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Cervical Screening Performance

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To the Editor

Kaufman et al[1] present an analysis of cervical screening performance in a large commercial laboratory system that performs a sizable fraction of cervical screening in the United States, challenging recently revised consensus guidelines.[2,3] The laboratory system predominantly offers cotesting (human papillomavirus [HPV] testing and liquid-based cytology [LBC]). The authors evaluate the contribution of cotesting vs HPV alone and stress added value of LBC for detection of prevalent cancer diagnosed within 1 year.

Recently released American Cancer Society Cervical Screening Guidelines[2] and ASCCP Management Consensus Guidelines[3] were based on scientific inquiry by a large and varied group, considering many sources of salient data, such as large health plans, screening trials, statewide registries, and federal screening programs, and extensive consensus deliberations. Both guidelines recognize that the major goal of cervical screening is to detect cancer precursors before invasion. Both conclude, based on evidence from randomized clinical trials and multiple prospective studies lasting 15+ years, that protection against cervical cancer is best achieved by testing for the carcinogenic HPV types, the causal factor of virtually all cervical cancer cases. The aggregate data show that the value of adding cytology to HPV testing comes at a very high cost in terms of extensive overdiagnosis of trivial abnormalities.

A previous presentation from the group[4] elicited substantial methodologic criticism.[5,6] Kaufman et al[1] present an incomplete and misleading consideration of their large convenience sample. There is no information about timing and clinical presentation of the cancers, prior screening history, or the impact of different HPV tests they offer. The conclusions are mostly based on

findings from women with cancer detected within a year of the cotest. Many cancers in that window are already symptomatic and diagnosed at an advanced stage,[7] and the cotest is conducted as part of the clinical evaluation of symptoms, not as a screening test. HPV testing may be negative when advanced cancers are detected by microscopic signs of necrosis. To what extent has cotesting helped this group of patients? More broadly, among HPV negatives, what percentage of cytologic results observed within 1 year of diagnosis would actually speed diagnosis to improve cancer outcomes? For example, HPV-negative atypical squamous cells of undetermined significance, representing a large proportion of cytologic abnormalities, would not lead to colposcopic referral within the year. Also, what were the "other" cancers that showed higher yields for cytologic tests? Lacking presentation of these details limits interpretation of these findings and the endorsement of cotesting.

Kaufman et al[1] confirm that HPV testing is more sensitive than LBC in detection of cervical intraepithelial neoplasia grade 3 (CIN3) but minimize this finding. The suggestion that not detecting some CIN3 would be acceptable is at odds with clinical practice, is counter to regulatory processes, and would put women at risk of developing cancer. The stated concern about overtreatment is also at odds with their preference for cotesting, which has the highest positivity of all approaches and inevitably results in more overtreatment.

Recently published management guidelines involved clinical societies, federal agencies, clinicians representing relevant disciplines, and patient representatives.[3] Cost was not considered in the decision process; the consensus group was motivated to provide optimal care. Guidelines will continue to evolve, and new data analyses are important. Such analyses should be conducted with the same painstaking care and multiorganizational involvement that underly recent guidelines. Real-life databases are attractive to evaluate clinical questions and can provide data for guidelines but require thorough evaluation of the population, timing of testing, and assurance that sophisticated epidemiologic approaches are used.[8] We encourage a reanalysis of the database used by Kaufman et al[1] to address critical questions outlined above to rigorously compare cotesting with its component parts.

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