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Cervical cancer screening in women over 65. CON: Reasons for uncertainty

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Among the most hotly debated topics in medicine are decisions regarding cancer screening, specifically the ages to begin and end, how often it should occur and the techniques to use [1]. In this issue of *Gynecologic Oncology*, Rosenblatt and colleagues re-visit the question of the age to end cervical cancer screening.[2] Their analysis suggests a protective effect of cytology among women aged 65 and older. Although their study is limited by observational methodology and data source, it adds to an emerging body of literature with similar findings [3] and led the authors to conclude that cervical cancer screening may be useful in the aged United States population.

First, it is important to note that all major current guideline groups in the United States endorse cervical cancer screening after the age of 65 years in women with a cervix who do not have a documented history of prior normal testing within the prior 10 years, with the most recent being within the prior 5 years [4–5]. Normal testing is defined as either 3 consecutive negative cytology results or 2 consecutive negative results on cytology plus testing for oncogenic human papillomavirus (HPV) types. It is the low-risk status conferred by this history that underlies the recommendation by all of these groups to end screening at age 65. None of the guidelines suggests an age over which never-screened women should not be screened. In fact, a modeling study commissioned by the US Preventive Services Task Force suggest that screening never-screened women aged older than 65 years every 2 to 5 years and ending in the eighth decade represents a “reasonable trade-off between the burden and benefits of screening” [7].

Cervical cancer screening is common in the United States, and relatively few women have not been screened at least once prior to age65. If the issue under consideration is continued screening among women aged 65 and older deemed low-risk by prior screening results, the following questions about this group are pertinent: what is the burden of disease (expected cervical cancer incidence and mortality)? To what extent could extended screening decrease cervical cancer incidence and mortality? What harms would be incurred by screening, and do they differ from those imposed on younger women? Is screening acceptable to women in

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this age group? What is the estimated magnitude of the net benefit (benefit minus harms)? And, finally, would such screening be considered “high-value”?

Surprisingly little is known about the incidence of cervical cancer and cervical cancer precursors (cervical intraepithelial neoplasia, CIN) among well-screened women aged 65 and older, although it appears to be quite small. In the Breast and Cervical Cancer Early Detection Program sponsored by the Centers for Disease Control and Prevention, 1 case each of CIN grades 2 and 3 were reported among 7500 women aged 60 to 65 years with three or more prior normal tests; no cases of cervical cancer were found [8]. In the Women’s Health Initiative, cervical cancer was diagnosed over a 6-year period in 8 women with normal baseline cytology among 15,415 participants aged 50 to 79 years [9]. Sexually active older women who are not married or living as married were at higher risk for developing cervical neoplasia, suggesting demographic variables that may identify a population of older women at risk. The number of cases that occurred among those aged 65 years and older meeting the criteria to end screening, however, was not reported.

Certainly, harms can be anticipated in the pursuit of disease detection and treatment. These include false-positive tests leading to unnecessary interventions that carry inherent risks as well as identification and treatment of lesions that would have never become clinically apparent in the woman’s lifetime. For example, a study of 2561 post-menopausal women (average age 67) in the United States with at least one prior normal cytology test followed over two rounds of annual screening identified only one case of histologically confirmed CIN grade 1 to 2 [10]. In this cohort followed for up to 4 years after the final screening round, abnormal cytology prompted 112 additional cytology tests, 33 colposcopies, 30 biopsies, 35 endocervical curettages, 8 endometrial biopsies, 4 dilations and curettages, 7 loop excisions and 2 cone biopsies to find one lesion of questionable clinical significance. The resources required to screen this group, and the potential benefit derived, would certainly strain the definition of “high-value” care.

Similarly, little is known about the accuracy of cervical cancer screening tests in this population. In a recent large study of women in the United States [11], screening (cytology or primary HPV testing with triage using genotyping for types 16 or 18) missed nearly 90% of all cases of CIN grade 2 or worse among women aged 50 and older (a group that included women up to age 93), raising legitimate concerns about test sensitivity in older women [12]. In that same study, about 5% of women aged 70 and older with normal cytology were HPV-positive, but no cases of CIN grade 2 or worse were found (n=525)[11]. Current screening with cytology plus HPV testing, deemed the preferred strategy in women aged 30 years and older by the American Cancer Society and the American College of Obstetricians and Gynecologists, extends screening past age 65 among women with normal cytology but positive HPV tests. This change in practice may ultimately provide additional protection to older women at potentially greatest risk of cervical cancer. Many, if not most, of these women, however, will not develop cervical neoplasia and will be placed in a surveillance cycle of unclear end.

Viewed through a clinical lens, frontline clinicians caring for older women know all too well the challenges of cervical cancer screening in this group. Colposcopy is often inadequate

and inaccurate. The cervix can be stenotic, making sampling difficult and painful. Those with abnormalities requiring an excisional procedure are often poor candidates for loop excision due to distorted cervical architecture (atrophy, prior cervical procedures) and may need to go to the operating room for cone biopsy with its accompanying harms; life-limiting co-morbid conditions, more common as women age, can easily tip the balance away from benefit and toward harm.

Rosenblatt's study suggests that cervical cancer screening is effective across the age spectrum, and we should be open-minded to the possibility that extending screening may be reasonable and valuable for some women over age 65. Prudent screening strategies, however, take a much more comprehensive approach. Whether extending screening past age 65 is an evidence-based, high-value practice involves knowing much more than we currently know about its consequences, intended and otherwise.

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