

Use of an expanded gold standard to estimate the accuracy of colposcopy and visual inspection with acetic acid

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We estimate the accuracy of colposcopy and visual inspection with acetic acid (VIA) while minimizing the effects of misclassification bias, and maximizing ascertainment of disease. VIA was performed by experienced physicians on a population-based sample of women aged 30 to 49 years in rural Shanxi province, China. Each woman received VIA, liquid-based cytology (LBC) and hybrid capture 2 (hc2, QIAGEN, Gaithersburg, MD; formerly Digene Corporation). Any woman who tested positive on any test had colposcopy, endocervical curettage (ECC) with directed biopsies as necessary and 4-quadrant random biopsies from normal-appearing areas of the cervix. A standard diagnosis based on colposcopy and directed biopsy, and an expanded diagnosis including ECC and 4-quadrant random biopsy were generated for each woman. In 1,839 women, use of the expanded *versus* the standard diagnostic criteria increased the prevalence of histologically confirmed high-grade cervical intraepithelial neoplasia and cancer (CIN2+) from 3.2% (59/1,839) to 4.2% (77/1,839) and decreased the sensitivity of VIA for CIN2+ from 69.5% (95% CI: 56.8–79.8) to 58.4% (95% CI: 47.3–68.8%) with little change in specificity of approximately 89%. Compared with the expanded diagnostic criterion, the sensitivity of a visual diagnosis of high-grade CIN or cancer by a colposcopist was 49.4% (95% CI: 38.2–60.5). The use of an expanded diagnostic criterion in this study yielded more conservative estimates of the sensitivity of VIA and colposcopy.

Cervical cancer kills almost 250,000 women each year in developing countries, representing more than 80% of the worldwide deaths due to this preventable cancer.¹ Few women in these countries have access to an effective screening and treatment regimen that can detect and eliminate precancerous lesions. Cervical cytology has seen success in the developed world in reducing the incidence and mortality of cervical cancer.² However, in the developed world, the sensitivity and specificity of cytology have been shown to vary widely with an average of 53.0% (48.6–57.4%) and 96.3% (96.1–96.5%), respectively.³ To address the moderate sensitivity, periodic retesting is required. Most developing countries lack the infrastructure, trained personnel, supplies and equipment to enable accurate, reliable and timely testing and

reporting of results for one screening visit, much less for periodic retesting.⁴ A separate visit is commonly required to investigate abnormal cytology, and this leads to increasing rates of women who are lost to follow-up.

Despite the best of intentions and many attempts it has proven difficult to implement cytology-based screening programs in low-resource settings, and the mortality and morbidity due to cervical cancer continue to rise,⁵ prompting a search for alternative approaches to screening. VIA involves washing the cervix with a 3–5% acetic acid (vinegar) solution, and then examining the cervix for acetowhite areas with the naked eye one minute later. Equipment and supply requirements are minimal, test results are immediately available allowing for immediate treatment, and a variety of nonphysician providers can be trained to perform and interpret this test.⁶ Given adequate training and sustained quality assurance, computer modeling has shown VIA to be cost-effective in a developing-world context.⁷ A randomized trial in India has demonstrated that a VIA-based screening program led to reductions in both cervical cancer incidence and mortality.⁸

Previous studies have found that sensitivity and specificity of VIA vary between approximately 60–90% and 43–95%, respectively.⁹ Possible sources for this variability include disease ascertainment bias, verification bias, misclassification bias and unblinding bias. Although colposcopically-directed

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