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*Editorial*

# Identifying a "Range of Reasonable Options" for Cervical Cancer Screening

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See related articles on pages 311, 317 and 330.

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This issue of *Obstetrics & Gynecology* includes three articles related to cervical cancer screening intervals: a commentary (see page 311), a survey (see page 317), and interim clinical guidance for use of a new screening test (see page 330).[1–3] All address an important question: what screening interval should apply to strategies that incorporate testing for high-risk types of human papillomavirus (HPV)?

Readers will recognize the salient elements of the debate about screening frequency and understand the tension: frequent screening with the most sensitive tests confers the lowest risk of cancer and cancer death but also leads to more invasive procedures, treatment harms, psychosocial distress, and life disruptions. Putting all of these elements together with attention to patient preferences and resource utilization is challenging for guideline committees. Yet, in the end, clinicians (and patients) want the answer to one simple question: which screening strategy has the highest likelihood of maximizing benefits and minimizing harms?

The authors of the study by Kinney et al,[1] many of whom are oncologists, rightly call for more transparency regarding the benefits and harms of various screening strategies. They believe that even after being informed of the potential harms of more intensive screening, significant numbers of patients and providers would not choose to accept the additional estimated lifetime cancer risk conferred by cytology plus HPV testing (co-testing) every 5 years (0.74%) compared with that conferred by co-testing every 3 years (0.47%). To that end, they argue that the risk achieved by annual cytology (0.25%) should be held as the benchmark for screening guidelines, a risk lower still than that achieved with co-testing every 3 years. Of course, caution must be exercised in singling out estimates from the cited study owing to their inherent imprecision. Moreover, as these authors point out, analyses of alternative screening strategies should reflect informed patient preferences regarding benefits and harms. Indeed, long gone are the days in which physicians were deemed the arbiters of how their patients value the potential outcomes of care and what tradeoffs they are willing to make to further decrease their risk of rare but serious medical conditions. However, evidence is lacking on how truly informed patients view the benefits and harms of cervical cancer screening, and assumptions that well-informed patients will always opt for more testing are not always borne out.[4]

Generating evidence on patient preferences is challenging, and, in the case of cervical cancer screening, it is complicated by decades-long public health messaging regarding the importance of annual screening. It is therefore not surprising that 74% of the women surveyed in the study by Silver et al[2] thought that women their age should have yearly cytology tests. Information on what the participants knew or were told about



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screening benefits and harms was not provided, so it is unclear if their responses reflect informed preferences. Importantly, 68% of these women were willing to extend screening intervals to every 3 years if recommended by their health care provider, underscoring the critical role that providers play in implementing evidence-based guidelines.

The interim clinical guidance by Huh et al[3] provides recommendations for the use of HPV testing as a primary screening test. These authors recommend that the periodicity of screening should not be more often than 3 years. Surprisingly, they state that screening may begin at age 25, despite recommendations in 2012 by major guideline groups[5–7] discouraging the addition of HPV testing to cytology in women under age 30, in part due to the high prevalence of HPV in this age group. In the sentinel study on which the recommendation is based, 21.1% of women aged 25–29 had positive HPV tests and were referred to colposcopy or placed in surveillance; in comparison, an estimated 7% of women would follow this path if screened with cytology alone.[8] Here, the measure of harm was confined to colposcopy referral; yet, as all front-line clinicians know, other harms are incurred: identifying combinations of positive test results of uncertain significance, treatment of cervical lesions destined to resolve without intervention, and burdening women with surveillance of unclear efficacy or endpoint. Such surveillance recently has been found to be associated with significant psychological distress in 39% of women.[9] The authors of the interim guidance state that they had concerns regarding the potential harms of initiating HPV testing so early, but do not describe the process by which the benefits and harms were weighed that led to their conclusion.

These articles add more information, but little clarity, to the shifting landscape of cervical cancer screening. To move forward, we suggest the following. First, women's experiences of the screening process must be better understood, and credible ways to integrate their informed preferences into recommendations should be a priority. Single-metric measures of benefits and harms such as quality-adjusted life-years will be useful. Additional discussion is warranted to define the appropriate role of patient preferences in screening decisions, specifically regarding screening interval. Many clinicians would not consider performing cytology more often than once a year a "reasonable" option, although a small percentage of survey respondents believed women should be screened that intensively.[2] Second, focus should shift from a single outcome of benefit (cancers and cancer deaths) to estimates of the net benefit a screening strategy provides to a population (benefit minus harms). Strategies that substantially decrease harms while minimally decreasing benefit provide greater net benefit. Third, resource utilization must be a mandatory part of the equation. In response to escalating health care costs, leaders in cardiology recently made a commitment to address the discordance between guidelines and value and to define high-value care.[10] Cost analyses are important to identify high-value screening options, but even more critical is the need for guideline committees to be attentive to their results. Fourth, an a priori agreed-upon process of performing and interpreting comparative effectiveness and cost analyses needs to be established to understand how new strategies compare with current approaches. It may be that a "range of reasonable options" can be identified to accommodate variations in screening setting and preferences.

Identifying high-value strategies that maximize benefits and minimize harms involves much uncertainty, and reasoned judgment will always be needed. Thus, it is crucial that those involved in the guideline process be free of both commercial and intellectual conflicts of interest to assure that recommendations stay focused on the goal of improving women's health.

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