Response

Cytology-based screening for cervical cancer prevention was introduced in high-income countries in the mid-20th century, and many low- and middle-income countries attempted to follow suit. Approximately 50 years later, results of the roll-out and implementation of cytology-based screening are clear and undisputable: high-income countries have experienced a 70% or greater reduction in the burden of cervical cancer, whereas low- and middle-income countries have not similarly benefited from cytology screening, and more than 80% of the global burden of cervical cancer resides solely in these countries (1). This disparity exists because cytology-based screening cannot be effectively implemented and sustained in lower-resource settings (2).

Ultimately, decisions by the local in-country leadership about cervical cancer screening and treatment strategies will require an honest assessment of feasibility and cost as well as trade-offs between programmatic sensitivity and specificity. For low- and middle-income countries in which women might be screened only once or twice in their lifetime, we favor programmatic sensitivity to maximize the impact on cervical cancer. Importantly, for many years following a single round of human papillomavirus (HPV) testing, HPV-negative women are reassured that they are unlikely to develop (3) or die of (4) cervical cancer, whereas HPV-positive women, who would be treated in a HPV screen-and-treat protocol, are at risk for cervical precancer and cancer for many years regardless of their concurrent cytological abnormalities (3) (if specimen adequacy and technician training were a major limitation for HPV testing, as they are for cytology, such performance would not be achievable). Although overtreatment is not desirable, treatment by cryotherapy is efficacious with few complications (5). Treatment may also reduce the risk of subsequent HPV infection, as inferred by the reduced incidence of cervical intraepithelial neoplasia grade 1 (CIN1) observed in the South Africa trial (6). A cytology-based program, even a cytology-based screen-and-treat strategy (assuming that it could be implemented), would have greater specificity than an HPV-based approach. However, a cytology-based program would still lead to overtreatment because most CIN2 and CIN3 will never develop into invasive cancer, and most cytology-positive results are not associated with CIN2 or more severe lesions (7). The bottom line is that regardless of the combination of tests used, successful screening programs result in intervention for screen-positive women who do not and will never have life-threatening conditions (ie, cervical cancer).

In the South African trial (6), there was no extensive confirmatory testing of screen-positive women (T.C. Wright Jr, Columbia University, personal communication): HPV-positive women received cryotherapy

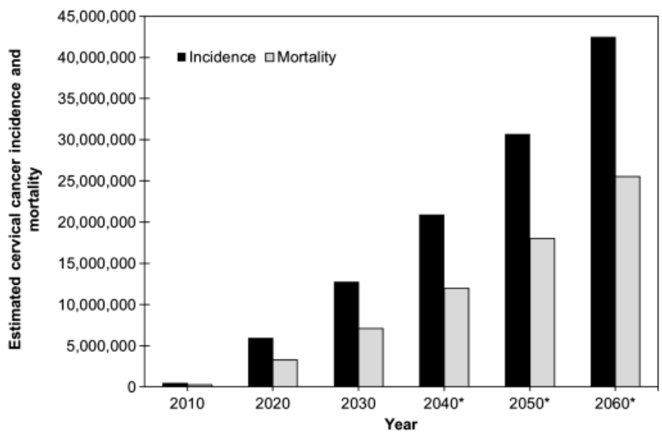

Figure 1. Estimated cumulative incidence of (**black bars**) and mortality due to (**gray bars**) cervical cancer in the less developed world assuming no large-scale medical or public health intervention. Data are as reported by http://globocan.iarc.fr/ (1). We suggest that these cervical cancer incidence and mortality rates in the less developed (low-resource) world are likely to be substantially underestimated because of the lack of resources for medical autopsies, medical records, pathology services, and pathology-based cancer registries. *The cumulative totals after 2030 were crude extrapolations, assuming a linear increase from the last estimate provided by GLOBOCAN for 2030.

unless visual inspection revealed contraindications for cryotherapy. Yet, more than 90% of cancers among women with contraindications were identified by an unaided visual examination before enrollment. The degree of acceptability for this intervention was high: 99.9% of the women reported that they would have referred friends and family to the program despite the lack of intermediate triage or diagnostic procedure.

Waiting to confirm the nonviability of cytology-based programs will likely result in millions of unnecessary cervical cancer deaths among underserved women (1) (Figure 1). The South African trial (6) may have provided the cervical cancer prevention community with a roadmap to sustainable cervical cancer prevention.

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Notes

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