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IMPACT OF PATIENT ADHERENCE AND TEST PERFORMANCE ON THE COST-EFFECTIVENESS OF CERVICAL CANCER SCREENING IN DEVELOPING COUNTRIES
The Case of Honduras

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Objective. **We examined the impact of patient adherence and screening test performance on the cost-effectiveness of visual inspection with acetic acid (VIA) and Pap smears when used with colposcopy for diagnosis.**

Materials and Methods. **Cost-effectiveness analysis was performed using computer modeling. The primary outcome was cancer prevalence in the 10 years after screening. Three hypothetical populations of 35-year-old women were compared: never-screened women, women screened with VIA, and women screened with Pap smears. We used community-based data from our screening program in Honduras to estimate screening test sensitivity and specificity, adherence to follow-up, and costs of screening and colposcopy services. Published data were used to model disease outcomes.**

Results. **VIA was more sensitive than Pap smears (70% vs. 4%), less expensive (U.S. $0.23 vs. $3.17), and the 2-vist VIA system had a higher rate of adherence to follow-up than the 3-visit Pap smear system (84% vs. 38%). VIA had a higher false-positive rate than Pap smears resulting in higher colposcopy referral rates, but more dysplasia was detected and treated. Cost-effectiveness analysis revealed that screening with VIA would cost U.S. $3,198 per cancer case avoided and reduce cancer cases by 42%, versus U.S. $36,802 and 2% for Pap screening. Although Pap smear quality was low in Honduras, sensitivity analysis showed that VIA was more cost-effective than Pap smears, even when test accuracy was equivalent.**

Conclusion. **In developing countries, systems barriers can limit the cost-effectiveness of Pap smears. VIA may be a cost-effective alternative for some resource-poor settings, although systems barriers, quality control, and feasibility issues must be considered.**

Introduction and Background

Cervical cancer is the most common cancer among women in developing countries, with an estimated lifetime risk of 2%–4% (Denny, 2005). Because health care resources are scarce; however, the cost-effectiveness of screening programs must be considered. Screening with Papanicolaou (Pap) smears, followed by colposcopy with biopsy for diagnosis and loop electrosurgical-excision procedure (LEEP) for treatment has become the standard of care

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for developed countries (Wright et al., 2007) owing to its effectiveness in reducing the population-wide incidence of invasive cervical cancer (Laara, Day, & Hakama, 1987) and its overall cost-effectiveness in this setting (Christopherson, 1983). However, there is currently no consensus regarding medical standards for cervical cancer screening in developing countries. Many developing countries in Latin America have existing Pap smear, colposcopy, and pathology services, and physicians follow the standards of care set in developing countries (Agurto, Sandoval, De La Rosa, & Guardado, 2006; Lazcano-Ponce, Moss, Alonso de Ruiz, Salmeron Castro, & Hernandez Avila, 1999; Robles, White, & Peruga, 1996). Unfortunately, cervical cancer mortality has remained high in Latin America, despite significant health care expenditures, owing to poor quality services and limited population coverage (Agurto et al., 2006; Lazcano-Ponce et al., 1999; Robles, White, & Peruga, 1996).

Visual inspection with acetic acid (VIA) has been proposed as an alternative to Pap smear screening in developing countries. VIA involves washing the cervix with 3%–5% acetic acid and then looking for changes indicative of precancerous lesions. The attractive features of VIA include low cost, simple administration, immediate availability of results, and accuracy comparable to that of good quality Pap smears (Denny et al., 2005; Megevand, Denny, Dehaeck, Soeters, & Bloch, 1996; Sankaranarayanan et al., 2004; University of Zimbabwe/JHPIEGO Cervical Cancer Project, 1999). VIA is typically recommended as part of a "see-and-treat" algorithm. The "see-and-treat" approach involves screening women with VIA and treating those with abnormal examinations using cryotherapy ablation in the same visit. This is very inexpensive, maximizes adherence to follow-up therapy, and has been shown to be more cost-effective than screening with Pap smears in low resource settings (Goldie et al., 2005; Goldie, Kuhn, Denny, Pollack, & Wright, 2001; Legood et al., 2005).

"See-and-treat" falls below the current standard of care in developed countries (Wright et al., 2007), however, because no pathologic diagnosis is obtained to ensure the adequacy of treatment. Physicians in developing countries who currently provide Pap smear, colposcopy, and LEEP services may be reluctant to adopt a "see-and-treat" system that falls below their standard of care, even if it is more cost effective (Suba et al., 2006). To maintain local standards of care, VIA can be used instead of Pap smears for initial screening, with colposcopy and LEEP performed to for diagnosis and treatment. VIA is a less expensive screening test than the Pap smear, but its false-positive rate is higher, resulting in more colposcopy referrals, which could limit cost savings. To date, no study has examined whether VIA is cost effective when used with colposcopy and LEEP services.

Existing studies comparing the cost effectiveness of VIA and Pap smears primarily used data from large research projects (Goldie et al., 2005; Goldie et al., 2001; Legood et al., 2005) and incorporated good quality Pap smears in their models. During our community-based screening and treatment project in Honduras (Perkins, Langrish, Stern, Figueroa, & Simon, 2007), we found that factors including lack of communication infrastructure (telephone, postal services), routine supplies (spatulas, fixative, laboratory dyes), and up-to-date cytopathologist training and certification negatively impacted both Pap smear quality and patient adherence. The impact of these local factors may be important when comparing the cost effectiveness of Pap smear and VIA screening programs. The purpose of our study is two-fold: 1) to compare the cost effectiveness of VIA and Pap smears when colposcopy is used for diagnosis, and 2) to examine the impact of systems barriers such as screening test performance and adherence to follow-up on cost effectiveness.

Methods

Primary data collection: Cervical cancer screening project in Honduras

Honduras is the second poorest country in the Western Hemisphere; two thirds of the population lives below the poverty line and half lacks basic sanitation and potable water. The average person receives 2–3 years of schooling, and 30% of the population is illiterate (Secretary of State of Honduras Presidential Report: nformation by Department and Municipality, 2004). The cervical cancer incidence in Honduras is 39.1/100,000 and the mortality is 16.8/100,000 (Arrossi, Sankaranarayanan, & Parkin, 2003). These rates are over four times higher than in the United States and over 10 times higher than in Finland (Aareleid, Pukkala, Thomson, & Hakama, 1993; U.S. Department of Health and Human Services, 2000). Honduras has no nationwide cervical cancer screening program, but Pap smears are widely available through local health centers, private clinics, or special screening days organized by a variety of private organizations. VIA is available in a handful of clinics nationwide.

The primary data for this cost effectiveness analysis were collected during our cervical cancer screening and treatment project which took place in Honduras between June 2003 and September 2004 (Perkins et al., 2007). During the project, we provided no-cost screening and treatment services to women in an underserved region of Honduras. We screened 1,370 women with Pap smears alone and an additional 339 women with both Pap smears and VIA. Women with abnormal results on either test underwent colposcopy with colposcopic-directed biopsy for diagnosis, and treatment with LEEP excision when appropriate. All pathologic specimens were processed, interpreted,