV-driven disease, a Pap test can be a wealth of knowledge, providing the ability to diagnose microorganisms and non-HPV related cancers such as gastric-type endocervical adenocarcinoma, endometrial, ovarian, and other rare metastatic carcinomas.

Prevalence of HPV-Negative Cervical Cancers

It is well established that not all cervical cancers will test positive for HPV. This can be due to failure to detect integrated HPV DNA, assay or specimen detection issues, loss of HPV DNA, or HPV never being present. In fact, approximately 15% of all adenocarcinomas are not related to HPV infection. A shift away from cytology and co-testing would lead to these cancers being missed.

A number of studies have found that up to 31% of invasive cancers will test negative for HPV by commercially available tests, and that 8.3%-14% of high-grade squamous intraepithelial lesion (HSIL) cases may also be negative for high-risk HPV.[12,13] Delayed diagnoses could then result in higher-stage tumors due to the longer (5-year) screening intervals after a negative HPV result.[14] The continued inclusion of cytology into the screening process will add much-needed sensitivity, as women diagnosed with cervical cancer will be more likely to have their disease detected by liquid-based cytology rather than by a positive HPV test.

Due to the documentation of HPV-negative carcinomas as well as high grade lesions (HSIL/AIS), women should have a Pap test at some time in their screening history and should not be screened solely with HPV tests.[9] This is especially important for women with an uncertain screening history or with any clinical symptoms.

Guidelines Ignore Practical Realities

The Pap and HPV tests are fundamentally different, of course, but together as a co-test they provide higher sensitivity than either test does separately. In the United States, it is important for primary cervical cancer screening to be as sensitive as possible in order to detect precancerous abnormalities to the best of our ability–given the opportunistic screening paradigm and heterogeneous nature of the healthcare system. To combat any potential overtreatment, the recently published American Society for Colposcopy and Cervical Pathology management guidelines recommend observation of CIN2 for women interested in future pregnancy, knowing that a significant number of cases will resolve spontaneously.

The new ACS guidelines rely primarily on international randomized clinical trials and mathematical data modeling that assumes perfect adherence to screening and follow up, largely ignoring the practical realities of screening in the U.S. The guidelines also fail to account for the different racial and socioeconomical backgrounds of women in the U.S. and the impact of lagging HPV vaccination uptake. Ignoring these real-world considerations could easily lead to even greater disparities in care.

A recently published retrospective longitudinal study from Quest Diagnostics and the University of Pittsburgh Medical Center offers new real-world evidence from a highly-diverse, heterogeneous U.S. population. This study examined prior co-testing results for women with a precancer or cancer diagnosis to determine how each screening modality (HPV alone, cytology alone, or co-testing) performed. In all analyses of CIN3/AIS and cancer data, co-testing was more sensitive than HPV alone or cytology alone. In fact, HPV alone missed twice as many cervical cancers compared to co-testing, which outperformed both HPV alone or Pap alone in detecting cancer and precancer in women over 30 years of age. The study concluded that its findings "should put to rest any notion that HPV alone achieves the same bar for quality cancer screening." [11]

Changing these guidelines also comes at a particularly concerning time given the COVID-19 pandemic. According to a recent Wall Street Journal article, "Hundreds of thousands of cancer screenings were deferred after worries about Covid-19 shut down much of the U.S. healthcare system starting this spring."[15] Altering guidelines now only creates more barriers to women receiving this essential preventative care.

Unintended Consequences for Healthcare Providers and Patients:

Compliance with HPV-only screening every 5 years is extremely challenging given that patients often do not come in for medical appointments on regular intervals. In addition, changing the recommended screening age from 21 to 25, and eliminating the Pap test recommendation altogether, will imprudently reduce the number of possible touchpoints between patients and providers—thus negatively impacting the overall health of women in the U.S., and negating the positive impact of preventive medicine.

Simply put, the Pap test gets women into their doctor's office, where preventive medicine can take place and be most effective. Eliminating the Pap test may cause general confusion and will create the potential that more women will not get the proper testing and treatment they need on a regular basis. To put that into perspective, most cases of cervical cancer in the U.S. are due to a failure of access to screening rather than a failure of the screening methodologies, which is why it is crucial for all screening options to be available.[3]

Call-To-Action: A Need for Advocacy and Guidance

It is difficult to understand why the ACS is making these changes to the guidelines, when laboratory and healthcare professionals understand better than anyone the positive impact the Pap test has on women's health. We need to not only understand what is driving these changes, but we must strive to be a crucial part of the decision-making process, rather than merely vocal critics.

Indeed, our perspective should be more widely-shared and central to any substantive changes to cervical cancer screening guidelines in the future.

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