

# Impact of Increasing Papanicolaou Test Sensitivity and Compliance: A Modeled Cost and Outcomes Analysis

F. J. MONTZ, MD, KM, FREDRIC L. FARBER, ROBERT E. BRISTOW, MD, AND  
TERRI CORNELISON, MD, PhD

**Objective:** To model the impact of increasing screening compliance or implementing liquid-based cytology in populations with known compliance patterns and risk profiles on rates of detection of cervical precancers.

**Methods:** An adaptation of a time-varying Markov model was used to follow a theoretic cohort of 100,000 women from age 20 through age 80. Separate analyses of all women, white, and black women were completed using three compliance rates (self-reported, Healthy People 2000, and Healthy People 2010 compliance) and two Papanicolaou test sensitivities (conventional Papanicolaou smear and liquid-based cytology).

**Results:** All populations benefited from both increased compliance and liquid-based cytology use. Increasing compliance to Healthy People 2010 goals resulted in 23%, 21.7%, and 17% reductions in cervical cancer incidence for all women, white, and black women, respectively. Substituting liquid-based cytology for traditional Papanicolaou smear collection and processing with no change in compliance resulted in 32%, 32%, and 33% reductions in cervical cancer incidence for the same three subpopulations. In addition, cost-effectiveness of the liquid-based technology indirectly related to the risk profile of the population: for black women, the cost-effectiveness ratio was \$10,335 per life year saved, whereas for white women, the ratio was \$17,967 per life year saved.

**Conclusion:** Using liquid-based cytology in all populations would be cost-effective in improving outcomes from cervical cancer. In high-risk populations, this new technology may represent the most cost-effective approach to improve cervical cancer outcomes. (Obstet Gynecol 2001; 97:781–8. © 2001 by The American College of Obstetricians and Gynecologists.)

In 1998, there were an estimated 13,700 new cases of squamous cell carcinoma of the cervix and an associated 4900 deaths in the United States.<sup>1</sup> This represents a remarkable 79% reduction in incidence and a 75% reduction in mortality since 1950.<sup>1</sup> This reduction is largely attributable to the widespread use of cervical cancer screening using exfoliative cytology (ie, the Papanicolaou smear). Unfortunately, it is evident that not all members of American society have benefited equally from the introduction of the Papanicolaou smear as there is a significant difference in disease incidence based on risk profiles, many of which are socioculturally linked. According to Surveillance, Epidemiology, and End Results (SEER) data, black and Hispanic women have cervical cancer incidence rates 39% and 85% higher than white women, respectively.<sup>1</sup>

There is a generally held belief that subpopulations having higher incidence rates are also not screened as frequently.<sup>2</sup> Over the past decade, there have been concerted efforts to increase the proportion of the population of the United States that undergoes regular Papanicolaou smear screening. Healthy People 2000, a goal-setting white paper published in 1990 by the United States Department of Health and Human Services, listed as an objective to “increase to at least 95% the proportion of women aged 18 and older with uterine cervix who have ever received a Papanicolaou test, and to at least 85% those who received a Papanicolaou test within the preceding 1 to 3 years.”<sup>3</sup> This program has been recently updated to the Healthy People 2010 goals, which call for 97% of women to have

---

From the Kelly Gynecologic Oncology Service, The Johns Hopkins Hospital and Medical Institutions, Baltimore, Maryland.

Supported, in part, by an unrestricted grant from Cytyc Corporation, Boxboro, MA.

## Financial Disclosure

Dr. Montz has received an honorarium for participating in a conference sponsored by Cytyc Corporation.

ever received a Papanicolaou smear and 90% to have been screened within the preceding 3 years.<sup>4</sup> In 1990, Congress passed the Breast and Cervical Cancer Mortality Act, which resulted in the Center for Disease Control's National Breast and Cervical Cancer Early Detection Program.<sup>5</sup> These programs have been successful in increasing the number of women screened as measured by the Behavioral Risk Factor Surveillance System.<sup>6</sup>

However, when collating compliance data and incidence rate information for the various subpopulations, it is not clear that lack of prescribed Papanicolaou smear screening can fully explain the increased incidence of disease in all cases. In particular, black women have consistently reported a higher compliance with regular Papanicolaou smear screening since the late 1980s, yet these women continue to have elevated incidence and mortality rates of cervical cancer.<sup>1,6-8</sup> Therefore, there is still needed improvement in providing the most efficient screening program for high-risk populations.

Despite the success of Papanicolaou smear-based screening for cervical cancer precursors, considerable debate remains regarding the sensitivity of this test with published reports ranging from 15% to 95%.<sup>9</sup> A recently published report from the Agency for Health Care Policy Research determined, using an extensive meta-analysis, that the best estimate for the sensitivity of the Papanicolaou smear in a screening setting is approximately 51%.<sup>8</sup>

The recent regulatory approval of new devices purporting to improve the sensitivity of the Papanicolaou test may provide additional technologies to reduce cervical cancer incidence and mortality in a variety of populations. In particular, liquid-based cytology testing has been approved by the Food and Drug Administration.<sup>10</sup> This technology apparently decreases difficulties in specimen preparation by providing a standardized fluid for collection and automates the process of transferring the specimen to a microscope slide. The reported result is at least a 50% reduction in the false-negative rate compared with the traditional Papanicolaou smear including a significant increase in the detection rate of high-grade squamous intraepithelial lesion.<sup>9</sup> Use of this test in conjunction with ongoing efforts to increase the coverage of the cervical cancer screening program may yield even greater benefits in terms of a reduction in cervical cancer mortality.

A theoretical model has been developed to determine the advantage of using liquid-based cytology<sup>11</sup> in populations with different risk profiles for cervical cancer. To show the impact of compliance and test sensitivity, a variety of assumptions concerning these two variables were modeled in the populations. We proposed to use a modification of this model that includes outcome changes related to different risk profiles and frequency

of screening, to determine the cost-effectiveness of liquid-based cytology.

## *Materials and Methods*

A time-varying, longitudinal model that submits a theoretical cohort of women to Markov state transitions each year over the course of screening has been developed and described in detail elsewhere.<sup>11</sup> In simple terms, the model follows an idealized group of women over a given time period, subjecting them to death and other disease states at standard rates, using reference statistics such as those reported by the National Center for Health Statistics. Simultaneously, other events or interventions are added to the model with any impact on death or other disease states determined. Again, standard or widely accepted reference values are used in determining the effect the event or intervention may have.

Our model was implemented as an Excel (Microsoft Corp., Redmond, WA) spreadsheet and applied to 100,000 20-year-old women screened until age 80. Three specific and different populations were evaluated: all women, white, and black women.

For each year in the model, members of the cohort were assigned to a variety of health outcomes. These outcomes included: death from other causes, contraction of cervical cancer, death from cervical cancer, cervical cancer survivor, hysterectomy, true negative screening, true positive (all grades of cervical intraepithelial neoplasia [CIN], carcinoma in situ [CIS], or squamous cell cancer found on colposcopy) screening, false-negative screening, and false-positive screening. All women who had a positive screening test were forwarded to colposcopy and treated appropriately. The model assumes a woman treated for CIN is returned to the screening pool and has the potential to develop CIN again over the course of screening. Women who were cervical cancer survivors or who had a hysterectomy for any reason were removed from the screening pool.

In reporting the results of the model, the different screening modalities were compared with a reference strategy (conventional Papanicolaou smear screening with 10% rescreening). Hence, the cost-effectiveness of each of the methods is presented separately in comparison with this reference strategy.

The women in the model were subject to death from all causes at the rate reported by the National Center for Health Statistics<sup>12</sup> for the subpopulations being modeled. Data from the National Cancer Institute's SEER Cancer Statistics Review were used for the cervical cancer incidence rates, death rates from cervical cancer,

as well as 5-year survival rates for cervical cancer<sup>1</sup> for the specific subpopulations being modeled.

Over the course of the screening regimen, a significant proportion of the cohort underwent a hysterectomy for benign conditions. These women were considered to be no longer at risk for squamous cell carcinoma of the cervix and were hence removed from the screening pool and modeled not to receive any further screening tests. Age-specific rates of hysterectomy as published by the Center for Disease Control were used to estimate the number of hysterectomies that would occur in the subpopulation being modeled.<sup>13</sup>

For purpose of modeling, the baseline value for the false-negative rate of the conventional Papanicolaou smear was estimated to be 49% and that of liquid-based cytology 27%. Sensitivity analyses were run using these baseline values for the false-negative rate of the conventional Papanicolaou smear and liquid-based cytology. In addition, the model was executed for liquid-based cytology substituting two other false-negative rates (20% and 40%), which bracketed the base case estimate of 27%.

A subanalysis was performed for the remaining members of the cohort once they reached age 50 until the final screening at age 80. This was done to compare the effect of increased compliance with the effect of liquid-based cytology on disease outcomes in elderly women in terms of average number of cancers per year.

The model makes certain assumptions about the course of the disease as it progresses to cervical cancer. The incidence of CIN lesions in the population is age specific as described by Reid and Fu.<sup>14</sup> The mean age of women with any CIN lesion is 35 with a peak incidence of 3550 per 100,000 women at age 29. In this model, all CIN lesions regress at the rate of 65% over 6 years for ages 20–34 and 40% over 6 years for ages 35 plus.<sup>9,14</sup> Thirty-five percent of CIS lesions regress over 6 years.<sup>9</sup> Progression proceeds in two stages from CIN of any grade to CIS and from CIS to cancer. Progression is modeled based on the incidence rates at each stage. Progression from CIN to CIS occurs in 6 years, whereas progression from CIS to cancer occurs in ten.<sup>15</sup> To account for interval cancers, 10% of all CINs that will ever progress to cancer will do so within 1 year.<sup>16</sup>

The model computes the age-specific potential likelihood of a CIN progressing to cancer based on the population-specific SEER incidence rates of cervical cancer,<sup>1</sup> the rate of CIN in the population,<sup>14</sup> and the age-specific rate ratio between an unscreened population and a screened population as reported by Gustafsson et al.<sup>17</sup> The rate ratio is the ratio of cancer incidence in an unscreened population to the cancer incidence in a screened population.

Three sets of compliance assumptions were modeled

for each of the three subpopulations: self-reported compliance rates, compliance using Healthy People 2000 goals, and Healthy People 2010 goals. Compliance rates were divided into the following three categories: 1) never compliant: women who have never had a Papanicolaou smear, 2) partially compliant: women who have had a Papanicolaou smear but not in the last 3 or more years, and 3) fully compliant: women who have had a Papanicolaou smear in the last 3 years or less.

The self-reported compliance rates are based on data reported by the Behavioral Risk Factor Surveillance System for 1997.<sup>6</sup> Rates of women never having had a Papanicolaou smear were used as a surrogate for non-compliance. Rates of women reported having had a Papanicolaou smear in the last 2 years were used to determine the rate of compliant women in the population. The difference in the rates between noncompliant and compliant women was used as the partially compliant rate. The Healthy People 2000 rates were modeled as 5% never compliant, 85% fully compliant, and 10% partially compliant women.<sup>3</sup> Healthy People 2010 compliance rates were modeled as 3% never compliant, 90% fully compliant, and 7% partially compliant.<sup>4</sup>

The model further makes the arbitrary assumption that fully compliant women are divided equally between those women screened annually, biannually, and triennially. Half of the partially compliant women are screened every 5 years, and the other half are screened once every 10 years. Noncompliant women have incidence rates of cervical cancer equal to the rate in an unscreened subpopulation.

Table 1 shows the costs associated with the screening methods analyzed. The reference visit at which the initial Papanicolaou smear is obtained is assumed to be well-woman health care. As such, there is no cost applied for these visits in the model. In reality, it may be that a given percentage of well-woman visits are purely the end result of a woman desiring cervical cancer screening. This percentage is unknown and therefore the above assumption was made.

The median charges to indemnity insurers for the specified Common Procedural Terminology-4 codes<sup>18</sup> were used for follow-up of squamous intraepithelial lesion and treatment of CIN. Charges<sup>19</sup> were used so as to bias the model against new technologies that could result in more cases forwarded to follow-up. The estimated costs for initial and end-stage treatments for cervical cancer were weighted averages of the SEER incidence rates by stage and the costs as reported by Brown and Garber.<sup>20</sup> The incidence by stage is assumed to be constant regardless of the screening frequency modeled. All costs are in 1997 United States dollars.

The main outcome measure of the model is the average incidence of cervical cancer over the course of

**Table 1.** Intervention Costs (1997 United States Dollars)

	Cost	Comments
Revisit cost <sup>17</sup>	\$37.00	CPT 99212—median reimbursement
Conventional Papanicolaou smear with 10% rescreening	\$9.75	\$1.50 preparation \$7.50 screening \$0.75 manual rescreening
Liquid-based cytology	\$19.50	\$1.50 preparation \$7.50 screening \$0.75 manual rescreening \$9.75 disposable
Colposcopy <sup>17</sup>	\$362	CPTs 57454 and 88305
CIN I treatment <sup>17</sup>	\$185	CPT 57511
CIN II/III treatment <sup>17</sup>	\$796	CPTs 57522 and 88307
Treatment costs for cervical CA <sup>18</sup>	\$18,880	Mean charges with hysterectomy as principal procedure plus radiation therapy
Costs for dying of cervical CA <sup>18</sup>	\$30,363	
Yearly costs for CA survivors <sup>19</sup>	\$1000	
Survivor and monetary discount rates	3%	

CPT = common procedural terminology; CIN = cervical intraepithelial neoplasia; CA = cancer.

Base case values for CPT-4 codes are median values for charges to indemnity insurers and are used to bias results against tests that would increase the number of follow-up examinations.

Device costs are based on manufacturer's quoted prices.

Costs for dying and ongoing treatment of cervical cancer are based on a weighted average of the costs by stage at diagnosis.

screening. This can be directly compared with the average reported incidence of cervical cancer for the same ages (20 through 80). The model produces results in terms of life years saved compared with conventional Papanicolaou smear screening with 10% rescreening. The number of cervical cancer cases and deaths in the unscreened cohort are predicted from the SEER data<sup>1</sup> for incidence and the age-specific rate ratio.<sup>17</sup> The costs in 1997 dollars of a particular screening program are calculated based on the costs shown in Table 1.

Both benefits (life years saved) and costs (dollars) are discounted on an annual basis. The purpose of this discounting is to correct for the impact of inflation, realizing that the so called "buying power" of a single dollar in 1 year is generally less than the "buying power" of a single dollar in the subsequent year. This discounting allows for results to be reported in dollars using a fixed date (1997 for the purposes of this study). The results presented in this paper use a 3% per year discount rate for both costs and benefits. The model also reports the undiscounted average yearly incidence of cervical cancer that would occur in the cohort during the course of screening.

## Results

Table 2 shows the base results of the model in terms of yearly average cancer incidence over the course of the screening regimen. The expected incidence is calculated for each population based on reported SEER incidence data.<sup>1</sup> For the full population, the SEER data predict 12.4 cancers per year, and the base model predicts 11.8 cancers per year for the reported compliance numbers in the full population using the conventional Papanicolaou smear with a 51% sensitivity. The SEER data predict that there would be 11.8 yearly cancers in the white population and the model predicts that white women would have an average of 10.8 cancers per year. For black women, the SEER data predict there would be 15.1 cancers per year, and the model predicts 13.5 cases per year. The fact that the model predicts values that are generally within 10% of the reported data from SEER validates this approach as a means to test the effectiveness of cervical cancer screening programs.

The use of a liquid-based cytology test with current compliance patterns has the potential to reduce cervical cancer incidence for all subpopulations by approximately 32% regardless of the subpopulation studied. Increasing compliance to Healthy People 2000 goals using conventional Papanicolaou smears has the potential to reduce cervical cancer incidence for the full population by 10.9%, white women by 10.8%, and black women by 6.8%. If Healthy People 2010 goals were achieved with the conventional Papanicolaou smear, the model predicts reductions in cancer incidence of 22.9%, 21.7%, and 17% for all women, white, and black women, respectively. If Healthy People 2010 goals were achieved in conjunction with the use of liquid-based cytology, there would be reductions in cancer incidence of 50%, 50%, and 46.7% for all women, white, and black women, respectively, compared with reported compliance rates with the conventional Papanicolaou smear.

Table 2 also shows the results of the sensitivity analyses for liquid-based cytology. It can be seen from the table that even at a 20% improvement in the false-negative rate as compared with the conventional Pap smear (40% false-negative rate), liquid-based cytology has the potential to improve outcomes by more than 17% for all populations and all compliance rates studied.

Table 3 shows that use of liquid-based cytology would be cost-effective if implemented in any of the three studied populations. Based on current compliance patterns, a liquid-based cytology test would cost an incremental \$15,296 per life year saved for the full population, \$17,967 per life year saved for white women, and \$10,335 for black women screened for cervical cancer. If the Healthy People 2010 goals are



**Table 2.** Average Yearly Cancer Incidence of Cervical Cancer for Women Screened From Age 20 Through Age 80 at Different Compliance Rates

		Self-reported compliance rate <sup>4</sup>		
		All women	White women	Black women
Expected incidence <sup>1</sup>		12.4	11.8	15.1
Conventional smear	Papanicolaou	11.8	10.8	13.5
	40% FNR	9.7	8.9	11.2
Liquid-based cytology	Base case	8	7.3	9.1
	20% FNR	7.2	6.6	8.2
Healthy People 2000 compliance goals*				
Conventional smear	Papanicolaou	10.5	9.6	12.6
	40% FNR	8.6	7.8	10.3
Liquid-based cytology	Base case	7	6.4	8.3
	20% FNR	6.2	5.7	7.4
Healthy People 2010 compliance goals <sup>†</sup>				
Conventional smear	Papanicolaou	9.1	8.4	11.3
	40% FNR	7.3	6.8	9
Liquid-based cytology	Base case	5.9	5.4	7.2
	20% FNR	5.2	4.8	6.4

FNR = false-negative rate.

\* Healthy People 2000 compliance goals are 95% of women ever having a Papanicolaou smear and 85% of women having a Papanicolaou smear in the last 3 y.

<sup>†</sup> Healthy People 2010 compliance goals are modeled as 97% of women ever having a Papanicolaou smear and 90% of women having a Papanicolaou smear in the last 3 y.

used for compliance modeling, liquid-based cytology would cost an incremental \$20,424 per life year saved, \$23,503 per life year saved, and \$11,346 per life year saved for the full population, white, and black women, respectively. It is important to note that use of liquid-based cytology has an improved cost-effectiveness ratio as the risk profile of the population being screened is increased.

Table 3 also illustrates the cost-effectiveness sensitivity analyses. For liquid-based cytology at a 40% false-negative rate (a 20% improvement on the conventional

Pap smear), use of the new technology would still cost less than \$50,000 per life year saved standard of cost-effectiveness in all populations at all compliance levels.<sup>21</sup> If liquid-based cytology operates at a 20% false-negative rate (a 60% improvement over the conventional Pap smear), the cost-effectiveness ratio is less than \$20,000 per life year saved for all populations and less than \$10,000 per life year saved for black women.

Table 4 shows the cost-effectiveness ratios for increasing the compliance to Healthy People 2010 goals. This analysis does not take into account the cost of the

**Table 3.** Cost-effectiveness of Liquid-Based Cytology in Preventing Cervical Cancer in Populations Screened From Age 20 Through Age 80 With Different Risk Profiles

Compliance	Sensitivity analysis	All women	White women	Black women
Self-reported <sup>4</sup>	40% FNR	\$33,988/lys	\$39,102/lys	\$23,549/lys
	Base case	\$15,296/lys	\$17,967/lys	\$10,335/lys
	20% FNR	\$11,329/lys	\$13,473/lys	\$ 7550/lys
Healthy People 2000 goals*	40% FNR	\$36,962/lys	\$41,837/lys	\$23,358/lys
	Base case	\$16,796/lys	\$19,466/lys	\$10,244/lys
	20% FNR	\$12,576/lys	\$14,712/lys	\$ 7480/lys
Healthy People 2010 goals <sup>†</sup>	40% FNR	\$43,388/lys	\$49,313/lys	\$25,387/lys
	Base case	\$20,424/lys	\$23,503/lys	\$11,346/lys
	20% FNR	\$15,553/lys	\$18,020/lys	\$ 8385/lys

FNR = false-negative rate; lys = life years saved.

Cost-effectiveness presented in discounted dollars per discounted life years saved. These are incremental cost and benefits as compared with the equivalent compliance using the conventional Papanicolaou smear.

\* Healthy People 2000 compliance goals are 95% of women ever having a Papanicolaou smear and 85% of women having a Papanicolaou smear in the last 3 y.

<sup>†</sup> Healthy People 2010 compliance goals are modeled as 97% of women ever having a Papanicolaou smear and 90% of women having a Papanicolaou smear in the last 3 y.

**Table 4.** Cost-Effectiveness of Increasing Compliance in Preventing Cervical Cancer in Populations Screened From Age 20 Through Age 80 With Different Risk Profiles and Different Screening Strategies

	All women	White women	Black women
Compliance	Conventional smears		
Healthy People 2000 goals*	\$57,999/lys	\$63,962/lys	\$ 8847/lys
Healthy People 2010 goals†	\$37,262/lys	\$47,533/lys	\$12,046/lys
	Liquid-based cytology		
Healthy People 2000 goals*	\$22,122/lys	\$24,755/lys	\$10,655/lys
Healthy People 2010 goals†	\$25,818/lys	\$30,577/lys	\$11,384/lys

lys = life years saved.

Cost-effectiveness presented in discounted dollars per discounted life years saved. These are incremental cost and benefits as compared with the self-reported compliance rates using the conventional Pap smear.

\* Healthy People 2000 compliance goals are 95% of women ever having a Pap smear and 85% of women having a Pap smear in the last 3 y.

† Healthy People 2010 compliance goals are modeled as 97% of women ever having a Pap smear and 90% of women having a Pap smear in the last 3 y.

program to attract more women into screening but simply the extra cost associated with the increased number of screening tests. The high-risk, black subpopulation fares the best in this analysis because of the fact that black women are already nearly compliant with the Healthy People 2000 goals. Hence, there is little incremental cost associated with increasing the compliance of black women. As shown in the bottom section of Table 4, when combining liquid-based cytology to increase the test sensitivity with increased compliance, the cost-effectiveness ratios are improved compared with increased compliance alone at virtually all compliance levels in each subpopulation.

To demonstrate the effect of increased compliance in elderly women, the results of the model were extracted for the cohort once they reached age 50 until they reached age 80. These results are shown in Table 5. The results for increasing compliance in the elderly population were more dramatic than the results for the full population especially among black women.

## Discussion

It is generally believed that populations at higher risk for cervical cancer have lower participation rates in screening programs.<sup>2</sup> However, when comparing the self-reported compliance patterns and cervical cancer incidence for three populations in the United States, this belief is not necessarily verified: self-reported compliance with Papanicolaou smear screening has been at least as high for black women for the past decade as for

**Table 5.** Average Yearly Cancer Incidence of Cervical Cancer for Women Age 50 Through Age 80 at Different Compliance Rates

	Self-reported compliance rate <sup>4</sup>		
	All women	White women	Black women
Expected incidence <sup>1</sup>	13.8	12.5	19.2
Conventional Papanicolaou smear	13.7	12.1	17.3
Liquid-based cytology	8.8	7.6	11.3
Healthy People 2000 compliance goals*			
Conventional Papanicolaou smear	11.6	10.3	15.2
Liquid-based cytology	7.2	6.3	9.5
Healthy People 2010 compliance goals†			
Conventional Papanicolaou smear	9.5	8.7	12.7
Liquid-based cytology	5.8	5.2	7.8

\* Healthy People 2000 compliance goals are 95% of women ever having a Pap smear and 85% of women having a Pap smear in the last 3 y.

† Healthy People 2010 compliance goals are modeled as 97% of women ever having a Pap smear and 90% of women having a Pap smear in the last 3 y.

white women (Table 6). Nonetheless, the incidence of cervical cancer for black women has been higher than that for white women throughout this time period and was predicted to be higher by 38% in 1998.<sup>1</sup>

Table 6 also demonstrates that black women have come close to the Healthy People 2000 goals of 95% of ever receiving a Papanicolaou smear and 85% being screened in the last 3 years. Therefore, without increased efforts to attract more women to screening, the ability of the Papanicolaou smear to further reduce cervical cancer incidence in a high-risk, compliant population may have reached the point of exponentially diminishing returns. To illustrate this point, the model was run with compliance assumptions equal to the Healthy People 2010 goals. With only 3% of the population never receiving a Papanicolaou smear and 90% fully compliant with the conventional Papanicolaou smear, the model predicted that there would still be 11.3 cancers per year in the black population. This value is little improved over the 11.8 cancers predicted for all women with actual compliance assumptions. It may be that there are underlying, unrecognized processes that cause black as well as other high-risk groups to manifest a greater than average disease risk profile.

Elderly women of all three subpopulations have a higher risk of developing cervical cancers. Elderly women are also the least likely to report high levels of compliance with recommended screening guidelines.<sup>6</sup> Not surprisingly, the results for increasing compliance in the elderly population are more dramatic than the results for the full population, especially among blacks

**Table 6.** Comparison of Self-reported Compliance With Pap Smear Testing Among Different Populations Between 1987 and 1997

Year	All women		White women		Black women	
	Ever screened (%)	Screened recently (%)	Ever screened (%)	Screened recently (%)	Ever screened (%)	Screened recently (%)
1987 <sup>5</sup>	88	67	91	69	88	73
1997 <sup>4</sup>	93.7	79.7	93.7	80.1	94.3	83.9

(Table 5). Nonetheless, the impact of liquid-based cytology used at current compliance levels is approximately as effective as increasing compliance to a level beyond the Healthy People 2000 goals.

One reason why the Papanicolaou smear may have reached its optimal efficacy is the inherent limited sensitivity of the test. In an attempt to determine what impact improved Papanicolaou sensitivity would have on cancer rates, we modeled the effect of using a recently approved alternative that offers a 50% reduction in the false-negative rate.<sup>22</sup> Using current compliance assumptions, liquid-based cytology has the potential to reduce the incidence of cervical cancer by more than 30%, regardless of the risk profile of the population. This improvement in outcomes compares favorably to widely implemented model screening programs for other cancers.<sup>23,24</sup> The magnitude of this reduction is greater than that possible even with the high compliance assumptions outlined above. Additionally, this technology could be deployed in a population at increased risk for cervical cancer at a cost of approximately \$11,000 per life year saved.

Because of the absence of concrete data, many of the assumptions used in this model were arbitrary (ie, the division of fully and partially compliant women into different screening rate groups, the fact that women did not solely undergo well-women care for the purpose of cervical cancer screening, etc). Though this is a potential weakness of the modeling, it is our opinion that the assumptions are rational and within the realm of probability. Another proviso that must be appreciated is that the modeling results, especially as they address the cost-effectiveness of liquid-based cytology, represent a best case scenario. It may be that there are hidden and unappreciated costs that would increase the estimated \$11,000 per life year saved.

The results of this paper vary markedly from a recently published cost-effectiveness study by Brown and Garber,<sup>20</sup> but are similar to the results of the Agency for Health Care Policy Research study.<sup>9</sup> In the Brown and Garber<sup>20</sup> study, the base Papanicolaou smear sensitivity used was 80%, whereas the report here presented and the Agency for Health Care Policy Research report used a sensitivity of 50.4%. A complete discussion of the results of this model and how it

compares with the two previously published reports is available in a prior report.<sup>11</sup> However, it is important to note that one of the goals of this work was to show the impact of known compliance rates on the efficacy of cervical cancer screening. The Agency for Health Care Policy Research report used compliance rates to validate the model by using managed care utilization data but did not predict the effect of new technologies in real world utilization settings.

An argument that is generally made against the implementation of new screening technologies in an attempt to reduce the impact of cervical cancer is that resources would be better spent increasing the actual percentage of women being screened as opposed to being spent on technologies. As shown in Table 4, the use of liquid-based cytology in conjunction with increased compliance may provide a more cost-effective approach than increasing compliance alone. Therefore, the choice of increasing compliance versus using liquid-based cytology is an artificial distinction. Efforts should be made to use both approaches in parallel.

## References

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Cancer Statistics Review, 1973–1995: Tables and graphs. Bethesda, MD: National Cancer Institute, 1998.
2. National Institutes of Health. Consensus Statement 1996;43:1–38. Available from the National Institutes of Health via the Internet. Accessed 2000 Jan 17.
3. United States Department of Health and Human Services. Healthy People 2000 Review. Washington, DC: Department of Health and Human Services, 1997.
4. Centers for Disease Control and the National Institutes of Health. Healthy People 2010 Conference Edition. Available from the Center for Disease Control via the Internet. Accessed 2000 Feb 29.
5. United States Department of Health and Human Services. The National Breast and Cervical Cancer Early Detection Program, At-A-Glance. Washington, DC: United States Department of Health and Human Services, 1999.
6. Blackman DK, Bennett EM, Miller DS. Trends in self-reported use of mammograms (1984–1997) and Papanicolaou tests (1991–1997). Behavioral Risk Factor Surveillance System. Centers for Disease Control and Prevention. October 8, 1999. MMWR CDC Surveill Summ 1999;48:10–22.
7. Ackermann SP, Brackbill RM, Bewerse BA, Cheal NE, Sanderson LM. Cancer screening behaviors among U.S. women: Breast cancer, 1987–1989, and cervical cancer, 1988–1989. MMWR CDC Surveill Summ 1992;41:17–25.

8. Harlan LC, Bernstein AB, Kessler LG. Cervical cancer screening: Who is screened and why? *Am J Pub Health* 1991;81:885-90.
9. Agency for Health Care Policy and Research. Evidence Report/Technology Assessment. Number 5. Rockville, MD: Agency for Health Care Policy and Research, 1999.
10. United States Food and Drug Administration Center for Devices and Radiological Health. Database of releasable premarket approval applications. Available from the United States Food and Drug Administration via the Internet. Accessed 2000 Feb 29.
11. Hutchinson ML, Berger BM, Farber FL. Clinical and cost implications of new technologies for cervical cancer screening—The impact of test sensitivity. *Am J Manag Care* 2000;6:766-800.
12. National Center for Health Statistics. Division of Vital Statistics. Table 250. Washington, DC: National Center for Health Statistics, 1999.
13. Lepine LA, Hillis SD, Marchbanks PA, et al. Hysterectomy surveillance—United States, 1980-1993. *MMRW CDC Surveill Summ* 1997;46:1-15.
14. Reid R, Fu YS. In: Peto R, Zur Hausen H, eds. Banbury Report 21: Viral etiology of cervical cancer. Cold Spring Harbor, NY, 1986: 100, 117.
15. DeMay RM. The art and science of exfoliative cytopathology; exfoliative cytology. Chicago, IL: American Society of Cyto Pathologists Press, 1996:74-83.
16. Eddy DM. Screening for cervical cancer. *Ann Intern Med* 1990;113: 214-26.
17. Gustafsson L, Pontén J, Zack M, Adami H. International incidence rates of invasive cervical cancer after introduction of cytological screening. *Cancer Causes Control* 1997;8:755-63.
18. American Medical Association. Physician's Current Procedural Terminology CPT '96. Chicago, IL: American Medical Association, 1995:9-10, 206, 208, 333, 327.
19. Practice Management Information Corporation. Physician fees: A comprehensive guide for fee schedule review and management. Los Angeles, CA: Practice Management Information Corporation, 1997:184-5, 346, 348, 388.
20. Brown AD, Garber AM. Cost-effectiveness of three methods to enhance the sensitivity of Papanicolaou testing. *JAMA* 1999;281: 347-53.
21. Raab SS. The cost-effectiveness of cervical-vaginal rescreening. *Anat Path* 1997;108:525-36.
22. Soler ME, Blumenthal PD. New technologies in cervical cancer precursor detection. *Curr Opin Oncol* 2000;12:460-5.
23. Kerlikowske K, Grady D, Rubin SM, Sandrock C, Ernster VL. Efficacy of screening mammography. A meta-analysis. *JAMA* 1995;273:149-54.
24. Hendrick RE, Smith RA, Rutledge JH, Smart CR. Benefit of screening mammography in women ages 40-49: A new meta-analysis of randomized controlled trials. *J Nat Cancer Inst* 1997; 22:87-92.

Address reprint requests to:

F. J. Montz, MD, KM

The Kelly Gynecologic Oncology Service

Departments of Obstetrics and Gynecology, and Oncology

The Johns Hopkins Hospital and Medical Institutions

600 North Wolfe Street, Phipps 248

Baltimore, MD 21287-1248

E-mail: [fmontz@jhmi.edu](mailto:fmontz@jhmi.edu)

Received August 10, 2000.

Received in revised form December 14, 2000.

Accepted January 12, 2001.

Copyright © 2001 by The American College of Obstetricians and Gynecologists. Published by Elsevier Science Inc.