PSI Health Impact Estimation Model for Cervical Cancer Prevention: Screening and Referral/Treatment

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PSI shares its models with all interested individuals or organizations. Please note that the models are updated periodically based on the latest available epidemiological, demographic, intervention effectiveness, and utilization data. As a result, numbers used in this document should be considered illustrative only. They show how the model works, but they may have changed since the time of writing.

For more information or the latest model updates, contact Hongmei Yang at hyang@psi.org.

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Background

Population Services International (PSI) is a social marketing organization that promotes healthy behaviors in low-income and vulnerable populations. PSI has programs in 65 countries (www.psi.org) and covers a wide range of health areas including prevention of cervical cancer through screening for precancerous cases, referral, and treatment. PSI uses the disability-adjusted life year (DALY) as the metric for measuring the impact of interventions in health areas. A DALY model has been developed for each of PSI’s product/services and behavior change communications (BCC) interventions. The DALY model presented here is the cervical cancer prevention (CCP) DALY model for early detection and treatment of precancerous lesions through screening and referral/treatment.

Cervical cancer is a leading cause of cancer death among women in low-income countries (WHO, 2011). Estimates from GLOBOCAN 2008 (Ferlay et al., 2010) indicate that there were 530,000 new cases of cervical cancer and 275,000 deaths from cervical cancer worldwide. The regions with the highest incidence of cervical cancer are Eastern and Western Africa, with age-standardized rates (ASRs) greater than 30 per 100,000. They are followed by Southern Africa (26.8 per 100,000), South-Central Asia (24.6 per 100,000), South America, and Middle Africa (ASRs 23.9 and 23.0 per 100,000, respectively).

Cervical cancer is almost always caused by the human papillomavirus (HPV) (Boshart et al., 1984; Parkin, 2002), which is transmitted through sexual intercourse. There are about 50 known types of HPV that can infect the genital areas but not all types cause abnormal changes in the cervix. The types of HPV commonly known to be carcinogenic (i.e., can cause cancer) include HPV types 16, 18, 31, 33, 35, 45, 52, and 58. Types 16 and 18 are responsible for about 70% of the cervical cancer cases (Clifford et al., 2006; Smith et al., 2007). The lifetime risk of HPV infection is high (50% to 80%) among sexually active women (Crum et al., 2003; Koutsky, 1997). Most HPV infections are transient and the virus is eliminated by the immune system 4 to 18 months after onset (Brown et al., 2005; Moscicki et al., 2006; Woodman et al., 2001). Sometimes, however, a small amount of the infection persists and causes lesions that may progress to invasive cancer. Such lesions are called precancerous lesions. Depending on histological changes, precancerous lesions are commonly classified as cervical intraepithelial neoplasia grades 1, 2, and 3 (CIN1, CIN2, and CIN3). Mild precancerous lesions (CIN 1) usually regress to normal. Moderate to severe precancerous lesions (CIN 2 and CIN3) are more likely to progress to invasive cancer (Goldie et al., 2001; Holowaty et al., 1999). The natural history of the development of cervical cancer is illustrated below in Wright and Schiffman, Figure 4 (Wright and Schiffman, 2003).
According to GLOBOCAN 2008, the worldwide deaths to cases ratio of cervical cancer is high, greater than 0.5 (Ferlay et al., 2010). One of the main reasons for the high deaths to cases ratio is the difficulty of early diagnosis. Women with precancerous lesions usually do not have any symptoms and therefore are unaware they have the disease. As a result, diagnosis and treatment are delayed. However, cervical cancer is a slow-growing disease; from the initial HPV infection, it usually takes many years for the cancer to develop. Cervical cancer is preventable if the precancerous lesions or other abnormalities are detected early and treated early.

Because women with precancerous lesions are typically unaware that the lesions are present, it is critical to screen women of reproductive age (15-49). The Pap smear, long used as the main screening method for cervical cancer, has been successful in reducing cervical cancer incidence rates and death rates in some developed countries (Sarian et al., 2005). However, because use of the Pap smear requires 1) multiple visits by the woman, 2) collection of cervical samples, and 3) skilled cytologists, the method has limited use in less developed (low-resource) countries. Similarly, HPV DNA testing is not suitable in these countries because it is expensive and requires a skilled lab specialist. A promising screening method for use in low-resource settings is visual inspection, which involves washing the cervix with diluted acetic acid or Lugol’s iodine, and then observing the cervix with naked eye—visual inspection with acetic acid (VIA) and visual inspection with Lugol’s iodine (VILI). The application of acetic acid causes the lesion areas to turn white. The application of iodine causes the normal tissue to be stained while the lesion areas appear unstained. The visual inspection method is safe, affordable, easy to do, and has good testing characteristics. Performance in detecting precancerous lesions is comparable to the Pap smear (Gaffikin et al., 2003; Gaffikin et al., 2007; Sarian et al., 2005).

A precancerous lesion that has been detected can either be destroyed or removed, depending on the size. For a lesion that does not exceed 75% of the transformation zone (the area adjacent to the border of the endocervix and ectocervix), cryotherapy—the use of freezing to destroy abnormal cells—is usually recommended. Otherwise, cold-knife conization—the use of a scalpel to remove a cone-shaped wedge from the cervix—or LEEP (loop electrosurgery excision procedure) are used. All three treatment methods have high efficacy: cryotherapy (85% to 95%), cold-knife conization (90% to 94%), and LEEP (90% to 98%) (WHO, 2006).

Currently, PSI has screening and treatment programs in Myanmar and Zimbabwe, and screening and referral programs in Cameroon, Kenya, Guatemala, Nicaragua, and Caribbean:

- For screening and treatment programs, PSI/local offices provide VIA screening services to women of reproductive age (15-49) and treat lesions that do not exceed 75% of the transformation area with cryotherapy. Women with larger (more advanced) lesions are referred to other health centers for excision treatment (i.e., conization).
- For screening and referral programs, PSI/local offices screen women of reproductive age (15-49) using VIA (except for Caribbean where PSI office uses Pap smear for screening) and refer those with lesions detected to other health centers for treatment.

The cervical cancer prevention health impact estimation model developed by PSI provides an estimate of DALYs averted per screening and referral/treatment (i.e., DALY coefficient). This report 1) describes the principles and structure of a simple deterministic model (in Excel) that estimates the health impact of screening and referral/treatment programs in DALYs averted per screening and referral or per screening and treatment, and 2) identifies the parameters and assumptions used in the model.
Section 1: Principles and Structure of the Model

1.1 Principles of the mathematical model

This section uses the example of the program that offers screening and treatment to describe the principles of the mathematical model. In a program that does not offer treatment (i.e., has only screening and referral) women found to have precancerous lesions are referred to other health centers for treatment. The proportion of referred women who seek for and receive treatment needs to be taken into consideration.

The model assumes the following:

\[ N = \text{Population of females who are at risk of cervical cancer} \]

\[ P = \text{Prevalence rate of precancerous lesions} \]

\[ S = \text{Sensitivity of VIA or Pap smear} \]

\[ Sp = \text{Specificity of VIA or Pap smear} \]

For a given female population at risk of cervical cancer \((N)\), \(x\) women test truly positive (i.e., women with precancerous lesion are detected to have the lesion) and \(y\) women test truly negative (i.e., women having no precancerous lesion are detected as having no such lesion). According to the definition of sensitivity and specificity, the following formulas are obtained:

\[ S = \frac{x}{N \times P} \quad (1) \]

\[ Sp = \frac{y}{N - N \times P} \quad (2) \]

Therefore, \(x = S \times N \times P\) and \(y = Sp \times N \times (1 - P)\).

The results of the screening for precancerous lesions are shown below in Table 1.1, a 2x2 table.

<table>
<thead>
<tr>
<th>Result</th>
<th>Precancerous lesions</th>
<th>No precancerous lesions</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIA positive</td>
<td>(X=S<em>N</em>P)</td>
<td>(N*(1-P)*(1-SP))</td>
<td>(S<em>N</em>P+N*(1-P)*(1-SP))</td>
</tr>
<tr>
<td>VIA negative</td>
<td>(N<em>P</em>(1-S))</td>
<td>(Y=Sp<em>N</em>(1-P))</td>
<td>(N<em>P</em>(1-S)+Sp<em>N</em>(1-P))</td>
</tr>
</tbody>
</table>

| Total      | \(N*P\)              | \(N-N*P\)              | \(N\)         |

Note: Numbers in black are original.

Given that precancerous lesions progress differently to invasive cancer and that visual inspection with acetic acid (VIA) of lesions of different grades (CIN1, CIN2, and CIN3+) can result in differences in the detection of positive cases (Arbyn et al., 2008; Melnikow et al., 1998; Myers et al., 2000; Sarian et al., 2005), the three cancer grades are considered separately in the modeling process. Table 1.2 shows the distribution of results of cervical cancer screening by grade of precancerous lesions.
### Table 1.2 Results of cervical cancer screening by grade of precancerous lesion

<table>
<thead>
<tr>
<th>Result</th>
<th>CIN1</th>
<th>CIN2</th>
<th>CIN3+</th>
<th>No precancerous lesions</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIA +</td>
<td>$S_1^*N^<em>P^</em> \text{ Prop}_1$</td>
<td>$S_2^*N^<em>P^</em> \text{ Prop}_2$</td>
<td>$S_3^*N^<em>P^</em> \text{ Prop}_3$</td>
<td>$N^<em>(1-P)^</em>(1-Sp)$</td>
<td></td>
</tr>
<tr>
<td>VIA -</td>
<td>$N^<em>P^</em> \text{ Prop}_1$</td>
<td>$N^<em>P^</em> \text{ Prop}_2$</td>
<td>$N^<em>P^</em> \text{ Prop}_3$</td>
<td>$N-N^*P$</td>
<td>$N$</td>
</tr>
</tbody>
</table>

$\text{Prop}_i = \text{Proportion of CIN1, CIN2, and CIN3+}$;  
$S_i = \text{sensitivity of VIA in detecting CIN1, CIN2, and CIN3+}$

Women who test positive when screened for cervical cancer receive cryotherapy immediately if the lesion area does not exceed 75% of the transformation zone. Those who test positive but have a larger lesion receive a referral for advanced treatment. From this, it is assumed that $a$ percent of the women screened have a lesion $\leq 75\%$ and receive cryotherapy, and $(1 - a)$ percent of the women screened have a lesion larger than 75% of the transformation zone and receive a referral for advanced treatment. Among women in the second group, $b$ percent seek and receive the advanced treatment (i.e., conization). The two figures below illustrate the cervical cancer screening and treatment process; Figure 1.1 shows PSI treated women, and Figure 1.2 shows PSI cases referred.

The last column in each figure shows the number of cervical cancer cases averted, given the lifetime likelihood that a precancerous lesion progresses to cancer ($r_i$), and the effectiveness of cryotherapy ($PE_i$) and conization ($PE_i'$) in treating precancerous lesions.

The total number of women screened is $N$.

The number of women who received treatment from PSI after screening is $N(1 - P)(1 - Sp)a + NPa \sum_{i=1}^{3} (S_i * \text{ Prop}_i)$ [see Figure 1.1].

The number of cases averted (lifetime) from PSI treatment is $NPa \sum_{i=1}^{3} (S_i * \text{ Prop}_i * r_i * PE_i)$ [see Figure 1.1].

The number of women who received a referral after screening is $N(1 - P)(1 - Sp)(1 - a) + NP(1 - a) \sum_{i=1}^{3} (S_i * \text{ Prop}_i)$ [see Figure 1.2].

The number of cases averted (lifetime) if $b$ percent of the referrals are treated is $NP(1 - a)b \sum_{i=1}^{3} (S_i * \text{ Prop}_i * r_i * PE_i')$ [see Figure 1.2].

Similarly, if the first-year progression rate to invasive cancer after the lesions are detected is $t_i$, the number of cases averted from PSI treatment in the first year after the detection of a lesion is $NPa \sum_{i=1}^{3} (S_i * \text{ Prop}_i * t_i * PE_i)$.  

The number of cases averted from PSI referral in the first year after the detection of a lesion is $NP(1 - a)b \sum_{i=1}^{3} (S_i * \text{ Prop}_i * t_i * PE_i')$. 

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**PSI**
Because PSI programs are implemented among women of reproductive age (15-49), the estimate of the burden of disease is restricted to this age group. Given that the risk of developing cervical cancer is related to age, it is appropriate to analyze women by age group in the modeling process. The GLOBOCAN 2008 (Ferlay et al., 2010) data provide age-specific incidence rates for three age groups (i.e., 15-39, 40-44, and 45-49). Therefore, the same age groups are used to estimate the burden of disease and the health impact of the PSI cervical cancer prevention program (see Sections 2 and 3 below).

1 Because the risk of developing cervical cancer varies substantially among women age 15 to 39, it would be informative if this broad age group were disaggregated into the smaller age groups 15-29, 30-34 and 35-39. The editor of GLOBOCAN 2008, Jacques Ferlay, was contacted about this matter but informed PSI that disaggregated data for the suggested age groups was not available from GLOBOCAN 2008 (personal communication from Jacques Ferlay, May 25, 2011). For all PSI platforms with cervical cancer prevention programs (except Zimbabwe), cervical cancer incidence and mortality data reported in GLOBOCAN 2008 are based on data from neighboring countries. This is because five of the six PSI countries covered in this report do not have cervical cancer databases, and Zimbabwe’s data come from a local cancer registry (Harare) and are not representative of the entire country.

Jacques Ferlay suggested the Cancer Incidence in Five Continents series (ci5.iarc.fr) as a source for cancer incidence data because it reports incidence from local cancer registries in five-year age groups. However, this source again only has data on Zimbabwe, and most of the data are from the Harare local cancer registry (covering the black population 1990-2002). Additionally, Ferlay advised that these figures should be used with caution because the Harare registry has the lowest histological verification rate in the series. Because no detailed prevalence data were available for five of the six PSI countries, and because the data available from Zimbabwe was described as being of poor quality, it was decided not to pursue estimating five-year incidence rates as described in a simulation model in an article by Mandelblatt et al. (Mandelblatt et al., 2002).
Figure 1.1 Cervical cancer screening and treatment process and number of people involved in each process, PSI treated

<table>
<thead>
<tr>
<th># Screened</th>
<th>Tested +</th>
<th>PSI Treated</th>
<th>Lifetime Risk of cancer if untreated</th>
<th>Cases averted</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN1</td>
<td>N<em>P</em> Prop1</td>
<td>S1<em>N</em>P* Prop1a</td>
<td>S1<em>N</em>P* Prop1a</td>
<td>S1<em>N</em>P* Prop1a*r1</td>
</tr>
<tr>
<td></td>
<td>S1<em>N</em>P* Prop1</td>
<td>S1<em>N</em>P* Prop1*(1-a)</td>
<td>referred</td>
<td>referred</td>
</tr>
<tr>
<td></td>
<td>&gt;75%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIN2</td>
<td>N<em>P</em> Prop2</td>
<td>S2<em>N</em>P* Prop2a</td>
<td>S2<em>N</em>P* Prop2a</td>
<td>S2<em>N</em>P* Prop2a*r2</td>
</tr>
<tr>
<td></td>
<td>S2<em>N</em>P* Prop2*(1-a)</td>
<td>referred</td>
<td>referred</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;75%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIN3</td>
<td>N<em>P</em> Prop3</td>
<td>S3<em>N</em>P* Prop3a</td>
<td>S3<em>N</em>P* Prop3a</td>
<td>S3<em>N</em>P* Prop3a*r3</td>
</tr>
<tr>
<td></td>
<td>S3<em>N</em>P* Prop3*(1-a)</td>
<td>referred</td>
<td>referred</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;75%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No precancerous lesions</td>
<td>N-N*P (1-Sp)*a</td>
<td>N*(1-P)*(1-Sp)*a</td>
<td>n/a</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>N*(1-P)<em>(1-Sp)</em>(1-a)</td>
<td>referred</td>
<td>referred</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;75%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total: \[
N = \frac{N(1 - P)(1 - Sp) + \sum_{i=1}^{3} (S_i \times Prop_i)}{NP} + \frac{N(1 - P)(1 - Sp)a + \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE_i)}{NPa} + \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE_i)
\]
Figure 1.2 Cervical cancer screening and treatment process and number of people involved in each process, PSI referred
Section 2: Estimating the Disease Burden of Cervical Cancer

The population size and age distribution of females age 15-49 are obtained from the United Nations’ world population prospects (United Nations Population Division, 2009). Detailed information about parameter values and data sources is available in Section 4 below.

For individuals in each age group, cases are estimated by multiplying the population at risk by the incidence rate of the disease. Deaths are estimated by multiplying the cases by case fatality rate, which is the ratio of cumulative death rate to cumulative case rate. To estimate the burden of disease in DALYs\(^2\), the methodology used is that presented in the Disease Control Priorities in Developing Countries (DCP2) report (Jamison et al., 2006). A woman with cervical cancer is assumed to go through four stages—an average of six years (Goldie et al., 2008)—before dying of cervical cancer at age 55 (Jamison et al., 2006). Stage I cancer (i.e., cancer that has invaded the cervix but is not growing outside the uterus) and Stage II cancer (i.e., cancer that has grown beyond the cervix and uterus but has not spread to the walls of the pelvis and the lower part of the vagina) are considered local. Stage III cancer is considered regional because it has spread either to the lower part of the vagina or to the walls of the pelvis or the lymph nodes in the pelvis, and stage IV cancer has spread to distant organs (American Cancer Society, 2010). It was estimated that 90% of the stage I cancer cases progressed to stage II within four years. It took three years for 90% of the stage II cancer cases to progress to stage III, and it took two years for 90% of the stage III cancer cases to progress to stage IV (Myers et al., 2000). The transition from a lower cancer stage to the next cancer stage is assumed to follow the Poisson distribution. The duration of each stage was therefore a stochastic variable following exponential distribution. Years of life lost due to disability (YLD) was then calculated by multiplying the duration of each stage by disability weight. Years of life lost due to premature death (YLL) was discounted at 3% for future years. Because cervical cancer occurs many years after high risk HPV infection and detection of precancerous lesion, the YLDs and YLLs of cervical cancer are discounted at 3% per year for number of years after detection of precancerous lesion but before diagnosis of the cancer (i.e., age at diagnosis minus age at screening).

Section 3: Estimating the Health Impact of the PSI Cervical Cancer Prevention Program

The second component of the DALY model estimates the impact of the cervical cancer prevention (CCP) program. For women in each of the three age groups, the model runs a scenario to estimate 1) how likely it is that a woman with a precancerous lesion will test positive and be treated by PSI or other health care providers, 2) how likely it is that she will develop invasive cancer if left untreated, and 3) how likely it is that she will be prevented from developing cancer if treated (see Figure 1). To estimate the cases averted per screening and treatment (i.e., cases averted coefficient for screening and treatment), we divide the cases averted from the population by the number of women treated. To estimate the cases averted per screening and referral (i.e., cases averted coefficient for screening and referral), we divide the cases averted from the population by the number of women referred. Deaths averted coefficients were obtained by multiplying cases averted coefficients by the case fatality rate. The cases averted and deaths averted

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\(^2\) A DALY is defined as one healthy year of life lost due to premature death and/or disability from a disease. It measures the gap between current health status and an ideal situation where everyone lives into old age free from disease and disability. In our model, a global standard life expectancy at birth of 81.25 years and an average age at death from cervical cancer of 55 years were used to calculate the number of years of life lost (YLL) due to premature death. A 3% time discounting was applied for future years but no age weighting was applied in the modeling (i.e., DALY (0.03,0)).
coefficients are then translated into an equivalent figure measured in DALYs averted per screening and treatment or per screening and referral.

Section 4: Parameters and Data Sources

Table 4.1 Incidence rate and death rate for cervical cancer among women, by age group (15-39, 40-44, and 45-49), selected countries

<table>
<thead>
<tr>
<th>Country</th>
<th>15-39</th>
<th>40-44</th>
<th>45-49</th>
<th>Cumulative risk (0-74)</th>
<th>15-39</th>
<th>40-44</th>
<th>45-49</th>
<th>Cumulative risk (0-74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameroon</td>
<td>0.00007</td>
<td>0.000377</td>
<td>0.000598</td>
<td>2.5%</td>
<td>0.000027</td>
<td>0.00019</td>
<td>0.000361</td>
<td>1.9%</td>
</tr>
<tr>
<td>Guatemala</td>
<td>0.00018</td>
<td>0.000654</td>
<td>0.000858</td>
<td>2.9%</td>
<td>0.000041</td>
<td>0.000262</td>
<td>0.000382</td>
<td>1.5%</td>
</tr>
<tr>
<td>Kenya</td>
<td>0.000059</td>
<td>0.00047</td>
<td>0.000376</td>
<td>2.7%</td>
<td>0.000024</td>
<td>0.000235</td>
<td>0.000226</td>
<td>2.1%</td>
</tr>
<tr>
<td>Myanmar</td>
<td>0.000114</td>
<td>0.000548</td>
<td>0.000688</td>
<td>2.8%</td>
<td>0.000026</td>
<td>0.000159</td>
<td>0.00031</td>
<td>1.6%</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>0.000216</td>
<td>0.000743</td>
<td>0.001046</td>
<td>4.1%</td>
<td>0.000051</td>
<td>0.000278</td>
<td>0.000466</td>
<td>2.3%</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>0.000099</td>
<td>0.000935</td>
<td>0.000991</td>
<td>5.3%</td>
<td>0.000038</td>
<td>0.000446</td>
<td>0.000566</td>
<td>3.9%</td>
</tr>
<tr>
<td>Caribbean</td>
<td>0.000145</td>
<td>0.000308</td>
<td>0.000428</td>
<td>2.1%</td>
<td>0.000031</td>
<td>0.000114</td>
<td>0.000172</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

Source: GLOBOCAN 2008 (Ferlay et al., 2010)

Table 4.2 Percentage of women at risk of cervical cancer by age group (15-39, 40-44, and 45-49), selected countries

<table>
<thead>
<tr>
<th>Country</th>
<th>15-39</th>
<th>40-44</th>
<th>45-49</th>
<th>Population at risk (all ages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameroon</td>
<td>39.88%</td>
<td>4.13%</td>
<td>3.46%</td>
<td>8929000</td>
</tr>
<tr>
<td>Guatemala</td>
<td>39.19%</td>
<td>4.12%</td>
<td>3.35%</td>
<td>6509000</td>
</tr>
<tr>
<td>Kenya</td>
<td>41.31%</td>
<td>3.94%</td>
<td>3.33%</td>
<td>17935000</td>
</tr>
<tr>
<td>Myanmar</td>
<td>44.42%</td>
<td>6.36%</td>
<td>5.60%</td>
<td>24659000</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>42.63%</td>
<td>4.84%</td>
<td>4.22%</td>
<td>2747000</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>42.03%</td>
<td>3.50%</td>
<td>3.39%</td>
<td>6429000</td>
</tr>
<tr>
<td>Caribbean</td>
<td>39.80%</td>
<td>6.90%</td>
<td>5.40%</td>
<td>20233000</td>
</tr>
</tbody>
</table>


Table 4.3 Characteristics of cervical cancer screening and treatment methods and variables related to precancerous (PC) lesions

<table>
<thead>
<tr>
<th>PC lesions</th>
<th>Proportion of PC lesions</th>
<th>Sensitivity of VIA</th>
<th>Treatment efficacy of cryotherapy</th>
<th>Treatment efficacy of conization</th>
<th>Progression to invasive cancer, lifetime</th>
<th>Year-1 progression rate to cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN 1</td>
<td>58.5%</td>
<td>49.4%</td>
<td>90.0%</td>
<td>92.0%</td>
<td>1.0%</td>
<td>0.05%</td>
</tr>
<tr>
<td>CIN 2</td>
<td>29.2%</td>
<td>77.7%</td>
<td>87.9%</td>
<td>87.9%</td>
<td>5.0%</td>
<td>0.15%</td>
</tr>
<tr>
<td>CIN 3+</td>
<td>12.3%</td>
<td>82.9%</td>
<td>84.1%</td>
<td>88.6%</td>
<td>13.0%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

Source: aArbyn et al., 2008; bAlliance for Cervical Cancer Prevention (ACCP), 2003; cOstor AG, 1993; dHolowaty et al., 1999 (estimated by halving the progression rate in the first two years reported in Table 1).

Specificity of VIA in detecting CIN1+: 87% (Arbyn et al., 2008)
Specificity of Pap smear in detecting CIN1+: 96.8% (AHCPR, 1999; Mayrand et al., 2007)
Sensitivity of Pap smear in detecting CIN1: 49.4%, CIN2 and CIN3: 55.4% (AHCPR, 1999; Mayrand et al., 2007)

Proportion of detected lesions that are ≤75% of the cervical area: 80%. Goldie et al. (2005) has used visual inspection to determine whether women with positive results on screening are eligible for cryosurgery. A lesion covering more than 75% of the cervix is a major criterion for ineligibility. The study reported that 15% of those with CIN grade 1 and 25% of those with CIN grade 2 or 3 lesions would be ineligible for cryotherapy based on visual inspection. From these figures, PSI assumes that 20% of women will be ineligible (mainly because the detected lesion is greater than 75% of the cervical area).

Proportion of filled referrals: 20% (assumption; platforms are suggested to collect such data to update this assumption)

Table 4.4 Cancer-related variables by cancer stage (I-IV)

<table>
<thead>
<tr>
<th>Cancer stage</th>
<th>Progression rate to next stagea</th>
<th>Duration (years)b</th>
<th>Disability weightc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I (T1, N0, M0)</td>
<td>0.9/4 yrs</td>
<td>1.745</td>
<td>0.08</td>
</tr>
<tr>
<td>Stage II (T2, N0, M0)</td>
<td>0.9/3 yrs</td>
<td>1.102</td>
<td>0.08</td>
</tr>
<tr>
<td>Stage III (T3, N0, M0 or T1-3, N1, M0)</td>
<td>0.9/2 yrs</td>
<td>0.532</td>
<td>0.75</td>
</tr>
<tr>
<td>Stage IV (T4, N0, M0 or any T, any N, M1)</td>
<td>-</td>
<td>2.621</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Source: aMyers et al., 2000; bCalculated by assuming that the transition from a lower cancer stage to the next stage follows Poisson distribution; cJamison et al., 2006

Duration of cervical cancer to death (years): 6 (Goldie et al., 2008)

Age at death: 55 (calculated based on age-specific death data reported by GLOBALCANC 2008 (Ferlay et al., 2010)

Life expectancy (years): 81.25 (PSI default, which equals life expectancy for the Japanese (Jamison et al., 2006))

Section 5: Limitations

The PSI model is static, capturing the current situation only. It does not account for changes in the distribution of CINs that may result from sustained large-scale implementation of the intervention. If, after a rollout phase, most women are regularly screened and positive results are treated, it can be expected that (at a population level) most lesions tested and treated will be CIN grade 1 and that CIN grades 2 and 3 lesions will be observed less frequently. Because most CIN1 lesions regress to normal and only 1% progress to cancer, the number of DALYs averted per screen & treat or per screen & refer will decrease over time. There may be an optimal frequency for screen & treat/screen & refer to maximize DALY coefficients without significantly reducing the total number of DALYs averted.
Incidence rates and death rates for women age 15 to 39 are the same in the PSI model although, in reality, they increase non-linearly with age. The incidence and death data for all PSI platforms except Zimbabwe were obtained based on data from neighboring countries. Because carrying out in-depth calculations on such data is risky, PSI did not estimate the five-year age group rates for women age 15 to 39.

Section 6: Selected Formulas in the Excel Model

6.1 Formulas for burden of disease for cancer

Cancer cases in age group j =
Population at risk in age group j × Incidence rate in age group j

Deaths in age group j =
Cancer cases in age group j × Case fatality rate

DALYs in age group j =
Cancer cases in age group j × YLD + Deaths in age group j × YLL

6.2 Health impact of screening and treatment programs

Formulas for lifetime impact (PSI treated and PSI referred)

Cases averted in age group j per screening and treatment, **PSI treated**, lifetime =

\[
P_j \times \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE_i) \\
\frac{1 - P_f}{(1 - S_p) + P_j \sum_{i=1}^{3} (S_i \times Prop_i)}
\]

Cases averted in age group j per screening and treatment, **PSI referred**, lifetime =

\[
P_j \times b \times \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE'_i) \\
\frac{1 - P_f}{(1 - S_p) + P_j \sum_{i=1}^{3} (S_i \times Prop_i)}
\]

Where,

- \( r_i \) = Lifetime progression rate from precancerous lesions (CIN1, CIN2 and CIN3+) to invasive cancer
- \( Prop_i \) = Proportion of CIN1, CIN2, and CIN3+
- \( S_i \) = Sensitivity of VIA in detecting CIN1, CIN2 and CIN3+
- \( Sp \) = Specificity of VIA in detecting precancerous lesions (i.e., CIN1+)
$P_j = \text{Prevalence rate of precancerous lesions in age group } j, \text{ which equals } l_j / \sum_{i=1}^{3} (prop_i \times t_i)$

Where,

$I_j = \text{Incidence rate of cervical cancer in age group } j.$

$t_i = \text{First year progression rate of precancerous lesions to invasive cancer since dysplasia was detected}.$

$PE_i = \text{Treatment efficacy of cryotherapy}$

$PE_i' = \text{Treatment efficacy of conization}$

**Formulas for year one impact (PSI treated and PSI referred)**

*Cases averted in age group } j \text{ per screening and treatment, PSI treated, year one =}*

$$\frac{P_j \times \sum_{i=1}^{3} (S_i \times Prop_i \times t_i \times PE_i)}{(1 - P_j)(1 - Sp) + P_j \sum_{i=1}^{3} (S_i \times Prop_i)}$$

*Cases averted in age group } j \text{ per screening and treatment, PSI referred, year one =}*

$$\frac{P_j \times b \times \sum_{i=1}^{3} (S_i \times Prop_i \times t_i \times PE_i')}{(1 - P_j)(1 - Sp) + P_j \sum_{i=1}^{3} (S_i \times Prop_i)}$$

Where,

$Prop_i = \text{Proportion of CIN1, CIN2, and CIN3+}$

$b = \text{Proportion of referred women who received treatment}$

$S_i = \text{Sensitivity of VIA in detecting CIN1, CIN2 and CIN3+}$

$Sp = \text{Specificity of VIA in detecting precancerous lesions (i.e., CIN1+)}$

$P_j = \text{Prevalence rate of precancerous lesions in age group } j, \text{ which equals } l_j / \sum_{i=1}^{3} (prop_i \times t_i)$

Where,

$I_j = \text{Incidence rate of cervical cancer in age group } j.$

$t_i = \text{First year progression rate of precancerous lesions to invasive cancer since dysplasia was detected}.$

$PE_i = \text{Treatment efficacy of cryotherapy}$

$PE_i' = \text{Treatment efficacy of conization}$
6.3 Health impact of screening and referral programs

Figure 6.1 below shows the PSI cervical cancer screening and referral process, and the number of people involved in each step of the process. The formulas used to calculate the health impact of PSI screening and referral programs follow similar logic to those used to calculate the health impact of PSI screening and treatment programs (discussed above in Section 6.2), and are presented below for lifetime and year one screening and referral programs.

Figure 6.1 Cervical cancer screening and referral process, and number of people involved in each step of the process

Formulas for calculating cases averted per screening and referral (lifetime and year one)

Cases averted in age group j per screening and referral, lifetime =

$$ P_j \times a \times b \times \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE_i) + P_j \times (1 - a) \times b \times \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE_i) $$

$$ \frac{(1 - P_j)(1 - Sp) + P_j \sum_{i=1}^{3} (S_i \times Prop_i)}{1 - P_j} \times \sum_{i=1}^{3} (S_i \times Prop_i \times r_i \times PE_i) $$
Cases averted in age group \( j \) per screening and referral, year one =

\[
P_j \times a \times b \times \sum_{i=1}^{3} (S_i \times \text{Prop}_i \times t_i \times \text{PE}_i) + P_j \times (1 - a) \times b \times \sum_{i=1}^{3} (S_i \times \text{Prop}_i \times t_i \times \text{PE}')
\]

\[
\frac{1 - P_i}{(1 - P)}(1 - Sp) + P_j \sum_{i=1}^{3} (S_i \times \text{Prop}_i)
\]

Where,
\( r_i \) = Lifetime progression rate from precancerous lesions (CIN1, CIN2 and CIN3+) to invasive cancer
\( \text{Prop}_i \) = Proportion of CIN1, CIN2, and CIN3+
\( a \) = Proportion of precancerous lesions that do not exceed 75% of the transformation zone
\( b \) = Proportion of referred women who received treatment
\( S_i \) = Sensitivity of VIA in detecting CIN1, CIN2 and CIN3+
\( Sp \) = Specificity of VIA in detecting precancerous lesions (i.e., CIN1+)
\( P_j \) = Prevalence rate of precancerous lesions in age group \( j \), which equals \( l_j / \sum_{i=1}^{3} (\text{Prop}_i \times t_i) \)

Where,
\( l_j \) = Incidence rate of cervical cancer in age group \( j \).
\( t_i \) = First year progression rate of precancerous lesions to invasive cancer since dysplasia was detected
\( \text{PE}_i \) = Treatment efficacy of cryotherapy
\( \text{PE}'_i \) = Treatment efficacy of conization
References


