

Cost-Effectiveness Analysis of Diagnosis and Management of Cervical Squamous Intraepithelial Lesions

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Objective: To compare five strategies for the diagnosis and treatment of cervical squamous intraepithelial lesions (SILs), including those that incorporate colposcopy and a new technology, fluorescence spectroscopy.

Methods: On the basis of a health care perspective, we performed a cost-effectiveness analysis using a decision-analytic model for the diagnosis and management of SILs. We compared the five strategies based on the expected costs and number of cases that were treated appropriately, missed, treated inappropriately, and appropriately not treated in a hypothetical cohort of 100 patients referred after an abnormal Papanicolaou smear. Data on prevalence and operating characteristics were derived from the medical literature. Costs were adjusted from hospital charge data.

Results: A see-and-treat strategy based on fluorescence spectroscopy was the least expensive but least effective strategy, costing \$160,479 to detect 31.55 cases of cervical precancer accurately in 100 patients. The most expensive strategy was colposcopically directed biopsy, at \$311,808 to find 45.78 cases; however, when both tests were used in a see-and-treat modality, slightly more cases were found (46.05) at a lower cost (\$285,133). Other strategies were dominated in the base case. The incremental cost-effectiveness of the joint strategy compared with the spectroscopy-only strategy was \$8596 per case of cervical precancer detected. Sensitivity analysis showed that the analysis was sensitive to the cost of the new technology of fluorescence spectroscopy.

Conclusion: Fluorescence spectroscopy should be considered an important innovation in the diagnosis of SILs as demonstrated by its efficacy and economic advantages. (*Obstet Gynecol* 1998;91:270-7. © 1998 by The American College of Obstetricians and Gynecologists.)

Despite the availability of Papanicolaou smear screening, cervical cancer and its precancers remain important and costly health problems, especially in socially disadvantaged and minority women. Worldwide, approximately half a million women are diagnosed with cervical cancer each year, making it the second most common malignancy in women in the world.¹ In the United States, approximately 16,000 women are diagnosed each year with invasive cervical cancer and 4800 women die from the disease annually.²

Colposcopy currently represents the standard of care for the treatment of women with abnormal Papanicolaou smear results. The technique has been demonstrated to have good sensitivity but poor specificity in expert hands in the diagnosis of cervical precancers.³ The current strategy for evaluating a patient with abnormal smear results is an initial visit at which a comprehensive history and physical examination with colposcopy and colposcopically directed biopsies are undertaken. Patients return 1-2 weeks later for treatment including cryotherapy, laser ablation, loop electrosurgical excision procedure (LEEP), or cone biopsy.

Many investigators⁴ have attempted to omit the second visit by diagnosing and treating (if appropriate) patients at a single visit using LEEP, known as a "see-and-treat" strategy. Because of the low specificity of colposcopy, there are many false positives. This means up to 40% of patients have negative specimens.

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Improving the specificity of colposcopy would decrease the number of patients who are treated inappropriately.

Fluorescence spectroscopy is an emerging new diagnostic technique that probes the morphologic and biochemical properties of tissue using ultraviolet or visible light.⁵ A variety of mathematical algorithms have been presented to classify tissue type given a tissue fluorescence spectrum,⁶ potentially enabling automated or semiautomated diagnosis in near real-time of pathology with little training. This new technique has proven beneficial in the diagnosis of bronchial neoplasms⁷ and now is being investigated as a tool in the diagnosis of cervical precancer.

This study is a cost-effectiveness analysis from a health care perspective of various strategies for the diagnosis and management of cervical squamous intraepithelial lesions (SILs), comparing the current standard colposcopy with the recently developed technique of fluorescence spectroscopy. In addition, we compare these two strategies with three other see-and-treat strategies that are based on variations of these technologies (colposcopy and fluorescence spectroscopy), in which patients who test positive are treated at the same visit.

Materials and Methods

We structured a decision tree⁸ to identify the possible outcomes of the diagnosis and management of cervical precancer. Patients were classified into one of four categories: true positives—appropriately treated; false negatives—inappropriately not treated; false positives—inappropriately treated; and true negatives—appropriately not treated. We calculated the number of patients that we would expect to find in each of these categories from a hypothetical cohort of 100 patients seen in a referral clinic.

For this analysis, the term *diseased patient* was defined as a patient with high-grade SILs or invasive cervical cancer. Recognizing that controversy exists regarding the appropriate treatment of patients who have low-grade SILs or atypical cells of uncertain significance, we took a conservative approach. In this model, our goal was to treat only those patients with true diagnoses of high-grade SILs or invasive cervical cancer. In addition, we calculated the expected monetary costs that would be incurred for these patients. Consequently, we performed a cost-effectiveness analysis of the strategies for the diagnosis, treatment, and subsequent management of cervical precancer.

Strategies

We compared the following five strategies for the diagnosis and treatment of high-grade SILs, including

those that incorporate the new technique of spectroscopy [strategy is in brackets]: 1) Colposcopically directed biopsy followed by treatment with LEEP at a second visit if high-grade SILs are found at biopsy [Colposcopy]. This is usual care. 2) See and treat based on colposcopic diagnosis and treatment with LEEP in one visit [See-and-treat colposcopy]. “See and treat” refers to the fact that if high-grade SILs are suspected at the time of colposcopic evaluation, the patient will be treated immediately, rather than after confirmatory biopsy results, which would be available 1–2 weeks later. Thus, the treatment is based on the initial colposcopic impression and no biopsy is performed. 3) Spectroscopically directed biopsy followed by treatment with LEEP at a second visit if high-grade SILs are found at biopsy [Spectroscopy]. 4) See and treat based on spectroscopic diagnosis and treatment with LEEP in one visit [See-and-treat spectroscopy]. Similar to the strategy for see-and-treat colposcopy (strategy number 2 above), this strategy implies that if high-grade SILs are suspected at time of spectroscopy, then the patient will be treated immediately, rather than await biopsy results and an additional office visit 1–2 weeks later. 5) See and treat based on spectroscopy and colposcopy used together and treatment with LEEP in one visit [See-and-treat spectroscopy and colposcopy]. In this strategy, at the time of the first visit, if both spectroscopy and colposcopy indicate high-grade SILs, then the patient is treated immediately. If both spectroscopy and colposcopy indicate no lesions, then the patient is not treated. Finally, if the results of spectroscopy and colposcopy conflict, then a biopsy is performed; in that case, the decision to treat with LEEP (at a second visit) is based on the results of the biopsy.

Probabilities

Probability data for the decision-analytic model were based on the medical literature as well as data collected at our clinic. To estimate the prevalence of cervical SILs in a referral population, we computed a weighted average of the prevalence values of studies that analyzed the operating characteristics of colposcopy. We included only studies in which all patients had both colposcopy and biopsy, in which biopsy was considered the criterion for diagnosis.^{9–17} These nine studies^{9–17} analyzed the accuracy of colposcopy in patients with abnormal Papanicolaou smear results, representing a broad range of referral populations, numbers of patients, and standard practices. In this same analysis, we determined the weighted average of patients who had high-grade SILs compared with all patients with SILs to generate the fraction of patients who should be treated appropriately. The prevalence of patients with SILs was found to be 72% of those referred. Of all

Table 1. Prevalence of Squamous Intraepithelial Lesions and High-Grade Squamous Intraepithelial Lesions

Reference	n	High-grade		(High-grade)	
		SILs	SILs	SILs/n	SILs/SILs
Benedet et al ⁹	549	431	366	0.785	0.849
Benedet et al ¹⁰	3252	2407	1722	0.740	0.715
Cristoforoni et al ¹¹	188	130	34	0.691	0.262
Edebiri ¹²	222	120	104	0.541	0.867
Ferris and Miller ¹³	205	115	43	0.561	0.374
Javaheri and Fejgin ¹⁴	903	675	334	0.748	0.495
Lozowski ¹⁵	151	111	85	0.735	0.766
Sheshadri et al ¹⁶	152	53	36	0.349	0.679
Stafil and Mattingly ¹⁷	659	483	335	0.733	0.694
Total*	6281	4525	3059	0.720	0.676

* Weighted averages of fraction of squamous intraepithelial lesions (SILs) compared with all samples and fraction of high-grade SILs compared with all SILs based on sample size.

patients with SILs, 68% were found to have high-grade SILs (Table 1).

Calculations for the sensitivity and specificity of fluorescence spectroscopy were based on a series of 92 patients suspected of having cervical intraepithelial neoplasia (CIN).¹⁸ Between two and five spectroscopy measurements were taken from colposcopically normal- and abnormal-appearing sites in each patient. Colposcopically directed biopsies were taken from colposcopically abnormal areas measured spectroscopically in all patients, and a diagnosis was determined by a consensus panel of four pathologists. Each pathologist individually made a diagnosis of the biopsy, blinded to the decisions of the others. If there was any disagreement among the members of the panel, the pathologists were brought together as a panel and collectively forced to make a diagnosis based on unanimous opinion. Therefore, the operating characteristics of biopsy are assumed to be 100%.

As cited in the study by Ramanujam et al¹⁸ the operating characteristics of colposcopy are based on a meta-analysis³ of previously published studies that evaluated the use of colposcopy in the referral setting. The characteristics of the three diagnostic tests (fluorescence spectroscopy, colposcopy, and biopsy) are summarized in Table 2.

Costs

We documented from a health care perspective the expected costs that would be incurred for each of the clinical strategies for the diagnosis and management of cervical precancer. Our institution has established a clinical pathway for the diagnosis and treatment of cervical SILs beginning with colposcopy at the time of the referral visit; the other strategies examined in the analysis were modeled after this plan.

Table 2. Operating Characteristics of Diagnostic Tests

	Presence vs absence of SILs (stage I)		High-grade vs low-grade SILs (stage II)	
	Sensitivity	Specificity	Sensitivity	Specificity
	Colposcopy ³	0.94	0.48	0.79
Fluorescence spectroscopy ¹⁸	0.82	0.68	0.79	0.78
Biopsy*	1.00	1.00	1.00	1.00

SIL = squamous intraepithelial lesion.

* By assumption.

Costs were based on charge data obtained from our hospital's billing information system. Charges then were multiplied by the 1995 hospital cost-to-charge ratios to obtain estimated costs of care.¹⁹ Only direct medical costs were included and measured in 1995 dollars. The 1995 cost-to-charge ratios were determined from the 1994 experience, but these ratios have not changed appreciably at our hospital over the past few years. Table 3 denotes the components of health care costs for each of the clinical strategies represented in the model.

Based on the clinical pathway for SILs, treatment and subsequent follow-up visits occur over a 2-year period. We discounted the costs that occurred 1 and 2 years after the initial visit by a discount rate of 3%. The 3% discount rate is intended to reflect the real consumption rate of interest (ie, time preference for money). It does not include inflation, because the cost portion of the analysis was performed in 1995 dollars. These assumptions were chosen in accordance with the Panel on Cost-Effectiveness in Health and Medicine²⁰ convened by the U.S. Public Health Service (Joseph Lipscomb, PhD, personal communication).

Costs for professional encounters with physicians were based on 1995 Medicare Resource-Based Relative Value Scale amounts.²¹ These amounts, based on both the type and complexity of procedure and adjusted for performance in the Houston geographic area, were used as the approximated cost of the physician's time. The adjustments for the Houston area are appropriate because they permit consistency with the other Houston-based costs in our model.

It is difficult to assess accurately the costs of fluorescence spectroscopy because the technology still is in development. In estimating the cost of any diagnostic technology, one must consider two components: 1) the cost of the diagnostic test itself and 2) the cost of physician time. (The two components are detailed in Table 3 for each of the five strategies evaluated.) To address the first component, we assumed that the cost

Table 3. Resources Used for the Clinical Strategies in the Diagnosis and Management of Cervical Intraepithelial Neoplasia

	Colposcopy	See-and-treat colposcopy	Spectroscopy	See-and-treat spectroscopy	See-and-treat spectroscopy and colposcopy
Diagnosis					
Hospital component					
Papanicolaou smear	5	4	5	4	4
Chlamydia	1		1		
Gonorrhea	1		1		
Viral smears	1		1		
ECC	5	4	5	4	4
Pregnancy test	1		1		
Clinic visit	7	6	7	6	6
Professional component					
Papanicolaou smear (technician)	5	4	5	4	4
Papanicolaou smear (interpretation)	5	4	5	4	4
Chlamydia	1		1		
Gonorrhea	1		1		
Viral smears	1		1		
ECC	5	4	5	4	4
Treatment and follow-up					
Hospital component					
Spectroscopy with biopsy			5		
Colposcopy with biopsy	5				
Spectroscopy with LEEP			1	5	5
Colposcopy with LEEP	1	5			5
Local anesthesia	1	5	1	5	5
Gross/microscopic slide evaluation (3 slides)	1		1		
Gross/microscopic slide evaluation (6 slides)	1	1	1	1	1
Gross/microscopic slide evaluation (1 slide)	4	4	4	4	4
Professional component					
Spectroscopy with biopsy			5		
Colposcopy with biopsy	5				
Spectroscopy with LEEP			1	5	5
Colposcopy with LEEP	1	5			5
Pathology	6	5	6	5	5

ECC = endocervical curettage; LEEP = loop electrosurgical excision procedure.

Numbers in the table indicate the maximum theoretical frequency of resources used for each strategy, including the initial visit and follow-up visits in the subsequent 2-y period.

of fluorescence spectroscopy would be 80% of the cost of colposcopy because the technology itself is not expected to exceed the cost of colposcopy. Because of the uncertainty of cost estimates for a technology still in its developmental phase, we varied the cost of fluorescence spectroscopy from 80% to 100% of the cost of colposcopy; as stated above, spectroscopy costs are not expected to exceed the cost of colposcopy.

The second component, cost of physician time, depends directly on the degree to which the new technology has diffused into clinical practice. Specifically, the salary costs of a physician's time typically exceed those of a nurse practitioner. In the early phases of fluorescence spectroscopy diffusion into clinical practice, physicians will perform the diagnostic test. As the technique becomes accepted widely and fine-tuned, nurse practitioners or trained technicians can be expected to perform spectroscopy procedures. Therefore, we iden-

tified two phases of technology diffusion. For the base case, we assumed that spectroscopy would be diffused fully into clinical practice. In this scenario, nurses, not physicians, performed the spectroscopy and consequently no physician costs were incurred. In the second scenario, fluorescence spectroscopy has not been implemented fully into clinical practice. In this scenario, physicians performed the spectroscopy procedures, thereby incurring physician costs.

Analysis

We evaluated the various algorithms for the diagnosis and treatment of high-grade SILs in the referral setting by a cost-effectiveness analysis. The projected outcomes for using fluorescence spectroscopy, colposcopy, and a combination of the two techniques were compared to

Table 4. Expected Costs and Benefits and Incremental Cost-Effectiveness Analysis for 100 Referral Patients for the Diagnosis and Management of Squamous Intraepithelial Lesions

Strategy	Cost	No. of true positives	No. of false negatives	No. of false positives	No. of true negatives	Incremental cost-effectiveness ratio (\$/case of high-grade SILs found)	Incremental cost-effectiveness ratio* (\$/case)
See-and-treat spectroscopy	\$160,479	31.55	17.15	5.99	45.31	—	—
See-and-treat colposcopy	\$210,962	36.16	12.54	8.10	43.20	\$10,935	Weak dominance
Spectroscopy	\$246,381	39.93	8.76	0.00	51.30	\$9397	Weak dominance
Colposcopy	\$311,808	45.78	2.92	0.00	51.30	Dominated	Strong dominance
See-and-treat spectroscopy and colposcopy	\$285,133	46.05	2.65	2.01	49.29	\$6337	\$8596

SIL = squamous intraepithelial lesion.

In a sample of 100 referral patients, a perfect test would identify 48.7 cases with disease and 51.1 cases without disease (based on the prevalence data as demonstrated in Table 1).

* Computed using extended dominance.

determine the expected costs and effectiveness of the various strategies. We evaluated the strategies using the metric of dollars per case of high-grade SILs detected. However, we were most interested in the additional cost required to detect an additional case of high-grade SILs; therefore, we performed an incremental cost-effectiveness analysis comparing the expected costs and effectiveness of the various strategies to diagnose and treat cervical precancer.

The cost-effectiveness analysis was modeled using SMLTREE 2.9 software (Hollenberg JP, New York, NY). We first determined results of the model using the initial parameters as presented previously; this is the “base case” analysis. We then performed sensitivity analysis to determine how variation in the model’s parameters would affect the overall costs and health effectiveness of the various clinical strategies. Given the inherent uncertainty in a mathematic model, sensitivity analysis examines the stability of conclusions by varying the model’s parameters over a range of plausible alternatives.

Results

Table 4 shows the results of the base case analysis, which is based on an 80% cost of spectroscopy compared with colposcopy and full diffusion of the fluorescence spectroscopy technology. See-and-treat spectroscopy was the least expensive but least effective strategy, costing \$160,479 to detect accurately 31.55 cases of cervical precancer in 100 patients. The most expensive strategy was colposcopically directed biopsy, at \$311,808 to find 45.78 cases; however, when both tests were used in a see-and-treat modality, slightly more cases were found (46.05) at a lower cost (\$285,133). Thus, the usual strategy is dominated (less benefit at a greater cost) by a new, potentially viable strategy.

Table 4 also shows the results of the incremental cost-effectiveness analysis, using the outcome measure of dollars per case found of cervical precancer. On the basis of this analysis, both the strategies of see-and-treat colposcopy and spectroscopically directed biopsy are eliminated from considerations of cost-effectiveness using the principle of extended dominance.²² In the situation of extended dominance, while the costs of the clinical strategies increase, their incremental cost-effectiveness ratios decrease. This leads to a situation in which a strategy of intermediate cost will not be cost-effective. For example, compare the incremental cost-effectiveness ratios for the strategies in Table 4: if the health care system is willing to pay \$10,935 to detect a case of high-grade SILs using the see-and-treat colposcopy strategy, then it will be able to spend \$9397 to detect an additional case using the spectroscopy strategy. After removing from consideration those strategies that are weakly dominated, the incremental cost-effectiveness of the see-and-treat spectroscopy and colposcopy strategy compared with the see-and-treat spectroscopy strategy was \$8596 per case of cervical precancer detected. In the language of cost-effectiveness analysis, weak dominance is different from strong dominance—one strategy strongly dominates another when it is both less expensive and more effective. (Further explanation of the cost-effectiveness analysis concept of dominance can be found in the article by Cantor.²²)

Sensitivity Analysis

We performed a sensitivity analysis varying the prevalence of SILs in the referral population. Even over a wide interval of prevalence rates, the model demonstrated a potential for significant cost savings using the alternative technology of fluorescence spectroscopy. In a one-way sensitivity analysis varying the prevalence of

Table 5. Sensitivity Analysis for Stage-I Sensitivity of Fluorescence Spectroscopy Reduced to 0.65

Strategy	Expected cost	No. of cases of high-grade SILs detected	Incremental cost-effectiveness ratio (\$/case of high-grade SILs detected)
See-and-treat spectroscopy	\$134,462	25.01	—
See-and-treat colposcopy	\$210,962	36.16	\$6857
Spectroscopy	\$214,113	31.65	Strong dominance
See-and-treat spectroscopy and colposcopy	\$282,867	45.57	\$7641
Colposcopy	\$311,808	45.78	\$142,381

SIL = squamous intraepithelial lesion.

SILs from the minimum to the maximum prevalence rates for the studies listed in Table 1, the structure of the results followed the same pattern of weakly and strongly dominated strategies. The incremental cost-effectiveness ratio for the joint spectroscopy and colposcopy strategy compared with see-and-treat spectroscopy ranged between \$8444 and \$10,560 to detect a case of high-grade SILs. Similarly, when the proportion of high-grade SILs compared with all SILs ranged from the minimum to maximum values for the individual studies, the same pattern of weakly and strongly dominated strategies emerged; in this one-way sensitivity analysis, the incremental cost-effectiveness ratio for the joint spectroscopy and colposcopy strategy compared with see-and-treat spectroscopy ranged between \$8526 and \$9093 to detect a case of high-grade SILs. Thus, variation in the prevalence rates changed the total costs and effectiveness of the various strategies but had little effect on their incremental cost-effectiveness.

We performed a sensitivity analysis on the value of the test sensitivity (proportion of diseased patients identified correctly) for each stage of the fluorescence

spectroscopy. Variations in the first-stage test sensitivity (distinguishing SILs from non-SILs) led to significant changes in the incremental cost-effectiveness analysis. For example, if the first-stage test sensitivity decreased to 0.65, then the results changed markedly, as shown in Table 5. (The number 0.65 was chosen as a lower bound; it may not make practical sense to use a diagnostic test for cervical precancer with a test sensitivity lower than 0.65.) The incremental cost-effectiveness ratio for fluorescence spectroscopy was strongly dominated by see-and-treat colposcopy; however, the standard colposcopy strategy had an unusually high cost-effectiveness ratio, ie, an incremental cost-effectiveness ratio of more than \$142,000 to detect a case of cervical precancer. With increased first-stage test sensitivity (data not shown), the basic pattern of cost-effectiveness remained unchanged.

When we increased the discount rate to 5%, the basic structure of the results once again did not change. The same pattern of dominated strategies emerged; the joint spectroscopy and colposcopy strategy compared with see-and-treat spectroscopy had an incremental cost-effectiveness ratio of \$8461 per case of cervical precancer found (Table 6). Similarly, when we increased the cost of the fluorescence spectroscopy to be equal to the cost of colposcopy (exclusive of physician costs), the results remained essentially the same. The same pattern of dominated strategies emerged; the joint spectroscopy and colposcopy strategy compared with see-and-treat spectroscopy had an incremental cost-effectiveness ratio of \$8713 per case of cervical precancer found.

However, in the early diffusion of spectroscopy scenario, in which physician costs for performing the diagnostic test are included, a different pattern emerged. When all of the base case assumptions remained constant except for the addition of physician

Table 6. Sensitivity Analysis of Changing Model Parameters Affecting Cost in the Cost-Effectiveness Analysis

Strategy	No. of cases detected	Cost of spectroscopy set to 100% cost of colposcopy					
		Discount rate 5%		Cost of spectroscopy set to 100% cost of colposcopy		Early diffusion of spectroscopy	
		Expected cost	Incremental cost-effectiveness ratio (\$/case detected)	Expected cost	Incremental cost-effectiveness ratio (\$/case detected)	Expected cost	Incremental cost-effectiveness ratio (\$/case detected)
See-and-treat spectroscopy	31.55	\$158,362		\$170,681		\$187,784	
See-and-treat colposcopy	36.16	\$207,860	Weak dominance	\$210,962	Weak dominance	\$210,962	\$5150
Spectroscopy	39.93	\$244,129	Weak dominance	\$256,969	Weak dominance	\$274,096	Weak dominance
Colposcopy	45.78	\$308,600	Strong dominance	\$311,808	Strong dominance	\$311,808	\$10,490
See-and-treat spectroscopy and colposcopy	46.05	\$281,037	\$8461	\$297,027	\$8713	\$316,267	\$16,421

Early diffusion of spectroscopy implies physician cost for performing diagnostic test.

costs for fluorescence spectroscopy, not all of the strategies were dominated. In this scenario, the joint spectroscopy and colposcopy strategy increased to \$16,421 per case of cervical precancer found. On the basis of how we defined stage of diffusion in the decision-analytic model, ie, whether physicians performed the diagnostic testing for fluorescence spectroscopy (and if they did, incorporating these costs in the model), we found that the extent of technology diffusion is an important factor to consider in a cost-effectiveness analysis of clinical strategies that include technologic innovation.

Discussion

The potential magnitude of the diagnosis of CIN is considerable. The National Cancer Institute²³ estimated that 50 million Papanicolaou smears are obtained annually. Kurman et al²⁴ surveyed university and commercial cytopathology laboratories and found a 5% rate of low-grade cervical cytologic abnormalities. Therefore, there are at least 2.5 million abnormal Papanicolaou smears each year in the United States that at least should be evaluated further (some of these may be false positives). Substantial cost savings (across 2.5 million abnormal Papanicolaou smear results) may be possible if methods are devised that are less expensive and more effective than current standard practice. On the basis of the findings presented in this paper using the outcome measure of dollars per case of cervical precancer found, we can use a see-and-treat strategy combining fluorescence spectroscopy and colposcopy and save more than \$25,000 per 100 referral patients to identify correctly at least the same number of cases identified correctly by the current standard of care of colposcopy. When these results are extrapolated to the estimates made by Kurman et al,²⁴ one finds there is the potential to save \$625 million annually (\$250 per patient for 2.5 million abnormal Papanicolaou smear results) in the United States.

The results of this study should be generalizable to other sites that treat referral patients. The prevalence of SILs was based on a meta-analysis of studies⁹⁻¹⁷ that did not occur at our institution. Our institution is a comprehensive cancer center, but it is also a referral center at the county and state levels for patients with abnormal Papanicolaou smear results. Although the operating characteristics of fluorescence spectroscopy are based on measurements taken from patients at our institution, these patients should not be different than the patients at community practices regarding follow-up of abnormal Papanicolaou smear results.

Further work is planned to analyze the cost-effectiveness of the various strategies using a standard measure of health (eg, life-year or quality-adjusted

life-year). With a standard measure of effectiveness, the economic and clinical concerns of false positives and false negatives can be incorporated better into the analysis. Similarly, the present study also is limited by the fact that the health care perspective was selected for analysis. The ideal perspective for cost-effectiveness analysis is the more comprehensive societal perspective. The resulting evaluation that incorporates both quality-adjusted life-years and a societal perspective then can be compared appropriately with other technologies and procedures that have been evaluated previously with the same methodologies.²⁵

We recognize that this study is an early attempt to evaluate the cost-effectiveness of a technology that has not been established as a diagnostic standard. However, while this technology is being developed, it is important to analyze and document its potential impact on both clinical and economic outcomes. If, for example, the diagnostic technology of fluorescence spectroscopy were to be perfectly accurate but also exorbitantly expensive, then serious questions of its practicality and feasibility would have to be raised. Therefore, it is crucial to evaluate emerging technologies for their clinical implications as well as their economic implications.

Fluorescence spectroscopy has been shown to improve the specificity of colposcopy. Diagnostic information can be obtained in near real-time. There is significant potential for economic savings with this technique, specifically by reducing the cost of operator time and the number of office visits. Thus, fluorescence spectroscopy should be considered as a cost-effective adjunct or replacement for colposcopy for the diagnosis of cervical precancers.

References

1. Nieminen P, Kallio M, Hakama M. The effect of mass screening on incidence and mortality of squamous and adenocarcinoma of cervix uteri. *Obstet Gynecol* 1995;85:1017-21.
2. Preventive Services Task Force. Guide to clinical preventive services. Baltimore, Maryland: Williams & Wilkins, 1996.
3. Mitchell MF. The accuracy of colposcopy. *Clin Consult Obstet Gynecol* 1994;6:70-3.
4. Ferris DG, Hainer BL, Pfenninger JL, Zuber TJ. 'See and treat' electrosurgical loop excision of the cervical transformation zone. *J Fam Pract* 1996;42:253-7.
5. Richards-Kortum R, Sevick-Muraca E. Quantitative optical spectroscopy for tissue diagnosis. *Annu Rev Phys Chem* 1996;47:555-606.
6. Gindi GR, Darken CJ, O'Brien KM, Stetz ML, Deckelbaum LI. Neural network and conventional classifiers for fluorescence-guided laser angioplasty. *IEEE Trans Biomed Eng* 1991;38:246-52.
7. Lam S, MacAulay C, Hung J, LeRiche J, Profio AE, Palcic B. Detection of dysplasia and carcinoma in situ with a lung imaging fluorescence endoscope device. *J Thorac Cardiovasc Surg* 1993;105:1035-40.

8. Weinstein MC, Fineberg HV. Clinical decision analysis. Philadelphia: WB Saunders, 1980.
9. Benedet JL, Anderson GH, Maticic JP, Miller DM. A quality-control program for colposcopic practice. *Obstet Gynecol* 1991;78:872-5.
10. Benedet JL, Boyes DA, Nichols TM, Millner A. Colposcopic evaluation of patients with abnormal cervical cytology. *Br J Obstet Gynaecol* 1976;83:177-82.
11. Cristoforoni PM, Gerbaldo D, Perino A, Piccoli R, Montz FJ, Capitanio GL. Computerized colposcopy: Results of a pilot study and analysis of its clinical relevance. *Obstet Gynecol* 1995;85:1011-6.
12. Edebiri AA. The relative significance of colposcopic descriptive appearances in the diagnosis of cervical intraepithelial neoplasia. *Int J Gynaecol Obstet* 1990;33:23-9.
13. Ferris DG, Miller MD. Colposcopic accuracy in a residency training program: Defining competency and proficiency. *J Fam Pract* 1993;36:515-20.
14. Javaheri G, Fejgin MD. Diagnostic value of colposcopy in the investigation of cervical neoplasia. *Am J Obstet Gynecol* 1980;137:588-94.
15. Lozowski MS, Mishriki Y, Talebian F, Solitare G. The combined use of cytology and colposcopy in enhancing diagnostic accuracy in preclinical lesions of the uterine cervix. *Acta Cytol* 1982;26:285-91.
16. Seshadri L, Jairaj P, Krishnaswami H. Colposcopy in the diagnosis of cervical neoplasia. *Indian J Cancer* 1990;27:180-6.
17. Stafil A, Mattingly RF. Colposcopic diagnosis of cervical neoplasia. *Obstet Gynecol* 1973;41:168-76.
18. Ramanujam N, Mitchell MF, Mahadevan-Jansen A, Thomsen SL, Staerckel G, Malpica A, et al. Cervical precancer detection using a multivariate statistical algorithm based on laser-induced fluorescence spectra at multiple excitation wavelengths. *Photochem Photobiol* 1996;64:720-35.
19. Finkler S. The distinction between costs and charges. *Ann Intern Med* 1982;96:102-9.
20. Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996.
21. Health Care Financing Administration. Physicians' Medicare fee schedule. January 1, 1995. Chicago: CCH, Inc., 1995.
22. Cantor SB. Cost-effectiveness analysis, extended dominance and ethics: A quantitative assessment. *Med Decis Making* 1994;14:259-65.
23. National Cancer Institute. National health survey supplement of cancer control. Bethesda, Maryland: National Center for Health Statistics, 1989.
24. Kurman RJ, Henson DE, Herbst AL, Noller KL, Schiffman MH. Interim guidelines for the management of abnormal cytology. The 1992 National Cancer Institute Workshop. *JAMA* 1994;271:1866-9.
25. Mason J, Drummond M, Torrance G. Some guidelines on the use of cost effectiveness league tables. *BMJ* 1993;306:570-2.

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