

Safety, Acceptability, and Feasibility of a Single Visit Approach to Cervical Cancer Prevention: Results from a Demonstration Project in Rural Thailand

Roi-et Province, Thailand

By

*Lynne Gaffikin, DrPH
Margo Lauterbach, MD
Mark Emerson, BS*

and the

*Cervicare Thailand
Group*

October 2003



Cervical Cancer Prevention Program Office,
JHPIEGO, an Affiliate of
Johns Hopkins University

With funding from the
Bill and Melinda Gates Foundation through the
Alliance for Cervical Cancer Prevention

**Safety, Acceptability, and
Feasibility of a Single Visit
Approach to Cervical
Cancer Prevention: Results
from a Demonstration
Project in Rural Thailand**

Roi-et Province, Thailand

By

**Lynne Gaffikin, DrPH
Margo Lauterbach, MD
Mark Emerson, BS**

for the

Cervicare Thailand Group

October 2003

**With funding from the Bill and Melinda Gates Foundation
through the Alliance for Cervical Cancer Prevention**

JHPIEGO is a nonprofit international health organization dedicated to improving the health of women and families. Established in 1973, JHPIEGO – affiliated with Johns Hopkins University and headquartered in Baltimore, Maryland – works in more than 30 countries through its collaborative partnerships with public and private organizations, and local communities.

Copyright © 2003 by JHPIEGO Corporation. All rights reserved.

JHPIEGO
Brown's Wharf
1615 Thames Street
Baltimore, Maryland 21231-3492, USA
www.jhpiego.org

Editors: Katrin DeCamp, Dana Lewison

Cervicare Thailand Group members:

Thailand: K Limpaphayom, MD; P Lumbiganon, MD, MS; S Srisupundit, MD; S Warakamin, MD; B Chumvorathayee, MD; S Kanavacharakul, MS

USA/JHPIEGO: L Gaffikin, DrPH; PD Blumenthal, MD, MPH; M Emerson, BS; R Lewis, MPH; P Ringers, PhD

Cover photo: Thai women waiting for testing (February 2000, during the initial launch of the SAFE Project). Photographer: Robbyn Lewis, JHPIEGO CECAP Program Manager.

Printed in the United States of America

October 2003

PREFACE AND ACKNOWLEDGMENTS

Between February and October 2000, JHPIEGO's Cervical Cancer Prevention Program (CECAP) and colleagues from Chulalongkorn and Khon Kaen Universities in Thailand had the opportunity to work collaboratively with the Thai Ministry of Public Health (MOPH) to introduce and assess an alternative testing and treatment option for preventing cervical cancer. We are grateful to the Thailand MOPH for this opportunity, as well as for their support and encouragement.

Roi-et Province MOPH nurses carried out the fieldwork under the direct supervision of clinical supervisors from Khon Kaen University Hospital (Bundit Chumworathayee, Sanguanchoke Luanratanakorn) and Khon Kaen Provincial Hospital (Sumontha Prasertpan, Suwaree Paojirasinchai). Supervision of data collection and data entry in the field was provided by Kesara Phutthong, with assistance from Sodsuy Kanavacharakul and Rabiab Poomban-khor. We thank the Roi-et Provincial Medical Director for his assistance with this project, and the district hospital directors and other facility staff who supported the project implementation.

Our gratitude goes to Khon Kaen University for providing backup clinical support and supervision, and to the Royal Thai College of Obstetricians and Gynecologists for logistical and advocacy assistance. The village health volunteers deserve acknowledgment for their contribution to participant education and recruitment. Finally, the team owes a debt of gratitude to the women and their families who participated in this project.

We also thank the following JHPIEGO staff: Noel McIntosh for overall program guidance; Sarah Slade for training and clinical input; Sapna Sharma for project coordination; Karen Mazziott for financial assistance, Saifuddin Ahmed for help with statistical analyses; Sonia Elabd for assisting with training materials; and Mark Fritzler for equipment support.

This project was funded by a grant to JHPIEGO from the Bill & Melinda Gates Foundation through the Alliance for Cervical Cancer Prevention and by the MOPH of Thailand.

TRADEMARKS: All brand and product names are trademarks or registered trademarks of their respective companies.

TABLE OF CONTENTS

PREFACE AND ACKNOWLEDGMENTS	i
ABBREVIATIONS AND ACRONYMS	iv
EXECUTIVE SUMMARY	v
INTRODUCTION	
BACKGROUND.....	1
THAILAND.....	2
METHODOLOGY	
TIME FRAME.....	6
SITE SELECTION.....	6
PROVIDER SELECTION	6
STUDY PARTICIPANTS.....	7
CLINICAL PROTOCOL	7
RECRUITMENT.....	9
VIA TESTING.....	10
TREATMENT: CRYOTHERAPY AND REFERRAL.....	10
COUNSELING FOLLOWING CRYOTHERAPY.....	13
FOLLOWUP VISITS.....	13
SUPERVISION	14
RESULTS	
INITIAL VISIT	16
VIA	20
DETERMINING ELIGIBILITY FOR IMMEDIATE TREATMENT.....	21
POST-VIA COUNSELING QUESTIONS AND POST-VIA INTERVIEW	22
CRYOTHERAPY RESULTS	
PRE-PROCEDURE COUNSELING	24
CRYOTHERAPY PROVIDER OBSERVATIONS.....	24
POST-CRYOTHERAPY COUNSELING.....	25
POST-CRYOTHERAPY INTERVIEW	25
FIRST FOLLOWUP VISIT	
PERSONAL QUESTIONNAIRE INFORMATION.....	27
PROBLEM VISITS	
SYMPTOMATOLOGY	32
CLINICAL ASSESSMENT	33
ONE-YEAR FOLLOWUP VISIT	
PERSONAL QUESTIONNAIRE	35
HEALTHCARE PROVIDER INFORMATION	39
DISCUSSION	40
REFERENCES	

ABBREVIATIONS AND ACRONYMS

CECAP	Cervical Cancer Prevention Program
CIN	Cervical intraepithelial neoplasia
DH	District hospital
DMPA	Depot-medroxyprogesterone acetate
HPV	Human papillomavirus
IUD	Intrauterine device
KKU	Khon Kaen University
LEEP	Loop electrosurgical excision procedure
MOPH	Ministry of Public Health
PID	Pelvic inflammatory disease
SAFE	Safety, acceptability, feasibility, and program effort
SCJ	Squamocolumnar junction
STI	Sexually transmitted infection
SVA	Single visit approach
VIA	Visual inspection with acetic acid

EXECUTIVE SUMMARY

To increase screening and treatment coverage, innovative approaches to cervical cancer prevention are being investigated in Thailand. This evaluation assessed the value of a single visit approach (SVA) using a combination of visual inspection of the cervix with acetic acid (VIA) and cryotherapy in a rural area. Although a variety of treatment options exist for use in an outpatient setting, cryotherapy was the treatment of choice for this joint JHPIEGO/Thailand project because it: 1) has a cure rate comparable to other commonly performed procedures (Andersen and Husth 1992; Mitchell et al 1998; Nuovo et al 2000); 2) is easy to learn, does not require electricity, requires few consumables, and has a long history in the scientific literature of low complication rates (Cox 1999; Nuovo et al 2000); and 3) has an established, safe, and effective performance record with nonphysicians in developed countries (Morris et al 1996).

This project was conducted in four districts in the northeast province of Roi-et. The project was limited to 4 (of 16) districts to balance human and financial resource requirements with the desire for results that are easier to generalize. Twelve nurses were trained in VIA and cryotherapy as part of mobile (village health center-based) and static (hospital-based) teams in four districts of Roi-et Province. Over 7 months, 5,999 women were tested for cervical cancer or precancer using VIA. If positive, after being counseled, these women were offered cryotherapy and counseled again about its benefits, potential risks, and likely side effects. Data were collected measuring safety, acceptability, feasibility, and program effort (SAFE).

The overall VIA test-positive rate was 13.3% with 94.9% of those eligible accepting immediate treatment. In total, 756 women received cryotherapy; 83.2% returned for their first followup visit. There were no major complications and less than 5% of those treated returned for any perceived problem. Only 2.2% ($\pm .010$) of the treated women required any management other than reassurance regarding side effects. Both VIA and cryotherapy were highly acceptable to the patients – more than 95% were satisfied with the experience – and, at 1 year, the squamo-columnar junction was clearly visible for the majority of the women, with a VIA test-negative rate of 94.3%.

By combining the use of testing with VIA and the immediate treatment of test-positive cases (or referral), the SVA has the potential to increase disease detection at an earlier stage when it can be treated successfully. This report describes the key results of this demonstration project involving an alternative, field-based, resource-appropriate approach to cervical cancer prevention. Furthermore, it clearly illustrates that an SVA using VIA followed by immediate treatment with cryotherapy for those testing positive is safe, acceptable, and feasible in rural Thailand, and has the potential to be an efficient method of cervical cancer prevention in similar rural, low-resource settings.

INTRODUCTION

BACKGROUND

Cervical cancer continues to be a widespread public health problem throughout the world because access to screening and treatment of precancerous lesions is not widespread (Pisani 1998). Each year there are approximately 400,000 new cases of cervical cancer – almost 80% of which occur among women living in developing countries – and at least 200,000 women die of the disease. Worldwide, cervical cancer is the second most common cancer among women. The vast majority (99.7%) of cases are associated with infection of one or more types of human papillomavirus (HPV), which is sexually transmitted (Walboomers et al 1999). The HPV virus first enters the cells covering the cervix and then slowly causes changes that, with time, can result in cancer. Although women generally are infected with HPV in their teens, twenties, or thirties, invasive cancer may not develop for as long as 10–20 years after infection.

Cervical cancer is almost always preventable through the introduction of sustainable testing and treatment programs. For example, where cytology-based (Pap smear) testing has become widely available, cervical lesions are detected at an earlier stage when treatment is effective. As a result, deaths from cervical cancer have been considerably reduced in a number of developed countries. Furthermore, in countries where the quality of Pap smears is good and testing coverage is high (70% or more), the incidence of cervical cancer has been substantially reduced.

There are a number of reasons why traditional, cytology-based testing has failed to curb the high rates of cervical cancer in developing countries. First, there is a relative lack of effective testing programs. There are too few trained and skilled professionals to make such a program work effectively, and cyto-technicians, pathologists, and diagnosticians often work in facilities with less than optimal equipment. Moreover, healthcare resources available to sustain the program are limited. Despite the fact that 80% of cervical cancer cases are in developing countries, only approximately 5% of eligible women actually undergo testing in developing countries in a 5-year period (World Health Organization 1986). Some women are simply unaware of the necessity and availability of testing; others have limited access to healthcare interventions. Because many women – particularly those who live in rural settings – are not informed about when to return for treatment, they become lost to followup. Knowing this, they may be discouraged to undergo testing in the first place. Similarly, those who provide the testing for these women are often discouraged to do so because of the lengthy turn-around time involved in getting the results.

Recent studies have demonstrated the potential of visual inspection using acetic acid (VIA) as an alternative test to Pap smears in the identification of cervical lesions (Abwao et al 1998; Sankaranarayanan et al 1999; University of Zimbabwe/JHPIEGO Cervical Cancer Project 1999). VIA testing is not only inexpensive and simple, it can also be provided at all levels of the healthcare system by nurses and midwives. A key advantage of VIA testing over cytology-based services is that the results are immediately available. This means that management decisions, especially whether to offer outpatient treatment if the cervix is found to be abnormal, can be made during a woman's initial visit (Kitchener and Symonds 1999; Parkin and Sankaranarayanan 1999).

Given the evidence to date supporting VIA as a viable testing method, demonstrating whether VIA can be efficiently linked to safe treatment in low-resource settings was a logical next step in assessing its potential role in cervical cancer prevention programs in developing countries. One strategy for optimizing the preventive effects of testing in low-resource settings is to couple testing with an immediate offer of diagnosis and/or treatment for test-positive cases – essentially a “single visit” approach (SVA) (Holschneider et al 1999). A VIA-based SVA differs from the traditional approach to cervical cancer prevention in that referral for diagnostic testing (e.g., colposcopy and biopsy) is limited *only* to cases that are not eligible for treatment (e.g., due to lesion size) immediately following testing.

THAILAND

Since World War II, advancements in medical and public health services in Thailand have led to a decrease in the incidence of infectious diseases and of some diseases that can be prevented by vaccination. Female life expectancy has increased while the mortality rate has markedly decreased. There has also been a change in the causes of death among the Thai female population. Between 1983 and 1987, for example, carcinoma was the third leading cause of death with a mortality rate of 17.8 per 100,000. Statistics show that, between the years 1970 and 1980, death in women from carcinoma of all types doubled from 10.5 to 24 per 100,000.

The most common carcinomatous lesion in women in Thailand is carcinoma of the cervix, accounting for 18.1% of all cancers found in Thai women (IARCPress 2001). According to the National Cancer Institute, the number of cases has continued to increase.

Pap smears have existed in Thailand for more than 30 years, but they are mainly performed in tertiary or secondary health centers (e.g., the University Hospital or large provincial hospitals). Therefore, Pap smears are not available to two-thirds of the country’s population living in rural areas.

Training in Pap smears has been part of the medical school curriculum in Thailand since the 1960s. The Family Health Division of the Thailand Ministry of Public Health (MOPH) established a policy of early cancer detection in 1989. Pap-based screening was integrated into family planning services so that most nurses, especially those trained in IUD (intrauterine device) insertion, received training to perform Pap smears.

A pilot project of early cervical cancer detection was started in 1989 with the goal of reaching at least 20% of women aged 30–60. To achieve this goal, Pap smear centers were established in various parts of Thailand. Quality control was to be done periodically by trained medical cytopathologists.

In 1991, the service was expanded throughout the country to 61 of 75 provinces. As of 1993, the service covered 20–30% of the female population between the ages of 30 and 60. The National Cancer Institute’s screening program strategy targets every women 35 years or older and suggests screenings once every 5 years. The Institute established a target of 60% screening coverage of all eligible women by 1996, and 80% by the year 2000. Currently, coverage remains low. A problem, however, was that various institutions lacked well-trained cytologists due to movement to the private sector and promotions within the MOPH. For example, in 1997, it was estimated that there were only 200 cytologists in the country, mostly in urban centers. To address this training shortage, the MOPH conducted training courses in 61 provincial hospitals from 1980–1993. Despite this training, other problems continued to impede the successful implementation of a

national cytology-based program. At the district level, fixative was not routinely available, and outside of the major cities, the time for receiving returned results was 1–3 months.

Coupled with the logistical problems associated with cytology-based screening, there have also been problems with the quality of Pap smears. In Chulalongkorn Hospital, a tertiary health center, Pap smears have been done for more than 30 years. In the early 1990s, it was observed that there were proportionately more suspicious and positive cases for outpatient clinic women than for women who had Pap smears done at the family planning clinics. As a result, in 1992, an analysis was done of false-negative Pap smears from women with cancerous cervix lesions. Of 194 cases proven to have cervical malignancy, 142 (73.19%) were abnormal according to cytological examination, and the remaining 52 (26.8%) were false-negatives (Gaffikin et al 2003). The majority of the false negatives (82.7% or 43 cases) resulted from errors in taking the smear and the rest (17.3% or 9 cases) were due to interpretation error. The study results highlighted the need for stricter quality control in how to obtain and interpret a Pap smear.

Because rural healthcare workers in Thailand face many challenges when attempting to implement a cytology-based cervical cancer prevention program, it was felt that VIA might be an appropriate alternative means for identifying those women who otherwise may not have access to any testing for precancer or cervical cancer. VIA was identified as the potentially optimal alternative technique to use in a setting with few resources because it is a relatively noninvasive and inexpensive procedure that is easy to perform. In addition, healthcare workers at all levels of the system can be adequately trained to perform VIA, including those in the most rural areas where the majority of women who need testing reside. Moreover, the requirements for VIA are available on a local level, and the results of VIA are immediately available, thus treatment and/or referral can be provided at the same time that the examination is conducted.

In some countries, the most widely used procedures for treating precancerous lesions remain surgical, namely cone biopsy and hysterectomy. Both require hospitalization, general anesthesia, and are associated with considerable risks (Program for Appropriate Technology in Health 1998). This is the case despite equally effective outpatient methods, which are safer and easier to perform, having been available since the 1970s. These methods include cryotherapy, which involves destroying the abnormal cervical tissue by freezing it with a coolant (compressed carbon dioxide or nitrous oxide gas), and electrocautery (Sivanesaratnam 1999). More recently, LEEP (loop electrosurgical excision procedure), wherein the abnormal tissue is excised, has replaced the need for cone biopsy in many situations (Mitchell et al 1998). In Thailand, LEEP is available, but only at the medical school hospital in Bangkok and most of the regional hospitals and medical schools outside Bangkok. Conization and cryotherapy are performed, but only in hospitals in large cities. Unfortunately, at the district and subdistrict facilities, there is no treatment option available for treating pre-invasive cervical lesions. Women have to be referred to one of the approximately 20 large regional hospitals that can provide these services.

Although a variety of treatment options exist for use in an outpatient setting, cryotherapy was the treatment of choice for this joint JHPIEGO/Thailand project because: 1) it has a cure rate comparable to other commonly performed procedures (Andersen and Husth 1992; Mitchell et al 1998; Nuovo et al 2000); 2) it is easy to learn, does not require electricity, requires few consumables, and has a long history in the scientific literature of low complication rates (Cox 1999; Nuovo et al 2000); and 3) has an established, safe, and effective performance record with nonphysicians in developed countries (Morris et al 1996).

By combining the use of testing with VIA and the immediate treatment of test-positive cases (or referral), the SVA has the potential to increase disease detection at an earlier stage when it can be treated successfully. This translates into the potential to reduce disease progression and death in women who currently do not have access to Pap smears and physician-based services. In addition, by offering immediate treatment to eligible test-positives, this approach has the potential to reduce referrals of women with suspect precancerous lesions to higher levels of the healthcare system. Finally, once treated with cryotherapy, a woman's risk of developing an infection with other types of HPV may be reduced for several years, and those women found to be normal on VIA testing may not need retesting for 5 years or more (Lonky et al 1997).

Ideally, the implementation of a SVA to cervical cancer prevention as part of large-scale national programs would enable most at-risk rural women to be reached. Some stakeholders, however, believe this approach is inappropriate for developing countries because the safety of nonphysicians treating precancerous lesions in low-resource settings has never been established (Cullins et al 1999). Additionally, a *Lancet* commentary noted that identifying many women with low-grade lesions (using VIA) may not be cost-effective (Kitchener and Symonds 1999). To address these information gaps, a JHPIEGO team from the USA and a team from two universities in Thailand, in collaboration with the Thailand MOPH, initiated a multi-site demonstration project in rural Thailand where testing coverage remains low.

The project aimed to establish the safety, acceptability, feasibility, and program effort (SAFE) associated with implementing a VIA- and cryotherapy-based SVA to cervical cancer prevention in a rural, low-resource setting (see **Table 1**). In addition to safety, acceptability, and feasibility, other objectives of the project centered on both local and national goals. To carry out testing under realistic settings, it was important to demonstrate the ability to train nurses and midwives to competently perform both VIA and cryotherapy under field conditions, and to have them confidently treat or refer women with abnormal (suspect precancerous) lesions. To do this, field-based, competency-based learning materials had to be developed, and a group of providers, supervisors, and clinical coordinators had to be trained to implement and support project activities (including quality assurance). Finally, ways in which large-scale VIA-based SVA programs could be implemented nationally had to be identified. This report describes key results of this demonstration project involving an alternative, field-based, resource-appropriate approach to cervical cancer prevention.

TABLE 1. SAFE PROJECT QUESTIONS

TOPIC	QUESTION(S)
Safety	<ul style="list-style-type: none"> ● What were the rates of minor and major post-treatment complications? ● Were women with large lesions or advanced disease appropriately referred?
Acceptability	<ul style="list-style-type: none"> ● How many women in the clinic opted for testing when it was offered? ● How many women who were test-positive agreed to be treated on the spot? How many were referred or refused treatment? ● To what extent were women successfully able to carry out post-treatment home care as prescribed by the provider? ● To what extent did the women’s partners support the women in carrying out the prescribed home care, including abstinence or use of condoms for 4 weeks following treatment, and returning for followup visits? ● To what extent were women satisfied with the decisions they had made regarding cervical cancer prevention? ● To what extent are participating providers willing to continue to use a test-and-treat approach? ● To what extent do these providers feel the benefits of this approach outweigh any risks? ● To what extent are participating clinics willing to continue to use this approach?
Feasibility	<ul style="list-style-type: none"> ● To what extent were providers able to test and treat target numbers of women during the project period? ● To what extent were supervisors able to carry out their tasks as outlined in the protocol? ● To what extent could project staff make the project quality assurance system operational? ● What effect did offering VIA-based testing and immediate treatment for 6 months, coupled with patient followup for 12 months, have on routine service delivery?
Program Effort	<ul style="list-style-type: none"> ● What was the 12-month test-negative rate (absence of acetowhite lesions) among women choosing to have treatment?

METHODOLOGY

TIME FRAME

The project was designed to provide testing and treatment for women during a 6-month period, followed by 12 months of monitoring for women treated.

SITE SELECTION

This project was conducted in four districts in the northeast province of Roi-et. The project was limited to 4 (of 16) districts to balance human and financial resource requirements with the desire for results that are easier to generalize. Roi-et was selected because it is mostly rural, cervical cancer prevention services had not been successful there in the past, and it is adjacent to Khon Kaen Province where a health facility – Khon Kaen University (KKU) – exists to adequately treat referral cases. This referral hospital is accessible within a few hours' transport time and was officially linked to the selected sites for the duration of the project (one of the project managers, Pisake Lumbiganon, is an obstetrician/gynecologist at that university).

PROVIDER SELECTION

Two or three providers who met provider eligibility criteria were selected per site (see text box below).

Provider Eligibility Criteria

- Nonphysician – nurse, midwife, or other types of healthcare provider (i.e., registered nurse)
- Experience performing pelvic examinations
- Adequate eyesight (natural or lens-corrected)*
- Willing to attend and be assessed as competent during a training course involving VIA and treatment for cervical lesions
- Able to make a treatment decision and competently and confidently perform the treatment procedure immediately (if appropriate) following testing

**Assess eyesight through the use of a visual acuity chart and inspection for cataracts.*

Given that no organized program was ongoing in the province prior to initiating services, providers, supervisors, and other project-related staff needed to be trained. Additionally, permission for trained nurses to be able to provide treatment for suspect precancer had to be obtained from the MOPH. The project recruited women between February and October 2000, and was approved by two institutional review boards (Johns Hopkins Bayview Medical Center, USA, and the MOPH, Thailand) and received the official support of the MOPH.

Twelve nurses with current or previous reproductive health experience were selected by local MOPH officials and trained in VIA and cryotherapy during a 2-week competency-based course. The course involved both classroom and clinical practice and was supervised by experienced medical consultants from JHPIEGO and local academic medical institutions. During training, enough clinical practice was provided for all nurse trainees to be assessed as competent according to guidelines agreed upon by the participating institutions. Before the clinical practice, anatomic models were extensively used to achieve facility with VIA and cryotherapy.

This approach has been shown to reduce the time required to achieve competency during clinical practice (Limpaphayom et al 1997).

Formal training was followed by a 1-month pilot phase during which the nurses were intensively supervised by local physician supervisors, all with prior experience in colposcopy. Immediately before the nurses were trained, these supervisors had received similar competency-based training in VIA and cryotherapy, followed by a 1-month period of clinical practice to achieve proficiency in both procedures.

STUDY PARTICIPANTS

During the 7-month enrollment period, the objective was to enroll and provide VIA testing to approximately 3,000 women. The proposed target group was 30–45 years of age. The upper age limit reflects the fact that recent studies on VIA test qualities in developing countries have typically included women under age 50. This age limit is also based on the fact that the transformation zone in menopausal women is less visible, making visual inspection more difficult and potentially less accurate. Because the project focuses on identifying and treating precancerous lesions, the lower age limit was established as the peak age at which high-grade squamous intraepithelial lesion (cervical intraepithelial neoplasia [CIN] II and III) is thought to occur – approximately 10 years younger than the peak age of invasive cancer (PATH 1998). Assuming the test-positive rate in the population would be a maximum of 20%¹, 600 women (of the 3,000 screened) would potentially qualify for, and be offered, immediate treatment.

Exclusion criteria for women participating in the project included those who:

- Had a total hysterectomy (cervix and body of uterus removed) or their cervix removed
- Had previous known diagnosis of cervical cancer
- Were more than 20 weeks pregnant by clinical examination (because treatment can be delayed without disease progression until after childbirth)

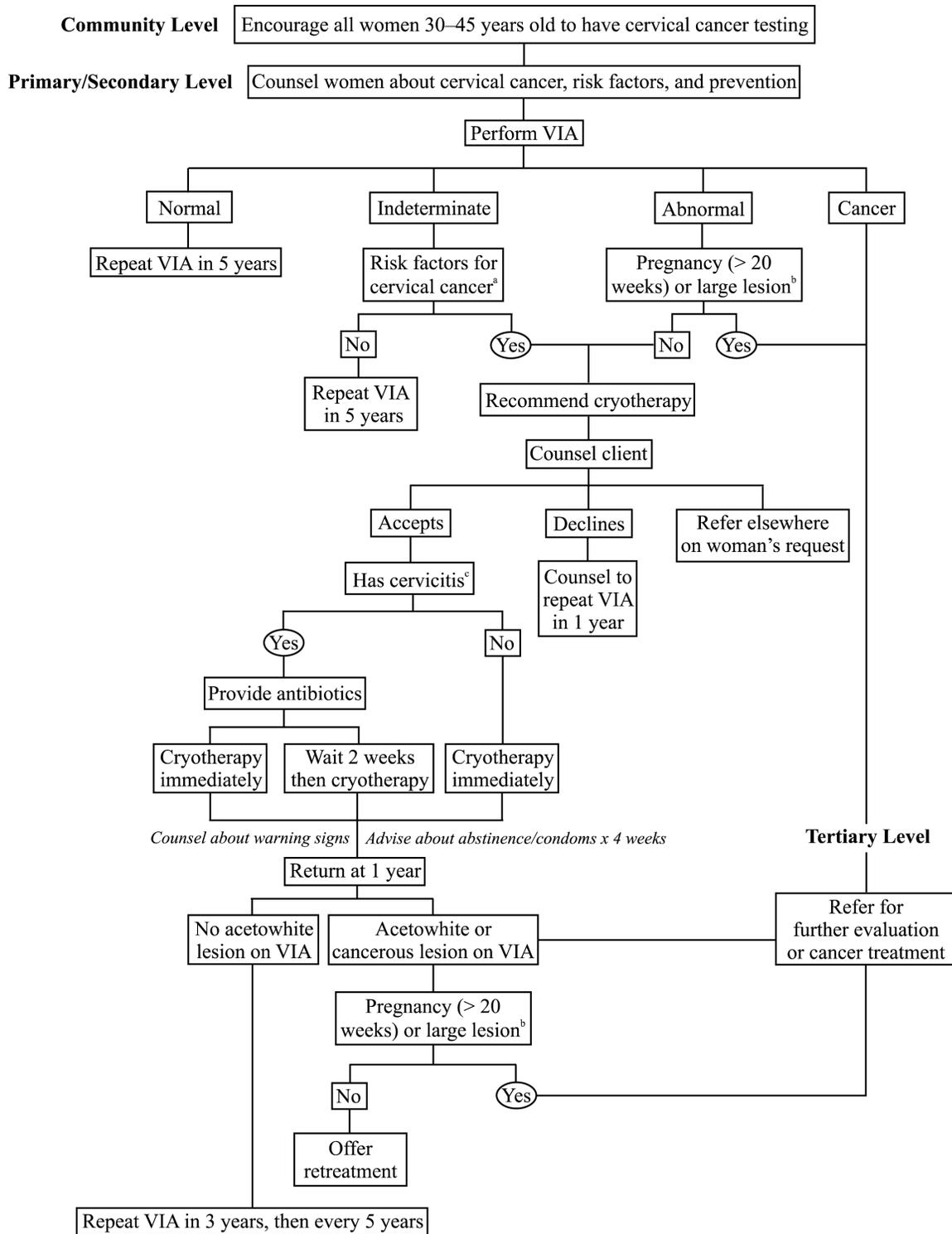
CLINICAL PROTOCOL

Three nurses per district hospital (DH) provided VIA and cryotherapy, as indicated, either at the hospital itself (static services) or as two-person itinerant teams that regularly visited 36 rural health centers located in the DH catchment area (mobile services).

The clinical protocol for the SAFE Project was designed to fit into ongoing testing and treatment activities in each country. **Figure 1** outlines how the VIA-based test-and-treat protocol spans all levels – from the community to the family planning/maternal and child health clinic, where patients are seen and treated, to the nearby referral facilities (the polyclinic or DH), where some patients may be referred, if necessary.

¹ A test-positive rate of 10–20% has been observed in studies of populations with high prevalence of and minimal screening for cervical cancer.

FIGURE 1. SAMPLE FLOW DIAGRAM FOR CERVICAL CANCER PREVENTION



^a High risk for STIs (e.g., previous STI, multiple sex partners), previous abnormal Pap smear, mother or sister had cervical cancer, smokes, chronic corticosteroid use

^b Lesion > 75%, extends onto vaginal wall or extends more than 2 mm beyond diameter of cryotherapy probe

^c Mucopus in os, cervix bleeds easily, or urethral discharge

For the purposes of this project, the clinical protocol involved a minimum of three visits:

- An initial intake visit included testing and, if appropriate, treatment.
- If the woman was treated, an initial followup visit occurred at 12–16 weeks.
- A final followup visit happened at 12 months (to assess the persistence or absence of acetowhite lesions).

RECRUITMENT

Women of eligible age attending the DH or mobile site for any reason during the 7-month recruitment period were invited to participate. Additionally, women were actively recruited from participating DH and health center catchment areas. MOPH village health volunteers who routinely conduct health promotion activities in catchment villages provided basic information about the project by distributing brochures, personally telling women about the services, and making loudspeaker announcements on the day of the service. Women were informed about when services would be provided in the respective facilities and what the prevention services involved.

Sample Size

One of the key questions regarding the use of cryotherapy in low-resource settings is the safety of the procedure when provided by nonphysicians. Clinical experience with cryotherapy in developed countries has been associated with a complication rate of less than 5%, which we anticipated would also be the case in this project. To ensure that we could detect a rate this low with adequate ($\pm .02$) precision, the number of women who needed to be treated during the project period was determined as follows²:

$$N = 1.96^2 \cdot 0.04 \cdot 0.96 / .02^2 = 368.79 \text{ or } 370 \text{ women treated with cryotherapy}^3$$

For 370 women to be treated, a minimum of 3,700 women needed to be recruited. The final sample size was twice this number (7,400) to allow for approach-specific (mobile versus static) post-complication rates to be calculated with the same precision level.

Health Education

Women who were interested in being tested for cervical cancer participated in a group or individual health education session. During this session, the site nurses discussed the following topics:

- The nature of cervical cancer as a disease and the consequence of a sexually transmitted infection (STI)
- Risk factors for disease
- Role and importance of VIA testing
- Consequence of not being tested
- Treatment options if the VIA test is abnormal
- Expected side effects of treatment
- Possible treatment complications (minor and major)

² Assume a binomial distribution for estimating the confidence interval around a proportion and that project women represent part of an infinitely large population.

³ p = estimated proportion = 0.04; $q=1-p = 0.96$; d = margin of error = .02; Z = value of alpha at .05 = 1.96; and N = required sample size = 370.

After the education session, a brief reproductive health history was obtained for all eligible women who agreed to be tested.

VIA TESTING

Once the woman had been counseled by the provider and positioned on the examination table, the speculum was inserted, the cervix brought into view, and the speculum locked in place. A dilute (3–5%) solution of acetic acid was then applied and, after 1 minute, the entire cervix was examined using a good light source. Special attention was paid to seeing the entire transformation zone. Service providers referred to JHPIEGO’s VIA cervical atlas, which was used during training, to make their VIA assessment. The assessment findings were recorded using the standardized categories on the VIA form along with other relevant information (see **Table 2**).

TABLE 2. VIA CLASSIFICATION RELATIVE TO CLINICAL FINDINGS

VIA CLASSIFICATION	CLINICAL FINDINGS
Test-positive	Raised and thickened white plaques
Test-negative	Smooth, pink, uniform, and featureless; ectropion, polyp, cervicitis, inflammation, nabothian cysts
Cancer	Cauliflower-like growth or ulcer; fungating mass
Indeterminate	No distinct acetowhite lesion is visible, but some white area is apparent that could represent an abnormality; cervicitis or inflammatory changes are so severe that the cervix cannot be adequately assessed for acetowhite lesions

Note: “Indeterminate” is no longer used as a classification.

TREATMENT: CRYOTHERAPY AND REFERRAL

Test-positive women meeting any of the following criteria were considered eligible for treatment:

- Lesion was not cancerous
- Lesion did not extend onto the vaginal wall
- Lesion occupied less than 75% of the cervix
- Lesion extended less than 2 mm beyond the diameter of the cryotherapy probe

Treatment decisions for women assessed as indeterminate using VIA were made considering the woman’s age and other potential risk factors for cervical cancer.

Risk Factors

- Sexual activity (begun at less than 20 years old)
- Multiple sexual partners
- Exposure to STI
- Mother or sister with cervical cancer
- Previous abnormal Pap smear
- Smoking
- Immunosuppression
- HIV/AIDS
- Chronic corticosteroid use (for asthma and lupus)

After the woman was assessed as eligible for treatment, nurse providers explained the meaning and implications of the test results to the woman. In addition, the providers reviewed in more detail what was involved with the treatment procedure – the benefits, risks, potential side effects, and their management – as well as the advantages and disadvantages of immediate treatment (see **Table 3**). The woman then made an informed choice regarding treatment.

TABLE 3. EXPECTED SIDE EFFECTS OF CRYOTHERAPY

SIDE EFFECT	MANAGEMENT
Cramping	<ul style="list-style-type: none"> ● Counsel patient before the procedure that she should expect some degree of cramping during and after the procedure, and that cramping usually stops shortly after the procedure. ● Reduce cramping by pressing lightly on the cervix with the cryotherapy probe. ● If cramping is severe, provide oral analgesic (acetaminophen or ibuprofen).
Vaginal Discharge (Profuse, Watery)	<ul style="list-style-type: none"> ● Counsel patient to expect a discharge lasting 4–6 weeks. ● Counsel patient to expect discharge color to change from a pink tint to clear white or a yellow tint (occasionally streaked with blood). ● Counsel patient to return if discharge changes to foul-smelling or is pus-colored (if so, evaluate for infection and treat with antibiotics). ● Strongly advise abstinence for 4 weeks. ● If abstinence is unlikely, advise condom use for 4 weeks to prevent pelvic infection.
Spotting/Light Bleeding	<ul style="list-style-type: none"> ● Counsel patient to expect spotting/light bleeding for 1–2 weeks. ● Counsel patient to return for evaluation if there is heavy bleeding.

Women assessed as test-positive who had evidence of purulent cervicitis⁴ were given a single oral dose of two antibiotics (2 grams azithromycin for *Chlamydia trachomatis*⁵ and 400 mg cefixime for *Neisseria gonorrhoeae*) prior to cryotherapy. They were offered the choice of either having cryotherapy immediately (the same day as taking antibiotics) or returning in 2 weeks for repeat VIA. For pregnant women with an abnormal VIA test who had evidence of purulent

⁴Purulent cervicitis is defined as yellowish mucopus in the cervical os or canal, a cervix that is beefy red and bleeds easily when touched, or a urethral discharge.

⁵Doxycycline (100 mg orally, 2 times daily for 7 days) is an acceptable alternative, but compliance is often poor. Doxycycline should not be used in pregnancy.

cervicitis, both azithromycin⁶ and cefixime could be used. Patients who were allergic to cephalosporins (cefixime) were to be offered a single intramuscular injection of 2 grams spectinomycin. Providing antibiotic treatment to women suspected of having purulent cervicitis could potentially reduce the very small risk (less than 1%) of pelvic infection following cryotherapy.

For women choosing immediate treatment, the steps involved in the treatment procedure were explained in greater detail. They were then provided with a place to sit comfortably until cryotherapy could be performed. Waiting time for treatment was not to be longer than 1–2 hours. If a longer wait was unavoidable, the woman was to be invited to return the following day or another day for treatment (or be given the choice to remain and wait for treatment).

Cryotherapy was provided according to the treatment protocol. A standard probe was applied and the double freeze technique used as outlined in Chapter 6 of JHPIEGO’s VIA training manual (McIntosh, Blumenthal, and Blouse 2001). Following treatment, the woman was allowed to rest in a private area for 15 minutes (or until she had fully recovered) before leaving the health facility. Oral analgesics (acetaminophen or ibuprofen) were given if the patient had severe cramping following treatment.

Table 4 lists what actions were to be taken for women who were either not eligible for, or chose something other than, immediate treatment. All referral decisions were documented on the intake form.

TABLE 4. RECOMMENDED REFERRAL ACTIONS

STATUS	REFERRAL ACTION
Women suspected of having cervical cancer	Refer immediately to a facility that can adequately provide treatment for invasive cancer.
Test-positive women whose lesions occupy greater than 75% of the cervix or extend more than 2 mm beyond the outer edge of the standard cryotherapy probe	Refer for treatment at the project referral site or the nearest facility offering LEEP or cone biopsy. If travel to the other facility is not possible or judged not likely to happen, counsel about the greater likelihood of persistence of the lesion at 12 months and the need for having treatment again.
Test-positive women who fulfill criteria for immediate treatment but who request to be treated using a procedure other than cryotherapy	Counsel about the advantages and disadvantages of all treatment methods. Refer to closest facility offering treatment of the woman’s choice.
Test-positive women who request further (more diagnostic) testing, not offered at the site	Refer to closest facility offering colposcopy and biopsy (as indicated).
Test-positive women declining any treatment	Counsel about the likelihood of disease progression and prognosis. Recommend a return visit within a year for a repeat VIA test to reassess disease status.

⁶ Erythromycin stearate (500 mg orally, 4 times daily for 7 days) is an acceptable alternative, but many patients cannot tolerate the gastrointestinal problems. Erythromycin estolate should not be used in pregnancy.

COUNSELING FOLLOWING CRYOTHERAPY

Before leaving the health facility, women received counseling regarding:

- The details of self-care at home
- When they should return for their next visit
- Conditions under which they should come to the clinic for care outside of the scheduled visits

Women were instructed to come in as soon as possible and not wait if they experienced symptoms of any complications/warning signs (see text box below).

Warning Signs

If you have any of the following, you should return to this or the nearest health facility:

- Fever for more than 2 days
- Severe lower abdominal pain, especially if you have a fever
- Bleeding heavier than your heaviest days of menstrual bleeding for more than 2 days
- Bleeding with clots

Women were counseled to abstain from sexual relations for 4 weeks following treatment and were given a supply of condoms to reduce the risk of pelvic infection. Women also were provided with a daily diary on which to record the time of onset of any side effects or symptoms of complications, sexual activity, use of condoms, and any other information related to the recommended home care. These women were instructed to bring the diary back with them every visit (scheduled or not) and they were given a visit schedule card as a reminder of when to come back for their followup visit.

FOLLOWUP VISITS

Initial Followup Visit

This visit was scheduled sometime between 12 and 16 weeks following treatment to review the woman's post-treatment experience (e.g., when watery discharge ceased) and to enquire about any concerns or problems she had since being treated. The visit also included a question and answer period to assess how well she had been adhering to home care instructions. If a woman complained of lower abdominal pain or persistent vaginal discharge, a pelvic examination was considered necessary to check for potential vaginal, cervical, or pelvic infection.

The diary provided to women during their treatment visit was reviewed. All data collected during this 12 to 16 week visit were recorded on the initial followup visit form. During the scheduled followup visit, women were asked questions about their own and their partners' attitudes toward the test-and-treat experience. Women were reminded of the date of their 12-month visit and the importance of returning, when scheduled, to have the condition of their cervix assessed by a trained provider. Their visit schedule card was used to remind them of the date of this visit.

Unscheduled Problem Visit

Any unscheduled visit was defined as a problem visit if it occurred outside of the time ranges established for scheduled visits. A special form was used for recording data pertaining to any problem visit.

Final Followup Visit

This visit was scheduled at 12 months following treatment and involved a pelvic examination. Because the squamocolumnar junction was visible, and the transformation zone could have been visible, a speculum examination was performed during which the cervix was carefully checked to assess how it had healed and whether any lesion persisted. All women who were test-positive at 1 year were referred to KGU as part of a separate study to assess the value of VIA compared to colposcopy among women who had been treated with cryotherapy. These women were provided with a second VIA examination by a doctor/supervisor trained in VIA as part of the project, a magnified visual inspection using a video camera, and a colposcopy and biopsy, as indicated (results not included herein). All women test-negative at 1 year were enrolled in a second separate study, which was designed to assess the test qualities of VIA at 1 year. These women were given a colposcopic examination by a colposcopic specialist at another referral hospital (Roi-et Provincial Hospital), followed by a biopsy, as indicated (results not included herein).

Women were counseled during the 1-year visit about what additional care might be needed, depending on their treatment status. In addition to the clinical examination, their responses to questions about their attitude and those of their partners about their treatment experience were recorded on the designated form.

SUPERVISION

A critical component of the project was regular supervision of the trained service providers by one of the trained supervisors assigned to the country project team. Supervision involved an assessment of how the quality assurance and referral systems were working. As noted earlier, before assuming the role of supervisor, potential candidates were trained and qualified as experts in both VIA testing and cryotherapy.

At least one supervisor visited each of the sites within the first 2 weeks of when the site began to implement the project protocol. The purpose of the visit was two-fold – to ensure adequate implementation of the SAFE Project protocol, and to reassess the competency of the service providers following completion of their training and the start-up of services.

Subsequently, monthly and/or more frequent supervisory visits were made to each site as deemed appropriate by country team members and/or as determined through the monitoring of select quality assurance indicator values (see **Table 5**).

TABLE 5. PROJECT QUALITY ASSURANCE INDICATORS

AREA	INDICATOR	HOW TO CALCULATE
Overall Services	Recruitment rates	<ul style="list-style-type: none"> Number of women recruited for VIA during last month/Total number of women eligible for VIA testing
	Initial and final followup visit rate	During a period of time: <ul style="list-style-type: none"> Number of women coming for repeat VIA testing/Number of women getting first VIA testing Number of women coming for followup after cryotherapy/Number of women getting cryotherapy treatment
Counseling	Proportion of providers providing counseling to standards	<ul style="list-style-type: none"> Number of providers performing VIA and cryotherapy counseling to standards/Total number of providers providing VIA and cryotherapy counseling
	Proportion of women adhering to home care requirements	<ul style="list-style-type: none"> Number of women adhering to home care requirements/Total number of women advised on home care requirements
VIA Testing	Test-positive rates	<ul style="list-style-type: none"> Number of women testing positive to VIA/Number of women getting VIA test
	Proportion of providers able to delineate the extent of the acetowhite lesions	<ul style="list-style-type: none"> Number of providers able to delineate the extent of acetowhite lesions/Number of providers performing VIA at the site
Clinical Decision-Making	Proportion of providers making appropriate case management recommendations	<ul style="list-style-type: none"> Number of providers making correct case management recommendations/Total number of providers providing VIA services
Cryotherapy	Cryotherapy rate	<ul style="list-style-type: none"> Number of women getting cryotherapy/Number of women getting VIA tests
	Complication (minor and major) rate	<ul style="list-style-type: none"> Number of women experiencing complications following cryotherapy/Number of women getting cryotherapy

Supervisors assessed the VIA test skills of providers by direct observation using the appropriate checklist, and the disease recognition capabilities of providers using the standardized cervix slide set or computer-generated images. Supervisors also assessed the appropriateness of treatment decisions made by providers by referring to the standardized treatment criteria set up for this project. During all visits, supervisors followed the supervisory protocols and recorded their findings on a designated supervisory form.

Providers' skills in performing cryotherapy and their overall performance were also assessed during this visit by review of the providers' client records and by direct observation using the checklist. The supervisors also used a special form on which to record findings of an independent VIA co-assessment examination (whereby the provider and supervisor independently assessed the same woman using VIA and recorded their results on separate forms before discussing their findings).

RESULTS

The following sections describe in detail the data analysis findings. The data were recorded on the following forms: the initial intake form, the VIA and cryotherapy forms, the first followup visit form, the problem visit form, and the final (1-year) followup visit form. On occasion, women did not provide answers for every question on the form. For these questions, the number of omitted answers was subtracted from the overall sample size when calculating valid percentages. (This explains why sample sizes for the question responses vary throughout this report.)

INITIAL VISIT

This section describes the findings from the initial visit questionnaire, which was filled out by a trained nurse during a woman's first visit to the healthcare facility. The form contained questions regarding general demographic and personal information, followed by inquiries about the woman's medical and reproductive history.

Demographics and Personal Information

Age

The project targeted women aged 30–45 years. Each participant's age was verified, to the extent possible, by her date of birth to validate her eligibility for the study. Of the 5,999 women who took part in the project, all ages from 30 to 45 were represented. (In addition, the age for one woman is recorded as 29 years.) The mean, median, and mode for age were 37.8, 36.0, and 32.0 years, respectively. More than half (58.5% or 3,503/5,985) were younger than 38 years old.

Access

To help define the catchment area of the study, and to later devise strategies for outreach planning, questions targeted the relative locations of the facilities and how the women reached them. At their initial assessment, women were asked how they had arrived at their facilities. The majority of women (51.6% or 3,095/5,993) used a motorcycle as their primary means of transport, while 19.3% (1,154/5,993) walked to the facility. Only 3.6% (217/5,993) of the women drove their own car, 4.9% (296/5,993) rode a bicycle, 8.6% (514/5,993) drove someone else's car, and 9.0% (541/5,993) used the public bus to travel. Fewer than 3.0% (175/5,993) of the women chose other modes of transportation, such as a hospital van or a *tuk tuk* (tricycle taxi). Travel times to the facility varied from 1 minute to 2 hours; however, almost all of the women (99.5% or 5,956/5,988) arrived at the facility within an hour. Many women (80.5% or 4,821/5,988) took 20 minutes or less to reach the facility, and more than half (54.2% or 3,248/5,988) took 10 minutes or less.

Reasons for Attending the Health Facility

Women were asked the question: "Why did you come to the health facility today?" An overwhelming majority of these women (98.2% or 5,887/5,995) responded that the reason for their visit was to get tested for cervical cancer. Additional reasons (given by less than 2.0% or 108/5,995 of the women) for visiting the facility included: a well baby visit; other health

problems for the woman or her child; a family planning visit; accompanying another individual to the facility; or other, miscellaneous reasons.

The women were also asked who had originally suggested that they have VIA testing. The sources of this suggestion were staff at the facility where the initial visit took place or staff at another health facility for 40.7% (2,441/5,994) of the women. Village health workers were the source for 22.7% (1,361/5,994) of the women. In addition, 16.2% (972/5,994) of the women said that they came for testing after talking to people who had previously been tested as part of the project. Only 7.0% (420/5,994) of the women said that they came to the facility after talking to an outreach health promotion worker. The village information center was the source of information for 6.8% (406/5,994) of the women, and 6.0% (359/5,994) of the women attended because a family member, friend, or neighbor had proposed the idea. The remaining 0.6% (35/5,994) of the women indicated that some “other” source had prompted them to get tested.

Marital Status and Schooling

The majority of women (81.4% or 4,876/5,993) were married at the time of their initial examination; 16.0% (958/5,993) were not married but living with someone (“in union”). A small percentage of women (0.1% or 3/5,993) were either single or never married, and 2.6% (155/5,993) were either widowed, divorced, or separated at the time of testing.

Twenty-four respondents provided no data about education level. Of those who responded, more than half (58.3% or 3,484/5,975) claimed that they had completed at least 4 years of schooling. Almost one-quarter of the women (26.7% or 1,597/5,975) reported finishing at least 5–6 years of schooling, 9.8% (588/5,975) had completed 7–12 years, and 4.0% (241/5,975) had attended school for more than 12 years (this higher level of education spanned from 13–23 years of total schooling). Another 0.6% (37/5,975) of the women had completed 1–3 years of education, and only 0.5% (28/5,975) indicated that they had received no schooling whatsoever.

Reproductive and Medical History

The women were asked many questions about their gynecological, sexual, and medical histories. The information gathered was used to determine a woman’s eligibility for treatment, and to identify any factors that might make her at risk for cervical cancer.

Gynecological History

To further ensure that women were eligible to receive testing as part of the project, all were asked if they had ever had a hysterectomy. Four participants (0.1% of 5,999) responded that they did not know whether or not they had ever undergone this procedure, and 10 women (0.2% of 5,999) failed to respond to this question. Thus, 99.7% (5,984/5,999) of the women specifically responded that they had not had a hysterectomy. Another question verified that all women had previously engaged in sexual intercourse. Almost all of the women (99.8% or 5,990/5,999) responded “yes” to this question and/or provided their age at first sexual intercourse. (The remaining 0.2% [9/5,999] of the women accounted for the “unknown” [5/9] or missing [4/9] data.) Furthermore, the women were asked if they had ever been diagnosed with or treated for cervical cancer. The vast majority (99.1% or 5,947/5,999) indicated that they had not, whereas 11 women (0.2%) responded “yes” to this question. Among these 11 women, 10 had negative tests and 1 had a positive test in the study. Five women (0.1% of 5,999) responded

that they did not know about such a diagnosis or treatment, and 35 women (0.6% of 5,999) had no response recorded for this question.

Parity

The date of each participant's last menstrual period was recorded, and each woman was asked whether or not she knew or suspected that she was currently pregnant. Fifty women (0.8% of 5,999) gave no response, and 9 women (0.2% of 5,999) responded "yes" to this question or gave a number of weeks that they believed they were pregnant (2/5,999 or .03%). Six women (0.1% of 5,999) indicated that the answer to this question was "unknown." The remaining 5,931 women (98.9%) believed that they were not pregnant. The latter were then asked how many weeks into their pregnancies they believed they were. Only 6 women responded to this question, and they knew or suspected that they were anywhere from 2–11 weeks pregnant. (According to the protocol used in Thailand, anyone less than 20 weeks pregnant at the clinical examination was deemed eligible to participate.)

In addition, all women were asked if they had ever been pregnant, and an overwhelming majority (98.6% or 5,915/5,999) specified that they had. The number of pregnancies (answered by 5,865 women) ranged from 1–13, the majority (52.3% or 3,066/5,865) having had two pregnancies. Three pregnancies were recorded for 28.8% (1,687/5,865) of the women, four pregnancies for 8.6% (507/5,865), 5 pregnancies for 2.5% (149/5,865), and one pregnancy for 6.9% (404/5,865). The few remaining respondents (0.9% or 52/5,865) indicated they had had six or more previous pregnancies. The mean number of pregnancies among those who had been pregnant was 2.5; the median and mode were both 2.0.

Contraception

To gain a better understanding of the ways in which the women attempted to prevent pregnancies, questions were asked regarding contraception use. Only 2.2% (131/5,966) of the women indicated that they currently used condoms, whereas more than half (53.3% or 3,196/5,992) said that they had received a tubal ligation to prevent pregnancy. A small percentage of women (0.5% or 27/5,992) indicated that they were not sexually active at the time of their initial visit, and 9.8% (586/5,992) indicated that they currently used no form of contraception. Another 17.2% (1,033/5,992) of the women were currently taking oral contraceptives, 7.6% (456/5,992) utilized depot-medroxyprogesterone acetate (DMPA), 1.6% (94/5,992) had received Norplant® implants, and 8.5% (511/5,992) used an IUD. Only 0.5% (32/5,992) of the women indicated that their partners had undergone a vasectomy, 0.3% (18/5,992) used the withdrawal method (coitus interruptus), and 0.2% (14/5,992) refrained from intercourse during suspected ovulation (natural family planning). Twenty-five women (0.4% or 5,992) indicated an unspecified, "other" form of contraception.

The women were also asked which form of contraception, other than condoms, they had utilized in the *past* to prevent pregnancy. Of those women who answered and who said they used contraception in the past, the most popular forms of contraception included: tubal ligation (53.6% or 3,210/5,992); birth control pills (45.1% or 2,704/5,992); DMPA (33.0% or 1,979/5,992); and the IUD (31.3% or 1,875/5,992). (Totals add up to more than 100% because women could answer yes to more than one method.)

Menstruation

Questions regarding menstruation were asked to establish a baseline for menses-related issues that could potentially be affected by cryotherapy treatment. Each woman was first asked if she was menopausal (i.e., if her regular menses had ceased), to which 99.1% (5,808/5,860) of those who responded said “no.” When asked about the duration (in days) of her regular menses, more than half (56.3% or 3,376/5,999) of the women responded that their periods generally lasted 3 days. Another 16.9% (1,015/5,999) of the women said 2 days, and 12.6% (755/5,999) said 4 days. Only 2.0% (121/5,999) of the women claimed to menstruate for 1 day, and 3.3% (199/5,999) said that they menstruate for 6 or more days per cycle. When asked about the usual blood flow during each menstrual period, 13.8% (825/5,999) of the women stated that they generally had a heavy flow, 47.7% (2,860/5,999) had a medium flow, and 16.3% (975/5,999) had a light flow. A blood flow pattern that varied from month to month was typical for 2.2% (133/5,999) of the women, whereas 18.4% (1,106/5,999) said that they had varying blood flow from light to heavy. Inter-menstrual bleeding or spotting occurred for 5.5% (329/5,999) of the women, and 3.2% (194/5,995) claimed to have post-coital bleeding. A significant proportion (45.0% or 2,702/5,994) of the women indicated that cramping accompanied their last menses.

Risk Factors for Cervical Cancer

The following are risk factors for cervical cancer: smoking; having a first-degree relative with cervical cancer; having had a previously abnormal Pap smear; starting sexual activity early (e.g., before 20 years of age); having multiple sexual partners; being exposed to an STI; and having an immunosuppressive disease such as HIV/AIDS or immunosuppression via chronic corticosteroid use (McIntosh, Blumenthal, and Blouse 2001). The women were asked about the presence or absence of these risk factors, and any woman with one or more of these factors and whose VIA assessment was considered indeterminate was considered a candidate for immediate treatment.

Smoking, Family History, and Pap Smear History

Fewer than 2% of the women who responded (116/ 5,995) claimed that they had ever smoked or chewed tobacco. With respect to first-degree blood relatives, only 3.1% (186/5,999) knew that they had a positive family history of cervical cancer. A small percentage of women (0.5% or 27/5,999) did not know whether or not there was a positive family history of the disease. With respect to previous Pap smears, 53.9% (3,236/5,999) reported a previous test, 45.6% (2,735/5,999) reported not having had the test, and 0.5% (28/5,999) said that they did not know whether or not they were previously tested. Of the women with previous Pap smear testing, 83.5% (2,703/3,236) knew their test result: 93.5% (2,528/2,703) had normal test results; 4.7% (126/2,703) had abnormal test results; and 1.8% (49/2,703) had “other” results. Most of these “other” results were not specified; the ones that were specified include candida (8 women), cervicitis (2), and yeast (1).

Sexual History, Partner Sexual History, and Partner Involvement

Approximately 4 out of every 10 women (40.9% or 2,448/5,988) had engaged in consensual or non-consensual sexual intercourse before the age of 20, and more than three-quarters of the women (75.4% or 4,514/5,988) had done so by the age of 22. The age of their first sexual encounter ranged from age 10–40 (with the exception of a single woman who reported first intercourse at age 2), and the majority of the women (97.5% or 5,839/5,988) reported having their first sexual encounter between the ages of 15 and 30. The mean age of first sex was 20.8

years, and both the median and mode were 20.0 years. Most women (91.0% or 5,448/5,987) denied ever having had intercourse with someone other than their current or latest partner. Thus, with respect to this risk factor, fewer than 10% of the women claimed to have had multiple sexual partners. When asked if their husbands/partners had engaged in sexual intercourse with someone else, 30.9% (1,854/5,999) indicated that they had; 40.7% (2,441/5,999) indicated that they had not; and 28.3% (1,698/5,999) indicated that they did not know the answer to this query. Of those women whose husbands/partners had engaged in sexual intercourse with another person, 10.5% (193/1,840) said that their husbands/partners had used condoms, 54.4% (1,001/1,840) said that condoms were not used, and 35.0% (645/1,840) said that they did not know if condoms were used.

When asked if they had discussed getting tested and possibly treated for cervical cancer with their husbands/partners before attending the facility, 75.8% (4,466/5,895) of the women said that they had, and 24.2% (1,429/5,895) said that they had not.

HIV/AIDS and Other STIs

All 3 women (0.1% of 5,999) who indicated that they had been diagnosed with HIV/AIDS had negative VIA tests. Another 29 of the women (0.5% of 5,999) said that they did not know if they had HIV/AIDS, and 35 women (0.6% of 5,999) failed to respond to this question. The remaining women responded that they were HIV negative. Ten of the women (0.2% of 5,999) said that they had partners who had been diagnosed with HIV/AIDS, and 63 women (1.1% of 5,999) indicated that they did not know the HIV/AIDS status of their partners. With respect to other STIs, 309 women (5.2% of 5,999) indicated that they suspected or had been told by a health professional that they had an STI. Approximately 10% (582/5,999) of the women indicated that their partners had suspected or been told by a health professional that they had an STI, and 2.8% (166/5,999) of the women said they did not know about the STI status of their partners/husbands.

VIA

After the initial intake form had been filled out, all participating women were counseled about the upcoming examination and a VIA form was filled out by a designated data collection nurse. The participants also provided their opinions about the VIA procedure by answering questions after the procedure. The nurses recorded observations about the VIA procedure itself, as well as opinions regarding pain experienced by the women and whether or not each woman was counseled on all key points of the service. This section describes the frequency distribution results for each variable on the VIA form.

Procedure

During the examination, the nurse providers were to visualize the squamocolumnar junction (SCJ) of the cervix, perform the VIA assessment, and record the descriptive characteristics of any lesions present. The SCJ was easily visualized for 98.0% (5,836 of 5,958) of the women for whom these data were recorded; it was visualized, but with difficulty, for only 0.9% (56 of 5,958) of the women. The SCJ cannot be visualized if it is inside the cervical canal, as was the case for the remaining 64 women (1.1% of 5,958). Two women (.03 % of 5,958) had a visible benign lesion, such as a polyp, which obscured the view of the SCJ.

Considering the project VIA classification categories, 85.8% (5,146 of 5,999) of the women were labeled as test-negative, and 13.3% (798 of 5,999) were classified as test-positive. Subsequently, the latter group of women was evaluated for their eligibility for treatment. Cancer was suspected for 4 woman (0.1% of 5,999), and 51 women (0.9% of 5,999) were classified as indeterminate. Consequently, the latter group was assessed for treatment eligibility based upon any risk factors for cervical cancer that they may have had.

A followup question about the 4 women suspected of having cancer was, “What proportion of the cervix is covered by the cancerous lesion?” Of these women, 2 had suspect lesions covering less than 25% of the cervix and 2 had lesions covering 25–50% of the cervix.

DETERMINING ELIGIBILITY FOR IMMEDIATE TREATMENT

If a woman was assessed as test-positive or indeterminate, the health providers were to proceed to a specific set of questions on the form regarding the woman’s eligibility or candidacy, respectively, for treatment.

Of the women classified as test-positive, if the proportion of the total cervix that was acetowhite was greater than 75.0%, the protocol dictated that they would be ineligible for treatment. This was the case for 15 of the 785 women (1.9%) for whom these data were recorded. The remaining 770 women (98.1%) were eligible for treatment according to that criterion. For the majority (83.9% or 646/770) of these women, acetowhite cervical coverage was less than 25.0%; 14.8% (114/770) had lesions covering 25–50% of the cervix; and 1.3% (10/770) had lesions covering 50–75% of the cervix. If the acetowhite area extended beyond the cervix and onto the adjacent vaginal wall, the woman was also considered ineligible for treatment. Another 1.9% (15/779) of the women were eliminated from the treatment eligibility group for this reason.

Other exclusion/ineligibility criteria included: a 12-week fibroid mass; an ovarian/adnexal mass greater than 5 cm; and current menstruation or menstruation due in the next 7 days. Only 1.0% (8/776) of the women for whom these data were recorded had a fibroid mass; 0.4% (3/772) had an ovarian/adnexal mass; and 13.0% (101/778) were due to menstruate within the next week. In addition, 0.4% (3/752) of the women reported here that they were HIV positive.

Considering the responses to the eligibility criteria questions, and referring to the treatment status categories, the health providers judged that 85.9% of the 780 test-positive women for whom the data were recorded were eligible for treatment. Another 14.1% (110/780) of these women were ineligible for treatment, and recommendations for treatment were made according to the clinical protocol.

Women classified as indeterminate and who answered “yes” to having any risk factors were considered candidates for treatment. Although 51 women (0.9% of 5,999) were assessed as indeterminate, data on most of the risk factor variables exist for only 50 women. Five of these 50 women claimed to have had more than one sexual partner during their lives; 3 said that they had a partner/husband with a suspected STI or HIV; and 1 said that she smoked or chewed tobacco. Of the 51 women who responded, 18 women said that they had sexual intercourse for the first time before the age of 20. Of the indeterminates for whom informative data exist, 43.1% (22 of 51) qualified as candidates for treatment as a result of having one or more risk factors; 18 of the 22 had only one risk factor; and 4 had two risk factors.

Cases of Cervicitis

All women who assessed as test-positive or indeterminate but at risk (n=820) were to be investigated for signs of cervicitis. Of those evaluated and whose results were recorded (n=688), 1.2% (8/688) had signs of cervicitis. Of these 8 women, the data indicate that 6 were provided with pills to treat cervicitis, and 1 did not receive pills. The data are missing for 1 person, and it is not known if the remaining woman was given pills or not. Only 1 of these 6 women took the pills in the presence of a health provider.

Clinical Management Plans, Referrals, and Consent for Treatment

A clinical management plan was to be devised for all test-positive women, for those assessed as indeterminate with one or more risk factors, and for those with suspect cancerous lesions (n=824). Data were recorded for 807 of these women. For each, the provider indicated an initial recommendation, asked the woman what she wanted to do, and then recorded the final recommendation, based on the woman's decision. The nurse providers initially recommended immediate treatment for more than three-quarters (76.1% or 614) of the 807 women for whom these data were recorded. The providers also recommended that 15.6% (126/807) receive treatment at a later date, and that 8.3% (67/807) be referred to another (specified) facility. Most women who responded and whose treatment was recommended for postponement (79.3% or 69/87) were to be treated within 14 days, and most women for whom a location was specified (76.1% or 48/63) were referred to the Roi-et Provincial Hospital. Reasons for referrals to other facilities were recorded for 67 women, the predominant reason (in 27 or 40.3% of cases) being an extensive cervical lesion. Other reasons included polyps (8/67 women or 11.9%); fibroids (8/67 women or 11.9%); ovarian/adnexal masses (3/67 women or 4.5%); the need for additional diagnostic tests (3/67 women or 4.5%); and suspected cancer (2/67 women or 3%). For 16 women (23.9% or 67), the reason for referral is listed as "other" (no further explanation provided).

On the basis of the provider's recommendation, 96.6% (774/801) of the women for whom these data exist consented to immediate treatment. Of the remaining 27 women (3.4% of 801) who did not give their consent for immediate treatment, 17 provided reasons why: 5 indicated they needed to consult with their partners first; 1 wanted more time to think about her options; and the remaining 11 had "other" reasons for not consenting.

The final case management recommendations recorded for 810 women were: immediate treatment with cryotherapy (that day) for 74.4% (603/810); referrals for 8.1% (66/810); and postponed treatment (request to return for cryotherapy) on a future specified date for 17.3% (140/810). The majority of the latter postponements (80.0% or 101/125 women) occurred because these women expected their menstrual periods to occur within the next week.

POST-VIA COUNSELING QUESTIONS AND POST-VIA INTERVIEW

The nurses recorded that 99.7% (5,981/5,999) of the women who took part in the project were counseled about three important issues: the meaning of their VIA results; their case management, including available treatment options; and when they should return to the clinic for additional cancer prevention services. Following this counseling, each participant gave responses to seven questions about her experience during and after the VIA procedure. Of the 5,740 who responded, the majority (89.0% or 5,107) said that they experienced no discomfort during the VIA procedure, and 11.0% (633) indicated that they did experience discomfort. Additionally, most of the women (89.6% or 5,133/5,729) claimed that their testing experience

was better than expected. For a small percentage of the women (0.6% or 33/5,729), their experience with VIA was worse than expected; 4.8% (276/5,729) had an experience that matched expectations; and 5.0% (287/5,729) said they had no expectation before the procedure. Almost all of the women (99.8% or 5,699/5,709) believed that they were informed enough about what they would experience during the testing procedure, and 98.5% (5,658/5,742) were either very satisfied (71.9%) or satisfied (26.7%) with their decision to have VIA testing. Furthermore, based on the results of their test, 98.8% (5,671/5,742) of the women were either very satisfied (74.6%) or satisfied (24.1%) with the management recommendation of the provider. Nearly all (99.8% or 5,732/5,744) of the women declared that they would, in the future, recommend the VIA test to female friends and/or family members. Only 1.7% (98/5,744) of the women for whom there are informative data had final questions or concerns which were expressed in writing on the back of their questionnaires.

CRYOTHERAPY RESULTS

Of the 5,999 women tested, 756 (12.6%) received cryotherapy and had individual cryotherapy intake forms filled out. These forms contained information about pre- and post-procedure counseling, general patient observations, and post-cryotherapy attitudes of the women. This section summarizes the responses to questions on the cryotherapy forms.

PRE-PROCEDURE COUNSELING

All women eligible and interested in receiving cryotherapy was counseled about four important points: 1) their treatment options; 2) what the cryotherapy treatment entails and what they should expect during the procedure; 3) home care recommendations (such as the necessity for abstinence and the use of condoms for 4 weeks following cryotherapy); and 4) the need to return for two separate followup visits as part of the project protocol. The first followup visit was scheduled for 12–16 weeks after cryotherapy, and the final followup visit was scheduled for 1 year after cryotherapy.

Data for various questions were missing for some women. Overall, the data indicate that more than 98.9% (748/756) of the women who received cryotherapy also received counseling regarding each of these four points.

CRYOTHERAPY PROVIDER OBSERVATIONS

Of the 755 women for whom there were available data, the majority (81.3% or 614/755) received cryotherapy on the same day that their VIA testing took place. (The procedure was postponed for the remaining 18.7% [141/755] of the women.) Information regarding the facility where the cryotherapy took place was also available for 755 of the women. Cryotherapy was performed at a different facility than the VIA testing for only 4.9% (37/755) of the women. The majority of the women (95.1% or 718/755) had their VIA assessments and cryotherapy at the same facility.

Nurses perceived that 39.6% (299/756) of the women experienced pain or cramping during or immediately after the procedure. When asked to rate the perceived severity of the women's pain, of the 290 women for whom there is a response to this question, 79.0% (229/290) were perceived to have experienced mild pain. Moderate pain level was perceived for 18.3% (53/290) of the women, and the remaining 8 women (2.8% of 290) were perceived to have experienced severe pain. Of 746 women for whom there was a response, 6.3% (47/746) received an analgesic, and 45 of these 47 women (95.7%) received the analgesic after the procedure. (Data were missing for 8 women.)

Of the 748 women for whom there were data, bleeding occurred immediately after the cryotherapy probe was removed for 1.7% (13/748). The bleeding was assessed as mild for 84.6% (11/13) of the women; 2 answers were missing.

There were no occurrences of moderate or severe bleeding immediately after the cryotherapy probe was removed. When asked how the bleeding was controlled, of the 10 responses given, nurses applied cervical pressure to control the bleeding 100% of the time. None of the following were recorded as being used to control the bleeding: surface cervical medications (0/10);

vaginal packing (0/10); sutures (0/10); admission (0/10) or referral (0/9) to the hospital; transfusion (0/10); or “other” (0/9).

With the exception of bleeding, there were no immediate adverse post-treatment events recorded for the 749 women who responded to this question. Further clinical action (e.g., a hysterectomy or an exploratory laparotomy) was not needed for any of the 752 women for whom there were informative data.

POST-CRYOTHERAPY COUNSELING

After treatment, nurses were instructed to counsel each woman about eight pertinent points: 1) possible side effects that may occur secondary to treatment; 2) expected vaginal discharge changes; 3) post-treatment symptoms that may indicate a possible complication; 4) the importance of seeking medical attention if any of these symptoms occur; 5) how to obtain services at the DH if these symptoms develop; 6) the risk of putting anything in the vagina and/or 7) engaging in sexual intercourse within the first 4 weeks post-treatment; and 8) the importance of using condoms if intercourse does occur within 4 weeks of treatment. Some data were missing for the eight questions; however, 99.7% (754/756) of respondents indicated that the women received counseling about all eight points.

POST-CRYOTHERAPY INTERVIEW

As a means of measuring immediate acceptability of the cryotherapy procedure, each woman was asked to first comment on the treatment, and then on how she felt about her experience. Of the 753 women who commented on their treatment, 40.8% (307/753) reported pain or cramping during the procedure. Only 306 women quantified their pain/cramping, and the majority of these women (80.4% or 246/306) described their pain/cramping as mild. Moderate pain was reported by 17.0% (52/306) of the respondents, and 2.6% (8/306) said that they had experienced severe pain. Of the 307 women who commented on how they felt about their experiences, the majority (66.1% or 203/307) said that the pain was less severe than their worst menstrual cramps. Another 27.7% (85/307) of these women believed that the pain was comparable in severity to their worst menstrual cramps. Only 4.6% (14/307) of the women indicated that the pain during the procedure was more severe than their worst menstrual cramps. The remaining 1.6% (5/307) of these women said that they were unable to make such a comparison.

The majority of women (91.5% or 688/752) said that their treatment experience was better than they had expected. Only 0.3% (2/752) of the women indicated that their experience was worse than they had expected. The experience matched the expectations of 1.7% (13/752) of the women, and 6.5% (49/752) said that they had no expectations before the treatment.

For the 744 women who answered the next question (about what to expect during treatment), the majority (99.5% or 740/744) felt that they were sufficiently informed about what to expect during the treatment. The remaining 0.5% (4/744) of women indicated that they were not sufficiently informed.

With respect to their husbands/partners, 2.3% (17/750) of the women believed that they would have problems convincing them to postpone intercourse for the recommended 4 weeks. This issue was not relevant for 4.8% (36/750) of the women who either did not have husbands/partners, or whose husbands/partners would not be present for the subsequent 4 weeks. The remaining 92.9% (697/750) of the women did not think at the time they received treatment that

they would have any problems convincing their husbands/partners to postpone intercourse for 4 weeks. Similarly, the majority of women (94.5% or 704/745) did not anticipate any problems convincing their husbands/partners to use condoms if they did have intercourse within the recommended abstinence period; however, 0.5% (4/745) of the women believed that this suggestion might be problematic. (For this question, 5% [37/745] of the women indicated that they did not have husbands/partners or that their husbands/partners would not be present for 4 weeks.)

With the exception of 1 woman (0.1% of 753) who was unsatisfied with her decision to have the condition of her cervix assessed with the VIA test, 99.9% (752/753) of the women were either very satisfied (70.4% or 530/753); satisfied (28.7% or 216/753); or neutral (0.8% or 6/753) about this decision. Regarding their treatment decision, 72.3% (544/752) of the women who responded were very satisfied with their decision to be treated for suspect cervical disease; 26.7% (201/752) were satisfied; and 0.9% (7/752) were neutral regarding this decision. Most women (97.5% or 732/751) who responded indicated that they would recommend this treatment to their friends and/or female family members in the future; only 2.5% (19/751) said that they would not make this recommendation. After both counseling sessions and the cryotherapy procedure itself, only 2.7% (20/749) of the women had final questions or concerns, which were expressed on the back of their cryotherapy intake forms.

FIRST FOLLOWUP VISIT

Between 12–16 weeks post-treatment, the women were instructed to return for their first followup visit. This section describes the results, taken from the women’s forms, of their first followup visits. Of the 756 women who originally received cryotherapy, 83.2% (629/756) returned for the first followup visit. At this visit, the women responded to questions regarding compliance with home care recommendations, any treatment side effects that had occurred, their perspectives on their experiences thus far, and how much support they had received from their husbands/partners. Furthermore, if any woman had a major physical problem or complaint, the healthcare providers were to record the symptomatology and, if indicated, perform a clinical assessment.

PERSONAL QUESTIONNAIRE INFORMATION

If the date a participant attended her first followup visit was not within approximately 12–16 weeks of her cryotherapy treatment, she was asked to provide a reason for not returning during that time. In total, 153 women did not come back within the designated time period (calculated here as 10–16 weeks). Of these, 10 (6.5%) claimed that their husbands/families did not want them to return as scheduled; 106 (69.3%) said that it was not convenient to come at the scheduled time; 30 (19.6%) did not remember the scheduled date to return; and 3 (2.0%) needed to come to the facility on a different day for another reason. Four women had “other” reasons for postponing their scheduled return date – 2 because they “felt normal;” 1 because she worked in a different district; and 1 who did not specify her reason. Only 2.5% (16/629) of the women had moved or changed contact addresses after their cryotherapy treatment.

Women’s Compliance with Home Care Recommendations

Each woman had been counseled about the risks associated with inserting anything into the vagina, having intercourse, and not using condoms should they have sexual intercourse within 4 weeks post-treatment. To document compliance and to enquire about other factors affecting the acceptability and safety of treatment, these women were asked about these home care recommendations during the visit.

First Sexual Intercourse Post-Treatment

Of the 628 of the women who responded, 72.3% (454/628) had engaged in sexual intercourse in the 4-month interim since treatment. Of the 91.8% (417/454) who knew approximately when this occurred, 34.5% (144/417) said that they had done so within 4 weeks/28 days of their treatment. This indicates that 65.5% (273/417) of the women had abstained from intercourse for the recommended 4-week time period. By 32 days post-treatment, more than half (59.5% or 248/417) of the women had had intercourse. By 60 days post-treatment, the same was true of 97.1% (405/417) of the women. When the numbers were analyzed in weekly increments, it was found that 1.5% (7/459) of the women who responded indicated that they had resumed intercourse within 7 days; 11.1% (51/459) had done so within 1–2 weeks; 18.3% (84/459) had done so within 3–4 weeks; and 69.1% (317/459) had done so after 4 weeks. The source of this information was two-fold – from the daily diaries of 54.1% (250/462) of the women, and from verbal estimates given by 37.4% (173/462) of the women when they were interviewed. The remaining source of the information was unknown/unrecorded.

When asked why they had engaged in intercourse earlier than recommended, 141 women responded. The majority of these respondents (89.4% or 126/141) said that they did not want to disappoint or say no to their husbands/partners. The remaining women had intercourse for six reasons: 3 women (2.1%) indicated that their husbands/partners forced them; 1 woman (0.7%) claimed that her husband/partner(s) threatened to have intercourse with others if she were unwilling; 2 women (1.4%) said that they were afraid of this latter possibility; 4 women (2.8%) said that they wanted to; 2 women (1.4%) said that they forgot about the 1-month waiting time; and 3 women (2.1%) were not convinced that the abstinence period was important.

Condom Use

With respect to the use of condoms during intercourse, 63.3% (292/461) of the women claimed to have used condoms since their cryotherapy. Information regarding the date when condom use was initiated was recorded for 279 women. The sources for these data were the daily diaries of 61.3% (171/279) of the women, and the verbal estimates of 35.8% (100/279) of the women when they were interviewed. For the remainder of the women, the source of information was unknown/unrecorded.

Of the 264 women who estimated the number of days that had passed between their treatment and their use of condoms, 6.1% (16/264) said that they had used condoms within the first week; 14.0% (37/264) had done so within the second week; 12.5% (33/264) within the fourth week; and 51.9% (137/264) sometime after 4 weeks. When asked to estimate by weekly increments when the use of condoms began, the data were slightly different, but the distribution was similar. Of the 291 respondents, condoms were used by 3.1% (9/291) in less than 1 week; by 16.5% (48/291) within 1–2 weeks; by 24.4% (71/291) within 3–4 weeks; and by 56.0% (163/291) after 4 weeks post-cryotherapy. When asked how often condoms were used during intercourse, only 131 women responded to this question (compared to the 292 women who originally said that they used condoms). Of these 131 women, 90.1% (118/131) claimed to have used condoms all of the time; 1.5% (2/131) said most of the time; and 8.4% (11/131) said some of the time. Of 13 women who did not use condoms all of the time, 10 gave reasons: 45.5% (5/11) said that they did not feel comfortable asking their husbands/partners to use condoms, and 27.3% (3/11) said that their husbands/partners refused to use them. One woman (9.1% of 11) did not think that the use of condoms really mattered; another woman (9.1% of 11) lost/ran out of condoms.

Vaginal Insertion

Of the 629 women who attended their first followup appointment, 4.6% (29/629) claimed to have inserted something into their vagina post-treatment. This information came from the diaries of 58.6% (17/29) of the women, and 17.2% (5/29) of the women's verbal estimates. For 24.1% (7/29) of these women, this information was not known/recorded. Most of the women (72.4% or 21/29) were able to provide the number of days between their cryotherapy treatment and any vaginal insertion, which ranged from 1–61 days. More than half of these 21 women (61.9% or 13/21) had inserted something into their vaginas within 30 days of the cryotherapy. When asked to estimate by weeks, 29 women responded: 10.3% (3/29) indicated that this event had occurred within 1 week of treatment; 10.3% (3/29) said within 1–2 weeks; 17.2% (5/29) said within 3–4 weeks; and 62.1% (18/29) said within 4 weeks. Five of the women gave specific examples of what they had inserted vaginally – a vaginal tablet (1 woman), a finger (3 women), and soap (1 woman).

Treatment Side Effects

In total, 84.1% (450/535) of the women recorded information in their diaries regarding their first post-cryotherapy menses; another 13.6% (73/535) gave a verbal account of this information. (The source is unknown/unrecorded for the remainder.) For 88.4% (555/628) of the women who responded to this question, menstruation had occurred since cryotherapy; any change from their normal menses was subsequently recorded by 552 women. With respect to menstrual blood flow, 90.0% (497/552) of the women who responded had experienced no change; 4.0% (22/552) had less blood flow than normal; and 1.6% (9/552) had significantly less blood flow than normal. On the contrary, 3.4% (19/552) of these women reported having more blood flow than normal, and 0.9% (5/552) had significantly more blood flow. Menstrual cramping had also changed for some women. Of the 552 women who responded, 4.3% (24/552) experienced much less cramping, and 5.6% (31/552) experienced less cramping. Additionally, 1.3% (7/552) of the women experienced more cramping, and 0.2% (1/552) experienced much more cramping. Most of the remaining 88.4% (488/552) of the women indicated no change in cramping levels, and 0.2% (1/552) reported no cramping. The duration of menses changed after treatment for a minority of the 552 respondents. Only 1.4% (8/552) of these women said that they bled significantly less, and 2.9% (16/552) bled less than normal. However, 2.4% (13/552) of the respondents bled more than normal, and 0.7% (4/552) bled significantly more than normal. This indicates that 92.6% (511/552) of these women had periods that lasted the same number of days before and after cryotherapy treatment.

Of the 627 women who responded to the question regarding bleeding not associated with menstruation, this type of bleeding was noted for 2.9% (18/627). Of these 18 women, 72.2% (13/18) recorded the date of these events in their diaries, and 22.0% (4/18) gave a verbal account. (The source was unknown/unrecorded for 5.6% [1/18] of the women.) Similarly, 18 women provided an estimate of the number of days after cryotherapy that the abnormal bleeding occurred, which was anywhere from 1–36 days post-treatment. For the majority of women (55.6% or 10/18), abnormal bleeding occurred within the first week after cryotherapy. For the remaining 44.4% (8/18) of the women, it occurred after 1 week post-cryotherapy. When asked to estimate this bleeding by weekly increments, again 55.6% (10/18) of the women claimed that the abnormal bleeding occurred within the first week post-cryotherapy. Of the remaining 44.4% (8/18) of the women, 22.2% (4/18) estimated abnormal bleeding to have occurred between 1–2 weeks post-cryotherapy; 11.1% (2/18) between 3–4 weeks; and 11.1% (2/18) after 4 weeks.

Information about blood clots (e.g., balls or clumps of blood) and pain/cramping episodes was provided by 627 women. Blood clots were noted by 0.6% (4/627) of the women—75% (3/4) had experienced these within the previous month, and the remaining woman had experienced blood clots more than 1 month prior to her first followup visit. Intermenstrual pain or cramping was experienced by 13.6% (85/627) of women. Of the 79 women who responded, 68.4% (54 women) recorded information in their diaries about the dates of their intermenstrual bleeding. A verbal account of this information was given by 31.6% (25/79) of the women. Many respondents who had felt pain/cramping (41.8% or 33/79) experienced it within 1 day of their cryotherapy; 54.4% (43/79) cumulatively experienced it within 2 days; 77.2% (61/79) cumulatively by 1 week; and nearly all (96.2% or 76/79) of the women who had experienced pain/cramping did so within 3 weeks. Two women (2.5% of 79) indicated that the pain occurred 30 days after treatment, and 1 woman (1.3%) indicated that her pain occurred 90 days after treatment. When estimating by week, 70.7% (58/82) of those who answered estimated that their pain/cramping had occurred within 1 week of treatment; 20.7% (17/82) estimated within

1–2 weeks; 2.4% (2/82) estimated 3–4 weeks; and 6.1% (5/82) estimated that more than 4 weeks had elapsed before they had any pain/cramping.

Pain was classified by 82 women, and the pain/cramping was described as mild for 69.5% (57/82); moderate for 26.8% (22/82); and severe for 3.7% (3/82). The pain/cramps were compared to the women's worst menstrual cramps. Of the 82 respondents, 42.7% (35/82) claimed that these episodes were less painful; 14.6% (12/82) said that they were much less painful; and 9.8% (8/82) said that the episodes were comparable to their typical menstrual cramps. The intermenstrual pains/cramps were much more painful for 7.3% (6/82) of the women; 15.9% (13/82) said they were more painful; and 9.8% (8/82) said that they could not be compared.

Of the 623 women who responded to the question on pregnancy, 7 (1.1%) said that they had become pregnant since treatment, and one of these pregnancies was recorded as being aborted. Another pregnancy was recorded as ending, but with no record of the pregnancy's outcome. Thus, 0.8% (5/623) of these women were pregnant at the time of their first followup visit. Three women (0.5%) responded that they did not know if they had become pregnant since their treatment. The remaining 98.4% (613/623) of the women claimed that they had not become pregnant or given birth since their treatment. When asked if they had experienced any other problems in the cervix, vagina, or pelvic area since treatment, 0.5% (3/628) of the women who answered claimed that they had experienced problems trying to become pregnant.

Other than the problems covered above, 6 women had experienced one or more problems since their treatment, including: abnormal vaginal discharge (0.5% or 3/628); chills/fevers/hot sweats (0.3% or 2/628); and 1 woman who had vaginal discharge also had vaginal itching/leukorrhea (0.2% or 1/626). When asked what measures were taken when such other problems arose, 7 of 11 women (63.6%) who responded indicated that they had visited the same health facility as they did for their first followup visit. None of the 11 women indicated that they had attended another health facility, visited a traditional healer, or used a pharmacological or traditional remedy for any other health problem that they perceived to be associated with their treatment.

Patient Perspectives

Of the 629 women who returned for their first followup visit, the majority (90.0% or 566/629) characterized their post-treatment experiences as better than they had anticipated; 4.5% (28/629) said that the experience matched their expectations; and 4.1% (26/629) indicated that they did not have expectations before the treatment. Only 1.4% (9/629) of the women felt that their experiences were worse than what they had expected. Women were asked, "Do you think that the staff counseled you enough about what to expect after treatment?" Of the 627 women who responded, 40.2% (252/627) said "mostly," and 59.8% (375/627) responded "very much so." No particular aspect of the counseling, such as the expected side effects or risk-associated behaviors, was specifically identified as being inadequately addressed.

Of the 628 respondents who answered the question about their decision to have their cervix assessed with VIA, 99.7% (626/628) indicated that they were either very satisfied (71.0% or 446/628) or satisfied (28.7% or 180/628) with their decision to have the condition of their cervix assessed using VIA. A small proportion (0.3% or 2/628) felt ambivalent about the decision. All 629 women who returned for a first visit responded about their treatment experience and indicated that they were either very satisfied (70.3% or 442/629), or satisfied (29.7% or 187/629)

about their decision to be treated with cryotherapy for suspect cervical disease. Of the 627 women who answered the next question about recommending VIA, most (97.9% or 614/627) had already recommended to friends and/or family members that they get VIA tested. VIA was not recommended to friends and/or family members by 2.1% (13/627) of the women; 98.9% (620/627) thought that they would make this recommendation in the future. This indicates that only 1.1% (7/627) did not think that they would make this recommendation to get VIA in the future.

Post-Treatment Partner Support

To aid in the assessment of treatment acceptability, questions concerning the supportiveness of women's husbands/partners were asked. Of the 628 respondents, 7.2% (45/628) said that they had problems trying to convince their husbands/partners to postpone intercourse for 4 weeks after treatment. An additional 3.7% (23/628) of the women did not ask their husbands/partners to postpone intercourse. The majority (89.2% or 560/628) indicated that they did not have any such problems. If they did have intercourse, the women were asked if they had any problems trying to convince their husbands/partners to use condoms. Of the 572 women who had sex, 2.4% said that they did have such problems, and 1.6% said that they chose not to ask their husbands/partners to use condoms.

Of the 628 respondents, the majority (91.6% or 575/628) felt that their husbands/partners were either very supportive (85.7% or 538/628), or supportive (5.9% or 37/628) about the need for abstinence and/or condom use for the designated time period post-treatment. Only 1.6% (10/628) of the respondents felt that their husbands/partners were not very supportive, and 0.5% (3/628) felt that they were not supportive at all. A minority (6.3% or 40/628) of the women indicated that they either did not have husbands/partners (2.2% or 14/628), or that their husbands/partners were not present post-cryotherapy (4.1% or 26/628). Women were asked, "How do you think your husband/partner feels about your decision to receive treatment?" Of the 628 women who responded, 94.9% (596/628) claimed that they thought their husbands/partners were either very satisfied (58.4% or 367/628), or satisfied (36.5% or 229/628) with their decision. Only 1.0% (6/628) of the women said that their husbands/partners were ambivalent about their decision to receive treatment. Another 2.4% (15/628) of the women claimed not to have husbands/partners, and 1.8% (11/628) reported that their husbands/partners were not around.

In total, 99.0% (623/629) of the women reported having none of the listed problems or complaints. Nurses were asked to assess whether or not they thought any of the women's complaints or health problems were likely to be related to cryotherapy treatment. According to the nurses, these women's health problems were related to the treatment in 5 of the 6 cases (83.3%). The other woman's concerns were recorded as unrelated to her treatment. Further questions or concerns were recorded by 4.6% (29/629) of the women on the back of their questionnaires.

In the clinical protocol, indication of major clinical problems due to the cryotherapy treatment was the criterion for a full examination at the time of the followup visit. Because there were no such indications at the time of the first followup visit, no women had any further clinical assessments at their 3-month followup visits.

PROBLEM VISITS

Women were encouraged to attend the healthcare facility if any problems, abnormalities, or worrisome side effects arose after they received cryotherapy. If they presented at the facility, a “problem visit” form was completed with information about their symptoms. Additionally, as indicated by the study clinical protocol, they were assessed and examined by one of the project nurses. This section summarizes the responses to questions on the problem visit forms and any clinical assessments made by the attending nurses.

SYMPTOMATOLOGY

Of the 756 women treated with cryotherapy, 4.4% (33/756) presented at a project healthcare facility for a problem visit. Among these 33 women, the symptoms that caused them to seek medical attention were: menstrual bleeding (9.1% or 3/33); non-menstrual bleeding (12.1% or 4/33); non-menstrual pain/cramping (27.3% or 9/33); abnormal vaginal discharge (45.5% or 15/33); headache (3.0% or 1/33); and chills/hot sweats/fevers (3.0% or 1/33). **Table 6** below summarizes the main presenting complaint of the 33 women for whom there was a problem visit form.

TABLE 6. MAJOR PRESENTING COMPLAINT

MAIN COMPLAINT	NUMBER OF WOMEN	PERCENTAGE OF WOMEN
Menstrual bleeding	3	9.1%
Non-menstrual bleeding	4	12.1%
Non-menstrual pain/cramping	9	27.3%
Abnormal vaginal discharge	15	45.5%
Headache	1	3.0%
Chills/hot sweats/fever	1	3.0%
Pregnancy-related	0	0%
Total	33	100%

Of the 3 women who presented at the clinic because of suspected abnormal menstrual bleeding, 2 women (66.7%) stated that the bleeding lasted longer than normal, and 1 woman (33.3%) claimed that the menstrual bleeding was shorter in duration. Although 4 women complained of non-menstrual bleeding, only 3 of these women estimated when the bleeding started. One woman (33.3%) started bleeding 2 days prior, and 2 women (66.7%) indicated that they began bleeding 4 days prior. When asked for how many days they had been bleeding, 1 woman (25%) said 1 day, 2 women (50%) said 2 days, and 1 woman (25%) said that she had been bleeding for 3 days. Although only 4 complained of non-menstrual bleeding, responses describing the bleeding at its heaviest were recorded for 5 women (therefore N = 5 for this question). This occurred throughout the dataset, which likely reflects that women experienced more than one symptom (although only the main one they presented for was recorded). Overall, 60% (3/5) of the women described the bleeding as being the same in amount as the lightest days of their menstruation; 1 woman (20% or 1/5) said that the bleeding was heavier than any part of her regular menstruation; and 1 woman (20% or 1/5) said that her non-menstrual bleeding was lighter than her normal menstruation (her main presenting complaint was problematic menstrual bleeding).

Of the 33 women for whom there was a problem visit form, 27.3% (9/33) indicated that pain/cramping was their main reason for the visit; however, 11 women responded to the

pain/cramping-related questions. The pain among these 11 women lasted anywhere from 1–29 days. Nine of the 11 women (81.8%) indicated an exact number of days, and the majority (88.9% or 8/9) said that they had pain for 7 or fewer days. The remaining 1 woman (9.1%) claimed that her pain/cramping lasted 29 days in duration.

Abnormal vaginal discharge was the main symptom for 45.5% (15/33) of the women who attended the health facility for a problem visit. However, 21 women described the color of their vaginal discharge as follows: black (4.8% or 1/21); yellow (76.2% or 16/21); white (.05% or 1/21); green (5.0% or 1/21); and “other,” such as “clear with no odor” (9.5% or 2/21). Eighteen women said that they had discharge that lasted for the following number of days: 1 day for 11.1% (2/18) of the women; 2 days for 11.1% (2/18); 3 days for 16.7% (3/18); 4 days for 27.8% (5/18); and 7 days for 16.7% (3/18). Another 3 women (each accounting for 5.5% or 1/18 of the group) said that they experienced vaginal discharge for 5 days, 14 days, and 18 days, respectively.

Regarding the remaining chief presenting complaints, 9.0% (3/33) of the women said that they had chills, hot sweats, and/or fevers (for 1, 3, and 9 days, respectively). Of the 28 women who responded to the question, 24 (85.7%) said that they were still experiencing problem(s) at the time of the problem visit. Of the 30 women who reported where they presented for these problem(s), 26.7% (8/30) said that they had visited another provider or clinic before that day for care perceived to be related to their problem(s). Five clinics were named: Chaturapakpiman Hospital (1 woman); Non Sawan Health Clinic (2 women); Sri Kotre Health Clinic (1 woman); Nong Pue Health Clinic (1 woman); and Kud Nom Sai Health Clinic (1 woman).

Of the 33 women who returned for a problem visit, 51.5% (17/33) of the presenting complaints were classified as minor complications due to the nature of the clinical problem (requiring an outpatient procedure by a trained provider); 21.2% (7/33) as problematic side effects; and the remaining 27.3% (9/33) as just problem visits (e.g., women returning with suspect health problems, but not assessed as having either an anticipated side effect or a complication of cryotherapy). None of the women were assessed as having a major complication (i.e., requiring inpatient care).

CLINICAL ASSESSMENT

All 33 women who presented for a problem visit had three vital signs measured and recorded: temperature, heart rate, and blood pressure. Valid temperatures (data available for 30 women) ranged from 36.0°C to 37.7°C; thus no women were febrile at the time of their clinical assessments. Valid radial pulses (data available for 32 women) ranged from 66 beats per minute to 96 beats per minute; thus no women were experiencing tachycardia.

If indicated, a pelvic examination was to be performed and any clinical abnormalities diagnosed, recorded, and treated. As indicated by the denominator values below, only some of the women had information recorded about the various conditions of interest. It was discovered by one of the trained attending nurses that 61.5% (16/26) of the women for whom there were data had evidence of cervicitis; 4.8% (1/21) had signs of an STI; and 1 woman (4.8%) had pelvic tenderness associated with suspected pelvic inflammatory disease (PID) (later confirmed not to be PID). In total, 22.7% (5/22) of the women for whom data were recorded had active vaginal bleeding, and 19.0% (4/21) showed signs of a cryotherapy-induced vaginal burn. Of the 32 women who presented for problem visits and for whom there were data recorded for this question, less than half (46.9% or 15/32) were assessed as having problems secondary to having

received cryotherapy. The nurses were unsure about making any association between the presenting complaint and the cryotherapy treatment for 21.9% (7/32) of the women. The remaining 31.3% (10/32) of the women presented with problems that were assumed by the nurses to be unrelated to their treatment.

Of the 33 women who had problem visits, 97.0% (32/33) were observed and provided with reassurance as part of their clinical management plan. There were data regarding prescription medication for 30 women – 27 (90.0%) of whom received some sort of prescription medication. These medications included (but were not limited to) paracetamol, doxycycline, and metronidazole. Among the 18 women with data recorded for the other clinical options, 27.8% (5/18) received medication for surface application to the affected area, and 1 woman (5.6%) received intravenous antibiotics (for suspected PID, which later was confirmed as a misdiagnosis). None of the following measures were required for any of the women for whom there were informative data: vaginal packing, sutures, transfusion, referral to another facility or hospital admission, hysterectomy, or exploratory laparotomy. Of the 17 women for whom there were informative data, 1 woman (5.9%) received some sort of unspecified (i.e., “other”) clinical action.

ONE-YEAR FOLLOWUP VISIT

The protocol called for women to return to the clinic 1 year after cryotherapy treatment for a VIA assessment and general evaluation. This section describes the results from these final followup visits.

The questionnaire from this visit contained information similar to that recorded for the first followup visit—compliance with home care recommendations, potential treatment side effects, overall patient perspectives about their experience, and post-treatment partner support. Of the 756 women who underwent cryotherapy, 93.5% (707/756) returned for their 1-year followup visit by the time the data were analyzed (data collection ended 3 months after the last followup visit was scheduled to take place).

PERSONAL QUESTIONNAIRE

Only women who did not present for their first followup visit (N=109) were asked about the date of their first sexual intercourse post-treatment, the use of condoms, and the act of inserting anything into the vagina. Where appropriate, the responses of these 109 women have been added to the responses of those who answered the same questions during the first followup visit, yielding as the denominator all those responding to the questions during either of the two followup visits.

Women's Compliance with Home Care Recommendations

First Sexual Intercourse

When asked at 3 months (or at 1 year if there was no first followup visit) about their first episode of sexual intercourse after treatment, specific days were indicated by 470 women ranging from 1 to 120 days. Of these 470 women, 321 (68.3%) estimated that intercourse had occurred after 4 weeks post-treatment. Of the 558 women who responded with either an exact number of days or a range of time, 406 (72.8%) said that sex occurred after 4 weeks; 15.9% (89/558) said between 3–4 weeks; 9.5% (53/558) said between 1–2 weeks; and 1.8% (10/558) reported that they had had sex within 1 week of their cryotherapy treatment.

Combining the 3- and 12-month followup responses, 150 of 152 women offered a main reason for why they had engaged in sex earlier than recommended: 131 (87.3%) said that they did not want to say no to or disappoint their husbands/partners; 6 (4.0%) said that they wanted to have sex; 4 (2.7%) said that they were not convinced that this time period was important; 3 (2.0%) said that their husbands/partners forced them; 2 (1.3%) said that they were afraid their husbands/partners would have sex with others if they did not; 2 (1.3%) said that they forgot about the waiting period; and 1 (0.7%) said that her husband/partner threatened to have sex with others.

Condom Use

Many of the women (63.7% or 356/559) said that they used condoms during intercourse after treatment. Among those who used condoms, 297 women reported the exact number of days that elapsed between cryotherapy and their use of condoms (between 1–120 days), and 354 were able to estimate this time in weeks. When estimated by weeks, the majority (62.1% or 220/354) estimated that condoms were used after 4 weeks post-treatment; 21.5% (76/354) estimated that condom use began between 3–4 weeks; 13.8% (49/354) estimated 1–2 weeks; and the remaining 2.5% (9/354) said they used condoms during the first week post-cryotherapy. Only 142 women responded to the question about frequency of condom use: 90.8% (129/142) said that they used condoms all of the time; 1.4% (2/142) claimed that they used condoms most of the time; and 7.7% (11/142) said they used condoms some of the time.

Among women who had sex before 4 weeks and did not use condoms: 31.3% (5/16) said that they did not use condoms because they felt uncomfortable asking their partners to use condoms; 25.0% (4/16) said that their husbands/partners refused to use condoms; 18.8% (3/16) lost/ran out of condoms; 12.5% (2/16) did not think using condoms was important; 1 (6.3%) said she was afraid her partner would choose to have sex with others rather than use condoms; and 1 (6.3%) said she did not want to use condoms.

Vaginal Insertion

Each woman was asked, “Have you inserted anything into your vagina in the interim since treatment (or in the 3 months since treatment, for those responding at 1 year)?” In total, 721 women responded to this question. Only 4.9% (35/721) answered “yes,” and 21 of these women provided the exact number of days post-treatment that this occurred. Another 29 women were able to estimate the week this occurred after treatment: 10.3% (3/29) estimated this happened in the first week after treatment; the same number said it occurred in weeks 1 and 2; 17.2% (5/29) estimated that it occurred 3–4 weeks post-treatment; and the remaining 62.1% (18/29) estimated that it occurred after more than 4 weeks post-treatment.

Treatment Side Effects

Menstruation, Pain/Cramping, and Vaginal Discharge

The majority (89.9% or 635/706) of the women who responded indicated that they had menstruated since their treatments. Most (97.0% or 592/610) who responded about timing said that this occurred within the first month following cryotherapy. Another 14 women (2.3% of 610) said that they first menstruated 2 months post-cryotherapy; 0.5% (3/610) said 3 months post-cryotherapy; and 1 woman (0.2% of 610) said 12 months post-cryotherapy. This first menses was painful for 25.7% (163/634) of the women who responded. Of the 154 women who answered the next question, 110 (71.4%) claimed that the pain was equivalent to what they experience during a normal menses. Another 5.8% (9/154) of the women reported having more pain, and 7.8% (12/154) experienced significantly more pain. Less pain was experienced by 9.1% (14/154) of the women, and 4.5% or (7/154) reported having much less pain. For this question, 1.3% (2/154) of the women claimed that they did not previously experience cramping.

Pain/cramping not associated with menstruation was noted for only 6.4% (45/703) of those who responded to this question. Of the 42 women who indicated the duration of this pain, it lasted less than 1 week for 54.8% (23/42); 1–2 weeks for 14.3% (6/42); 2–4 weeks for 4.8%

(2/42); 1–3 months for 7.1% (3/42); and longer than 6 months for 19.0% (8/42). Of the 45 women who responded about the severity of the pain/cramping, it was described as mild by 57.8% (26/45); moderate by 40.0% (18/45); and severe by 1 woman (2.2%). When asked to compare the pain/cramping to their worst menstrual cramps, 38.5% (15/39) of the women said that it was more painful; 20.5% (8/39) said much more painful; 17.9% (7/39) said similar; 7.7% (3/39) said less severe; 7.7% (3/39) said much less severe; and 7.7% (3/39) said that they could not make that comparison.

Vaginal discharge was recorded as lasting 1–60 days after treatment for 42 women, the majority of whom (97.6% or 41/42) experienced the discharge within 30 days post-cryotherapy. Twenty-four (57.1%) women experienced discharge within 10 days after their treatments. Only 3.4% (24/706) of the women said that they had experienced malodorous discharge, occurring anywhere from 1–30 days post-treatment. The majority of these women (95.8% or 23/24) said that the malodorous discharge occurred within the first 14 days after their procedures.

Feminine Pads and Condoms Distribution

Each woman received 8 feminine pads, 6 condoms, and 2 pairs of panties after their cryotherapy procedure. Of the 705 women who responded, slightly more than half (57.2% or 403/705) felt that the number of pads was sufficient given the amount and duration of discharge they experienced (50.6% [357/705] of the women said enough and 6.5% [46/705] said more than enough). However, 42.8% (302/705) of these women felt that the number was not sufficient. Of the 313 women who then suggested what they felt was an adequate number of pads per day to be distributed, 47.0% (147/313) suggested 3 pads; 36.1% (113/313) suggested 2 pads; and 8.6% (27/313) suggested 1 pad. Of the remaining 6.4% (20/313) of the women, 1.3% (4/313) and 0.6% (2/313) believed that 4, 5, or 6 pads per day, respectively, would be sufficient. The number of condoms distributed was considered “more than enough” by 65.4% (457/699) of respondents, and “enough” by 33.6% (235/699). Only 7 women (1.0%) felt that the number of condoms distributed was not sufficient. Of the 7 women who suggested a specific number of condoms as ideal for distribution, 28.6% (2/7) suggested 10; 14.3% (1/7) suggested 12; 14.3% (1/7) suggested 15; 14.3% (1/7) suggested 25; and 28.6% (2/7) suggested 30.

Pregnancy

Thirty-one women (4.4% of 705) claimed that they had tried to become pregnant since their cryotherapy treatment. Of these women, 17 provided a response to the number of months they had been trying to get pregnant, and the estimates ranged from 2–12 months. The specific numbers of months provided were: 2 months (5.9% or 1/17); 3 months (5.9% or 1/17); 4 months (11.8% or 2/17); 6 months (23.5% or 4/17); 10 months (5.9% or 1/17); and 12 months (47.1% or 8/17).

Among the 31 women who had tried in the past year to become pregnant, the outcome of this effort is unknown for 5 women, 15 (48%) did not conceive, and 11 (35%) became pregnant. The status of the 11 pregnancies was: 7 resulted in live, full-term births, 3 women were still pregnant at the time of the followup visit, and results were not indicated for 1 woman. Only 1 woman who said she had tried to become pregnant described having a “problem getting pregnant.”

Other Problems

Of the 706 respondents, 1 woman (0.1%) said that she experienced chills, hot sweats, and/or a fever. During the previous year, the majority of women (90.9% or 642/706) said that they had not returned to any facility for a perceived health problem. In total, 56 (7.9%) of the women who returned at 1 year indicated that they had gone to the same facility to receive care for a perceived health problem as they did for their VIA testing. However, for 28 of these 56 women, the day they went to the “same facility” was the same day as their first followup visit. Furthermore, there was a problem visit form filled out for only 3 of these women. This suggests that this question was not well understood by a number of women, and likely only 4.4% (31/706) of the women went to the same facility for a perceived health problem. (This correlates with the 33 problem visit forms collected from the same facility and reported on above.)

Only 1.8% (13/706) of the women said that they had visited another facility for a health problem they perceived as being associated with their treatment. However, 5 of these 13 women are among those who also said that they went to the same facility. A few facilities other than the facility where they had been originally treated were identified as having been visited for a perceived health problem including: Kittichote Clinic (1 woman); Lak Muang Hospital (1 woman); a private clinic (no specific name provided; 5 women); Roi-Et Hospital (1 woman); Roi-Et Thornburi Hospital (1 woman); Ruampat Hospital (1 woman); and the Siriporn Clinic (1 woman). To treat their perceived problems, 0.1% (1/705) of the women used a pharmaceutical remedy. Only 0.4% (3/704) of the women said that they visited a traditional healer, and only 0.3% (2/706) said that they used a traditional remedy.

Patient Perspectives

When asked to characterize their experience after treatment, 705 women responded to the questions: 89.4% (630/705) indicated that their experience was better than expected; 7.4% (52/705) said that their experience met their expectations; and 1.4% (10/705) said that they had no expectations of the visit. Only 1.8% (13/705) of the women said that their experience was worse than they had expected. Regarding the counseling the women received about what to expect after treatment, 58.9% (416/706) said that they were counseled enough, and 40.7% (287/706) said that they were counseled “mostly” enough. Only 0.4% (3/706) of the women said that they were counseled only “somewhat” enough. When all of the women were asked on what topics they would have liked more counseling, 4.5% (32/706) of the respondents said that they would have liked more information about the amount of pain/cramping that was to be expected, and 4.7% (33/706) said that they wanted more information about the duration of such pain/cramping. With regard to vaginal discharge, women said that more counseling should be provided about: the expected amount (5.1% or 36/706); its duration (5.2% or 37/706); and its odor (2.8% or 20/706). Other women felt that there should have been more counseling about the need for abstinence (2.4% or 17/706); condom use (2.1% or 15/706); the risks of inserting anything into the vagina (2.4% or 17/706); and the overall risk of infection (2.7% or 19/706).

The majority of the 706 women who responded were either very satisfied (64.0% or 452/706) or satisfied (35.3% or 249/706) with their decision to have the condition of their cervix assessed with the VIA test. Four women (0.6% of 706) said that they were neutral about this decision, and 1 woman (0.1% of 706) said that she was unsatisfied with this decision. Most of the women (99.3% or 701/706) had recommended the VIA test to their friends or family members, and 99.6% (703/706) indicated that they would do so in the future.

When asked if anyone had given them written material about cervical cancer prevention, 96.3% (680/706) of the women responded “yes.” Of the 691 women who responded to the next question, 650 (94.1%) said that healthcare workers were responsible for handing out this material. Friends (7.5% or 52/691), family members (1.7% or 12/691), partners (0.4% or 3/691), and others (0.1% or 1/691) were other cited sources for such written material. (Note: The sum of these numbers is greater than 100% because some women received written material from multiple sources.)

Post-Treatment Partner Support

Of the 685 women who responded, 82.5% (565/685) said that they had shared any written material they had received about cervical cancer prevention with their husbands/partners.

Of the 641 women who said that they resumed intercourse after their treatment, 3.7% (24/641) said that they had problems trying to convince their husbands/partners to use condoms. Another 0.8% (5/641) of the women said that they did not try to ask their husbands/partners to use condoms. Overall, 95.5% of these women (612/641) did not have any problems trying to convince their husbands/partners to use condoms after treatment.

As a final question, the women were asked if there was any additional information they would have liked to receive, and 3.3% (23/706) said that there was. In addition, 1.7% (12/706) of the women indicated that they would have liked their husbands/partners to have received additional information.

HEALTHCARE PROVIDER INFORMATION

After the interviews, the nurses examined the women, performed VIA, recorded the results, and provided followup care for any women who required it. Of those assessed at 1 year (704 women in total), the results of their VIA tests were as follows: 0.1% (1/704) was assessed as having suspect cancer; 5.7% (40/704) were VIA test-positive; 93.9% (661/704) were VIA test-negative; and 0.3% (2/704) were VIA test-indeterminate. Those who were test-positive, and the 1 woman with suspect cancer (41 women total), were referred to Khon Kaen Hospital for ongoing management (and to participate in a followup study to assess the correlation between nurse VIA results at 1 year and doctor colposcopy assessment findings). The remaining 94.2% (663/704) of the women were counseled at this visit about their results and told to return in 5 years for retesting. (Subsequently, the test-negative women were asked to go to Roi-et Provincial Hospital for colposcopy and biopsy, as appropriate, as part of a second followup study to assess the test qualities of VIA 1-year post-cryotherapy treatment.)

DISCUSSION

The results of this project clearly illustrate that an SVA using VIA followed by immediate treatment with cryotherapy for those testing positive (or referral as indicated) is:

- *Safe* – There are minimal complications.
- *Acceptable* – Women will come for testing when it is offered if they know that good followup care is likely, and they will recommend the service to others.
- *Feasible* – Nurses, after brief intensive training and supervision, can safely provide testing and treatment in a primary care setting, rural health systems can accommodate both static and mobile prevention services, and incorporating cancer prevention services does not necessarily affect the provision of other services like family planning.

Moreover, with sustained *effort* (including cost and infrastructure), an SVA using VIA followed by immediate treatment with cryotherapy can achieve moderate population coverage and low referral of test-positives 1 year post-treatment.

The results of this project provide important *safety* information for policymakers in developing countries who are considering how to strengthen fledgling cervical cancer prevention programs. According to all available followup data, no clinically apparent PID or stenosis occurred as a complication of cryotherapy. Moreover, the overall rate of minor complications (within 12 months of treatment) resulting from cryotherapy performed by a trained nurse in a rural facility without the use of colposcopy was low (2.2%). It is possible, but very unlikely, that serious problems post-cryotherapy went unreported because project staff routinely inquired at local facilities about anyone coming in for health problems post-treatment, and the 3-month project followup data validate the findings from the problem visit form.

The single visit approach – based on the combination of VIA and cryotherapy – appeared to be *acceptable* not only to women, but also to their partners and to the project providers. Other, more qualitative methods of measuring acceptability would provide further insights into how acceptable the project was and what aspects may be in need of attention. Results of such a qualitative assessment are reported separately (Corneli, Gaffikin, and Baldwin 2003).

This experience in Thailand also demonstrates that it is *feasible* to maintain the logistics of refilling the carbon dioxide tanks and transporting the cryotherapy units from one institution to another (i.e., the mobile team approach). The relatively low number of working parts of the cryotherapy unit (that could malfunction) as well as targeting training in equipment care and maintenance contributed to the ability to maintain these units in the field. There were very few treatment postponements for clinic-related reasons; those that were postponed were concentrated in the very early phase when project logistics were being worked out.

The mean/median time to perform VIA and cryotherapy were 7.4/6 minutes and 23.4/22 minutes, respectively. Although the protocol called for a daily maximum of 10 women tested per session (average two providers per session) to allow time for the project data collection, the actual number of women screened on average per daily session was higher in some sites, indicating consistent demand for the service and an ability to safely meet this demand.

Adherence to the home care requirements and scheduled return visit rates was high (more than 90% for the 1-year visit). This likely reflects the quality of counseling about the reasons for

abstinence/condom use, the fact that women were offered the opportunity to postpone treatment if they felt they needed to negotiate this with their husband or partner, and the relatively high level of regard for the government medical system among rural Thai women. Costs are an important component of the *effort* required to implement and sustain a cancer prevention program. To assess this in the context of rural Thailand, a wide variety of screening and test-positive (for cervical neoplasia) case management approaches were computer-modeled to predict incidence and mortality reductions as well as costs associated with each approach. A complete description of the model, developed by the Georgetown University Lombardi Cancer Center, and full results from a simulation exercise to identify the optimal prevention approach, are provided elsewhere (Mandelblatt et al 2002).

Briefly, comparing each prevention approach to *no organized screening* (estimated at \$2 per woman in rural Thailand), the most cost-effective approach identified in that paper was VIA for women aged 35–55 followed immediately with cryotherapy (or referral if the lesion did not qualify for immediate treatment) every 5 years (Mandelblatt et al 2002). The approach that achieved the highest predicted mortality reduction also involved VIA-based testing followed by immediate treatment every 5 years among a larger cohort of women (ages 20–70), but at a higher cost.

Using that computer model, mortality reductions of more than 25% were only predicted if at least 70% of targeted women were tested each cycle. In this project, the population coverage achieved for the four participating districts was approximately 17% within 7 months (this calculates to 30% within 1 year assuming the same average monthly recruitment rate). Project experience suggests that 100% coverage of the four districts could be achieved within 5 years if the same level of program effort (including funding) were expended.

Project women, however, reported that the average time it took them to come to the facility was 14.5 minutes; therefore, these coverage rates reflect use of services by women living relatively close to a project facility. This, coupled with the fact that so many of the project women (53.9%) reported having been Pap-tested in the past (compared to the estimated overall rate in rural Thailand [5%]), suggests that the project results are not likely representative of women living in more rural areas of Thailand. The amount of effort required to reach the additional 40%–70% of women in the four districts (to achieve 70%–100% coverage) has yet to be determined. The current phase of the project focuses on this important question.

Because this demonstration project was designed to test the SVA as it would actually be implemented in a project in the field, VIA was the only disease status obtained before treatment (Blumenthal et al 2001). Therefore, actual treatment cure rates were not measurable. However, acetowhite lesions 1-year post-treatment provide an indication of the need for retreatment (and/or referral) and can be easily measured and monitored under non-research program conditions (e.g., as part of a routine quality assurance system).

Importantly, among those treated in this project, the test-positive rate at 1 year was only 5.7% (0.7% of the total population initially tested), or one cancer – a low-stage adenocarcinoma. Despite the possible failure or inappropriate initial application of cryotherapy regarding this woman, it could be argued that a low stage, treatable cancer discovered as part of the project may otherwise have gone unnoticed completely or until a much later (less treatable) stage. Given that the negative predictive value of VIA has repeatedly been reported as 96% or greater, the low test-positive rate measured at 1 year is an important assurance to policymakers that cancers were not

misdiagnosed in the first place (Belinson et al 2001; Megevand et al 1996; Sankaranarayanan et al 1999; University of Zimbabwe/JHPIEGO Cervical Cancer Project 1999).

It is noteworthy that in 98% of those treated, the SCJ was visible to the nurses (and to the clinical supervisors when they were present) 1 year later. A commonly held opinion regarding cryotherapy disadvantages is that, after the ablative procedure, the SCJ recedes into the cervical canal, is no longer visible, and therefore cannot serve as a landmark for the detection of precancerous lesions. The reason for our findings may be that in many assessments of cryotherapy undertaken primarily in the United States or Europe, younger, often nulliparous women were involved. In experiences among older, more parous women, the SCJ initially appeared to be well out on the face of the exocervix, such that even after cryotherapy had been performed and the cervix healed, the SCJ remained visible and further assessment by VIA was possible.

For more than 30 years, Thailand has struggled to make a successful cervical cancer prevention program based on a “test and refer” approach (i.e., cytology-based testing and referral of all test-positives for additional diagnostic tests, including biopsy and treatment, if indicated). Despite efforts to develop cyto-technology as a viable profession, national annual Pap smear screening coverage is low. Treatment for rural women with precancerous lesions is available only in select hospitals. While more work exploring the programmatic potential of VIA combined with cryotherapy is ongoing (in order to answer questions related to coverage, cost, sustainability, and cryotherapy effectiveness in the hands of non-physicians), the results of this project indicate that a SVA based on VIA and cryotherapy and performed by nurse midwives is safe, acceptable, and feasible. As such, and in light of the mounting cost-effectiveness data on the SVA, it should be considered an alternative for high-risk areas where the likelihood of successfully implementing a more traditional approach to cancer prevention is low (Goldie et al 2001; Mandelblatt et al 2002).

REFERENCES

- Abwao S et al (eds). 1998. *Prevention and Control of Cervical Cancer in the ESA Region*. Meeting Report. AVSC International, PATH, Pathfinder International, and JHPIEGO. 29 March to 1 April.
- Andersen ES and M Husth. 1992. Cryosurgery for cervical intraepithelial neoplasia: 10-year follow-up. *Gynecologic Oncology* 45: 240–242.
- Belinson JL et al. 2001. Cervical cancer screening by simple visual inspection after acetic acid. *Obstetrics & Gynecology* 98 :441–444.
- Blumenthal PD et al. 2001. Innovative approaches to cervical cancer prevention. *Medscape Women's Health* (online serial).
- Corneli A, L Gaffikin, and L Baldwin. 2003. *A Qualitative Evaluation of the Acceptability and Feasibility of a Single Visit Approach to Cervical Cancer Prevention*. JHPIEGO: Baltimore, MD.
- Cox JT. 1999. Management of cervical intraepithelial neoplasia. *Lancet* 353: 857–859.
- Cullins VE et al. 1999. Cervical cancer prevention using visual screening methods. *Reproductive Health Matters* 1: 134–143.
- Gaffikin L et al. 2003. Safety, acceptability, and feasibility of a single-visit approach to cervical-cancer prevention in rural Thailand: A demonstration project. *Lancet* Vol 361: 814–820.
- Goldie S et al. 2001. Policy analysis of cervical cancer screening strategies in low-resource settings: Clinical benefits and cost-effectiveness. *Journal of the American Medical Association* 285: 3107–3115.
- Holschneider CH et al 1999. A single-visit cervical carcinoma prevention program offered at an inner city church: A pilot project. *Cancer* 86(12): 2659–2667.
- IARCPress. 2001. GLOBOCAN 2000: Cancer Incidence, Mortality, and Prevalence Worldwide, Version 1.0. IARC CancerBase No. 5.
- JHPIEGO. 1999. *Atlas of Visual Inspection of the Cervix with Acetic Acid (VIA)*. JHPIEGO: Baltimore, MD.
- Kitchener HC and P Symonds. 1999. Detection of cervical intraepithelial neoplasia in developing countries. *Lancet* 353: 856–857.
- Limpaphayom K et al. 1997. The effectiveness of model-based training in accelerating IUD skill acquisition. *British Journal of Family Planning* 23(2): 58–61.
- Lonky NM et al. 1997. Selecting treatment for cervical disease (part 2). *OBG Management* (January): 63–70.

Mandelblatt JS et al. 2002. The benefits and costs of alternative strategies for cervical cancer screening in less developed countries: a case study from Thailand. *Journal of the National Cancer Institute* 94: 1-15.

McIntosh N, P Blumenthal, and A Blouse. 2001. *Cervical Cancer Prevention Guidelines for Low-Resource Settings* (draft). JHPIEGO: Baltimore, MD.

Megevand E et al. 1996. Acetic acid visualization of cervix: An alternative to cytologic screening. *Obstetrics and Gynecology* 88: 383-386.

Mitchell MF et al. 1998. A randomized clinical trial of cryotherapy, laser vaporization, and loop electrosurgical excision for treatment of squamous intraepithelial lesions of the cervix. *Obstetrics and Gynecology* 92: 737-744.

Morris DL et al. 1996. A comparison of the evaluation and treatment of cervical dysplasia by gynecologists and nurse practitioners. *Nurse Practitioner* 23: 101-114.

Nuovo J et al. 2000. Treatment outcomes for squamous intraepithelial lesions. *International Journal of Gynaecology & Obstetrics* 68: 25-43.

Parkin DM and R Sankaranarayanan. 1999. Prevention of cervical cancer in developing countries. *Thai Journal of Obstetrics and Gynaecology* 11 (1): 3-20.

Pisani P. 1998. International Agency for Research on Cancer. Personal communication.

Program for Appropriate Technology in Health (PATH). 1998. Preventing cervical cancer in low-resource settings. *Outlook* 16: 1.

Sankaranarayanan R et al. 1999. Visual inspection of the uterine cervix with acetic acid in the detection of cervical carcinoma and its precursors. *International Journal of Cancer* 80: 161-163.

Sivanesaratnam V. 1999. Problems in management of CIN. *Thai Journal of Obstetrics and Gynaecology* 11(1): 27-30.

University of Zimbabwe/JHPIEGO Cervical Cancer Project. 1999. Visual inspection with acetic acid for cervical cancer screening: Test qualities in a primary care setting. *Lancet* 353: 869-873. (University of Zimbabwe: Chirenje ZM, T Chipato, J Kasule, E Ngwalle, S Rusakaniko, and R Makunike/JHPIEGO: Gaffikin L, P Blumenthal, J McGrath, and H Sanghvi.)

Walboomers JMM et al. 1999. Human papilloma virus is a necessary cause of invasive cervical cancer worldwide. *Journal of Pathology* 189(1): 12-19.

World Health Organization (WHO). 1986. Control of cancer of the cervix uteri. A WHO meeting. *Bulletin of the World Health Organization* 64(4): 607-618.