A Policy Analysis of Cervical Cancer Prevention in Honduras

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Abstract: In most developed countries, prevention programs using Pap screening have resulted in impressive decreases in cervical cancer morbidity and mortality over the past 50 years. However, in the developing world, it is quite a different story. In these countries, where over 80% of cases occur, cervical cancer is the leading cause of cancer death among women (Pisani, Parkin and Ferlay 1999). Globally, cervical cancer has been estimated to account for 2.1% of deaths among women aged 25-64, but in Latin America it accounts for 3.8% of these deaths (Parkin, Bray and Ferlay 2001). Because women in these age groups are fundamental to the fabric of life, not just within families but within economies and societies at large, the toll of this disease is significant. The reasons for this disproportionate burden throughout Latin America are not yet completely understood but are thought to be due in part to the high prevalence of human papilloma virus (HPV) and an inadequate health infrastructure to deal with incident cases (Eluf-Neto and Nascimento 2001). I suggest that this burden is also due to the inadequacies of current prevention programs.

This is an ideal time to reconsider cervical cancer prevention in the developing world. We now have a clear understanding of cervical cancer as a rare but possibly fatal complication of a sexually transmitted disease. After several decades of research, we know that HPV is a necessary but not sufficient cause of cervical cancer (Walboomers, Jacobs and Manos 1999). New methods for detecting infection with HPV, as well as new techniques for detecting cervical dysplasia, provide a unique opportunity to re-examine our efforts to decrease suffering from this preventable illness, especially in the developing world. Aside from medical advances, international collaboratives such as the Alliance for Cervical Cancer Prevention (ACCP) are directing funding, research, and model programs toward preventing cervical cancer, particularly in the developing world. We need to evaluate the potential effects of this confluence of new technology, knowledge, and interest among international donors on this important women’s health issue.

In this paper, I analyze the most effective way to approach cervical cancer prevention in Honduras. Honduras has a twenty year history of a national, Pap-based prevention program yet still suffers from mortality rates approximately five times higher than those in the United States. In an effort to re-consider these efforts, I examine three different cervical cancer prevention policies: the government’s current Pap-based approach; a see-and-treat approach (visual inspection with acetic acid followed by cryotherapy as necessary); and HPV vaccines. Using the medical and health systems literature, field notes, and key informant interviews, I evaluate each of these strategies along the following six criteria: efficacy, effectiveness, cost-effectiveness, acceptability, feasibility and equity. Despite significant resistance on the part of providers, I recommend a see-and-treat approach as the most cost-effective and equitable policy for decreasing cervical cancer incidence and mortality in Honduras.
Introduction

As with antibiotics and childhood immunizations, the Papanicolau (Pap) smear is considered to be one of the major public health successes of the last century. Used as a tool to screen for cervical cancer, the Pap smear has been an integral part of effective cervical cancer prevention programs. In most developed countries, prevention programs using Pap screening have resulted in impressive decreases in cervical cancer morbidity and mortality over the past 50 years. However, in the developing world, it is quite a different story.

Cervical cancer causes a disproportionately high degree of morbidity and mortality in the developing world. World-wide, cervical cancer is the second most frequent cancer and the fifth most frequent cause of death from cancer among women (Yang, Bray and Parkin 2004). In the developing world, where over 80% of cases occur, cervical cancer is the leading cause of cancer death among women (Pisani, Parkin and Ferlay 1999). Globally, cervical cancer has been estimated to account for 2.1% of deaths among women aged 25-64, but in Latin America it accounts for 3.8% of these deaths (Parkin, Bray and Ferlay 2001). Because women in these age groups are fundamental to the fabric of life, not just within families but within economies and societies at large, the toll of this disease is significant. The reasons for this disproportionate burden throughout Latin
America are not yet completely understood but are thought to be due in part to the high prevalence of human papilloma virus (HPV) and an inadequate health infrastructure to deal with incident cases (Eluf-Neto and Nascimento 2001). I suggest that this burden is also due to the inadequacies of current prevention programs.

For the past three years I have worked with a team of medical students and faculty to develop a reproductive health education and prevention program for rural Honduran women. The impetus for this annual month-long service project is Honduran women’s expressed fears of cervical cancer as well as the widely held misunderstanding that contraception is causing cervical cancer. These women’s fears, although not fully informed, are legitimate. In Honduras, cervical cancer mortality rates are almost quadruple what they are here in the United States. Thus, despite over a decade of Pap-based prevention programs, the impact of cervical cancer in Honduras is still large, and it disproportionately affects poorer and less educated women (Ferrera, Velema and Figueroa 2000).

The toll exacted by cervical cancer makes this an ideal time to reconsider cervical cancer prevention in the developing world. We now have a clear understanding of cervical cancer as a rare but possibly fatal complication of a sexually transmitted disease. After several decades of research, we know that HPV is a necessary but not sufficient cause of cervical cancer (Walboomers, Jacobs and Manos 1999). New methods for detecting infection with HPV, as well
as new techniques for detecting cervical dysplasia, provide a unique opportunity to re-examine our efforts to decrease suffering from this preventable illness, especially in the developing world. Aside from medical advances, international collaboratives such as the Alliance for Cervical Cancer Prevention (ACCP) are directing funding, research, and model programs toward preventing cervical cancer, particularly in the developing world. We need to evaluate the potential effects of this confluence of new technology, knowledge, and interest among international donors on this important women’s health issue.

In Honduras, which is the locale of our intervention as well as the focus of this paper, specific changes in the health care sector also make this an ideal time for reconsidering cervical cancer prevention efforts. Despite severe economic constraints, the current administration has voiced a commitment to health sector reform (The Economist Intelligence Unit 2004) and international donor agencies are responding. In February of this year, the World Bank approved a $25 million credit to assist development of the financial sector and to promote long-term economic growth and poverty reduction (World Bank 2005). This level of commitment implies faith in the current and future economic and political stability of the country. As Honduras moves through the demographic transition already experienced in many Latin American countries, development efforts including family planning programs will continue to spread to rural areas and women will continue to have questions and concerns about their reproductive health.
Currently, the Honduran Ministry of Health recommends screening Pap smears for sexually active women aged 30 to 59. Adherence rates to this policy are relatively high, with approximately 60% of women reporting having had a Pap smear in the past year (Secretaria de Salud 2002). However, after this screening test, many women, especially in rural areas, never get their results. Even when they do, their lack of knowledge often limits a clear understanding of the meaning of test results. Moreover, the financial and time investments required for follow-up care put it beyond the means of many women (Morse and Saleeby 2003).

Thus, current cervical cancer screening and prevention programs in Honduras are not associated with significant decreases in morbidity and mortality rates.

The World Health Organization advocates two major components of successful early cancer detection: education and screening (WHO 2004). The educational components of a prevention program can be instrumental not only by encouraging screening, but also by contributing to behavior change processes that lead to decreased risk. In much of Latin America, this educational process is often spearheaded by lay health advisors (LHAs), community members with additional training who serve as health resources in traditionally underserved areas.

Although much research is being done on this fundamental part of a comprehensive prevention program, analysis of the effectiveness of these LHA health education programs is outside of the scope of this work. This paper will

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1 For additional information on the educational/community development part of this intervention as it relates to LHAs, please see Erin Saleeby’s master’s paper.
instead focus more specifically on which screening modalities are most effective for cervical cancer prevention programs in Honduras. Some of these modalities, specifically visual inspection with acetic acid (VIA) and vaccines, can make use of LHA’s basic health training and status in the community to facilitate widespread implementation of prevention programs.

Within this context, the aim of this paper is to make recommendations about effective cervical cancer screening policies in Honduras. I will analyze one primary prevention approach and two secondary prevention approaches: (1) the government’s current policy regarding the use of Pap smears; (2) the use of VIA, also known as a “see and treat” method; and (3) primary prevention via an HPV vaccine. I will use the following criteria - efficacy, effectiveness, cost-effectiveness, equity, acceptability and feasibility - to evaluate each of these policies. Based on this analysis, I make recommendations for implementation of cervical cancer prevention policies appropriate to Honduras. The following pages offer evidence and support for the need to re-consider the current Pap-based prevention program in Honduras and recommend a shift to VIA with immediate treatment by cryotherapy as a more effective and equitable strategy to reduce the impact of cervical cancer.
Background

Natural History of Cervical Cancer

Cervical cancer is a progressive neoplastic syndrome of the cells of the cervix. Although most invasive cancer arises from squamous cells, about 20% of cervical cancer, known as adenocarcinoma, is associated with dysplastic glandular cells (Waggoner 2003). Over a period of years, cervical cells, either squamous or glandular, can develop changes resulting in precancerous or cancerous forms. The progression can range from cervical intraepithelial neoplasia (CIN) to squamous intraepithelial lesions (SIL) to carcinoma in situ and eventually to invasive cancer. Dysplastic changes may begin early in life, but the pre-invasive period is quite long, lasting decades. Hence, most women who are affected do not develop cancer until their late forties or fifties. During this pre-invasive period, the risk of metastasis is low, and appropriate treatment can be curative, making cervical cancer well suited for screening.

Treatment is based on the depth and extent of spread of lesions. For pre-invasive lesions, treatment can be performed on an outpatient basis using ablative or excisional procedures. Cryotherapy, the most common ablative procedure, involves spraying compressed carbon dioxide (CO$_2$) or nitrous oxide (NO$_2$) on to the diseased part of the cervix to kill the pre-cancerous cells. The procedure poses very few risks and requires only minimal medical follow-up. In general, it is minimally invasive, low-tech and very effective, even relative to more invasive treatments. Unlike excisional procedures, cryotherapy does not provide a sample
for histologic confirmation of the diagnosis. Loop electrosurgical excision procedure (LEEP), the most common excisional treatment, involves the physical removal of abnormal cells with an electrosurgical wire loop. It is also very low-risk but requires a more skilled provider and is usually done with colposcopic guidance. Both of these treatments have proven to be very effective in the treatment of CIN (Martin-Hirsch, Paraskevaidis and Kitchener 2004; Zasislak, Price, and McClelland 2003). For invasive cancers, major procedures such as radical hysterectomy, sometimes accompanied by chemotherapy or radiation therapy, are necessary. Without treatment, the cancer can metastasize to distant sites and result in death.

Morbidity from cervical cancer can include minor symptoms such as postcoital bleeding and pelvic pain. However, for non-metastatic cases, most of the morbidity stems directly from the treatment. Although most women with invasive cancer are past their childbearing years, infertility from surgery, radiation treatment, or chemotherapy is one of the major morbidities. Additionally, chemotherapy can result in significant nausea and vomiting, as well as hair loss and immunosuppression. Radiation treatment, although localized, can lead to burning and scarring of nearby tissues. Many women also experience significant psychological morbidity, whether from the cancer itself, or from fear of pain, infertility, or death.
Over the last decade, the pathophysiology of cervical cancer, and the link to HPV, has become better understood. Human papilloma virus, thought to be the most widespread as well as the oldest sexually transmitted infection in humans (Tjalma, Arbyn and Paavonen 2004; Lehitnen and Paavonen 2003), is now known to be central to the development of cervical neoplasia (Walboomers, Jacobs and Manos 1999). HPV infection alone is not enough for development of cervical cancer; it is thought to be a necessary but not sufficient cause. Many HPV infections, especially in young women, are transitory and regress spontaneously without ever resulting in any cervical cell changes. When infections are persistent, they can lead to dysplastic changes. Over 99% of cervical cancers and their precursor lesions (CIN) contain HPV DNA (Schreckenverger and Kaufmann 2004). Although over 100 strains of HPV are thought to exist, only some appear to be oncogenic. Eighty percent of cervical cancers are associated with four high risk HPV types, types 16, 18, 31 and 35. Type 16 alone is thought to be present in approximately 50% of cancers (Schreckenverger and Kaufmann 2004).

In Honduras, the association between HPV infection and the subsequent development of cervical cancer is not universally recognized by providers throughout the country (Morse and Saleeby 2003). This is despite the well documented high prevalence of HPV and cervical cancer there. In a recent case-control study published by Ferrera, Velema and Figueroa (1999), HPV was found to be highly prevalent (39%) even in their control sample. Data from Honduras are consistent with findings around the world. Human papilloma virus type 16 is
most commonly associated with invasive cancer cases, although the rate (42%) is somewhat lower than in other Latin American countries. Although Honduran rates of cancer associated with HPV 18 (10%) are comparable to that of other Latin American countries, rates of HPV 58 (6.5%) associated with invasive cervical cancer are almost double that typically found in other parts of Central and South America. These minor differences could be significant if HPV vaccines become a central component of cervical cancer prevention policies (see pp 34 ff).

Differences in HPV infection rates vary somewhat across the globe, although not as much as do differences in morbidity and mortality. World-wide, cervical cancer is the second most frequent cancer as well as the second highest cause of cancer-related morbidity and mortality among women (Yangh, Bray and Parkin 2004; Parkin, Pisani and Ferlay 1999). This burden disproportionately affects the developing world, where more than 80% of cases occur. In the year 2000, the World Health Organization (WHO) estimated that there were 471,000 new cases of cervical cancer diagnosed and 233,000 deaths worldwide (Parkin, Bray and Ferlay 2001). Approximately 92,136 of those cases and 37,640 of those deaths were in Latin America and the Caribbean (Lewis 2000). As I noted at the outset, cervical cancer is responsible for a higher proportion of deaths in 25-64 year old women in this region than anywhere else in the world.

Honduras appears to share a large part of this burden. Based on national cancer registry data, cervical cancer is the most common malignancy and accounts for
40% of the cancer cases that need follow-up care and 50% of the cancers in women (Ministerio de Salud 2004). In the year 2000, the Pan-American Health Organization (PAHO) reported an age adjusted incidence and mortality rate in Honduras of 39.6 cases per 100,000 women and 16.8 deaths per 100,000 women respectively (PAHO 2000). In an update on their cervical cancer prevention program in 2003, the Honduran Ministry of Health reported an incidence rate of 40 cases per 100,000 women and a mortality rate of 40 deaths per 100,000 women (Ministerio de Salud 2003). Although this discrepancy in mortality figures likely reflects data collection differences, both are strikingly large compared to data from the United States, which in 2000 experienced an age-adjusted incidence rate of only 9.3 cases per 100,000 women and a mortality rate of 2.9 deaths per 100,000 women (Jemal, Murray and Ward 2005). Unlike in the US, cervical cancer is the most common neoplasia among women in Honduras (Ferrera, Velema and Figueroa 1999) and in 1989-90 accounted for 4.9% of all deaths among women of childbearing age (PAHO 2001).

Moreover, unlike much of the developed world, where cervical cancer mortality has decreased over the last thirty years, mortality has remained almost constant in Latin America. This has resulted in a greater burden of years of life lost (YLL) in the developing world. Cervical cancer contributes over 2.7 million YLL among women aged 25-64 around the world. However, 2.4 million of these YLL lost occur in the developing world and only 0.3 million occur in developed countries. Latin America and the Caribbean is the only world region where cervical cancer
is the leading component of YLL (Eluf-Neto and Nascimento 2001). The WHO quantifies the burden of suffering in Latin America, reporting that cervical cancer now accounts for a loss of 471,000 daily adjusted life years (Lewis 2000). Exactly how much of this burden falls on Honduras has not been explicitly reported.

**Risk Factors**

Risk factors for cervical cancer are numerous and well-documented. Although women are usually over 35 when they are diagnosed, the disease is thought to begin much earlier, so risk factors early in life can influence development of cancer (Ferrera, Velema and Figueroa 1999). Universally agreed upon risk factors include HPV infection, having multiple sexual partners (or a partner who has multiple partners), early age at first intercourse, a history of sexually transmitted diseases, immunosuppression, low socioeconomic status, low educational status, and smoking. Recent research in Honduras suggests that exposure to smoke from wood burning stoves in the kitchen is also a risk factor for invasive cervical cancer, independent of other factors such as education, parity and number of sexual partners (Velema, Ferrera and Figueroa 2002). In the 2001 National Epidemiology and Family Health Survey, 55.9% of homes (25.4% of urban homes and 84.7% of rural homes) reported burning wood for cooking (Secretaria de Salud 2002).

In a recent study examining risk factors for cervical cancer mortality in Mexico, Palacio-Mejía, Rangel-Gómez and Hernández-Avila (2003) found that poverty-
related factors such as lack of formal education, unemployment, low-socio-economic level, rural residence and insufficient access to health care were all significantly associated with higher risk of mortality from cervical cancer. They suggest that not just poverty, but also gender inequality, has an impact on the high mortality rates of cervical cancer in Mexico. Although Blanc’s (2001) review focuses on reproductive health more broadly, she corroborates the idea that gender inequality, especially power differences within sexual relationships, can have a negative effect on women’s reproductive health outcomes. Women’s inequality within these relationships can affect their ability to protect themselves from risks, obtain information about reproductive health, or seek care as needed. Other investigators have proposed methods to mitigate some of these independent risks in a meta-analysis of studies in the developing world including a case-control study in Honduras. These studies demonstrate that education is especially important in empowering women to foster lifestyles that result in decreased risk for cervical cancer. Involving men in prevention programs has also been shown to be important in developing programs that will be well accepted and accessible (Blanc 2001). Many of these gender-specific factors that put women at greater risk for disease overlap with the factors that make them less likely to get screened. Thus, without educating and empowering women, less wealthy and less educated women will continue to be disproportionately affected in terms of both incidence and mortality (Ferrera, Velema and Figueroa 2000; Parikh, Brennan and Boffeta 2003).
The Honduran Context

A basic understanding of the socio-demographic, economic, political and health care system dynamics that shape life in Honduras is essential to making sound policy recommendations. To that end, I will briefly describe the demographic factors relevant to cervical cancer prevention. I will also describe the Honduran health care system, as well as recent reform efforts that may open the door for policy change regarding cervical cancer prevention.

The predominant social force of day-to-day life in Honduras is poverty. Despite a fairly stable political history relative to many of its Latin American neighbors, Honduras remains a poor country. In 2001, per capita income in Honduras was $870.35, significantly lower than the average of $6,728 in the rest of Latin America (PAHO 2001). In relative terms, this means that 66% of households fall below the poverty line, and 49% of these fall below the indigent line. Perhaps even more striking, especially in light of recent national efforts to combat poverty, is the increasingly uneven distribution of resources. In 2001, the poorest 20% of the population received 4.3% of the income while the richest 20% received 59.3% (PAHO 2001). In 2004, Honduras ranked 115th out of 177 countries on the Human Development Index\(^2\), with an overall score of 0.672 and a gender-related

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\(^2\) The UN Human Development Index was developed in 1990 and is reported annually by the UN since 1993. The Index measures, among other things, poverty, literacy, life expectancy and GDP per capita. It is considered to be a good indicator of both social and economic development. The gender-related development index uses the same variables but adjusts for gender inequalities in several key aspects of human development: life expectancy, literacy, gross school enrollment, and income.
development index of only 0.662 (United Nations 2004). This low score reflects, in part, the adult literacy rate of 16.8% overall: 8.9% in urban areas and 23.3% in rural areas. Average schooling for adults is 4.3 years, with women generally being less educated than men (Burlone 2003). Living conditions reflect these poverty levels, with 38% of rural women living in homes with open air latrines and 85% of them using wood fires in the home for cooking (Secretaria de Salud 2002).

These and other factors associated with poverty make the delivery of comprehensive preventive health services difficult. The rurality of Honduras is a particularly important variable. Fifty-six percent of the population lives in rural areas. Poverty tends to be concentrated in these areas, although marginalized zones in the two major urban areas are also growing. Despite a decrease in total fertility and crude birth rate over the past decade, the population is still growing and 53% of the population is under the age of 19, posing a major demand on the health care system in the years to come as they age and require more services.

Although data to support the contention are virtually non-existent, migration appears to have an increasing effect on health care delivery, as well as on cervical cancer incidence. Many young men migrate locally to work on large farms or to urban areas in search of industrial work. Increasingly they are migrating to the United States as well. Away from their homes, they often adopt less restrictive sexual practices, resulting in increased spread of communicable diseases among their urban partners, as well as an introduction of those diseases to their rural
partners (Linthicum 2004). My experience in Southern Honduras reveals that most migrating men leave families in rural areas but return home to them. Thus, human movement and changes in sexual behaviors may increasingly affect the spread of HIV, HPV, and the incidence of cervical cancer.

These challenges confront a health sector that is predominantly driven by the Ministry of Health (MoH). The MoH assumes all regulatory responsibility and is also the main, public provider of care. Operating hospital and ambulatory care networks that are linked together by a very weak referral system, the MoH provides care to just over half of the population (PAHO 2001; Omaha, Melendez and Uehara 1998). The Instituto Hondureño de Seguridad Social (Honduran Social Security Institute, or IHSS) serves much the same role as does Medicare and covers about 10% of the population. Although the private health sector is growing, it covers only about 10-15% of the population, mainly through for-profit clinics and hospitals and a small insurance market. Some non-governmental organizations (NGO) or church-sponsored non-profit providers exist, but they represent only a small fraction of health care services. Unlike the public sector, the private sector devotes few resources to public health activities.

This analysis will focus primarily on the MoH, not only because it is the main public provider of care, but also because it is engaged in the function of health promotion, health protection, and health recovery. Moreover, along with the Ministry of the Presidency, the MoH, through its Management, Planning and
Evaluation Unit, is tasked with planning and developing national health policy. Although the main source of financing for this system is taxes, as recently as 1999, foreign funds contributed 37% of the monies spent in the public health sector (The Economist Intelligence Unit 2004). Data on health care expenditures per capita vary widely depending on the source. Figures range from $49 per capita in 2001 to $165 per capita in 2004, putting it below all of its neighbors except Nicaragua (The Economist Intelligence Unit 2004). Regardless of the exact figure, resources are limited to fund the changes that need to be made to create a more effective, accessible system.

Changes to the health care system, as well as general social and economic development, remain on the political agenda, at least in rhetoric. Health sector reform was espoused in 1990, but no official policies were developed or implemented during state modernization efforts at that time. In 1999, as part of post-Hurricane Mitch reconstruction efforts, the government established “1999-2001 Policy Guidelines” to meet population concerns about equity, quality, solidarity and citizen participation in the use and delivery of health care. Since that time, the MoH has created the Technical Council on Management and Institutional Development. Although it is responsible for developing an improvement plan, no goals have been outlined, nor new programs implemented. Thus, the health sector continues to have major problems in the areas of health care access, information systems (for disease surveillance and reporting and
general health statistics), human and technical resources, and quality and licensing standards.

Each of these problem areas is significant to a consideration of implementing a cervical cancer prevention program. Access to care, especially screening services, is of great concern, especially for poor, rural women or women living in marginalized urban areas. In the communities where I have worked, most of the women must travel by foot, or first by foot and then by bus, to reach a health outpost, which is typically staffed by a nurse or a community health worker. To get a Pap smear, most women in these communities go to the closest outpost or wait until a Cuban doctor, who does outreach to rural communities, is in town. Once at the health post, if more advanced care is needed, they take a bus for over an hour to reach a city with fully-staffed clinics and a hospital. The links between these different levels in the health care system are weak, at best, resulting in less than ideal referral processes. These experiences seem fairly typical for the majority of the population that lives in rural areas.

The lack of good data collection efforts exacerbates the challenges posed by physical distances, and makes the referral process much more cumbersome. Electronic data collection is not feasible because of cost constraints and the undependable electricity supply in many of the rural outposts. Thus, recordkeeping, at least in the non-urban centros (health care centers/rural outposts) is completely paper-based. A recent report by PAHO suggests
significant underreporting of deaths (47%), as well as problems in indicating the exact cause of death (PAHO 2001). Despite the initiation of a national cancer registry at the main hospital in the capital city of Tegucigalpa, we probably do not know the full impact of cervical cancer morbidity and mortality.

The two other main weaknesses affecting cervical cancer prevention programs are a general lack of health care infrastructure, both human and physical, and a lack of licensing guidelines and quality standards throughout the health care system. Despite recent increases in the physician and nursing workforce, the human capital in the public sector is still quite limited. In 1999, Honduras had 8.7 physicians per 10,000 people, 3.2 nurses, and 0.6 mid-level laboratory technicians. Consideration of these workforce limitations is fundamental to establishing a more effective cervical cancer prevention policy. Associated with these workforce limitations are physical limitations, such as 2.03 clinical laboratories per 100,000 inhabitants. For a screening program based on cytology or HPV DNA testing, this lack of adequate lab resources is a significant barrier to prompt processing of tests. Delays in return of results raise serious concerns about loss to follow-up. Although I have not been able to locate data specific to Honduras about loss to follow-up, Gage, Ferreccio and Gonzales (2003) suggest that in developing countries, the percentage can be as high as 80%. My experiences in Honduras do not contradict this. In addition to these human and physical infrastructure shortages, a lack of standardized guidelines for health care provider licensing and accreditation, as well as maintenance and quality control of
labs and other facilities poses major challenges to effective screening and prevention.

Despite what may seem to be a fragile system, there are numerous successes as well as initiatives for reform that make this an ideal time to be re-assessing cervical cancer prevention efforts. One of the most recent successes has been a significant decrease in maternal mortality. From 1990-1997, Honduras’ maternal mortality rate fell 40%, from 182 per 100,000 live births to 108 per 100,000 live births (Shiffman, Stanton and Salazar 2004). This precipitous reduction, the largest ever documented in such a short period of time in the developing world, is thought to be due, in part, to the cooperative relationships that developed between international donors and national health officials. This bodes well for openness to improving other parts of women’s health, including cervical cancer prevention, especially considering the significant interest of several international agencies (Pan American Health Organization (PAHO), the Alliance for Cervical Cancer Prevention (ACCP)) as well as donors (Bill & Melinda Gates Foundation, the World Bank) in addressing this global problem through new technologies adapted to the developing world.

A second recent victory is the decrease in measles, with no reported cases for the years 1997-1999. This accomplishment illustrates the ability of the MoH to implement and sustain a comprehensive and effective national immunization program. This success also suggests that, if HPV vaccines are a reasonable option
for cervical cancer prevention in Honduras, there are replicable model programs. The third promising trend is a recent examination by the MoH of PAHO’s 11 essential public health functions, which coincided with an increase in spending on health promotion and preventive care. Thus, the success of effective models as well as internal and external policy agendas make this an ideal time to re-examine and improve Honduras’ cervical cancer prevention strategies.

The Key Players

Although the MoH and other Honduran institutions are clearly the key institutions in determining any changes to Honduras’ national prevention efforts, two international agencies merit mention because of their significant influence in international cervical cancer prevention efforts, especially in the developing world.

The Alliance for Cervical Cancer Prevention

Started in 1999 with funding from the Bill & Melinda Gates Foundation, ACCP is a consortium of five international agencies that are working together to invigorate a global campaign to prevent cervical cancer. The Alliance coordinates research and program implementation efforts to help develop effective strategies for prevention in the developing world. The Alliance is made up of a collaboration of the following five agencies: EngenderHealth, IARC (International Agency for Research on Cancer), JHPIEGO (an affiliate of Johns Hopkins University), PAHO, and PATH (Program for Appropriate Technology in Health).
The Pan-American Health Organization
PAHO serves as the regional office of the World Health Organization (WHO) for all of the Americas and falls under the rubric of the United Nations. As a public health agency with over 100 years of efforts to improve the public health and living standards throughout the Americas, PAHO serves a vital role in granting monetary and technical assistance, setting health policy standards and guidelines, and collecting data and conducting research to meet the specific public health needs of the countries in the Americas. These services often provide crucial resources for countries with limited means. At least in the United States, PAHO’s affiliation with the UN and its status as an international, non-partisan agency, lends credibility and legitimacy to their data and program and policy guidelines, which are thought of as non-biased or neutral.

The Current Policy
The current cervical cancer prevention program in Honduras was developed in 1991 as part of the National Program for Cancer Control. The program is specifically targeted at women aged 30 to 59, but the MoH recommends that all women get Pap smears every three years after the onset of sexual activity. The program is focused around decentralized sample collection with centralized processing at one of three regional labs. In May, 2002, the MoH carried out a major re-examination of the state of cervical cancer in Honduras, as well as an evaluation of the program’s major successes and failures as part of a two-year “Strengthening Project”. The report generated from this investigation, which received 65% of its funding from international donors, found three major
problems contributing to the high incidence of cervical cancer: (1) a low demand for cytology services; (2) a poorly linked network of health services; and (3) a lack of compliance with the “Manual of Norms and Procedures for the Prevention and Control of Cervical Cancer”. This combination of shortcomings was reported to be responsible for the high morbidity and mortality from cervical cancer, as well as the major economic and social investments required to care for patients who present in the advanced stages of cancer.

The MoH used these findings to set out three specific objectives for the “Strengthening Program” to improve cervical cancer prevention: (1) increase Pap screening rates and coverage areas; (2) improve the linkages between health services; and (3) apply the recommendations laid out in the “Manual.” Ancillary activities to help meet these objectives include a bilateral educational campaign targeted at women and health care providers. The general education for women is focused on risk factors and the importance of Pap smears. For health care providers, the focus is the guidelines detailed by the Manual, with an emphasis on the quality of samples, interpretation of results, and the provision of appropriate referrals. Provider training spans across care levels, from nurses to gynecologists, and across the health sector, including providers from both public and private facilities.

3 Unfortunately I have not been able to obtain a copy of this “Manual”. However, based on other manuals I have seen regarding treatment of sexually transmitted diseases, my best assumption is that the manual offers explicit documentation about the norms for screening and treatment of cervical cancer.
At a PAHO meeting in February, 2003, representatives from the MoH reported that the “Strengthening Project” has made several improvements toward meeting these goals. In the area of increasing Pap screening rates and coverage, several day training sessions were held for providers to increase their prevention knowledge and skills. In the area of improving linkages between the network of health care services available, significant improvements were reported but not detailed. Of note, the average time for return of Pap results dropped from three months to 30 days after the “Strengthening Project’s” introduction. Although there are still exceptions, this change is significant.

Screening Methods

Pap Smears

Pap smears, named for their inventor, Dr. George Papanicolau, offer a method for detection of abnormal cervical cells. The theory behind a Pap smear, also known as cervical cytology, is that changes in nuclear protein color and size that are associated with HPV infection and cancer development can be detected via microscopic examination of a sample of cervical cells. The actual process involves using a speculum to gain access to the cervix, and then collecting a sample of ectocervical cells with a paddle and endocervical cells with a thin brush that is inserted into the cervical canal. The cells are immediately smeared on a glass slide, fixed, and sent to a laboratory for examination by a cytotechnician and final reporting by a cytopathologist. Although uncomfortable, in the absence of any infection or other pathology, the procedure is usually not painful.
Results from a Pap smear, which can take anywhere from days to weeks, depending on the laboratory, serve only as a screening tool. They are not diagnostic but instead offer guidance about further examination. Results are reported by the level of cellular change noted. In 2001, a new reporting system, based on the degree of cellular change, or atypia, was adopted to allow for standardization between labs and clinicians. The new categorizations, designated the Bethesda System, characterize results as ASCUS (atypical squamous cells of undetermined significance), LSIL (low-grade squamous intraepithelial lesion) or HSIL (high-grade squamous intraepithelial lesion). Depending on the results, follow-up testing may include nothing other than continuing to get Paps at the recommended interval, repeating the Pap, colposcopy, or colposcopy with a biopsy. A colposcope allows a clinician to get a magnified view of cervical tissue and facilitates collecting a sample for biopsy.

Despite their widespread use, there has never been a randomized trial of the efficacy of cytologic screening for cervical cancer (Shingleton, Patrick and Johnston 2005). At this point, Paps are so widely used that such a trial will never be done. Observational trials in five Nordic countries comparing cervical cancer mortality before and after implementation of screening programs demonstrated reductions of 8-73% (Laara, Day and Hakama 1987). In the United Kingdom, recent debate over health care expenditures has called into question the value of a Pap-based prevention program. In response, Peto, Gilham and Fletcher (2004) analyzed and projected cervical cancer mortality rates before and after the 1988
launch of a national screening program. They suggest that 80% of projected cervical cancer deaths have been prevented in the United Kingdom due to the screening program. Although there are significant limitations to their methodology, an effect even half as large as was found is fairly impressive. In spite of this evidence, which has been supported in numerous developed countries with comprehensive screening programs, it is still prudent to question the efficacy of cytology as a screening tool, especially in the developing world.

The accuracy of a Pap’s detection of precancerous lesions is not established, and reported results vary. Published papers report divergent numbers for both sensitivity and specificity. The most recent review, published by Nanda, McCrory and Myers in 2000, compared 94 studies that used Pap testing with a reference standard (histology, colposcopy or cytology). In the 12 least biased studies reviewed, sensitivity ranged from 30-87% and specificity ranged from 86-100%. These figures are fairly consistent with the numbers reported by Fahey, Irwig and Macaskill in a review conducted in 1995. As, Nanda, McCrory and Myers point out, two major weakness in many Pap accuracy studies include selection bias and verification bias. Often, accuracy is assessed in a high prevalence group, such as women presenting to clinic for colposcopy after an abnormal Pap. Moreover, many studies verify only positive results with the gold standard. Both of these biases can make Paps appear more accurate than they are. The authors caution policy makers to use the low end of reported accuracy ranges, especially when conducting cost-effectiveness analyses.
The need for caution in applying these results to health policy decisions is especially true in the developing world. Although the two reviews described above are currently our best information, they rely on studies done in developed countries where greater access to resources often results in better accuracy due to better training of providers, better maintenance of laboratory equipment, and improved data collection. A recent assessment of cytology accuracy in developing countries based on six cross-sectional studies found that sensitivity ranged from 44% to 78% and specificity ranged from 91% to 96% (Sankaranaryanan, Gaffikin and Jacob 2005).

The wide range of sensitivity and specificity reported in the literature is not just due to differences in study design or geographic location. These figures range so widely in part because a Pap's accuracy varies with respect to the degree of dysplasia to be detected. Paps are generally more accurate at detecting more serious, high grade dysplasia. Thus, if a trial uses detection of low-grade dysplasia, the sensitivity appears lower than if measured for detecting invasive cancer. As the threshold for the test increases, sensitivity increases but specificity decreases (Nanda, McCrory and Myers 2000). Unfortunately, Pap sensitivity ranges quite widely, resulting in false negative rates of 6 to 55% in some trials (Shingleton, Patrick and Johnston 1995). Thus, the false negative rate, even in women with invasive cancer, can be concerningly high. Two-thirds of these false
negative results are thought to come from sampling errors, whereas the remainder is from detection error (Nanda, McCrory and Myers 2000.)

Accuracy is greatly affected by the adequacy of the sample, how it is fixed and stained, and the abilities of the cytotechnologist (Shingleton, Patrick and Johnston 1995). An inadequate or contaminated (bloody) sample is often unreadable. Inadequate smears, often a product of poorly trained providers, can have a significant impact on a program’s success. In a recent study in Peru looking at ways to improve Pap accuracy, 13.8% of smears were found to be inadequate for reading. In post-menopausal women whose endocervix is involuted, accuracy is often lower even with the use of endocervical brushes to collect the sample. Efforts to improve Pap’s accuracy include liquid-based cytology and computer-assisted cytology, both of which are still being assessed in the developed world and lie outside the financial reach of most developing countries. Despite variations in accuracy, there appears to be general agreement that high-quality Pap smears are very specific but their sensitivity is variable, at best.

In many respects, Pap-based prevention programs are resource-intensive. They require three types of health care personnel: a doctor or nurse to collect, prepare and fix the smear; a cytotechnician to process, stain and read the smear; and a cytopathologist who can supervise and accept ultimate responsibility for final reporting of results. Training for cytotechnicians is fairly extensive, often lasting for 12 to 24 months. Aside from human resources, cytology necessitates a
laboratory infrastructure, quality-control mechanisms, and information processing to get results back to women. Pap-based programs also require at least two, but usually three visits by the patient: a screening visit, a follow-up visit for additional testing, and a treatment visit. To date, combining all of these efforts effectively has proven difficult in much of the developing world.

**Visual Inspection with Acetic Acid**

Visual inspection with acetic acid (VIA), also known as the acetic acid test (AAT) or direct visual inspection (DVI), is a low-technology method for cervical cancer screening. The process involves inserting a vaginal speculum to gain adequate visualization of the cervix and then swabbing the cervix with a 3-5% acetic acid solution (table vinegar) for one to three minutes prior to inspecting it (Carr and Sellors 2004). Normal, healthy squamous epithelial cells are pink. When increased nuclear proteins associated with dysplastic changes are present, the cells turn white, differentiating them from neighboring cells even to the naked eye. A trained examiner records results as negative (no acetowhite changes), positive (acetowhite changes present), or suspicious for cancer. Although acetowhite changes are not specific to cervical neoplasia, a well-trained provider can distinguish the differences between inflamed and regenerating epithelium and cervical neoplasia. When acetowhiteness associated with neoplasia is found, treatment can be offered immediately to women with positive tests depending on the training of the provider, the equipment available and the patient’s preferences.
Since the widespread adoption of Pap smears, VIA has not been broadly used as part of comprehensive cervical cancer screening programs. However, with the recent increase in interest in the divergent success of Paps in the developed and developing world, new work is being done to validate the true accuracy of VIA, especially in low-resource settings. The most complete examination of the accuracy of VIA is a qualitative summary of the literature published by Gaffikin, Lauterbach and Blumenthal in Obstetrical & Gynecological Survey in 2003.

Authors searched for papers published from 1982 through 2002, resulting 16 studies that met their criteria (primary data analysis, only VIA, and no magnification). Because most VIA pilot programs are being done in the developing world, most of the included studies were from low-resource settings. Much like the Nanda team’s review of the accuracy of Paps, Gaffikin, Lauterbach and Blumenthal found significant variation, reporting sensitivity as 66-96% and specificity as 64-98%. They conclude, as do most of the studies and authors, that VIA’s performance compares favorably to that of Pap smears, offering perhaps increased sensitivity (and certainly a narrower range) but decreased specificity. However, as Gaffikin notes, their review prompts further research. This review is not a rigorous, quantitative assessment or meta-analysis. The included studies suffered from significant biases, most importantly verification bias. Although the studies varied, most only verified the results of VIA with colposcopy when the woman had a positive test. Thus, the actual specificity is likely lower than reported, as some of the negative results are likely false negatives. The authors offer a generally positive assessment of VIA for early detection of cervical cancer.
but call for quantitative studies and meta-analyses of trials that do not suffer from verification bias or selection bias.

Since this review, published data are now available from a massive (almost 57,000 women) trial of VIA in India and Africa. In this trial, which was designed to determine the accuracy of VIA and VILI (visual inspection with Lugol’s iodine, a technique similar to VIA), all women sequentially received each method, followed by colposcopy, and biopsy when clinically appropriate. Each test was done independently and blindly. Across the 11 study sites, detection of HSIL had a pooled sensitivity of 76.8% (95% CI: 74.2-79.4%), specificity of 85.5% (95% CI: 85.2-85.8%), positive predictive value of 9.4% (95% CI: 8.8-10.8%) and negative predictive value of 99.5% (95% CI: 99.4-99.6%). These values are consistent with the ranges reported by Gaffikin’s team and demonstrate the relatively high specificity and negative predictive value of VIA but also the poor positive predictive value due to the low sensitivity. Because of the ability to offer immediate results and treatment, this high false positive rate is a concern to some, because healthy women will get unnecessarily treated. Claeys, DeVuyst and Gonzales (2003) compared relative false positive rates between Paps and VIA in Nicaragua and expressed concerns about the effects of false positive rates on program planning and development of effective referral mechanisms.

In an effort to shift toward effectiveness trials, Sankaranarayanan, Basu and Wesley (2004) recently released a paper from the only published, randomized trial
of VIA screening in the last 20 years. The trial included over 78,000 rural Indian women between the ages of 30 and 59 who were randomized to either VIA screening or control (no screening). After screening, test positive women were counseled and offered colposcopy and punch biopsy, as necessary. They measured outcomes associated with program effectiveness - feasibility, participation rates, detection rates of CIN and invasive cancer, and program sensitivity to detect invasive cancer (calculated as the proportion of screen-detected biopsy confirmed cancer cases among the total invasive cancer cases recorded during the follow-up in the intervention arm). Women with invasive cervical cancer were referred to local treatment facilities for staging and treatment. Researchers used a population-based cancer registry to collect information about cancer incidence and mortality. Mortality rates were also extracted from death registries. The program demonstrated a 71.1% sensitivity to detect invasive cancer.

This trial is significant because it is the first randomized trial assessing a massive VIA screening program in low-resource settings. The study design does not allow for a better assessment of VIA accuracy. However, this trial does move in the right direction of assessing effectiveness. Although questions about acceptability and feasibility of VIA-based screening programs have already been positively answered in large, pilot programs in Thailand and Ghana, long-term effectiveness in terms of cervical cancer incidence and mortality are still not known. As the duration of some of these programs progresses, researchers will soon be able to
demonstrate whether VIA has any significant impact on cervical cancer incidence, morbidity and mortality.

Aside from a current lack of effectiveness data, there are other concerns about VIA-based prevention efforts. By its very nature, VIA relies on visual inspection of the ecto- and endocervix. Because the endocervix abuts the transformation zone, an area that is at high risk for developing cervical cancer, visualization of this area is fundamental. In post-menopausal women, the transformation zone often begins to involute as the endocervix atrophies. Thus, although there is not quantitative evidence demonstrating the effect of this anatomic change on VIA’s ability to detect cancer, specialists are rightfully concerned about its decreased applicability in postmenopausal women. Because glandular cancers (as opposed to the more common squamous cell cancers) are also more common in the endocervical canal, VIA is less adept at detecting them. (Sankaranaryanan, Gaffikin and Jacob 2005).

Despite these concerns, if one considers only technical issues and ignores for a moment test efficacy and effectiveness, VIA is ideal for low-resource settings. The process requires no electricity, only a light source which can easily be provided by a battery-powered lamp or headlamp. Moreover, nurses, midwives and even lay health advisors can be trained to provide this screening procedure. Several internationally focused health organizations (PATH, JHPIEGO, IARC) that work to provide appropriate health resources and technologies to low-
resource settings have developed manuals and protocols for training mid-level to lay health advisors in VIA. These programs, ranging from several days to two weeks, can be targeted to different levels of clinicians and include basic cervical anatomy, reference manuals, photographs and clinical practice. Use of these training protocols in several studies demonstrates their effectiveness in equipping health providers to perform this procedure. In Sankaranarayanan, Basu and Wesley’s clinical trial reported above, eight nurses completed a three-week training course using IARC training manuals. A photograph-based assessment of their competency prior to beginning any clinical screening activities demonstrated that all providers could correctly assess over two-thirds of the photographs. In an effort to maintain clinical skills and improve effectiveness, trainees took refresher courses every 6 months. In Sankaranarayanan, Basu and Wesley’s (2004) larger trial conducted in India and Africa, 51 female health workers took part in a five-day intensive course based on IARC manuals and also got one to two day refresher courses throughout the study. Their colposcopy-confirmed detection rates suggest adequate competence levels as well.

VIA also offers the benefit of immediate results and the possibility for immediate treatment, if the patient so desires. Often referred to as a “see and treat” approach, this method offers significant advantages in areas where women are traveling far to seek care and may not return for follow-up. Moreover, it allows for provider education and counseling of the patient to ensure that she understands the results of her screening test. The treatments offered post-VIA, cryotherapy and LEEP,
are minimally invasive and pose minimal risk. However, they do require additional provider training, as well as access to a medical facility that is able to deal with rare but possible complications such as bleeding and infection. At a population level, the ability to offer immediate treatment is fundamental to alleviating the significant loss to follow-up that occurs for Pap-positive women, especially in rural parts of Honduras where access to care is quite limited. However, at the individual level, the high false positive rate may lead to unnecessary treatment of healthy women.

**HPV Vaccine**

With the discovery of HPV as a necessary causal factor for cervical cancer, researchers have begun to explore the possibility of an HPV vaccine as primary prevention of cervical cancer. Although therapeutic vaccines are also being explored, because we are most interested in cervical cancer prevention, I will focus only on prophylactic vaccines. The data in this area are all very new, and still incomplete. Prophylactic vaccines against HPV can be developed in many ways but are all dependent on somehow stimulating an immune system response. The most promising prophylactic vaccines are composed of virus-like particles (VLPs) but lack any harmful viral genome. They initiate an HPV type-specific neutralizing antibody response that prevents primary HPV infection. Because preventing primary HPV infection is the goal, vaccines must be administered prior to the onset of sexual activity. The vaccines developed to date involve three
doses at months zero, one, and six of an intramuscular injection and have been well tolerated with no report of serious adverse events.

Vaccine trials are a work in progress, with new results in the pipeline and a significant part of the development process already underway. Phase I and II trials have already clearly established proof of principle, immunogenicity and safety (Lehtinen and Paavonen 2003; Tjalma, Arbyn and Paavonen 2004). Phase III trials, which demonstrate vaccine efficacy, are currently ongoing around the world. The first phase III trial, completed in 2002, was a placebo controlled trial of an HPV16 VLP vaccine. With an average of two years of follow-up, the vaccine was 91% effective at protecting against infection with HPV16 and 100% effective against persistent HPV16 infection. This trial paved the way for Phase III trials of a combined vaccine. This May, Harper, Franco and Wheeler (2005) published pilot results from an efficacy trial of a combined HPV16/18 L1 VLP vaccine. In this double-blind, multi-center, randomized trial in North America and Brazil, over 1,000 HPV-negative women aged 15 to 25 received either three does of the vaccine or placebo. Protection from persistent HPV 16/18 infection was 100%. The bivalent vaccine was also 92.9% effective at preventing cytologic abnormalities. This data represents the best information we have to date on vaccine effectiveness.

Clearly, these results need to be replicated in large, Phase III and Phase IV trials with much longer follow-up. The two main contenders to produce such results are
Merck’s quadrivalent HPV6/11/16/18 VLP vaccine and Glaxo-SmithKline’s bivalent HPV16/18 vaccine. Both companies are initiating large, multi-center trials in Europe, North America, Latin America and Asia over a forty-eight month period. Despite the longer follow-up times compared to previous trials, endpoints will still be intermediate and will include protection against persistent HPV 16 and HPV18, not incidence and mortality. Unfortunately, the long pre-invasive period for cervical cancer means that even well-designed trials will not be able to produce mortality endpoints for at least ten more years.

Although vaccine development has been very promising so far, there are still significant areas of uncertainty. The specificity of viral capsid proteins requires that VLP vaccines need to be targeted to the specific virus type. Initial development has been targeted at the most common types, specifically HPV16 and HPV18. Geographic variation in type prevalence will determine the relative effectiveness of a combined HPV16/18 vaccine in different parts of the world. In Honduras, HPV16 or HPV18 is found in 51.9% of cases of invasive cervical cancer (Ferrera, Velema and Figueroa 1999), so even a bivalent vaccine could prevent only about half of all cancer cases.

Aside from issues of vaccine HPV type make-up, we still do not have complete evidence about the existence of cross-reactivity between strains. A qualitative review published in 2003 concluded that cross-reactivity is very rare, but cited no primary or secondary data to justify that claim. Two more recent reviews cite
prospective data suggesting cross-reactive immunity to non-vaccine types (Bell and Alvarez 2005; Lehtinen and Paavonen 2003). Clearly, this issue is not yet fully understood, and perhaps will not be until vaccines have been widely used for at least ten years. Viral variation to develop vaccine resistance is also possible. Fortunately, HPV is a biologically stable virus that is thought to have remained the same for over 200,000 years (Lehtinen and Paavonen 2003), perhaps decreasing the chance that it will alter itself in response to new host immunity. We must also remain concerned about breakthrough infection, or infections by strains that were previously not oncogenic but become so to occupy a niche in response to vaccine-induced reductions of currently oncogenic types. Long-term monitoring of HPV type present in CIN and invasive cancers will be the only way to answer that question.

We still have numerous other unanswered questions about HPV vaccines. For example, although antibody titers post-vaccination have been substantially higher than those measured after infection, we do not know how long this immunity will last. Initial immunity is established in three doses, but it is possible that a booster dose will be required to maintain long-term protection. Some researchers are also considering whether different delivery methods (oral or via the nasal mucosa) could invoke levels of both systemic and cervical mucosal response similar to that of an intramuscular injection with just one dose (Tjalma, Arbyn and Paavonen 2004). Although this could possibly simplify vaccine program implementation, we still do not know if this will be possible. As with any vaccine, even with
incomplete coverage, unvaccinated persons might benefit somewhat from herd immunity. Even so, the heterogeneity of HPV types means that even with a completely effective vaccine and 100% coverage, there will still be sporadic cases of cervical cancer. Tjalma, Arbyn and Paavonen (2004) estimate that even complete coverage with a highly effective multivalent vaccine that combines the eight most common oncogenic HPV types could only prevent 95% of cervical cancers. Thus, even with an ideal vaccine, some type of screening will still be necessary.

**Study Design and Methods**

A policy analysis of a public health question requires a wide range of data sources to assess accurately the clinical and epidemiologic ramifications of cervical cancer screening and to place them within their appropriate social and political framework. This work combines the strengths of what have traditionally been defined as both quantitative and qualitative research by relying on the underlying “logic of inference” inherent in both (King, Keohane and Verba 1994). Clearly, to conduct such an analysis adequately is a massive undertaking and thus, I have tried to stay focused on the main question of determining the most appropriate screening modality. In this effort, I have used three main data sources: (1) a systematic review of the published literature, as well as archival and aggregate health and health services data, (2) personal field notes, and (3) key informant interviews. Combining these different sources will allow for triangulation of my methods, resulting in the most complete analysis possible. Using this information, I will apply a set of six evaluation criteria – efficacy, effectiveness, cost, equity,
acceptability and feasibility – to make final recommendations about the most appropriate screening method and prevention program in this setting.

**Data Sources**

I performed a systematic review of the published literature on cervical cancer incidence, screening, and prevention using standard databases such as MedLine, as well as within the publications of relevant organizations such as ACCP, FIGO (International Federation of Gynecologists and Obstetricians), PAHO and the WHO. My MedLine search included the terms cervical cancer, screening, prevention, accuracy, Papanicolau, VIA, DVI, see and treat, HPV vaccine, developing, low-resource, and Honduras. The search, which generated over one hundred articles, was generally restricted to those published in English, after 2000. To narrow the search, I focused on those articles most pertinent to the developing world, and to Honduras specifically. When they were available, I used randomized controlled trials, systematic reviews and meta-analyses as opposed to cohort and case control trials. Most of my analysis focused on approximately thirty of the most recent and methodologically sound articles generated from this search.

For information regarding Honduras’ health care system, as well as broader questions of acceptability and feasibility, I consulted social science databases such as JStor, Web of Science and Central American search engines, as well as publications from relevant organizations such as the World Bank, PAHO and WHO. This search included the same terms used for the MedLine search, with
the exception of accuracy, and also included the terms acceptability, feasibility, implementation, health care policy. This search was limited to English and Spanish-language articles. In addition, I sought source recommendations from a Central American politics expert at UNC-Chapel Hill and reviewed my own personal files.

Aside from using published information, whether in peer-reviewed journals or government or NGO documents, I made a significant attempt to place information within the appropriate context through the use of field notes and key informant interviews. My field notes come from two separate trips to Honduras, one during the planning stages of the community-based health education program I have referred to earlier, and one during implementation of the inaugural year of the program. In planning and carrying out this program, I have had significant contact with key public and private sector health care providers and program planners who are collaborating with us on this project. Moreover, through time spent doing educational workshops with women, providing clinical services, and living with families, I have also developed a keen understanding of the health knowledge base, concerns and desires of women living in southern Honduras.

To address some of my specific policy questions more systematically and directly, I also conducted in-depth, open-ended interviews with four key informants who represent different domains within the Honduran health care system. (Please see Appendix A for a sample of the survey instrument in English.) Although my
initial goal was to contact a known informant from each of four key sectors in cervical cancer prevention policy (national government sector; provider/clinician; research/academic; non-governmental organization/community-based organization), logistical difficulties with telephone and email communications to Honduras made this almost impossible. I have, nonetheless been able to obtain information, in person, by phone, and over email, from the following key informants who represent the same or similar key sectors of cervical cancer prevention policy:

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<td>Government</td>
<td>Regional</td>
<td><em>Zona 4 Director; Ministry of Health</em></td>
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<td>Clinical Care Provision</td>
<td>National</td>
<td>Chief of Division of Research, Evaluation &amp; Statistics; AHONPLAFA</td>
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<td>Non-Governmental Organization/Community-Based Organization</td>
<td>Local</td>
<td>Director; <em>Comunidades Unidas</em></td>
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<td>International Health Organization</td>
<td>International</td>
<td>Project Manager for Non-Communicable Diseases; PAHO</td>
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*This informant discussed the survey with the gynecologists who work at the main public hospital in his region. Thus, although his responses are taken to be the official MoH position on these issues, they are also reflective of the views of public sector gynecologists.

Each of these leaders offers a unique perspective on the Honduran health care system and on cervical cancer prevention policy in particular.

Even with the constraints imposed by language difficulties and technical obstacles, I have gained an indispensable third data source by conducting these survey interviews. The survey, designed to elicit in-depth responses from informants, consists of open-ended questions focusing in large part on acceptability and feasibility (political and economic) of each of the three policy alternatives. I wrote the surveys, as well as the initial email contact messages with
which they were introduced, in English and translated them into Spanish. They were then reviewed and corrected by a native Spanish speaker. After translating my notes from telephone interviews or written survey responses received via email, I used both content and textual analytical techniques to analyze the open-ended responses, following established methodological principles. I compared similarities and differences in response patterns, and searched the responses for the emergence of particular themes or perspectives to guide my analysis.

**Evaluation Criteria**

I have used conventional techniques of policy analysis, and more specifically those for assessment of prevention programs, to evaluate each screening method based on the following six criteria: efficacy; effectiveness; cost-effectiveness; equity; acceptability; and feasibility. I will briefly describe the working definition of each of these terms as I used them in the analysis, noting when primary and secondary prevention methods required different definitions:

**Efficacy**

Efficacy is generally taken to mean the performance of a test or intervention under ideal circumstances, i.e. *can* it work? Efficacy trials test whether the intervention can have the intended effect. In many cases, efficacy represents the immediate impact of a test or procedure, often an intermediate step that is divorced from its broader clinical implication. Thus, in the case of Pap smears and VIA, efficacy will be defined as the test's accuracy, as measured by its sensitivity.
and specificity in detecting abnormal cells (CIN or cancer). For HPV vaccines, efficacy will be defined as vaccine’s ability to prevent persistent HPV infection. Due to the long delay period in generating data regarding prevention of cervical cancer, vaccine trials are currently only reporting a vaccine’s ability to prevent primary and persistent HPV infection. However, this is not sufficient for demonstrating the true accuracy of vaccines. A recent WHO consensus conference determined prevention of HPV infection was not an adequate efficacy endpoint for use in program planning because although infection with high-risk type HPV is a powerful predictor for high-grade dysplasia or cancer, there is still no formal evidence demonstrating that preventing persistent HPV infections has an impact on cervical cancer development (Pagliusi and Teresa Aguado 2004).

**Effectiveness**
Effectiveness is generally taken to mean the performance of a test or intervention in real life settings, e.g. *does it work?* (Fletcher, Fletcher and Wagner 1996). Effectiveness trials weigh both the harms and benefits of interventions. More broadly, effectiveness demonstrates an intervention’s ability to meet broader clinical or public health goals, such as decreasing the incidence or mortality from cervical cancer. Thus, in this situation, for all of the policy alternatives, effectiveness will be defined as success in decreasing cervical cancer incidence and mortality in a real-world, Honduran setting.
Cost-effectiveness
Although cost-effectiveness analyses are driven by assumptions about the monetary value of situations that are hard to quantify accurately (death, health, years of life lost (YLL), etc.), they are still useful tools in policy analysis for comparing alternatives and determining the economic cost or benefit of a specific prevention program. Cost-effectiveness data specific to Honduras for each of the three policy alternatives are not currently available. Thus, I will review the cost-effectiveness studies that have been published and make recommendations based on their applicability to this discussion using a combination of outcomes.

Equity
An equity-focused criterion allows me to assess how fairly each prevention strategy can be implemented and to determine who will benefit most and least from it. Sociodemographic forces in Honduras, and access to services, both financial and geographic, are the main determinants of who benefits. Thus, I will compare these policy alternatives as they apply to low-resource versus high-resource women, and urban versus rural women.

Acceptability
Acceptability is defined as the policy’s acceptability to Honduran women and health care providers. Again, very few Honduran data exist. Work in other developing countries, as well as key informant reports and field notes, will guide this analysis.
Feasibility
Feasibility is a broad term intended to indicate whether or not a program could be implemented effectively. In this case, I will operationalize feasibility as key informants’ assessments of the political, economic and social constraints that may hinder prevention policy implementation.

Evaluation
Based on the definitions for evaluation criteria described above, I have analyzed each of the three prevention methods. When quantitative analysis is possible, such as comparing efficacy, effectiveness, and cost-effectiveness, I have used numbers to make a final evaluation. With the more qualitative criteria of equity, acceptability and feasibility, I have used the current MoH Pap-based program as the baseline and have determined whether the other two methods, if implemented, would be stronger or weaker along the same criterion. Based on the aggregate of these evaluations, I have made final recommendations about the most appropriate prevention strategy to be pursued in Honduras at this time.

Efficacy
Pap Smears
Best estimates of Pap accuracy based on recent reviews report a sensitivity of 30% to 87% and specificity of 86% to 100% (Nanda, McCrory and Myers 2000). However, using studies conducted in developing countries, Pap accuracy is somewhat lower, with sensitivity ranging from 44% to 78% and specificity ranging from 91% to 96% (Sankaranaryanan, Gaffikin and Jacob 2005). My
PAHO informant, as well as data from low-resource settings, both suggest that this discrepancy is due to sampling inadequacies (on the part of the examining provider) and reading errors (because of poor laboratory equipment or inadequate training of cytotechnians).

This same informant also reports the phenomena of many slides returning with the result of "inflamación" (inflammation). This is an indeterminate result, likely associated with some sort of change in the normal vaginal flora that obscures the true efficacy of the Pap in detecting pre-cancerous cells. We experienced this problem frequently while working in Honduras. Many women were upset and confused by this result, focusing on it and any possible ramifications for sexually transmitted infections, instead of the main focus of Pap smears, cancer detection.

It is unclear whether the high preponderance of this result is due to reading errors or actually reflects a true state of increased levels of gynecologic inflammation in these women. We can say with certainty that it obscures the clarity of Pap results and calls into question the test efficacy.

**VIA**

The most comprehensive review of VIA accuracy reports sensitivity ranging from 66% to 96% and specificity ranging from 64% to 98% (Gaffikin, Lauterbach and Blumenthal 2003). Despite sensitivity that is generally higher than that published for Paps, several of my MoH informants as well as public sector gynecologists expressed concerns about the accuracy of VIA, mainly the low sensitivity and high false positive rate. Contrary to their concerns, other informants who have helped with the implementation of pilot programs in El Salvador and other
Central American countries report program specific sensitivity and specificity rates higher than that of Paps, and these informants therefore recommend VIA as an efficacious alternative.

**HPV Vaccine**
So far, data from vaccine trials suggest that vaccines are very efficacious at preventing persistent HPV infection. In the most recent report of a bivalent (HPV16/HPV18) vaccine, Tjalma, Arbyn and Paavonen (2005) reported 100% efficacy for protecting vaccinated women against persistent HPV16 and/or HPV18.

**Effectiveness**

**Pap Smears**
Despite their widespread use, we do not know the true effectiveness of Pap smears in preventing cervical cancer. Laara, Day and Hakama (1987) reported 8-73% decreases in mortality in five Nordic countries after implementation of national Pap-based screening programs. Models in the United Kingdom suggest that 80% of cervical cancer deaths have been prevented due to their national, Pap-based screening program (Peto, Gilham and Fletcher 2004).

Although these decreases are impressive, similar results have never been achieved, either empirically or anecdotally, in any developing country. According to the Alliance for Cervical Cancer Prevention, cervical cancer screening programs in developing countries have had “little or no impact on cervical cancer mortality rates” (ACCP 2004). Although mortality from cervical cancer in
Honduras appeared to drop from 40.4 per 100,000 women in 1990 to 36.9 per 100,000 in 1999, in 2002, the rate was estimated to be back up to 40 per 100,000 (MoH 2004). Thus, despite over twenty years of a national prevention program, there has been no significant change in mortality rates and they are still very high, even in relation to other parts of the developing world.

**VIA**

Despite accuracy and efficacy fairly comparable to those of Pap smears, VIA has not been used in widespread prevention efforts for long enough to generate effectiveness data. Ongoing trials are moving in this direction, but data will not be available for as much as a decade. Direct evidence does not currently exist, but models have been developed to help policy makers and program planners develop more effective prevention programs for low-resource settings. In the most comprehensive of these models, Goldie, Kuhn and Denny (2001) used a mathematical model based on the natural history of HPV infection and cervical cancer to generate clinical and cost-effectiveness outcomes. Based on their model, once in a lifetime screening at the age of 35 with VIA followed by cryotherapy (a one-visit approach) could result in a 26% reduction in cervical cancer incidence. This was compared to Pap screening (as a two-visit strategy) once in a lifetime at the age of 35, which resulted in a 17% reduction in cervical cancer incidence.

Although this model suggests that VIA offers a distinct benefit over Paps, this model is built around numerous assumptions that do not apply to Honduras. The model is based on a population of previously unscreened South African women.
whose HIV infection rate is assumed to be approximately 8%. In Honduras, over 60% of sexually active women between the ages of 15 and 49 report having ever been screened for cervical cancer (Secretaria de Salud 2002). Moreover, at the end of 1999, the HIV/AIDS rate in Honduras was 1.9% (USAID 2000), approximately one fourth of the rate used in the South Africa model. The lack of prior screening and higher HIV rate suggest that any screening in this population would appear to perform much better than in the Honduran population. Although this is unlikely to vary the relative performance of each method, the absolute benefit is probably lower in Honduras. However, this analysis still suggests that the relative effectiveness of VIA is superior to that of Paps.

A second model to assess the clinical and cost effectiveness of different prevention strategies found similar results (Mandelblatt, Lawrence and Gaffikin 2002). This model compared the costs and benefits of various screening strategies based on a population-based simulation model developed in Thailand. In this model, a Pap smear every five years in women aged 35 to 55 resulted in a 13.5% predicted reduction in invasive cervical cancer. VIA, performed every five years on 35 to 55 year old women resulted in a 34.9% predicted reduction in invasive cervical cancer. Thailand’s rural population and HIV/AIDS rate of 1.5% (UNAIDS 2004) much more closely approximate that of Honduras. As with Goldie, Kuhn and Denny’s model, it is unreasonable to assume that this exact same level of effectiveness would be gained in Honduras. It is unlikely, however,
that the relative superiority of VIA over Pap would be significantly altered if the model were changed to reflect Honduran population dynamics.

**HPV Vaccine**

Because vaccine development is still a work in progress, effectiveness data are also a result of modeling at this time. Several models have been developed over the past three years to estimate the clinical and cost-effectiveness of vaccinations. Using a mathematical model based on disease progression, Hughes, Garnett and Koutsky (2002) estimated that a 47% reduction in invasive cervical cancer incidence could be achieved by a bivalent (HPV16/18) vaccine. The model assumes 95% coverage with a bivalent vaccine that is 75% effective and confers ten-year immunity.

A separate model developed by Kulasingam and Myers (2003) compared reductions in cervical cancer incidence and mortality between no screening, screening only (Pap), vaccine only and vaccine with screening at different intervals. Although Pap screening alone every three years was estimated to decrease incidence and mortality by 72.8% and 83.0% respectively, vaccine alone was only predicted to result in 16.8% and 17.7% decreases in incidence and mortality. If triennial screening is added to vaccines, incidence and mortality decrease by 74.3% and 83.5% respectively. The vaccine assumptions in this model were fairly similar to those used by Hughes, Garnett and Koutsky and assumed 100% coverage with a vaccine that covers 70% of oncogenic types and is 90% effective at conferring ten-year immunity.
The fairly significant differences predicted by these models raise two concerns. First, one cannot be certain how much of this discrepancy is dependent on the differing assumptions made in these models, and which is more closely reflective of Honduran reality. Second, aside from pointing out the weakness of such models, this discrepancy also highlights the fact that the true impact of a possible vaccine is not yet known. With these uncertainties, even once vaccines are ready for widespread implementation, they will not be a stand-alone strategy but will have to be combined with some form of secondary screening.

Cost-effectiveness

Pap Smears
Without better access to MoH officials and government documents, it is difficult to determine the true cost-effectiveness of Honduras’ Pap-based prevention efforts. Lacking additional data, it is simple to argue that, since the mortality from cervical cancer has remained basically unchanged since 1990 (one year prior to the implementation of the prevention program) to 2002 (MoH 2004), the program has not been cost-effective. In fact, the program may have been quite ineffective, spending limited resources with no discernible effect on mortality. Although it is quite possible that the program’s educational component has been beneficial, at least in rural areas, even these gains have not been documented to my knowledge.

In the absence of more detailed cost data from the government, I have compared the relative cost-effectiveness of each of these prevention efforts based on several
recently published mathematical models referred to above in the effectiveness discussion. Although the assumptions in these models, as discussed above, do not perfectly fit the Honduran context, the relative ranking of cost-effectiveness between strategies is unlikely to change, even when applied to Honduras.

In the Goldie, Kuhn and Denny model, Pap screening cost-effectiveness was always dominated by other strategies, meaning it was less cost-effective relative to VIA and HPV DNA testing. In Mandelblatt, Lawrence and Gaffikin's model, Pap screening every five years for women aged 35 to 55 had an incremental cost effectiveness ratio (US$/life years) almost six times greater than that of VIA. Despite any flaws in the model, it seems unlikely that a six-fold difference would be overcome, suggesting that, in low-resource settings such as Thailand and Honduras, Pap's are not the most cost-effective method for preventing cervical cancer. This idea was reiterated at the patient level by my NGO informant. She suggests that costs are one of the three main reasons that the Pap-based program has not been effective in Honduras.

**VIA**

As with VIA effectiveness, I have made cost-effectiveness comparisons based on models since no Honduran VIA programs exist. By comparing the relative cost-effectiveness of each of these prevention efforts based on the same recently

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1 According to my MoH and PAHO respondents, VIA is not currently in use in Honduras. However, my NGO representative reported that when she went to her gynecologist in April 2005 for a Pap smear, she was given the option of VIA. Her gynecologist told her that VIA is being used in Honduras at a lower cost to the patient and with immediate results. However, my informant reports that its use is not widespread and that most women do not have access to a provider who does it.
published mathematical models referred to above, I can draw conclusions about
the three methods under consideration in this discussion. As discussed above,
although the assumptions in these models do not perfectly fit the Honduran
context, the relative ranking of cost-effectiveness between strategies is unlikely to
change, even when applied to Honduras and provides a framework for research
when such data do become available.

In the Goldie, Kuhn and Denny model, VIA screening was the only strategy that
was found to be cost-saving. A single, lifetime VIA screen followed with
cryotherapy as necessary was more effective and less costly than no screening at
all. Increasing the number of times a woman is screened, up to every five years,
decreased the cost effectiveness, but it still remained more cost-effective than
other strategies. In Mandelblatt, Lawrence and Gaffikin’s model, VIA followed
by cryotherapy as needed every five years for women aged 35 to 55 had an
incremental cost effectiveness ratio (US$/life years) of $263, several-fold lower
than the next most cost-effective method. To put these costs in perspective, a
program based on these guidelines with 100% coverage would cost an extra $0.79
per Thai woman. That would increase the per capita health expenditures in
Thailand by 0.08%. Thailand currently spends $112 per capita. This lies within
the $49 to $165 range of that reportedly spent by Honduras per capita (The
Economist Intelligence Unit 2004). Thus, even with all of the cost and
demographic differences that likely exist between these two countries and
therefore alter the model, the relative size of such an investment is likely to be very small, even when applied to Honduras.

**HPV Vaccine**

Unfortunately, none of the models developed to date compare all three of the methods under discussion here. Most of the vaccine-relevant models compare vaccines to Paps alone or to a combination of the two, since early vaccine-based prevention programs will require Pap screening (or some other secondary prevention method) at least until long-term effectiveness data are available on vaccines. Kulasingam’s and Myers’ model (2003) found that a vaccine alone was not cost-effective in terms of incremental cost per life-year saved. In their model, Pap screening every five years had an incremental cost-effectiveness ratio of $6,030 per life-year saved. The two methods combined were also not found to be cost-effective. Although the cost figures generated were based on a hypothetical cohort of American women and the associated health care costs in the United States, the cost of the vaccine is listed as $200. This is based on an Institute of Medicine report that estimated the cost of a full course (three doses) of the vaccine as well as all associated direct costs. Although the direct costs are certainly higher in the US than in Honduras, even one half of the $200 amount is within the range of the entire per capita annual expenditures on health care services for Honduras (The Economist Intelligence Unit 2004), suggesting the vaccine is cost-prohibitive at this time.
Although other models like that of Goldie, Kohli and Grima (2004) may be useful in the long term in helping developed countries determine the most cost-effective way to add vaccines to their Pap-based screening programs (such as at what age they should initiate screening, or at what interval they should recommend secondary screening tests), their results are simply not relevant to a low-resource setting like Honduras. The lowest incremental cost-effectiveness ratio reported is $12,300 per quality-adjusted life year for combining a 100% effective vaccine with conventional cytology screening every five years, starting at the age of 35. This model serves to reiterate the relatively high cost of vaccine-based prevention, at least based on current projections, and the impracticality of considering such an intervention in a low-resource setting at current cost levels.

These models reiterate the views expressed by several of my key informants. Although my PAHO informant reported that most Latin American countries are “well-positioned” to start vaccines as soon as they are available, she agrees that they are currently cost-prohibitive. She repeated cost estimates of $35 to $50 per dose, making the vaccine much more expensive that of current Pap-based efforts, while not eliminating the concurrent need for them, driving costs up even further.

**Equity**

**Pap Smears**
Honduras’ current Pap-based prevention program is not completely equitable.

Although they did not address the problem in terms of equity, all informants thought that low coverage, especially in rural areas, was part of the problem with
current prevention efforts. The most recent national health survey, published in 2002, shows that rural, poor and less educated women have lower rates of Pap coverage than urban, wealthy and more educated women. Nationally, among women aged 15 to 49, 69.5% of urban women and 52.6% of rural women have ever had a Pap smear. In the two major urban centers, where services are most accessible, 86.3% (Tegucigalpa) and 65.1% (San Pedro Sula) of 15 to 49 year old women have ever gotten a Pap smear. Rural women are more likely to get Pap smears at public medical facilities (MoH facilities), and a fourth of them report not knowing the results of their Pap smears. My work in southern Honduras suggests that this number is actually much higher, and that the women who do receive their results often do not understand what they mean. MoH facilities are unfortunately quite slow at getting results back to women. Although the “Strengthening Project” has led to some improvement in this area, in 2001, 58.6% of women who got Pap smears at MoH facilities reported waiting 21 days or longer to get their results.

Differences in Pap rates are evident across income and educational levels as well. Of women aged 15 to 49 years with no education, only 42.6% have gotten a Pap smear in the past year and 27.5% of them do not know what the results were. Among similarly aged women with greater than a high school education, 62.6% have gotten a Pap smear in the past year and only 6.9% do not know what the results were. Among low-income women, only 46.1% have gotten a Pap smear in the past year, with 31.4% not knowing the results, as opposed to 58.1% of high
income women getting Paps in the past year and only 7.8% not knowing the results. Based on these national statistics, it seems fairly safe to say that although Pap services are accessible throughout the country, the current prevention program disproportionately benefits urban over rural women and wealthy, educated women over poor, less educated women.

VIA
Improved equity is one of the major strengths of a VIA-based cancer prevention program. Because nurses and LHAs can be trained to provide screening services, rural health centers with no physician coverage could provide these services. Thus, rural women would have much better access to preventive care. Moreover, because results are immediately available, women, both urban and rural, will not only receive their results but also counseling to ensure that they understand them and any need for follow-up. The ability to offer on-site results with counseling will also be of great benefit to less educated women who currently are less likely to know the results of their last Pap smear. Thus, a VIA-based program offers the distinct possibility of more equitably benefiting all women across geographic, education and income boundaries.

HPV Vaccine
Much like a VIA-based programs, a vaccine-based prevention program can make use of nurses and LHAs to provide primary prevention care, allowing for much broader geographic coverage of services. The ability to broaden the service delivery area and thereby decrease urban/rural differences in access to care is well-demonstrated by the childhood immunization program. Across all five
childhood vaccinations, less than one percentage point of difference exists between rates of urban and rural children who have received their vaccinations (Secretaria de Salud 2002). Broader access to services also diminishes the differences in utilization based on educational levels, with a difference of less than 5% in immunization rates for children of less- versus well-educated parents (Secretaria de Salud 2002). Information is not available for rates based on parents' income. Although increased access to vaccination services could help in prevention, the required, associated Pap smear services would likely suffer from the same access issues as a stand alone Pap-based program. Thus, although vaccine coverage would improve equity, the full benefits of the prevention program would still not be equally enjoyed by rural, less-educated and less wealthy women.

Acceptability

Pap Smears
In 2002, 60.9% of sexually active women aged 15 to 49 reported ever having had a Pap smear (Secretaria de Salud 2002). Their relatively high levels of compliance to recommended Pap screening recommendations suggest that Honduran women are fairly accepting of the current, Pap-based prevention program. Anecdotally, many women are uncomfortable with the sensitive nature of a screening visit but do it anyway because they recognize its importance. Although some young women may not get screened because such a clinic visit implies a degree of sexual activity that is not publicly permissible (Linthicum 2004), these are not the women who are at highest risk for development of cancer.
Because VIA is not currently used widely in Honduras, determining the acceptability of a see-and-treat model is largely dependent on the effectiveness of cryotherapy, key informant feedback and acceptability data generated from see-and-treat model programs in other developing countries. As already briefly discussed, cryotherapy is a low-tech, minimally invasive method for offering immediate treatment to women with positive VIA results. Even when performed by non-physicians, cure rate ranges from 88% to 99% for pre-invasive lesions, which is consistent with that found for other methods (Mandelblatt, Lawrence and Gaffikin 2002). Aside from being effective, cryotherapy has a very low complication rate. In Thailand, where a single-visit approach demonstration project was recently implemented, over 600 women were offered immediate treatment with cryotherapy. Of the 98.5% who consented to immediate treatment (suggesting it is also very acceptable to women), none experienced major complications and only 4.4% returned for perceived, minor problems such as vaginal discharge and cramping. (Royal Thai College of Obstetricians and Gynaecologists (RTCOG), CCJHPIEGO Corporation for Cervical Cancer Prevention Group 2003).

A similar but much larger single visit prevention program in Thailand also reported very high acceptability (Royal Thai College of Obstetricians and Gynaecologists (RTCOG), CCJHPIEGO Corporation Cervical Cancer Prevention Group 2003). Of the 5,146 women who had negative VIA results, 99.8% said they
would recommend the procedure. Of the VIA positive women who opted to have immediate cryotherapy, 97.5% said they would recommend both. Three months after their initial screening, 97.9% had recommended VIA to others and 94.5% said cryotherapy either met or exceeded their expectations. Because screening rates in this rural part of Thailand are very low, most of these women have likely never had a Pap smear. Thus, although their reported experience with VIA is very positive, we do not necessarily know that they would be any more or less accepting of Paps or an HPV vaccine. Two other very large trials of VIA accuracy in South India (>48,000 women) and Africa and India (~57,000 women) reported no recruitment issues, suggesting women in these areas are not resistant to VIA as a screening method.

These model programs suggest that, even across cultural differences, women are accepting of VIA. More applicable to this analysis is the feedback I received from key informants. El Salvador, which is reasonably similar to Honduras both socially and culturally, has had several, large-scale see-and-treat programs successfully implemented by PAHO without any problems with acceptability. Women have embraced the program and seem to appreciate the convenience of being able to receive treatment immediately. My clinical care provision informant, who oversees research and programming for the main private sector provider of Paps in Honduras, expected similar results. She thought that Honduran women would readily accept a VIA-based approach, assuming it was tied to an education program. With the right information about what VIA is and
how it can be important in the early detection of cervical cancer, she believes Honduran women will accept it.

Providers, however, have presented much greater concerns. Gynecologists have major uncertainty about the appropriateness of VIA and cryotherapy. These same PAHO programs in El Salvador that were so quickly accepted by women faced numerous barriers to initial implementation due to strong resistance from practitioners. VIA with immediate cryotherapy presents a whole new model for treating cervical dysplasia in the primary care setting. Similar concerns were voiced by my MoH informant, who talked to his gynecology colleagues at one of the major regional hospitals before responding to my survey. He reported their insistence that VIA is simply not an acceptable method due to the high false positive rate, without challenging their position. Although these gynecologists appreciate the advantage of being able to give women results immediately, they do not see it as outweighing the increased treatment of healthy women. This is of significant concern to them because cryotherapy is not currently practiced by most gynecologists. Thus a woman with a positive test would be referred to a specialist to receive a much more invasive procedure, such as conization, or even hysterectomy if she is past her childbearing years. In this context, a high false positive rate is quite concerning.

5 Conization involves the removal of a cone shaped sample of cervix from the transformation zone for diagnostic as well as therapeutic purposes. The procedure is typically performed under anesthesia with a scalpel, laser or electrosurgery. Immediate and long-term complications include bleeding, infection, uterine perforation, cervical stenosis, and pregnancy-related difficulties.
A see-and-treat approach challenges several of the common practices and beliefs of gynecologists. Gynecologists are trained as surgeons. Shifting treatment of cervical cancer to a primary care setting requires a significant shift in mindset for gynecologists, who are much more schooled in invasive but more definitive approaches to treatment, such as cervical conization and hysterectomy. Moreover, allowing nurses and LHAs to offer not only preventive services but also therapeutic care represents a significant shift of control down the medical hierarchy and will require a major acquiescence by gynecologists.

Although some of these barriers are specific to this field, there is a significant body of literature that details the challenges in disseminating and implementing innovations in medical care. Timely adoption of new practices is most effective if the innovation is evidence-based, well-perceived, and if the adopting institution supports “innovators” and “early adopters”, or physicians who are willing to accept changes (Berwick 2003). In the circumstance of using a see-and-treat approach to cervical cancer prevention in Honduras, the MoH could go far in initiating this innovation. By improving the perception of the practice by disseminating more evidence about its effectiveness in low-resource settings, the MoH could facilitate implementation by innovators and early adopters. Only with this institutional support will this type of approach, which offers the advantage of immediate results and treatment, become a fundamental part of an improved prevention policy.
HPV Vaccine
Determining the acceptability of an HPV vaccine in Honduras is quite difficult since they have not been implemented anywhere outside of clinical trials. Based on the high immunization rates of children, with approximately 89.2% of all five-year old children being fully immunized (Secretaria de Salud 2002), we can surmise that, in concept, Hondurans are accepting of vaccinations. One of my informants reiterated this idea, suggesting that Honduran women are very cognizant of the importance of immunizations in preventing disease and would adopt this attitude for and HPV vaccine as well.

However, vaccination for a sexually transmitted infection that may result in cancer is a much more complicated and culturally challenging concept that may not benefit from the same high levels of acceptance. Moreover, to be effective, the vaccine will need to be offered to girls, and possibly boys, before the onset of sexual activity. Due in part to difficulties with data collection in general, as well as the sensitive nature of the topic, it is unlikely that the MoH currently has national data about the average age at first sexual activity. Aside from a lack of necessary data, many parents may feel uncomfortable about vaccinating a child or adolescent for a sexually transmitted disease. In Honduras, where cultural norms about the permissibility of sexual activity outside of marriage are still restrictive of women’s behavior, it is not hard to imagine parents’ unwillingness to comply with such a vaccination. Despite possible cultural uncertainty about a vaccination for a sexually transmitted infection, my informants, especially at the grassroots, seem to believe that Hondurans would embrace a vaccine for cervical cancer.
Feasibility

**Pap Smears**
Clearly, implementing a Pap-based prevention program in Honduras is feasible since one has been in place since 1991. The MoH’s recent “Strengthening Project” suggests that within the Ministry there is hope that improvements to this program can be made. Their assessment of the main weaknesses of the program includes poor linkages within the health care infrastructure and lack of compliance to guidelines, or quality control. These major barriers affect the overall effectiveness of the program and will be important to consider for any prevention effort.

**VIA**
The existence of a Pap-based prevention program, which is in many ways more resource intensive than a VIA-based effort, suggests that much of the infrastructure necessary for a VIA-based program is already in place. The major structural changes required for implementing a VIA-based program is a shifting down of screening service provision from physicians to nurses and LHAs; as well as overcoming physician (mainly gynecologists) resistance to these changes. Lower level providers would need training in VIA and cryotherapy, for which modules already exist that have been implemented successfully in similarly resource-poor settings. Refresher courses, much like the regional trainings Honduran LHAs already attend, could serve as a way to maintain high quality services. Although such a major training endeavor would require a significant time and financial commitment up front, the money saved from laboratory fees
could be put towards this end. Some initial investment for cryotherapy equipment, assuming a see-and-treat approach is implemented, would also be necessary.

Despite the initial investments required, my health sector informants report that a single-visit approach with VIA and cryotherapy is feasible but will require a lot of convincing of physicians. My PAHO informant reported a two year process of advocating for a see-and-treat program in El Salvador with MoH and National Cancer Institute officials before being able to implement a pilot program. Once providers were convinced of VIA’s efficacy, the program was quite successful. She reports great frustration at the hesitance on the part of providers and MoH officials to consider VIA since Pap-based approaches, as they are currently structured, are not effective.

Similar concerns were raised by the gynecologists consulted by my MoH informant. Although a see-and-treat approach is feasible from a physical and human resources perspective, these Honduran gynecologists simply do not see a VIA-based program as feasible. Their main concern, as detailed above, is VIA’s high false positive rate which, they claim, makes it inappropriate for institutionalizing at a national level. Perhaps this resistance could be limited by using the success of programs in neighboring El Salvador. After almost a year in operation, the program has been very well accepted and no women have suffered serious complications from the immediate delivery of treatment. Perhaps a similar marketing strategy in Honduras could soften the resistance of gynecologists who
are currently open to the idea of a small, VIA-based pilot program but find the idea of a national program unacceptable.

**HPV Vaccine**
The successes of Honduras’ childhood vaccination campaigns suggest that an HPV vaccine program is probably feasible. The overwhelming success of the current childhood immunization program is due in part to a major decentralization of services so that vaccines are available at all health centers at all times; an immunization registry to allow for recordkeeping and tracing of unvaccinated children; and a well-maintained cold chain to allow for effective vaccine maintenance (Secretaria de Salud 2002). Although the target age group would likely be young adolescents, not infants, these same infrastructure and systems management mechanisms would facilitate smooth implementation of a vaccine-based prevention program. Because any vaccine program will also require secondary screening efforts, at least during the initial period, either Pap or VIA-based screening would need to continue.

Although current childhood immunization programs could help pave the way for smooth implementation of a vaccine-based prevention effort, there are still significant hurdles. Aside from the fundamental issue of the vaccine still being in the early stages of development, there are more concrete barriers to overcome. Ideally, adolescents would need to be vaccinated prior to onset of sexual activity to ensure no previous exposure to HPV. It is not clear whether the MoH has accurate data about the average age of onset of sexual activity in Honduras. Once
this age is established, what is the best way to capture this age cohort? Children in this age tend not to utilize health care services as frequently as do infants. Thus, a standard clinic-based approach to immunization would likely be ineffective.

While school could prove an ideal locale, many poor rural children, especially girls, are no longer attending school by adolescence. This suggests the need for some sort of mobile outreach effort, which would certainly complicate the maintenance of the cold chain. Although these barriers are all surmountable, policy planners would need to be very creative in developing a program that could overcome these obstacles to implementation.

Table 1: Summary Evaluation Table

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Pap Smears</th>
<th>VIA</th>
<th>HPV Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>Sens: 44%-78% Spec: 91%-96%</td>
<td>Sens: 66%-96% Spec: 64%-98%</td>
<td>100% for preventing persistent HPV16/18 infection</td>
</tr>
<tr>
<td><strong>Effectiveness</strong></td>
<td>8-73% in the UK 0% in Honduras 12% ↓ in incidence* 13.5% ↓ in invasive CA**</td>
<td>26% ↓ in incidence* 34.9% ↓ in invasive CA**</td>
<td>47% ↓ in invasive CA***</td>
</tr>
<tr>
<td><strong>Cost-effectiveness</strong></td>
<td>Incremental Cost-effectiveness ratio (US$/life years) 6 times that of VIA**</td>
<td>Incremental Cost-effectiveness ratio of $263/life years*</td>
<td>Estimated cost of $200 for 3 doses and all direct medical costs involved</td>
</tr>
<tr>
<td>Equity</td>
<td>0</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Acceptability</td>
<td>0</td>
<td>0/+</td>
<td>0/+</td>
</tr>
<tr>
<td>Feasibility</td>
<td>0</td>
<td>0/+</td>
<td>0/+</td>
</tr>
</tbody>
</table>

0: denotes a neutral evaluation with Paps serving as the baseline measure
+· better than Paps
-· worse than Paps

*Goldie, Kuhn and Denny (2001) model based on once in a lifetime screening at age 35
**Mandelblatt, Lawrence and Gaffikin (2002) model based on screening every 5 years in women aged 35 to 55
***Hughes, Garnett and Koutsuky (2002) model based on HPV16/18 vaccine with 95% coverage, 75% efficacy and 10-year immunity
Recommendations

From a purely medical perspective, a cervical cancer prevention program should apply the most accurate screening method available to bring about the best possible results. Within a policy context, especially in a low-resource setting such as Honduras, the accuracy of the screening method is but one of several important criteria that need to be considered to make recommendations about an effective program. Such a program should yield decreased incidence of and mortality from cervical cancer by employing a screening method that is cost-effective, simple, easy to apply, with minimal side effects or complications, and is equitable and culturally acceptable. This is a high demand that, under the constraints of the current health infrastructure in Honduras, perhaps cannot be met completely. However I would suggest that a see-and-treat approach of VIA with immediate cryotherapy when necessary would come closer to meeting these goals than do current Pap-based programs.

Although Pap-based screening programs have, perhaps by default, become the gold standard for effective screening programs in the developed world, they simply have not delivered the same benefits in Honduras. After over twenty years of a Pap-based prevention program, incidence and mortality rates are still unacceptably high. I would contend that this does not reflect inherent weaknesses in Pap smears as a screening method but instead exacerbates the broader, service delivery issues that are complicated by a Pap-based program. Most of these issues are simplified by a see-and-treat approach and address the specific concerns
raised by the MoH in their own recent assessment of Honduras’ current prevention efforts. As elucidated earlier, their major concerns were a low demand for services, poor networking within the healthcare system, and a lack of compliance to norms.

**Low demand for services**

Based on the relatively high adherence rates (~60% nationally but closer to 85% in major urban areas), I would suggest that the greater concern is not demand for services but access to them (Secretaria de Salud 2002). A see-and-treat approach, which can offer a much broader coverage area since nurses and LHAS would provide prevention services, could significantly alter utilization rates, most specifically in currently underserved rural areas. This could drive up demand for services, as well as significantly improve the equity of the program. This decentralization of preventive services could have additional benefits outside of the arena of cervical cancer as LHAS and nurses expand their scope of practice and underserved patients gain increased access to care.

**Poor networking within the healthcare system**

One of the major complaints about the current-Pap based system is that many women never get their results, and that even those who do often do not receive adequate referrals or cannot return for follow-up care. A see-and-treat approach mitigates many of these concerns. The provision of immediate results not only ensures that women will get their results, but also offers an opportunity to provide
counseling to ensure that they understand them. Moreover, the ability to offer immediate treatment in the form of cryotherapy minimizes loss to follow-up. Although women with invasive cancer will still need referral and linkage to the broader health care network, the ability to provide immediate results and treatment will significantly decrease the number of women who need follow-up in a more specialized setting.

This ability to combine screening with immediate treatment adds significantly to the effectiveness and the cost-effectiveness of the program. In Mandelblatt, Lawrence and Gaffikin’s (2002) model, VIA with referral to another facility for treatment was compared to VIA with immediate cryotherapy as necessary. If women 35 to 55 years old are screened every five years, the see-and-treat approaches results in a 30.8% reduction in incidence and 34.9% reduction in mortality whereas the screen and refer approach results in an 8.3% reduction in incidence and 12.3% reduction in mortality.

**Lack of compliance with norms**

Implementing a new prevention program, which would require training of new service providers, would offer an ideal opportunity to establish appropriate clinical care guidelines and recommendations as well as mechanisms for ensuring they are met. Most pilot see-and-treat programs have built refresher courses into the training and quality control standards for screening and treatment providers. Such courses could help to ensure the degree of compliance to norms that is lacking in the current Pap-based program. These quality assurances would also be
fundamental in helping gynecologists, who are currently resistant to a see-and-treat approach, feel more confident in its outcomes. Their advice in establishing appropriate cryotherapy treatment protocols could be helpful in ensuring a clinically sound program as well as securing physician buy-in to the new policy. Because quality control is of stated concern to the MoH as well, attention to quality issues would need to play an integral role in development of any new prevention program.

A see-and-treat approach would not only address many of the concerns raised by the MoH regarding the current Pap-based program, but would also fit well into the broader health policy agenda currently facing Honduras. The confluence of several events makes this an ideal time for Honduras to consider moving towards a see-and-treat approach to reduce the impact of cervical cancer. Internally, the MoH has recently enjoyed the much-publicized success of its program to reduce maternal mortality. The overwhelming success of this program not only illustrates the ability of the public health infrastructure to perform well, but also indicates a shift in priority towards women’s health issues. Cervical cancer prevention advocates would do well to make use of this window of opportunity while it still exists.

External factors are also forcing the policy window open. Among them is increased attention to the growing HIV/AIDS problem in Honduras, which could have a profound impact on cervical cancer if it is not well controlled. USAID
announced renewed efforts and funding to stem this growing epidemic in Honduras. Such attention will serve to increase public awareness of sexually transmitted infections and prevention efforts. This can help pave the way for easing cultural restrictions around discussing and accessing prevention services for other reproductive health issues such as cervical cancer.

The ACCP and other international agencies interested in cervical cancer prevention have been actively pushing the issue of re-assessing prevention efforts in the developing world. Over the past year, numerous articles addressing this topic have flooded the gynecologic, cancer and international health journals, sparking debate among researchers, clinicians and program planners. This academic discussion coincides with the continued implementation of numerous pilot programs and clinical trials throughout the developing world. Even traditionally conservative professional organizations such as the American College of Obstetricians and Gynecologists (ACOG) have entered the debate, issuing statements on the need for a re-consideration of prevention efforts in the developing world. They have gone so far as to deem see-and-treat approaches as appropriate within this context. This is significant: American gynecologists, who are accustomed to the benefits of Pap-based prevention, are indirectly endorsing the idea that perhaps such policies are not as efficacious in the developing world. All of these activities suggest significant external activity that could be instrumental in helping to tilt the policy agenda in Honduras toward a new approach to cervical cancer prevention.
Such external influences are not new to Honduras. Especially since Hurricane Mitch, external assistance, both financial and technical, has been a major part of many development and health promotion policies. Even the “Strengthening Project” for the current Pap-based program received 65% of its funding from external sources, mainly an international development organization. Thus, the possibility for external assistance with a prevention program is certainly not new.

Within this context, I recommend that the MoH implement a pilot see-and-treat prevention program. The program could be modeled after see-and-treat approaches currently ongoing in other parts of Central America. These programs are centered on the concept of bringing prevention and some treatment services into the primary care setting. This shift requires slowly building gynecologist acceptance, and training lower-level providers such as nurses and LHAs in the practice of VIA and, for more skilled nurses and LHAs, cryotherapy. The program will allow for much broader coverage of prevention services, especially in poorly served rural areas. Starting small, with a pilot program, offers the benefit of maximizing benefits while minimizing risks. It also allows more time for advocacy before initiating broader implementation plans. This advocacy will be fundamental to getting support from gynecologists, whose input is crucial for the program to work. Benefits of such an approach include the following:
**Improved equity:** All of my key informants expressed concerns about low coverage rates, especially in rural areas. A VIA-based approach will greatly improve coverage, especially for poor, rural women.

**Rapid return of results:** Much like coverage, the issue of delay in getting results was mentioned by all informants as a factor in the poor effectiveness of the current program. VIA solves this problem completely without major effort.

**Primary care focus:** A see-and-treat approach mirrors efforts in much of the developing world to shift care out of hospitals and to more community-based, primary care settings. Such a shift not only uses resources more effectively but also makes them more accessible to a broader segment of the population. This change also requires a move to less invasive treatments, when appropriate. Within the context of cervical cancer, this is ideal. A Honduran woman diagnosed with cervical cancer either gets a conization or, assuming she is past childbearing years, a hysterectomy (MoH informant 2005). However, if her cancer could be detected much earlier through screening, she could avoid these more invasive procedures and instead just get treated with cryotherapy. The lower costs in time, resources, and morbidities for both the patient and the health care system could be substantial.

**Increased role of LHAs:** LHAs are a greatly underused resource. Their integration within the community generally makes them trusted advisors. Thus,
their ability to provide much needed education about cervical cancer prevention is invaluable. Moreover, their training in VIA could open the door to more expanded roles. Some LHAs in southern Honduras currently manage birth control supplies for their communities, dispensing pills and giving Depo Provera shots. VIA training could be the next step in greater care provision in rural areas. Should a vaccine program be implemented in the next 10 to 15 years, LHAs would be ideal providers.

A see-and-treat approach, implemented first on a small scale, could be integral to mitigating the barriers that prevent the Pap-based program from being more effective. Models from neighboring Central American countries suggest that this will be the case. Financial support and technical assistance form international health and development organizations could help to ensure minimal costs to the MoH. If effective and implemented more broadly, such a policy could begin to decrease the significant morbidity and mortality of cervical cancer in Honduras.

Despite the possible benefits of such a policy, numerous unknowns remain. Although modeling suggests that VIA is both more effective and more cost-effective than Pap- and vaccine-based programs, we are still several years from evidence that could demonstrate positive effects on disease incidence and mortality. During that period, significant advancements in the development of HPV vaccines and HPV DNA testing could make these more viable alternatives for the future. Both of these alternatives currently lack the necessary effectiveness.
data to support their widespread use. However, such data should be forthcoming. If these methods prove to be successful, we can hope that they will also soon become more cost-effective so that they can be implemented even in resource-poor settings. Any of these alternatives share in the advantage of making use of LHAs to provide service in a more equitable manner. Only in these ways can we ensure a program that results in decreased incidence and mortality of this preventable disease for all women.
Appendix A: Survey of Experts on Cervical Cancer in Honduras

"Hello, this is Jessica Morse. I am a graduate student from the University of North Carolina at Chapel Hill. I emailed you earlier about participating in a telephone interview for my research study entitled "A Policy Analysis of Cervical Cancer Prevention in Honduras." Your participation in this survey is completely voluntary. This means that you do not have to participate in this survey unless you want to.

Did you have a chance to read the information I emailed you about participating in research studies?"

If "yes": "Do you have any questions or concerns about the research I am doing?"

- Answer all questions.
- If no questions or when all questions completely answered:

"Please be assured that I will not identify you by name, but only by general position, such as "Health Care Provider," "Researcher," "Organization Representative," or "Ministry of Health Official." If you have any questions about this study, please contact me (Jessica Morse, Jessica_morse@med.unc.edu) or the University of North Carolina at Chapel Hill Office of Human Research Ethics (IRB_subjects@unc.edu). As we discussed, I would like to tape this interview to assure that I have as accurate a picture as possible of your responses. I will be happy to send you a transcript if you like."

"Do I have your permission to begin asking questions?"

"Do I have your permission to tape this interview?"

If "no": Read Telephone Script to obtain informed consent.

After obtaining informed consent, begin here:

Thank you for helping me to study cervical cancer prevention programs in Honduras. Because I know your time is valuable, I will get right to the point. I want to get your views on some general questions and also some questions about specific areas of the Honduran health care system. You have special insight into each of these questions, and I value your responses.

1. The Honduran health system has used Papanicolaou (Pap) screening programs for cervical cancer prevention for years. What improvements might be made to this prevention program that would help to further reduce cervical cancer morbidity and mortality?

2. What do you think is the single most important reason for Honduras' cervical cancer morbidity and mortality rates?
3. And what about other reasons?

4. You have had experience with cervical cancer programs, either by implementing them or by conducting research on cervical cancer, or both. I want to know what factors you think help or hinder these programs. Please tell me anything that comes to mind.

Follow Up to “What do you mean?”: Well, any factors, like culture or politics or economics or anything else.

5. I know how challenging it is sometimes to be able to tell whether programs are succeeding. If you were trying to implement a new cervical cancer screening program, what measures of success would you use?

Follow Up to “What do you mean?”: For example, how would you measure whether it is effective, whether it is acceptable to women, whether it is politically feasible, and whether it is financially feasible?

6. Now I'd like to talk for a minute about a different screening technique called VIA, or visual inspection with acetic acid. Some research suggests that it can be better than Pap smears in some settings because it costs much less, and because the patient can get her results immediately. Do you think this could be an effective method in Honduras? Please tell me why you think this.

Follow-up if necessary: Could such a test be feasibly incorporated into a widespread program? Please tell me why or why not.

Follow-up if necessary: Do you think Honduran women would accept visual inspection with acetic acid (VIA)? Please tell me why you think this.

7. What about the HPV vaccine to prevent cervical cancer that is now being tested in other parts of Latin America? Do you think it could be used in Honduras? Please tell me why you think this.

Follow-up if necessary: Do you think an HPV vaccine could be feasibly implemented in a widespread program? Please tell me why you think this.

Follow-up if necessary: Do you think Honduran women would accept an HPV vaccine for prevention of cervical cancer? Please tell me why you think this.

Now I have a few last questions.
8. Where would you say improving cervical cancer morbidity and mortality falls on the agendas of the current administration and the Ministry of Health, understanding the many other needs that Hondurans have?

Why do you think cervical cancer falls where it does on the health care agenda?

9. Who are the key players need to support a cervical cancer prevention program? Why?

Who might be the strongest opponents of a new program? Why?

10. How long do you think it would take to see a new program accepted?

How long do you think it would take to see the new program achieve results?

11. Now I have just one last question: from your own perspective, and from the vantage point of the position you occupy, what do you see as the three main barriers to improving cervical cancer prevention in Honduras?

We are done! Thank you again for answering these questions! Please do not hesitate to contact me if you have any questions about this interview or about my research study.
Appendix B: Key Informant Interview Citations

1. Government Sector
   Regional Level
   *Zona 4* Director; Ministry of Health
   Conducted by telephone 6/13/05

2. Clinical Care Provision Sector
   National Level
   Chief of Division of Research, Evaluation & Statistics; ASHONPLAFA
   Conducted via email (written responses to survey) on 5/10/05

3. Non-Governmental Organization/Community-Based Organization Sector
   Local Level
   Director; *Comunidades Unidadas*
   Conducted via email (written responses) with in-person follow-up on 6/17/05

4. International Health Organization Sector
   International Level
   Project Manager for Non-Communicable Diseases; PAHO
   Conducted via telephone on 5/31/05
Citations


Burlone, S. (2003). Personal field notes from focus groups and personal interviews.


Claeys P., DeVuydt H., Gonzalez C., Garcia A., Bello R.E. Temmerman M. (2003). Performance of the acetic acid test when used in field conditions as a screening test for cervical cancer. Tropical Medicine & International Health, 8(8), 704-709.


Morse J. & Saleeby E. (2003). Personal fieldnotes and conversations with the National Director of Pathology, ASHONPLAFA.


