The Cost-Effectiveness of the Cytology Laboratory and New Cytology Technologies in Cervical Cancer Prevention

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Abstract

The effect of changes in cytology laboratory costs, including the costs of new technologies, on the cost-effectiveness of cervical cancer prevention has not been studied. Using University of Iowa laboratory detection rates and costs, a decision model determined the cost-effectiveness of the laboratory with and without new technologies. Compared with not performing a cervicovaginal smear, the cost to increase the discounted life expectancy per patient by 1 year was $2,805 for the laboratory component alone and $19,655 for the entire cervical cancer prevention strategy. In moderate- to high-risk women, cervical cancer screening was cost-effective even at high cytology laboratory costs (eg, $75 per smear). New technologies were cost-effective only if they resulted in a substantial increase in the detection of high-grade squamous intraepithelial lesions (eg, an additional 236 high-grade squamous intraepithelial lesions per 10,000 women). New technologies have not demonstrated these increased detection rates.

Since the widespread use of the Papanicolaou smear as a screening tool, there has been a marked decrease in the incidence of cervical cancer, resulting in an increase in patient life expectancy.[1–4] Other outcomes, such as cost-effectiveness, also have been reported, but these studies have not considered the detailed costs of cytology laboratories or the changes in cost-effectiveness, given advances in cytology technology.

Eddy,[1,2] one of the first to study the cost-effectiveness of cervicovaginal screening, incorporated estimates of cytology screening charges, rather than costs, in a decision model. Recent studies, such as the one by Bishop,[5] showed that cytology costs depend on a number of variables and need to be better estimated before detailed cost-effectiveness analyses can be performed. To illustrate this point, Raab[6] showed that rescreening, 1 component of laboratory interpretation, is cost-effective only in some patient scenarios and that there is a cutoff cost above which rescreening is not cost-effective.

Currently many cytology laboratories are studying the acquisition of new technologies, such as automated screening devices and monolayer preparation machines.[7–9] These technologies have been advocated to increase detection of cervical disease, albeit at a higher cost.[7–9] In the context of rescreening, O'Leary et al[10] reported that PAPNET(Neuromedical Systems, Upper Saddle River, NJ)-assisted rescreening did not detect a substantial number of lesions to justify the added cost. However, they did not test the efficacy of PAPNET in different patient scenarios (eg, high-risk patients) and did not recommend a detection rate that would be cost-effective. New cytology technologies have not been modeled to test their effect on cost-effectiveness of cervicovaginal screening.

In the present study, using decision analysis and actual cytology laboratory costs and cervical disease detection rates, the cost-effectiveness component of the

laboratory in cervicovaginal screening was studied.[6,11] This model was used to assess how the cost-effectiveness of cervicovaginal screening changed with the introduction of new technologies.

Materials and Methods

This study involved the following: (1) determining actual University of Iowa costs and cervical disease detection rates; (2) incorporating these costs and rates in a decision analytic model to determine the cost-effectiveness of cervicovaginal screening at the University of Iowa; and (3) performing sensitivity analyses to see how changes in costs and detection rates affected cervicovaginal screening cost-effectiveness.

Determining University of Iowa Costs and Disease-Detection Rates

The 1995 University of Iowa Hospitals and Clinics cytology files were retrospectively reviewed to determine the yearly number of slides reviewed, the rescreen rate, the diagnosis by the Bethesda system category, and the number of slides seen by each cytotechnologist and each cytopathologist. The 1995 year was similar in the percentage of cases by Bethesda system diagnosis to the preceding 5 years and the succeeding 2 years. Cases were classified in a Bethesda system category (benign, atypical [including atypical squamous cells of undetermined significance, or ASCUS, and atypical glandular cells of undetermined significance, or AGUS], low-grade squamous intraepithelial lesion [LSIL], high-grade squamous intraepithelial lesion [HSIL], or cancer) or in a non–Bethesda system category used at the University of Iowa (dysplasia, not otherwise specified, or "suspicious" for cancer).[12]

The total cytology laboratory costs were estimated by using the model described by Bishop[5] and are reported in 1997 US dollars. The total cost was composed of separate costs for laboratory supplies and personnel, hospital overhead, and cytotechnologist and cytopathologist screening and interpretation time.

Decision Model to Determine Outcomes of Cervicovaginal Screening

A decision model was developed for a reference case 30-year-old white women.[6,11] The decision model was developed in C++ by one of us (S.S.R.). The model used existing patient probabilities for risk of disease and cost to determine patient outcomes. The data sources, outcomes measured, and data used (assumptions) are described subsequently. The principles of decision analysis are outlined in reference 11.

It was assumed that the woman had the same risk to develop cervical cancer as an "average" woman for whom a smear was sent to the University of Iowa cytology laboratory. In the decision model, the protocol of having a single cervicovaginal smear was compared with not having a cervicovaginal smear. Several assumptions were made for simplification. First it was assumed that the probability of developing a second clinically significant cervical lesion was 0.[6,13] This assumption was made so that patient outcomes were not confounded by the rate of newly occurring clinically significant cervical lesions. Second, it was assumed that the probability of a sampling or screening error was 0.[13] This assumption was made because these errors would occur equally in both groups of women (ie, if a woman had a smear and developed disease because of a sampling error, she also would have developed disease if she did not have a smear). Third, it was assumed that if a woman had a preneoplastic lesion that was detected on a cervicovaginal smear, she would receive adequate treatment (eg, repeated smears, colposcopy, loop electrosurgical excision procedure).

Data Sources

Life expectancies were obtained from the Surveillance, Epidemiologic, and End Results Program and the National Center for Health Statistics.[14,15] Probability data were obtained from a MEDLINE search of the literature published between 1960 and 1997. Cost data were obtained from the University of Iowa Hospitals and Clinics and the medical literature.

Outcomes

Outcomes measured were patient life expectancy, number of women who developed cancer, number of women with a false-positive cytology diagnosis, cost, and cost-effectiveness.[6,16]

A woman had a false-positive diagnosis if she had a cytologic diagnosis other than benign and did not have evidence of disease on follow-up. It was assumed that a woman who did not have a SIL, who had a SIL that was treated, or who had a SIL that was not treated and did not develop into cancer had a normal life expectancy. A woman who had a SIL that developed into cancer had a decreased life expectancy because her risks of dying from cancer were increased. It was assumed that if invasive cancer developed, the cancer was a squamous cell carcinoma.[14] If a SIL progressed to cancer, the life expectancy depended on the cancer stage.[14] Life expectancies were discounted at a fixed annual rate of 5%.[17]

Cost-effectiveness was determined by comparing the strategy of having a cervicovaginal smear with the strategy of not having a cervicovaginal smear. Compared with the no smear strategy, the cost-effectiveness of the smear strategy

was expressed as the additional cost required to gain a discounted year of life expectancy per patient.[6,18]

Assumptions

The variables used in the decision model were characterized as probabilities, life expectancies, and costs and are shown in the **Appendix**, as recommended by Siegel et al.[18]

Sensitivity Analyses

Several of the variables were systematically changed in the decision model to study the effect of these changes on the cost-effectiveness of cervicovaginal screening.[11] The variables changed were the cytology laboratory cost of cervicovaginal screening and the SIL rate.

To study the effect of new cytology technologies on cost-effectiveness, it was assumed that the new technologies had higher detection rates and costs than did the conventional methods.[7–9] Different cutoff values of cost-effectiveness were studied.[6,18] Currently, there is not a consensus about a level of expenditure that is cost-effective.[19,20] However, a cost of $50,000 per discounted life year gained is viewed as a reasonable cost that has been used as a gauge of cost-effectiveness.[19] Thus, using the no smear strategy as a reference, if the cost-effectiveness of the smear strategy was less than $50,000 per discounted life year gained, the smear strategy was assumed to be cost-effective.[6,19] Other cutoff values of cost-effectiveness ($100,000 and $200,000 per discounted life year) also were studied to determine the effect of changing the cutoff value.[18] These higher values indicate that society would be willing to spend more to increase the discounted life expectancy per patient by one year.[13]

For the new technology to be cost-effective, it was assumed that there must be an increased detection of HSILs, because HSILs have a much higher probability to progress to cancer than any other SIL.[21] It would be unnecessary to diagnose all HSILs as HSIL using the Bethesda system (eg, HSILs also could be diagnosed as ASCUS, AGUS, or LSIL), but the net gain in the number of HSILs detected on follow-up would have to increase to justify the increased cost of the new technology. Also assumed in this model was that women had a yearly smear and that a large percentage of the lesions that may have been missed by not using the new technology would have been detected in the routine follow-up smear.[1] If cancer developed because the technology was not used, it was assumed that the cancer was low stage.[14] LSILs were not studied in this model because the 1-year rate of progression to cancer of LSIL is extremely low.[21]

Results

Determining University of Iowa Costs and Disease-Detection Rates

The cytopathology laboratory costs associated with cervicovaginal screening preparation and interpretation are given in **Table 1**.

The breakdown of the 26,352 University of Iowa smears for 1995 by Bethesda system diagnostic category was as follows: negative, 21,942 (83.26%); atypical, 2,330 (8.84%); LSIL, 1331 (5.05%); HSIL, 591 (2.24%); dysplasia, not otherwise specified, 39 (0.15%); carcinoma, 14 (0.05%); suspicious for carcinoma, 11 (0.04%); and unsatisfactory, 94 (0.36%).

Decision Model to Determine Outcomes of Cervicovaginal Screening

The patient outcomes of cervicovaginal screening are given in **Table 2**. The cancers developing from SIL were

Table 1
Cost per Case Associated With Interpretation of a Cervicovaginal Smear

	Cost per Case ($)	Explanation
Laboratory	0.89	Equipment: $0.03 (usage and repair costs) Reagents and consumables: $0.86 (stains: $0.45; chemicals: $0.26; disposables: $0.15)
Personnel		
Benign cases	4.18	80% of cases Average cytotechnologist salary $22.80/h × 7.0 min = $2.66 per case 15% rescreen; average cytotechnologist salary $22.80/h × 5.0 min = $0.44 Average clerical salary $14.47/h × 5.0 min = $1.20 Average time to process and stain $13.86/h × 4.0 min = $0.92
Atypical cases	2.97	20% of cases Average cytotechnologist salary $22.80/h × 8.5 min = $3.23 per case Average cytopathologist salary $87.63/h × 6.5 min = $9.49 Average clerical salary $14.47/h × 5.0 min = $1.20 Average time to process and stain $13.86/h × 4.0 min = $0.92
Overhead	7.11	*Includes section $0.61; department $1.81; hospital $4.69*
Total	15.15	—

Table 2
Outcomes of Women Who Received or Did Not Receive a Cervicovaginal Smear

Outcome	Strategy	
	Smear	No Smear
Cancers per 10,000	9.48	42.12
Cancers developing from SILs per 10,000	0	32.63
False-positive results per 10,000	492	0
Patient discounted life expectancy (y)	18.6032	18.5978
Per patient cost ($)		
Smear alone	15.15	0
Smear and treatment	214.84	108.70
Cost-effectiveness ($ per discounted life year)		
Smear alone	2,805	Reference
Smear and treatment	19,655	Reference

SIL = squamous intraepithelial neoplasia.

the cancers that would develop if a cervicovaginal smear was not performed (ie, 32.63 SILs would progress to cancer per 10,000 women, if cervicovaginal smears were not obtained). The difference in discounted life expectancy per patient between having and not having a cervical smear was 1.97 days. The per patient cost for a smear and treatment included the costs of treating a woman with an atypical diagnosis (assuming the woman had a smear) and the costs of treating women with cancer (assuming it was diagnosed on a cervicovaginal smear or it developed from an undiagnosed SIL). Using a cost-effectiveness cutoff value of $50,000 per discounted life year gained, the cervicovaginal smear considered by itself or in conjunction with treatment for SIL and cancer was more cost-effective than not having a smear.

Sensitivity Analyses

In **Figure 1**, the cost-effectiveness of having a cervicovaginal smear (compared with not having a smear) to detect SILs is plotted against the cytology laboratory atypical rate. Atypical diagnoses were considered to be ASCUS, AGUS, LSIL, HSIL, and dysplasia, not otherwise specified. The atypical rate was assumed to be the same percentage of Bethesda system diagnoses as at the University of Iowa (eg, if the atypical rate was 32.756%, 10.10% of the atypical diagnoses would be LSILs [double the University of Iowa rate]). The number of detected invasive cancers was not considered in this analysis because the University of Iowa women with detected cancer generally had a history of cancer, and these detections were recurrences. Smears in the women were for follow-up rather than primary screening. As the cost of the cervicovaginal smear increased from $10 to $75, the cervicovaginal smear became less cost-effective at the same cytology laboratory atypical rate. By choosing a cost-effectiveness cutoff value of $50,000 per discounted life year gained, cervicovaginal screening was cost-effective regardless of the cost of the cervicovaginal smear, unless the atypical rate of the laboratory was low. For high-risk populations (ie, in a population with a high atypical rate) cervicovaginal screening would be cost-effective even if the cost of the cervicovaginal smear was high.

In **Figure 2**, the cost-effectiveness of using new laboratory technology is shown. The additional cost of the technology is plotted against the number of HSILs that would have to be detected by that technology before that technology would be considered cost-effective from the patient perspective. Three different cost-effective cutoff values were used ($50,000, $100,000, and $200,000) and represented the costs that society would be willing to spend to increase the discounted life expectancy per patient by 1 year. For example, assuming a cost-effectiveness cutoff value of $50,000 per discounted life year gained, if the technology cost $10, 236 additional HSILs would have to be detected per 10,000 women, for that technology to be cost-effective. If the number of additionally detected HSILs was lower, then that technology would not be cost-effective. As the cost-effective cutoff value increased (ie, society viewed that a life year was valued at more than $50,000), and the cost of the technology remained the same, that technology would be cost-effective at a lower increased HSIL detection rate.

Discussion

At the University of Iowa, the cytology laboratory component of cervical cancer prevention is cost-effective from a patient perspective. The cost of the cytology preparation, screen, and interpretation to gain a year of discounted life expectancy compared with not performing a cervicovaginal smear was $2,805. This value is far below generally accepted cost-effectiveness cutoff values and provides a perspective of the cytology laboratory cost component in the overall care of patients with cervical disease.[6,19,20,22–24]

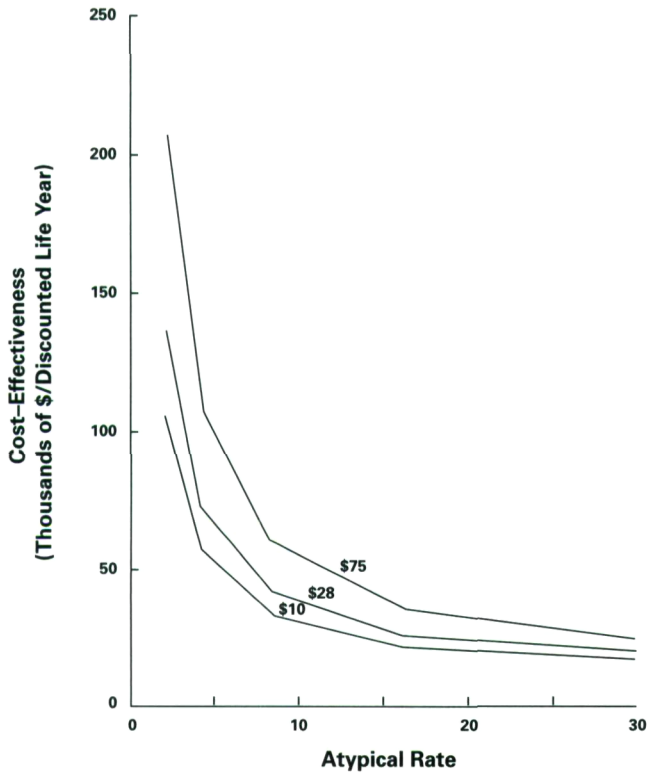

Figure 1 The cost-effectiveness of the cervicovaginal smear *vs* the laboratory atypical rate. The 3 curves represent 3 costs ($10, $28, and $75) of the laboratory component. As the laboratory atypical rate increases, the cost-effectiveness value of performing a cervicovaginal smear decreases (ie, performing the cervicovaginal smear becomes more cost-effective). As the cost of the cytology laboratory component increases and the atypical rate remains the same, the cost-effectiveness value of performing a cervicovaginal smear increases (eg, performing the cervicovaginal smear becomes less cost-effective).

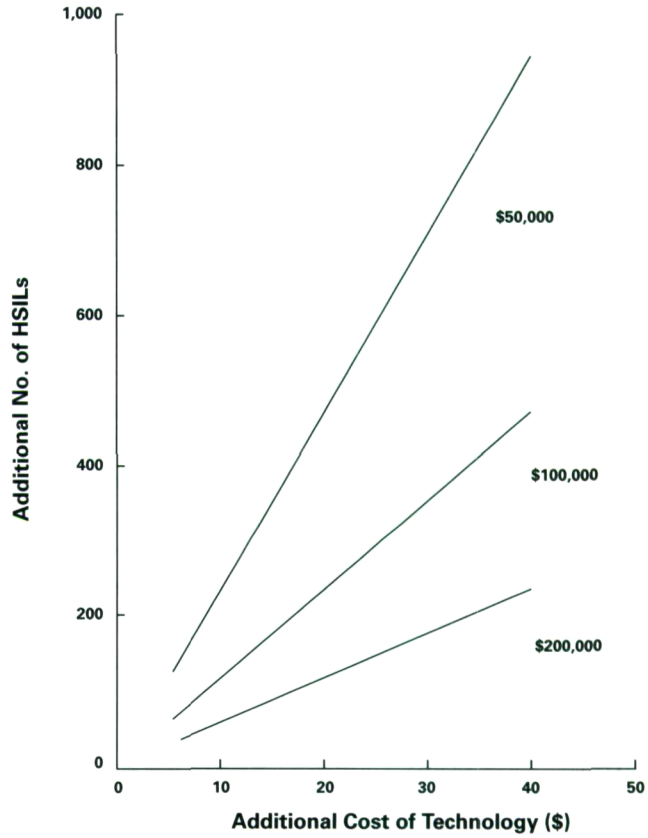

Figure 2 The additional number of high-grade squamous intraepithelial lesions (HSILs) *vs* the additional cost of the new technology. The 3 lines represent 3 cost-effectiveness cutoff values ($50,000, $100,000, and $200,000 per discounted life year gained). As the cost of the new technology increases, additional HSILs must be detected for that technology to be cost-effective. As the cost-effectiveness cutoff value increases and the cost of the technology remains the same, fewer HSILs need to be detected for that technology to be cost-effective.

As Eddy[1] reported, determining the cost-effectiveness of a test or treatment is a complex task, and in this study, the cytology cost is only one component. Incorporating treatment and follow-up costs and probabilities in the determination of the overall cost-effectiveness of cervicovaginal screening necessitates making assumptions about some data that rarely have been measured.[13] For example, detailed studies of the costs of treating women with cervical cancer have not been reported in the North American literature.[13] In fact, data related to treating cervical disease is generally reported in terms of charges instead of costs.[1] Nevertheless, using University of Iowa data, the entire process of cervical cancer prevention was cost-effective. This finding supports the conclusions of other cost-effectiveness studies that did not rigorously evaluate cytology laboratory costs.[1,3,4] Compared with the cost-effectiveness of the cytology component, the cost-effectiveness for the entire process of cervical cancer prevention was considerably higher, mainly because it was assumed that all women with an atypical smear were followed up aggressively. This indicates that the costs associated with preventing cervical cancer heavily depend on other aspects of prevention (eg, treating patients) rather than on pathology costs.

Calculation of cost-effectiveness depends on many variables, including the laboratory atypical rate, SIL progression to cancer rate, and rapidity of SIL progression to cancer.[6] The atypical rate is a composite of rates of different groups of patients who have different probabilities of having SIL or developing cancer. From the data shown in Figure 1, it can be seen that cervicovaginal screening of patient groups or laboratories with low atypical rates are problematic, at least in terms of population cost-effectiveness. Of course, other patient outcomes (eg, patient satisfaction or freedom of choice) may provide justification of screening low-risk groups.[18,25] For high-risk groups, cervicovaginal screening is

very cost-effective and remains cost-effective despite considerable increases in laboratory costs.

The use of new cytology laboratory technologies has been advocated for all patient groups, mainly because they reportedly increase detection of SILs compared with conventional methods.[7,9] However, in terms of cost-effectiveness, there is a trade-off between cost and increased detection. Technologies must show not only equivalent or better test performance characteristics (eg, sensitivity and specificity), but also that their cost is not out of line to limit cost-effectiveness. In the modeling performed in the present study, the number of additional "pick-ups" necessary to justify the additional cost of these technologies was determined. If women receive yearly smears, the additional pick-up of HSILs is key in determining if that technology is cost-effective.[21] This is because the medical literature indicates that an HSIL is the only lesion that is capable of progressing to cancer in the interval time.[21] An LSIL may progress to cancer, but because the progression time is so long, an LSIL would have a very high probability of being detected by subsequent smears before progressing to cancer.[2] Consequently, if women receive yearly smears, the added cost of a new technology to detect LSILs probably is not justified.

Although new technologies have demonstrated that they do detect some HSILs that conventional methods have missed, these data are based primarily on cytology diagnoses and not on long-term follow-up, which is the generally accepted "gold standard." In addition, some new technologies miss HSILs that conventional methods detect.[7–9] Based on the data in Figure 2, even assuming that society is willing to spend enormous amounts to gain an additional discounted life year per patient (eg, $200,000), the cost of the new technology would have to be low to justify an even modest gain in HSIL detection. For example, if the additional cost of the new technology was $10 per case, the new technology would have to detect an additional 59 HSIL cases per 10,000 women (at a cost-effectiveness cutoff of $200,000 per discounted life year saved) to be cost-effective. With lower cost-effectiveness cutoff values or higher technology costs, even more HSILs would need to be detected for that technology to be cost-effective. These high detection rates have not been demonstrated in the medical literature.[7–10, 26] This decision analytic study was not prospective, and additional prospective studies are needed to confirm automated cytology HSIL and LSIL detection rates in different patient populations.

In this model, a primary outcome of interest was life expectancy, and new technologies may add benefit besides increasing life expectancy.[18] For example, some new technologies may actually lower ASCUS rates, which could lower treatment costs, which could improve the cost-effectiveness of these technologies.[9] Other benefits of these technologies also were not addressed. For example, some technologies may lower costs of some laboratory components (eg, cytotechnologists may be able to screen more cases with a new technology) at the same time as increasing the costs of other components. The trade-offs of the cost benefits and limitations of new technologies have not been addressed, although currently, it may be assumed that overall laboratory costs increase with new technologies.

One benefit of some technologies is that they have been assigned their own *Current Procedural Terminology* code, indicating that these technologies may be billed for separately. Separate billing for using a new technology in cervicovaginal smears is important, given the well-recognized low per case rate for cytology reimbursement. Although using a new technology may increase reimbursement, the cost-effectiveness of using this technology still must be demonstrated for the cytology laboratory.[27] This shifts the focus of cost-effectiveness from patient-centered to laboratory-centered but still does not justify the use of new technologies from the patient perspective.

Even with high laboratory costs, cervical cancer prevention is cost-effective in moderate- to high-risk patient populations. Although new cytology technologies may increase the detection of SILs, current data have not shown that these new technologies are cost-effective in increasing patient life expectancy.

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References

1. Eddy DM. Screening for cervical cancer. *Ann Intern Med*. 1990;113:214–226.
2. Eddy DM. The frequency of cervical cancer screening: comparison of a mathematical model with empirical data. *Cancer*. 1987;60:1117–1122.
3. van der Graff Y, Zielhuis GA, Peer PGM, et al. The effectiveness of cervical screening: a population-based case-control study. *J Clin Epidemiol*. 1988;41:21–26.
4. Waugh N, Smith I, Robertson A, et al. Costs and benefits of cervical screening, III. *Cytopathology*. 1996;7:249–255.
5. Bishop JW. The cost of production in cervical cytology: comparison of conventional and automated primary screening systems. *Am J Clin Pathol*. 1997;445–450.
6. Raab SS. The cost-effectiveness of cervical vaginal rescreening. *Am J Clin Pathol*. 1997;108:525–536.
7. Mango LJ. Neuromedical Systems, Inc. *Acta Cytol*. 1996;40:53–59.
8. Patten SF, Lee JSJ, Nelson AC. NeoPath, Inc: NeoPath AutoPap 400 Automatic Pap Screener System. *Acta Cytol*. 1996;40:45–52.
9. Lee KR, Ashfaq R, Birdsong GG, et al. Comparison of conventional Papanicolaou smears and a fluid-based, thin-layer system for cervical cancer screening. *Obstet Gynecol*. 1997;90:278–284.
10. O'Leary TJ, Tellado M, Buckner S, et al. PAPNET-assisted rescreening of cervical smears: cost and accuracy compared with a 100% manual rescreening strategy. *JAMA*. 1998;279:235–237.

11. Weinstein MC, Fineberg HV. *Clinical Decision Analysis*. Philadelphia, Pa: Saunders; 1980:12–36.
12. The Bethesda Committee. *The Bethesda System for Reporting Cervical/Vaginal Diagnoses*. New York, NY: Springer-Verlag; 1994.
13. Raab SS, Steiner AL, Hornberger J. The cost effectiveness of treating women with a cervical vaginal smear diagnosis of atypical squamous cells of undetermined significance. *Am J Obstet Gynecol*. 1998;179:411–420.
14. Kosary CL, Ries LAG, Miller BA, et al, eds. *SEER Cancer Statistics Review, 1973–1992: Tables and Graphs*. Bethesda, Md: National Cancer Institute; 1995:145. NIH publication 96–2789.
15. National Center for Health Statistics, Public Health Service. *Vital Statistics of the United States: Life Tables*. Vol 2, section 6. Washington, DC: US Government Printing Office; 1988:6–67. DHHS publication (PHS) 88:1147.
16. Weinstein MC, Siegel JE, Gold MR, et al. Recommendations of the panel on cost-effectiveness in health and medicine. *JAMA*. 1996;276:1253–1258.
17. Lipscomb J. Time preference for health in cost effectiveness analysis. *Med Care*. 1989;27(suppl 3):S233–S252.
18. Siegel JE, Weinstein MC, Torrance GW. Reporting cost-effectiveness studies and results. In: Gold MR, Siegel JE, Russell LB, et al, eds. *Cost-Effectiveness in Health and Medicine*. New York, NY: Oxford University Press; 1996:276–303.
19. Owens DK, Sanders GD, Harris RA, et al. Cost-effectiveness of implantable cardioverter defibrillators relative to amiodarone for prevention of sudden cardiac death. *Ann Intern Med*. 1997;126:1–12.
20. Laupacis A, Feeny D, Detsky AS, et al. How attractive does a new technology have to be to warrant adoption and utilization: tentative guidelines for using clinical and economic evaluations. *CMAJ*. 1992;146:473–481.
21. Oster AG. Natural history of cervical intraepithelial neoplasia: a critical review. *Int J Gynecol Pathol*. 1993;12:186–192.
22. Gafni A, Birch S. Guidelines for the adoption of new technologies: a prescription for uncontrolled growth in expenditures and how to avoid the problem. *CMAJ*. 1993;148:913–917.
23. Naylor CD, Williams HI, Basinski A, et al. Technology assessment and cost-effectiveness analysis: misguided guidelines? *CMAJ*. 1993;148:921–924.
24. Laupacis A, Feeny D, Detsky AS, et al. Tentative guidelines for using clinical and economic evaluations revisited. *CMAJ*. 1993;148:927–929.
25. Raab SS, Hornberger J. The effect of a patient's risk taking attitude on the cost effectiveness of testing strategies in the evaluation of pulmonary lesions. *Chest*. 1997;111:1583–1590.
26. Stanley MW. Automated primary screening for gynecologic cytology: the time has not yet come. *Am J Clin Pathol*. 1998;109:10–15.
27. Raab SS, Bottles K. Cohen MB. Technology assessment in anatomic pathology: an illustration of technology assessment techniques in fine needle aspiration biopsy. Arch Pathol Lab Med. 1994;18:1173–1180.
28. DeMay RM. The Pap smear. *The Art and Science of Cytopathology*. Chicago, Ill: ASCP Press; 1996:61–206.
29. Fireman B, Quesenberry C, Somkin C. The Cost of Care for Cancer in a Health Maintenance Organization: Final Report to the National Cancer Institute. Oakland, Calif: Kaiser Permanente; 1994. Publication NO1-CN-05224-02-1.
30. Riley GF, Potosky AL, Lubitz JD, et al. Medicare payments from diagnosis to death for elderly cancer patients by stage at diagnosis. *Med Care*. 1995;38:828–841.

Appendix

Probabilities

Appendix Table 1 gives the probabilities used.

Progression to Invasive Cancer

Only a percentage of high-grade squamous intraepithelial lesions (HSILs) progress to invasive cancer, and the literature reports a wide range of progression rates.[1] Although different HSIL subtypes each have a different progression rate, these rates were combined in this model. Low-grade squamous intraepithelial lesions (LSILs) were not assumed to progress to cancer, assuming that women received yearly smears.[1]

Progression to Invasive Cancer in 1 Year

Of the HSILs that will progress to cancer, a percentage of HSILs will progress in 1 year.[1,2] The progression rates in Appendix Table 1 are a percentage of the HSILs that will progress to cancer and not a percentage of all HSILs.

Carcinoma Stage

If a patient had an HSIL that progressed to cancer, the cancer stage was assumed to be that described by the Surveillance, Epidemiology, and End Results program registry.[3]

Appendix Table 1
Probabilities Used in the Decision Model[1,3,5,9]

Variable	Probability (%)
Progression of HSIL to cancer	10
Progression of HSIL to cancer in 1 year	25
Carcinoma stage	
Local	51
Regional	33
Distant	8
Unstaged	7
Probability of HSIL given smear diagnosis	
HSIL	100
LSIL	20
Dysplasia, not otherwise specified	5
Atypia	10

HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion.

Appendix Table 2
Life Expectancies[3,6]

Stage of Disease	Life Expectancy (y)
No cancer	50.7
Local	46.3
Regional	26.6
Distant	6.6
Unstaged	32.0

Appendix Table 3
Treatment and Procedural Costs

Stage of Disease	Costs ($) by Stage of Disease in 6-Month Intervals*[7,8]			
	Initial	Continuing	Prefinal	Terminal
Local	8,500	3,000	7,200	10,600
Regional	10,000	3,300	7,700	11,700
Distant	1,200	4,700	9,900	11,900
Unstaged	7,200	3,900	8,100	9,800

Procedure	Procedural Costs by Service ($)†		
	Gynecology	Pathology	Total
Colposcopy	250	0	250
Colposcopy with biopsy	383	94	477
Loop electrosurgical excision procedure	855	374	1,229
Routine examination	50	—	50

* Initial cost is the cost of diagnosis and the first 6 months of treatment; continuing, the cost of the 6-month interval following initial treatment interval, but not including prefinal or terminal intervals; prefinal, the cost of the 6-month interval before the terminal interval; and terminal, the cost of the 6-month interval before death.
†From the University of Iowa Hospitals and Clinics, Iowa City and Raab et al.[2]

Probability of HSIL Given a Smear Diagnosis

There is a probability of an HSIL given any Bethesda system diagnosis.[4,5] The probability is highest for HSIL and lower for LSIL and atypical squamous cells of undetermined significance.[5]

Life Expectancy

Life expectancies with cancer were estimated from 5-year survival rates **Appendix Table 2**.[3,6]

Costs

The costs by stage of disease are costs associated with the diagnosis and treatment of invasive carcinoma **Appendix Table 3**. Because relatively few women in the United States have invasive cervical cancer, there are no large cost studies about their care. Costs were abstracted from the costs of treating noncervical cancers of similar stage.[7,8] The initial, continuing, prefinal, and final (terminal) costs were reported for 6-month intervals.[2,7,8] The initial cost represents the cost of the initial work-up and treatment (eg, operative, radiologic, and anesthetic costs).[2] These costs represent averages taken across a patient cohort during the first 6 months of care.[2,7,8] Because most patients were hospitalized, these costs were high compared with continuing, prefinal, and final costs. The continuing costs represent long-term costs (eg, repeat hospital visits, radiotherapy, home care, and pharmaceutical costs). The high prefinal and final costs reflect that costs increase if a patient dies of disease. For example, patients dying of cervical cancer may be hospitalized more frequently or may receive more intensive home care. These costs may be higher in other geographic regions. For a patient who had cancer but did not die of cancer, the overall cost consisted of an initial cost and 1 block of continuing cost. For a patient who died of cancer, the overall cost consisted of an initial, prefinal, final cost, and 3 blocks of continuing cost.

The procedural costs (Appendix Table 3) consisted of a gynecology charge and a pathology charge. Each charge consisted of a hospital and a professional charge.

Appendix References

1. Oster AG. Natural history of cervical intraepithelial neoplasia: a critical review. *Int J Gynecol Pathol*. 1993;12:186–192.
2. Raab SS, Steiner AL, Hornberger J. The cost effectiveness of treating women with a cervical vaginal smear diagnosis of atypical squamous cells of undetermined significance. *Am J Obstet Gynecol*. 1998;179:411–420.
3. Kosary CL, Ries LAG, Miller BA, et al, eds. *SEER Cancer Statistics Review, 1973–1992: Tables and Graphs*. Bethesda, Md: National Cancer Institute; 1995:145. NIH publication 96–2789.
4. Raab SS. The cost-effectiveness of cervical vaginal rescreening. *Am J Clin Pathol*. 1997;108:525–536.
5. DeMay RM. The Pap smear. *The Art and Science of Cytopathology*. Chicago, Ill: ASCP Press; 1996:61–206.
6. National Center for Health Statistics, Public Health Service. *Vital Statistics of the United States: Life Tables*. Vol 2, section 6. Washington, DC: US Government Printing Office; 1988:6–67. DHHS publication (PHS) 88:1147.
7. Fireman B, Quesenberry C, Somkin C. The Cost of Care for Cancer in a Health Maintenance Organization: Final Report to the National Cancer Institute. Oakland, Calif: Kaiser Permanente; 1994. Publication NO1-CN-05224-02-1.
8. Riley GF, Potosky AL, Lubitz JD, et al. Medicare payments from diagnosis to death for elderly cancer patients by stage at diagnosis. *Med Care*. 1995;38:828–841.
9. Weinstein MC, Siegel JE, Gold MR, et al. Recommendations of the panel on cost-effectiveness in health and medicine. *JAMA*. 1996;276:1253–1258.

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