**Systems Analysis of Real-World Obstacles to Successful Cervical Cancer Prevention in Developing Countries**

Papanicolaou screening is feasible anywhere that screening for cervical cancer, the leading cause of cancer-related death among women in developing countries, is appropriate. After documenting that the Vietnam War had contributed to the problem of cervical cancer in Vietnam, we participated in a grassroots effort to establish a nationwide cervical cancer prevention program in that country and performed root cause analyses of program deficiencies. We found that real-world obstacles to successful cervical cancer prevention in developing countries involve people far more than technology and that such obstacles can be appropriately managed through a systems approach focused on programmatic quality rather than through ideological commitments to technology. A focus on quality satisfies public health goals, whereas a focus on technology is compatible with market forces. (Am J Public Health. 2006;96:480–487. doi:10.2105/AJPH.2004.061606)

The great struggle to come, already emerging, is that between public health and personal responsibility, on the one hand, and the market on the other. The market can, and does already, overshadow both ‘genetics medicine’ and public health. It sets the stage and the social context, and thus has a commanding and still-rising power. The ultimate struggle I have in mind is between the population perspective of public health and the individualist perspective of the market.

—Daniel Callahan

**MOST OF THE WORLD’S premature deaths can be prevented with simple, available interventions; what is not clear is how to make these interventions more widely available to the people who need them.**

Cervical cancer, for example, is both preventable and curable, yet it remains the leading cause of cancer-related death among women in developing countries. Moreover, the impact of this disease is likely to increase over time. Declining birth rates throughout the developing world have induced a profound demographic transition that is leading to a shift in disease burden away from diseases of childhood toward cancer and other diseases of adulthood.

Human papillomavirus (HPV; the sexually acquired causative agent of cervical cancer) prophylactic vaccines, prospects for which remain uncertain, may potentially benefit only those generations of women who will not yet have initiated sexual activity by the time putative vaccines are first licensed, and 20 to 30 years may elapse from the time any vaccine is first licensed to the time most people in developing countries have access to it. Any future vaccinated populations will require less screening rather than no screening. When fully successful, conventional Papanicolaou (Pap) cyto logic screening reduces cervical cancer rates by 60% to 90% within 3 years of introduction to populations that have not previously been screened; these reductions in incidence and mortality are consistent and dramatic across populations.

We have advocated making Pap screening services available without further delay to women in high-risk demographic groups anywhere such services are feasible but unavailable, not because the Pap test will forever remain the most effective cervical screening option in all settings but because, in the case of any setting, it is both prudent and strategically necessary to implement Pap screening before rather than after completing research on either vaccines or what may become an endless series of novel screening technologies. Opportunity costs, borne by the underserved, are associated with prioritizing research on novel health interventions in settings where established interventions are feasible but unavailable, and research on novel screening technologies in developing countries has been justified by understandable yet incorrect assumptions that Pap screening is not feasible in such settings. Groups performing research on novel screening technologies have overestimated costs for Pap tests in developing countries 10- to 100-fold, overlooking the finding that Pap screening programs have been operational in several developing countries for more than 30 years.

The Pap test is one of the most inexpensive tests in American medicine, and we have suggested setting aside the paradoxical yet commercially useful belief that such a labor-intensive item will be inexpensive in settings where salaries are high but expensive in settings where salaries are low. Assuming that it is not appropriate to screen for cancer in communities without access to curative treatment services, Pap screening appears to be feasible anywhere that cervical screening is appropriate, in that it is difficult to envision either urban or rural communities with access to surgical and radiation therapy services but not to cytology laboratories.

Past failures of cervical screening efforts in developing countries can be directly related not to technological limitations of the screening test but to failures in system quality management, the goal of which is to confirm that women in targeted demographic groups are screened and receive appropriate follow-up. A shift in paradigmatic focus...
from technology toward quality is therefore essential. Sociopolitical obstacles to achievement of adequate programmatic quality are widespread and may arise when improved quality, which increases the likelihood of beneficial outcomes among recipients of care, does not increase the likelihood of increased incomes among providers of care.\textsuperscript{18}

We have suggested that interactions between programmatic quality and related sociopolitical obstacles will be elucidated by following the money as well as the science involved with cervical screening activities.\textsuperscript{18} Here we propose that real-world obstacles to successful cervical cancer prevention in developing countries are more appropriately addressed through a systems approach incorporating root cause analysis and focused on the concept of health care quality than through an ideological commitment to a single programmatic component. We also suggest that a focus on quality is more compatible with public health and humanitarian goals, whereas a focus on technology is more readily aligned with market forces.

**METHODS**

War is associated with male sexual promiscuity, which in turn contributes to the development of cervical cancer among sexually monogamous women.\textsuperscript{13} In 1996, a case-control study sponsored by Stanford University documented that the Vietnam War had contributed substantially to the problem of cervical cancer in contemporary Vietnam,\textsuperscript{19} and the Viet/ American Cervical Cancer Prevention Project was established as an all-volunteer nonprofit organization. Working as unpaid volunteers, project participants were free to obey the logic of the situation on the ground in Vietnam rather than the logic of competitive grant renewal.\textsuperscript{20} Publication of data linking war to disease was delayed for 8 years in an attempt to ease the process of reconciliation by offering what most would acknowledge to be a remedy,\textsuperscript{9,21} in advance of what some will perceive to be an accusation.\textsuperscript{9,20}

In 1999, we performed a cost-effectiveness analysis of Pap screening in Vietnam in response to concerns expressed by Vietnamese and global health policymakers about the feasibility of Pap screening in developing countries. Previous experience in the United States\textsuperscript{22} had shown us the uncertainties associated with reported prices for Pap tests. Rather than relying on Pap test prices based on local fee schedules, we used the total cost of a hypothetical Vietnamese screening system to deduce the cost of a single screening event. Our systems approach allowed groups of health workers prone to competition to view themselves in relation to other categories of workers, to their own shares of system costs and responsibilities, and to the system goal of improving health outcomes among women.

Our cost-effectiveness analysis documented that, contrary to widespread belief, Pap screening in developing countries such as Vietnam is extraordinarily inexpensive,\textsuperscript{21} and our findings enabled de novo establishment of population-based public-sector Pap screening services in Vietnam. Our analysis also implied that Pap screening in other developing countries was substantially more feasible than had previously been perceived. The validity of our analysis was challenged by the Alliance for Cervical Cancer Prevention (ACCP).\textsuperscript{23} The primary focus of ACCP, established in 1999 through a gift of $50 million from the Bill and Melinda Gates Foundation, is research on novel cervical screening technologies in developing countries.\textsuperscript{24}

Between 1999 and 2004, population-based Pap screening programs were established in 10 districts in southern and central Vietnam. High-risk target demographic groups were defined according to age and geographic location. The target age group, as defined by the natural history of cervical neoplasia, consists of women between the ages of 30 and 55 years.\textsuperscript{21} Cervical cancer rates are 26 per 100,000 in southern Vietnam\textsuperscript{32} and 4.4 per 100,000 in northern Vietnam,\textsuperscript{33} and these rates are associated with regional differences in HPV prevalence\textsuperscript{34} and the movement of soldiers during a previous epoch.\textsuperscript{28} At present, cervical cancer rates in northern Vietnam do not appear sufficiently high to warrant initiation of population-based screening.\textsuperscript{21}

All screening and treatment activities are being performed entirely by Vietnamese public-sector health providers. In certain districts, erosion of programmatic quality has been observed in the form of decreases over time in Pap test rates of atypia, follow-up rates of women with atypical test results, and yields of biopsy-confirmed cervical neoplasia. Public reporting of information on health care quality can improve health outcomes,\textsuperscript{25} but a crucial and ongoing challenge is finding methods to achieve measurement for public reporting of quality that do not undermine measurement for quality improvement.\textsuperscript{26} Detailed Vietnamese laboratory screening data are not presented in this article out of concern on the part of Vietnamese and American program participants that public reporting may lead to disciplinary action that would undermine future quality improvement efforts.

Because the true causes of problems are often hidden behind more obvious symptoms,\textsuperscript{27} we performed root cause analyses of cervical screening failures in Vietnam and other developing countries. Root cause analysis is a qualitative method that focuses on determining the underlying systems that set the stage for error,\textsuperscript{28} and such analyses are conducted to improve patient outcomes rather than to effect punitive change. The goal of any root cause analysis is to determine what happened, why it happened, and what to do to prevent it from happening again.\textsuperscript{29} Those most familiar with a situation are interviewed, and, through a persistent series of “why” questions, levels of health care processes at which failure occurs are determined.\textsuperscript{30}

We interviewed 5 Vietnamese public health department directors and vice directors, 8 nurses, 5 hospital directors, 5 cytopathologists, 5 laboratory directors, 5 gynecologists, 3 community outreach leaders, and 10 pathologists from Hanoi, Hue, and Ho Chi Minh City. All interviewees were involved with cervical screening activities in Vietnam. We interviewed as well laboratory directors and pathologists involved with cervical screening in developing countries other than Vietnam during international health conferences. Additional information pertaining to cervical screening failures in developing countries was obtained through literature.
reviews. Because certain research and commercial interests represent obstacles to success in Vietnam,31 we also conducted interviews with research personnel and industry representatives attending international health conferences and obtained further information through literature reviews. On the basis of our root cause analyses, we constructed a system map outlining obstacles to successful cervical screening to display how changes in each area of the system of cervical cancer prevention activities affect other areas.

## RESULTS

The results assembled from our interviews and literature reviews were categorized according to the perspectives of different groups of program participants and are presented in Table 1. This system map outlines some of the ways in which competing incentives among groups with shared interests in cervical cancer prevention affect program success, defined as ensuring that 100% of women in high-risk target demographic groups are screened and receive appropriate follow-up and treatment.

### Table 1—System Map of Real-World Obstacles to Successful Cervical Cancer Prevention in Developing Countries

<table>
<thead>
<tr>
<th>Program Group (Quality Goal)</th>
<th>Clients</th>
<th>Competing Incentives</th>
<th>Quality Measures</th>
<th>Obstacles to Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk women (100% program participation)</td>
<td>...</td>
<td>Higher prices for screening visits reduce program participation</td>
<td>Laboratory data linked to population registers</td>
<td>Higher net reimbursement for any other program group increases screening visit prices and reduces participation</td>
</tr>
<tr>
<td>Screening test collectors (100% coverage of high-risk demographic groups)</td>
<td>Public health departments and private-sector patients</td>
<td>Collecting cytologic, HPV, or visual screening tests in private rather than public sector increases net reimbursement</td>
<td>Laboratory data linked to population registers</td>
<td>Reimbursement often inversely linked to program coverage</td>
</tr>
<tr>
<td>Pathology laboratory personnel (diagnostic accuracy)</td>
<td>Public health departments and private-sector providers</td>
<td>Decreasing time and money spent analyzing each Papanicolaou test; or HPV test increases net reimbursement</td>
<td>Laboratory data analysis</td>
<td>Reimbursement often inversely linked to accuracy</td>
</tr>
<tr>
<td>Dysplasia treatment personnel (examine 100% of women with high-risk screening test results)</td>
<td>Public health departments and private-sector patients</td>
<td>Treating patients in private rather than public sector increases net reimbursement</td>
<td>Laboratory data analysis</td>
<td>Reimbursement often inversely linked to treatment of women in high-risk groups</td>
</tr>
<tr>
<td>Visual “screen and treat” personnel (100% coverage of high-risk demographic groups)</td>
<td>Public health departments and private-sector patients</td>
<td>Performing visual examinations in private rather than public sector increases net reimbursement</td>
<td>Laboratory data analysis</td>
<td>Neither coverage nor treatment adequacy can be confirmed; reimbursement often inversely linked to coverage and treatment of women in high-risk groups</td>
</tr>
<tr>
<td>Public health departments (goals defined by political leaders)</td>
<td>Political leaders</td>
<td>Competing sources of mortality (e.g., HIV, malaria, tuberculosis, avian influenza)</td>
<td>Budgetary allocation from government</td>
<td>Goals of political leaders often not linked to program coverage</td>
</tr>
<tr>
<td>Academic investigators and nongovernmental organizations (goals defined by grant donors, corporate sponsors, and academic journals)</td>
<td>Grant donors and corporate sponsors</td>
<td>Fund-raising and publications are required for academic career advancement and financial sustainability of nongovernmental organizations</td>
<td>Grants and publications</td>
<td>Grant donor goals, corporate sponsor goals, and academic journal publication acceptance criteria often not linked to program coverage</td>
</tr>
<tr>
<td>HPV and monolayer cytology test manufacturers (goals defined by equity stakeholders)</td>
<td>Equity stakeholders</td>
<td>Higher product price increases profit but lowers participation</td>
<td>Stock price</td>
<td>Equity stakeholder reward often not linked to program coverage</td>
</tr>
<tr>
<td>Vaccine manufacturers (goals defined by equity stakeholders)</td>
<td>Equity stakeholders</td>
<td>Vaccines will not eliminate screening requirements and may compete with screening for public health budgets; higher vaccine unit costs may lower coverage rates of both vaccination and screening programs</td>
<td>Stock price</td>
<td>Equity stakeholder reward often not linked to program coverage; public health departments may delay development of screening programs pending vaccine development</td>
</tr>
</tbody>
</table>

Note. HPV = human papillomavirus. *Measurement of screening and treatment activity limited to nonverifiable, self-reported activity logs.
Screening Test Collectors’ Perspective

The results from our literature review show the well-recognized obstacle to successful cervical cancer prevention in developing countries\textsuperscript{35} like Vietnam: an overreliance on reproductive health services for Pap test collection. Unfortunately, the target age group for reproductive health services and the target age group for cervical screening services barely overlap. As a result of the transition toward a market economy in Vietnam, increases in private-sector health provider incomes have dramatically outpaced increases in public-sector incomes, producing incentives against conducting Pap screening in the public sector.

Pathology Laboratory Personnel Perspective

Root causes of suboptimal diagnostic performance in Vietnamese laboratories were similar to those previously reported for American and Mexican laboratories\textsuperscript{36–38} and included obsolete supplies, poorly maintained microscopes, insufficient training, and suboptimal working conditions. The results from our interview with pathologists in developing countries show that cytootechnologists are often allocated insufficient time to perform microscopic examinations of Pap tests, which adversely impacts detection rates of cervical neoplasia.

Dysplasia Treatment Personnel Perspective

We found that salary differentials between the private and public sectors were far more pronounced for physicians than for other health providers, yielding few financial incentives to follow-up on women with positive screening test results when tests are collected in the public sector. Successful follow-up of screen-positive women in developing country settings, including Vietnam, has been achieved by allocating budgets for dedicated personnel to recontact women with positive test results.\textsuperscript{39} Successful follow-up of women from both urban and rural areas has been demonstrated in Cameroon (100\% follow-up),\textsuperscript{40} China (100\%),\textsuperscript{41,42} Costa Rica (97\%),\textsuperscript{43} South Africa (91\%),\textsuperscript{44} Venezuela (89\%),\textsuperscript{45} and Zimbabwe (98\%).\textsuperscript{46}

Visual “Screen and Treat” Personnel Perspective

Visual “screen and treat” specifically refers to the screening algorithm by which a visual screening test of the cervix (after application of dilute acetic acid or Lugol’s iodine, or both) is coupled with immediate cryosurgery in all test-positive cases. Visual screening tests have false-negative rates comparable to those associated with Pap tests, but they involve much higher false-positive rates.\textsuperscript{47} Because Pap screening is feasible wherever cervical screening is appropriate, visual screen and treat requirements in any particular setting are not apparent. However, the results from our literature review show a widespread tendency to incorrectly attribute past failures of cervical screening in developing countries to technological limitations of the Pap test, rather than to sociopolitical factors that impact any screening test. These incorrect perceptions produce incentives to implement noncytologic screening methods such as visual screen and treat. Because, in real-world settings, visual screen and treat programs produce no physical evidence on which to base meaningful program audits, the existence, let alone effectiveness, of such programs will not be verifiable outside of research settings.\textsuperscript{39} Although the long-term safety of large-scale overtreatment has not been established,\textsuperscript{39} the high false-positive rate associated with visual screening techniques will require performing cryosurgery on 18\% to 71\%\textsuperscript{42,46,48} of women who are screened.

In the case of visual screen and treat, screen-positive women undergo cryosurgery before the possibility of invasive carcinoma has been excluded, which has problematic implications for provider acceptance, patient safety, and informed consent.\textsuperscript{30} Approximately 18\% to 71\% of women screened will be informed that they have a positive cervical cancer screening test, that cryosurgery will probably render it impossible for anyone to determine whether cancer is present, and, if cancer is in fact present, that cryosurgery will be ineffective.

Public Health Departments’ Perspective

There appears to be a genuine lack of support for cervical cancer prevention efforts within the political structures of many developing countries,\textsuperscript{49} including Vietnam. Coverage of the target demographic population has not exceeded 40\% in any Vietnamese district where population-based Pap screening is currently being performed. Operational funding for all Vietnamese screening activities is being provided entirely by Vietnamese departments of public health, which are under significant pressure to support programs for control of competing sources of mortality, including HIV\textsuperscript{50} and avian influenza.\textsuperscript{31}

Academic Investigators’ and Nongovernmental Organizations’ Perspective

ACCP is a partnership involving 5 nongovernmental organizations: the Program for Appropriate Technology in Health, EngenderHealth, JHPIEGO, the Pan American Health Organization, and the International Agency for Research on Cancer of the World Health Organization. The ideological commitment of the Bill and Melinda Gates Foundation to novel technologies as the best route for improving health outcomes in developing countries explicitly ignores the sociopolitical and power structure changes necessary to redistribute resources within and between societies, and this commitment to such technologies has been criticized as potentially harmful in public conducted literature review.\textsuperscript{52}

Manufacturers’ Perspective

All for-profit corporations have fiduciary obligations to shareholders who are interested primarily in return on investment. Certain business strategies intended to benefit shareholders have been appropriately criticized by public health authorities.\textsuperscript{53}

DISCUSSION

As cervical cancer, a preventable public health problem, escalates with mathematical certainty throughout the developing world, our analysis shows that developing country health systems are struggling to succeed against an array of real-world obstacles, including nongovernmental organizations and academic investigators distracted by fund-raising.
Before root cause analyses determined the levels at which programmatic failure had occurred in the Costa Rican screening system, the US National Cancer Institute and corporate sponsors allocated millions of dollars to screen approximately 10,000 women in Guanacaste Province with an unprecedented array of novel screening technologies, some of which are now obsolete. Data collected from women in Guanacaste have been used to market novel screening technologies in the United States and formed the basis for numerous academic publications, thereby benefiting both research and commercial interests. However, it is uncertain whether the Guanacaste Project benefited women in any developing country setting outside of Guanacaste Province.

Technological refinements to the Pap test have not been associated with improved clinical outcomes in any setting, and they are unlikely to be associated with improved outcomes in the future. Although it is not meaningful to compare characteristics of novel screening tests analyzed in American reference laboratories with those of Pap tests analyzed in developing countries, all novel screening tests collected in Guanacaste were shipped to American reference laboratories for analysis. Only conventional Pap tests collected in Guanacaste were analyzed in Costa Rica.

At the time the Guanacaste Project was initiated, a system-wide quality improvement program also was proposed for Costa Rica that involved the establishment of a central coordinating unit, a colposcopy network, and consolidated laboratories. Between 1997 and 2000, age-standardized cervical cancer mortality rates in Costa Rica declined from 10.2 per 100,000 to 8.0 per 100,000. Because, to our knowledge, only conventional Pap tests have been used in public-sector screening in Costa Rica, it appears that the public health success documented in that country is attributable to a systems approach focused on quality rather than to an ideological commitment to a single programmatic component.

Within developing countries such as Vietnam, obstacles to the achievement of adequate programmatic quality are widespread. All health workers have incentives to increase net reimbursement, which may lead to low coverage of the targeted screening population, inadequate follow-up of screen-positive women, and poor laboratory performance. These patterns of programmatic failure have been observed in both developed and developing countries and serve as examples of the “prisoner’s dilemma” in game theory. Programmatic failures occur when participants uniformly pursue rational self-interests, whereas programmatic successes occur when at least some participants act in a manner partly contrary to rational self-interests.

Thus, successful cervical cancer prevention requires a combination of program managers who care about quality and program stakeholders who exert the political will to entrust managers with levels of authority commensurate with their responsibilities. Active participation by public health leaders is essential but requires support from appropriate governmental authorities, including ministries of finance. It is not appropriate to screen for cancer in communities without access to curative treatment services, and radiation therapy facilities in Vietnam meet only 10% to 20% of current actual demand. Although curative treatment facilities are in short supply throughout the developing world, it is paradoxical to cite shortages of required infrastructure as a reason not to develop more, and we continue to encourage potential donors to consider writing equipment costs for such facilities in Vietnam.

Novel technologies do not substitute for root cause analysis and may reinforce sociopolitical, technological, and financial obstacles to successful cervical cancer prevention. Ongoing ACCP randomized trials of novel screening technologies in developing countries include control groups of 75,000 unscreened women. The science and ethics of placebo-controlled trials in developing countries are complex, and we have entreated ACCP to publish a compelling scientific and ethical justification for the inclusion of no-screening arms in its ongoing randomized trials in order to prevent dissatisfaction of medically underserved groups such as that occurring after the Tuskegee syphilis experiment, which included an untreated control group of 399 men. Otherwise, we have suggested that women in the no-screening arms of these trials be reassigned to screening arms without further delay.

Both HPV and visual testing are vulnerable to the same quality control problems that have plagued the Pap test. In research settings, quality of visual testing degrades more rapidly
Visual screen and treat is the only cervical screening strategy that dispenses, in theory, with any requirement to establish a laboratory. To the extent that visual screen and treat is considered feasible, delays in the development of Pap screening services may continue to be rationalized. Because the Pap test will be a triage component of any other visual-based or HPV-based screening program, the obsolescence of visual screen and treat would immediately make viable a global consensus strategy by which Pap screening programs would be established immediately, with HPV or visual testing (or both) introduced later. Demonstration of an increased yield of biopsy-proven neoplastic lesions in a given population will remain the best proof of the value of any nontraditional screening methodology.

It would become strategically self-defeating for proponents of HPV or visual testing to delay implementation of Pap screening programs in any setting. The obsolescence of visual screen and treat, an intervention we have characterized as conceptually incompatible with the requirements of “first, do no harm,” is therefore of critical strategic importance in global cervical cancer prevention efforts. Visual screen and treat requires that women with positive cancer screening test results undergo ablative rather than excisional treatments before the possibility that cancer is present can be excluded. Visual screen and treat would necessitate regular acts of uncontested medical malpractice were it ever to be implemented in the United States, and in any setting it would generate considerable psychological morbidity owing to justifiable concerns about untreated cancer among up to 71% of women screened.

However, both ACCP and the American College of Obstetricians and Gynecologists have endorsed visual screen and treat as a safe, effective, and cost-effective approach to cervical cancer prevention in low-resource settings (including, presumably, those in the United States), raising concern about the global emergence of an iatrogenic public health problem. Correspondingly, the International Academy of Cytology has neglected to provide conceptual support for Pap screening in developing countries, without which donors and governmental authorities may be understandably reluctant to provide material support.

Disease prevention requires social change, which in turn requires the participation of those for whom the change is intended, including demographic groups at high risk for disease, appropriate governmental authorities, and essential medical personnel. Both locally and globally, sociopolitical problems associated with sustaining working coalitions from groups with shared interests but competing incentives constitute critically important real-world obstacles to successful cervical cancer prevention and will remain so irrespective of the screening method(s) eventually used. In settings where health systems cannot afford to ignore such incentives, laboratory data constitute an essential yet sometimes overlooked fulcrum against which to leverage the social change required to preserve life.

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Contributors

E. J. Suba supervised the study and led the writing. E. J. Suba and S. S. Raab performed the root cause analyses. All of the authors assisted with systems analyses and reviewed drafts of the article.

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Note. The views herein are those of the authors and not necessarily those of Kaiser Permanente, the University of California at San Francisco, the Brigham and Women’s Hospital, or the University of Pittsburgh.

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Reconsidering the Feasibility of Papanicolaou and Alternative Screening Tests for Low-Resource Countries

Despite the commendable commitment of Suba et al.1 to cervical cancer prevention in developing countries, several key conclusions in their article are made on the basis of inaccurate and misleading use of references. For example, they cite an International Agency for Research on Cancer document2 as saying that Papanicolaou test–based programs have been “operational” in developing countries for more than 30 years. However, no operational programs of any scale were identified in Africa or Asia. The same document concludes that even in Latin America, “attempts to organize screening programs have failed . . . in spite of a coverage of over 60%.” Further, the authors cite as “voluminous evidence” of the feasibility of Papanicolaou screening in developing countries just 3 references: a pilot project led by Suba et al. in a city in Vietnam, a set of guidelines in South Africa that have yet to be successfully implemented, and the same International Agency for Research on Cancer document previously cited as evidence that cytology-based programs have been operational (but not effective) in low-resource countries.

Suba et al. claim that successful follow-up of screen-positive women is feasible, as proven in 6 countries they name, but all 6 countries involved limited research studies done with external resources, not routine health services where the real-life problem of poor follow-up prevails.3,4

On visual “screen and treat,” Suba et al. state that use of visual inspection with acetic acid (VIA) would “require performing cryosurgery on 18% to 71% of women who are screened.” The 3 references they cite for this claim (all from 2001 or earlier) list screen-positive rates of 28%, 39%, and 18%. More recent studies (not cited by Suba et al.) produced test-positive rates from 7% to 33%, with most under 15%. Although some overtreatment is inevitable (because even cervical intraepithelial neoplasia identified by cytology will often regress spontaneously), VIA would not lead to treatment of up to 71% of all women screened, as repeatedly stated by Suba et al.

Contrary to the authors’ assertion, visual screen-and-treat algorithms by Alliance for Cervical Cancer Prevention partners and others all call for referring any woman with a lesion suspicious for cancer to further evaluation, and VIA studies have missed few, if any, cancers.6,10 In addition, many proponents of visual inspection for routine service also recommend taking a biopsy before the ablative treatment (wherever pathology services exist).10

The drawbacks of cytology are now well understood in resource-poor settings. VIA offers a viable alternative that deserves consideration on the basis of the evidence.

Vivien Davis Tsu, PhD, MPH

References
"Feasibility" refers to that which is possible, in addition to that which is operational, successful, or sustained. Papanicolaou screening is feasible anywhere cervical screening is appropriate, because it is not appropriate to screen for cancer among communities without access to curative treatment services, and because communities with access to curative treatment will also have access to cytology.
laboratories. Papanicolaou screening is the only preventive option currently available for public sector control of cervical cancer in developing countries. Because future screening programs based on alternative screening tests will require cytology as an essential triage component, visual inspection with acetic acid (VIA), human papillomavirus, and cytology tests may be appropriately regarded as complementary rather than competitive.

Research on alternative screening tests in developing countries has unfortunately been justified by incorrect assumptions that Papanicolaou screening is not feasible in low-resource settings where screening is appropriate. Because these incorrect assumptions undermine progressive public health leaders and empower apologists for the status quo, nongovernmental organizations and investigators distracted by fundraising obligations disconnected from public health goals engender significant obstacles to successful cervical cancer prevention in developing countries. Tsu does not specify why management procedures used for follow-up in research settings cannot be used in real-world settings.

We regret any confusion caused by the inference that “abnormal” rates of 20% to 39%, added to “atypical” rates of 37% to 49%, suggest a test-positive rate of 71% for VIA. VIA remains a feasible screening test for premenopausal but not postmenopausal women. Because individuals with positive screening tests understandably desire to know whether they truly have cancer, the implementation of VIA in real-world settings will require confirmatory testing, such as the biopsies suggested by Tsu, that will in turn require cytologic triage. Screening strategies—including VIA “screen and treat”—that do not provide required confirmatory testing should be considered obsolete.

Foege et al. have observed that a lack of management skills appears to be the single most important obstacle to improving health throughout the world. Our findings corroborate their observation in the context of cervical cancer prevention in developing countries, where critical real-world obstacles involve people far more than technology, and where skilled program managers are therefore critical for success. Failures of cervical cancer prevention efforts are not attributable to factors specific to the Papanicolaou test, but to lapses of political will and programmatic quality management to which all screening tests are vulnerable. The use of alternative screening tests may reinforce, rather than overcome, critical real-world obstacles.

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References
We strongly disagree with the authors’ comments about our work and have responded in detail to these criticisms previously. We refer Journal readers to our most recent response to Suba et al. and to the voluminous evidence describing our work, a small portion of which is cited here. The comprehensive work of the ACCP can be reviewed online (http://www.alliance-cxca.org); we invite readers to visit the site and make their own determinations regarding ACCP’s ethical, clinical, scientific, and public health value.

Another recurring criticism that Suba et al. make about ACCP’s work is that it is influenced by private-sector interests. We would like to take this opportunity to set the record straight. The ACCP has never received funding from any commercial entity. An erroneous statement about an ACCP link with Digene Corporation in a 2004 editorial has been corrected. Suba et al. may be misinterpreting PATH’s separate START project (http://www.path.org/projects/start_project.php), which is working to develop simple, rapid, and affordable biochemical screening tests (including a simpler human papillomavirus test) in partnership with 2 private-sector companies. The START project is funded by the Bill & Melinda Gates Foundation and the National Institutes of Health; PATH receives no funding from commercial partners for START work.

It is regrettable that Suba et al. discourage new approaches to cervical cancer prevention, often with arguments based on uninformed or inaccurate information. We believe that there are multiple strategies to prevent cervical cancer, including well-run cytology-based programs, human papillomavirus DNA testing–based programs, “screen-and-treat” programs, and human papillomavirus vaccine introduction. Women in developing countries clearly will benefit from the new policies, programs, and pilot efforts related to these approaches.

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ALLIANCE FOR CERVICAL CANCER PREVENTION: SETTING THE RECORD STRAIGHT

The recently published article by Suba et al. advocates for expanded access to Papanicolaou testing worldwide and for analysis of obstacles to effective screening programs. We are pleased to see discussion of this important topic in the Journal.

Suba et al. criticized the work of the Alliance for Cervical Cancer Prevention (ACCP), an alliance of 5 organizations with a goal of reducing cervical cancer deaths among the world’s poorest women. The article repeats previous criticisms the authors have made, including about the safety of visual screening approaches, the ethics of several ACCP studies, the assertion that ACCP leaders are “loath to recommend” cytology, and the theoretical underpinnings of ACCP cost analyses.
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References


SUBA RESPONDS

The participants of the Viet/American Cervical Cancer Prevention Project have agreed that research on novel screening approaches in certain low-resource settings may be appropriate, provided that such research is conducted subordinate to, not instead of, the development of Papanicolaou (Pap) screening services in the same settings. Opportunity costs, borne by the underserved, are associated with prioritizing research on novel health interventions in any setting where established interventions are feasible but unavailable. The debate to which Sherris et al. appropriately refer Journal readers may be considered part of a larger debate, articulated bluntly by President Jimmy Carter, over whether the Bill & Melinda Gates Foundation has become enamored with the promise of science and novel technologies at the expense of delivering available preventives today. That research on novel technologies in developing countries may be more compatible with market forces than with public health goals adds additional complexity to the situation.

It would be paradoxical to suggest that Program for Appropriate Technology in Health (PATH) is partnered with yet uninfluenced by human papillomavirus (HPV) test manufacturers. For example, PATH’s partnership with Digene Corporation (Gaithersburg, MD) presents a source of potential bias in favor of HPV screening that should be disclosed to readers of Alliance for Cervical Cancer Prevention cost-effectiveness studies. Because dozens of public–private partnerships have recently been established with philanthropic funding in global health, PATH should set a leading example by fully disclosing the terms of its public–private partnerships, including any arrangements for revenue sharing from future sales of HPV tests.

More than 7 years after the founding of the Alliance for Cervical Cancer Prevention, cytology remains the only preventive option available for public-sector cervical cancer control in developing countries. HPV vaccination, the long-term effectiveness of which remains uncertain, is currently unaffordable, as is HPV screening. Quality management methods are not established for visual inspection with acetic acid, which is not recommended for use outside of pilot projects and is inappropriate for postmenopausal women in any setting. Because cytology will be an essential triage component of future “screen and treat” or multiple-visit HPV-based or visual inspection with acetic acid programs, we entreat Sherris et al. to endorse, on the Web site for Alliance for Cervical Cancer Prevention, a patient-centered consensus policy whereby Pap screening will be implemented anywhere cervical screening is appropriate but unavailable, with consideration given to novel preventives as locality-specific research into novel preventives is completed.

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