Allocating Costs and Benefits in Disease Prevention Programs: An Application to Cervical Cancer Screening

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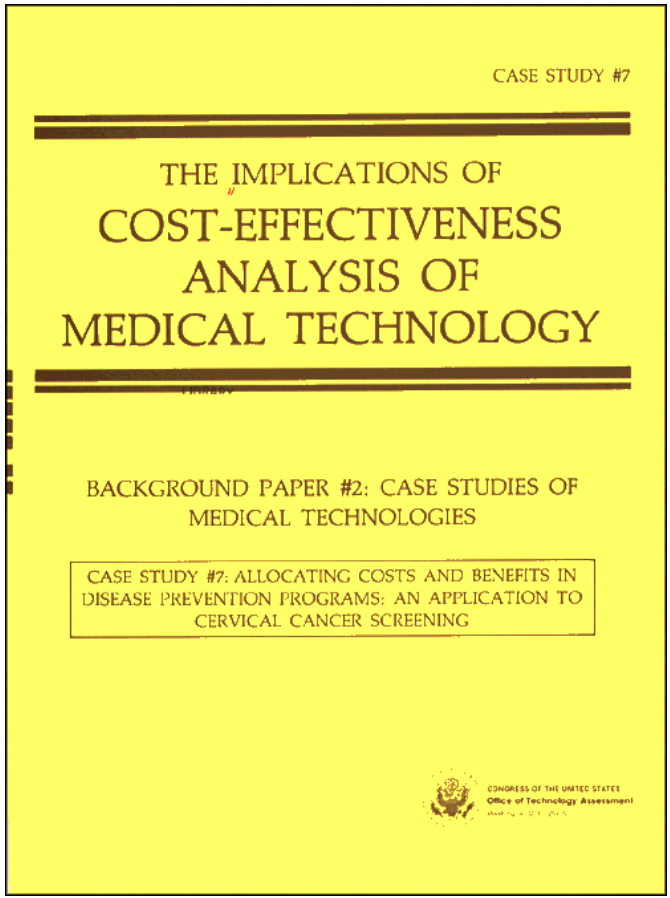

THE IMPLICATIONS OF COST-EFFECTIVENESS ANALYSIS OF MEDICAL TECHNOLOGY

JUNE 1981

BACKGROUND PAPER #2: CASE STUDIES OF MEDICAL TECHNOLOGIES

CASE STUDY #7: ALLOCATING COSTS AND BENEFITS IN DISEASE PREVENTION PROGRAMS: AN APPLICATION TO CERVICAL CANCER SCREENING

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OTA Background Papers are documents that contain information believed to be useful to various parties. The information undergirds formal OTA assessments or is an outcome of internal exploratory planning and evaluation. The material is usually not of immediate policy interest such as is contained in an OTA Report or Technical Memorandum, nor does it present options for Congress to consider.

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Foreword

This case study is one of 17 studies comprising Background Paper #2 for OTA'S assessment, The ***in-zpiications of Cost-Effectiveness Analysis of Medical Technology.*** That assessment analyzes the feasibility, implications, and value of using cost-effectiveness and cost-benefit analysis (CEA/CBA) in health care decisionmaking. The major, policy-oriented report of the assessment was published in August 1980. In addition to Background Paper #2, there are four other background papers being published in conjunction with the assessment: 1) a document which addresses methodological issues and reviews the CEA/CBA literature, published in September 1980; 2) a case study of the efficacy and cost-effectiveness of psychotherapy, published in October 1980; 3) a case study of four common diagnostic X-ray procedures, to be published in summer 1981; and 4) a review of international experience in managing medical technology, published in October 1980. Another related report was published in September of 1979: ***A Review of Selected Federal Vaccine and*** immunization Policies.

The case studies in ***Background Paper #2: Case Studies of Medical Technologies*** are being published individually. They were commissioned by OTA both to provide information on the specific technologies and to gain lessons that could be applied to the broader policy aspects of the use of CEA/CBA. Several of the studies were specifically requested by the Senate Committee on Finance.

Drafts of each case study were reviewed by OTA staff; by members of the advisory panel to the overall assessment, chaired by Dr. John Hogness; by members of the Health Program Advisory Committee, chaired by Dr. Frederick Robbins; and by numerous other experts in clinical medicine, health policy, Government, and economics. We are grateful for their assistance. However, responsibility for the case studies remains with the authors,

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Preface

This case study is one of 17 that comprise Background Paper #2 to the OTA project on the ***Implications of Cost-Effectiveness Analysis of Medical Technology.*** * The overall project was requested by the Senate Committee on Labor and Human Resources. In all, 19 case studies of technological applications were commissioned as part of that project. Three of the 19 were specifically requested by the Senate Committee on Finance: psychotherapy, which was issued separately as Background Paper *#3;* diagnostic X-ray, which will be issued as Background Paper #5; and respiratory therapies, which will be included as part of this series. The other 16 case studies were selected by OTA staff.

In order to select those 16 case studies, OTA, in consultation with the advisory panel to the overall project, developed a set of selection criteria. Those criteria were designed to ensure that as a group the case studies would provide:

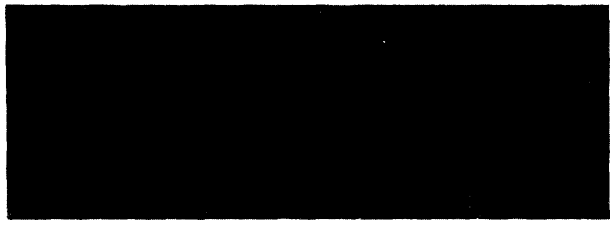
- examples of types of technologies by function (preventive, diagnostic, therapeutic, and rehabilitative);
- examples of types of technologies by physical nature (drugs, devices, and procedures);
- examples of technologies in different stages of development and diffusion (new, emerging, and established);
- examples from different areas of medicine (such as general medical practice, pediatrics, radiology, and surgery);
- examples addressing medical problems that are important because of their high frequency or significant impacts (such as cost);
- examples of technologies with associated high costs either because of high volume (for low-cost technologies) or high individual costs;
- examples that could provide informative material relating to the broader policy and methodological issues of cost-effectiveness or cost-benefit analysis (CEA/CBA); and
- examples with sufficient evaluable literature.

On the basis of these criteria and recommendations by panel members and other experts, OTA staff selected the other case studies. These 16 plus the respiratory therapy case study requested by the Finance Committee make up the 17 studies in this background paper.

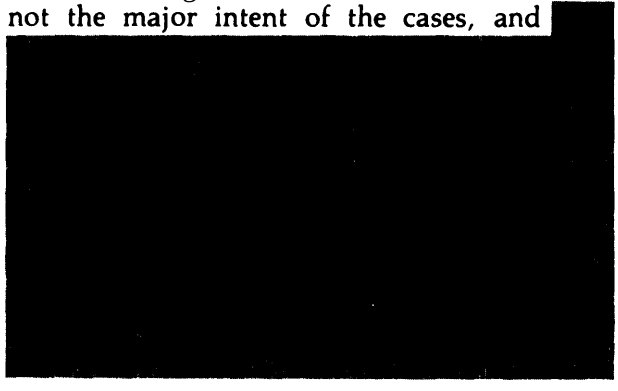
All case studies were commissioned by OTA and performed under contract by experts in academia. They are authored studies. **OTA subjected each case study to an extensive review process. Initial drafts of cases were reviewed by OTA staff and by members of the advisory panel to the project. Comments were provided to authors, along with OTA'S suggestions for revisions. Subsequent drafts were sent by OTA to numerous experts for review and comment. Each case was seen by at least *20,* and some by *40* or more, outside reviewers. These reviewers were from relevant Government agencies, professional societies, consumer and public interest groups, medical practice, and academic medicine. Academicians such as economists and decision analysts also reviewed the cases. In all, over *400* separate individuals or organizations reviewed one or more case studies. Although all these reviewers cannot be acknowledged individually, OTA is very grateful for their comments and advice. In addition, the authors of the case studies themselves often sent drafts to reviewers and incorporated their comments.

These case studies are authored works commissioned by OTA **The authors are responsible for the conclusions of their specific case study. These cases are not statements of official OTA position. OTA does** not make **recommendations or endorse particular technologies. ,During the various stages"of the** review and **revision process, therefore, OTA encourage the athors to present balanced information and to** recg**nize divergent points of view. In two cases. In two cases, OTA decided "that in order to more fully present divergent views on particular technologies a commentary should be added to the case study. Thus, following the case**

*Office of Technology Assessment, U.S. Congress, The Implications of Cost-Effectiveness Analysis of Medical Technology, GPO stock No. **052-003 -00765-7** (Washington, D. C.: U.S. Government Printing Off Ice, August **1980).**



The case studies were selected and designed to fulfill two functions. The first, and primary, purpose was to provide OTA with specific information that could be used in formulating general conclusions regarding the feasibility and implications of applying CEA/CBA in health care. By examining the 19 cases as a group and looking for common problems or strengths in the techniques of CEA/CBA, OTA was able to better analyze the potential contribution that these techniques might make to the management of medical technologies and health care costs and quality. The second function of the cases was to provide useful information on the specific technologies covered. However. this was not the major intent of the cases, and



Some of the case studies are formal CEAS or CBAS; most are not. Some are primarily concerned with analysis of costs; others are more concerned with analysis of efficacy or effectiveness. Some, such as the study on end-stage renal disease, examine the role that formal analysis of costs and benefits can play in policy formulation. Others, such as the one on breast cancer surgery, illustrate how influences other than costs can determine the patterns of use of a technology. In other words, each looks at evaluation of the costs and the benefits of medical technologies from a slightly different perspective. The reader is encouraged to read this study in the context of the overall assessment's objectives in order to gain a feeling for the potential role that CEA/CBA can or cannot play in health care and to better understand the difficulties and complexities involved in applying CEA/CBA to specific medical technologies.

The 17 case studies comprising ***Background Paper #2*** (short titles) and their authors are:

Artificial Heart: Deborah P. Lubeck and John P. Bunker
Automated Multichannel Chemistry Analyzers: Milton C. Weinstein and Laurie A. Pearlman
Bone Marrow Transplants: Stuart O. Schweitzer and C. C. Scalzi
Breast Cancer Surgery: Karen Schachter and Duncan Neuhauser
Cardiac Radionuclide Imaging: William B. Stason and Eric Fortess

Cimetidine and Peptic Ulcer Disease: Harvey V. Fineberg and Laurie A. Pearlman
Colon Cancer Screening: David M. Eddy
CT Scanning: Judith L. Wagner
Elective Hysterectomy: Carol Korenbrot, Ann B. Flood, Michael Higgins, Noralou Roos, and John P. Bunker
End-Stage Renal Disease: Richard A. Rettig
Gastrointestinal Endoscopy: Jonathan A. Showstack and Steven A. Schroeder
Neonatal Intensive Care: Peter Budetti, Peggy McManus, Nancy Barrand, and Lu Ann Heinen
Nurse Practitioners: Lauren LeRoy and Sharon Solkowitz
Orthopedic Joint Prosthetic Implants: Judith D. Bentkover and Philip G. Drew
Periodontal Disease Interventions: Richard M. Scheffler and Sheldon Rovin
Selected Respiratory Therapies: Richard M. Scheffler and Morgan Delaney

These studies will be available for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. *20402.* Call OTA'S Publishing Office *(224-8996)* for availability and ordering information.

Case Study #7

Allocating Costs and Benefits in Disease Prevention Programs: Application to Cervical Cancer Screening,

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AUTHOR'S ACKNOWLEDGMENTS

I acknowledge many debts of gratitude, but the primary one is to individual faculty members at the University of California at Los Angeles. Dr. Stuart Schweitzer worked with me throughout the entire project and spent numerous hours with me discussing the economic and theoretical constructs of the study; Dr. Shari Cretin was extremely helpful, particularly during the process of modeling the disease; Dr. Elizabeth Stern served as the resident expert on cervical cancer epidemiology—much of my data was drawn from her excellent work; Dr. Lester Breslow provided a valuable overview of the entire project; Dr. Robert Andrews helped a great deal, not only with the cost analysis, but also as an effective critic from outside the health field; finally, Dr. Michael GranfieId was instrumental in the reformulation of the financial analysis.

Regarding the gathering of data and information, I am particularly appreciative of Vicky Reyes, Administrator of the Porta-Pap Clinic at Los Angeles County/University of Southern California Medical Center. Her knowledge and insight were invaluable to the estimation of costs associated with the clinic model.

I also thank Sue Luce who spent hours editing the manuscript.

Contents

LIST OF TABLES

LIST OF FIGURES

Case Study #7:

Allocating Costs and Benefits in Disease Prevention Programs: An Application to Cervical Cancer Screening

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SUMMARY

This study is an attempt to advance the state of the art of cost-effectiveness analysis (CEA) as the technique pertains to disease prevention and health promotion programs. Cervical cancer screening is used as the subject of analysis to demonstrate the application of CEA to a disease prevention program. First, the disease process is modeled using a Markov chain technique to "age" a simulated population of 30- to 39-year-old women for 10 years, using disease transition probabilities reported in the literature. Then, the cost effectiveness of screening at different intervals, ranging from no screening to annual screening for the 10-year period, is calculated. The effects of the following are evaluated: 1) different migration patterns, 2) different risk groups, 3) different modes of administering Pap tests, and 4) joint production considerations. The sensitivity of the results both to various discount rates and to a range of Pap test error rates are also tested.

The results of the analysis indicate that a private party always has a financial incentive to postpone screening, whereas society finds it more cost effective to screen than not to screen, but *only* at infrequent intervals. The cost effectiveness of screening is markedly affected when a more efficient (i. e., less costly) delivery mode is simulated, and it is significantly affected when joint production effects are considered; however, it is not very sensitive to small changes in the discount rate, which initially was set at 10 percent, nor to varying assumptions regarding Pap test error rates.

Since private parties who may be interested in offering health promotion/disease prevention programs would incur the full cost of such programs while deriving only a portion of the benefits, we conclude that if society wants the private sector to screen for cervical cancer at a societally determined optimal rate, then society must be willing to subsidize the cost of the screening. We further conclude that the cost effectiveness of cervical cancer screening is much more affected by the costs assigned to screening than by different assumptions regarding the discount and error rates. These conclusions suggest that more attention should be paid to providing such programs at the most efficient level, that proper accounting measures should be used, and that less attention should be paid to the precise rates of discount and error.

INTRODUCTION

Prevention and early disease detection—The words alone suggest the saving of life, limb, misery, and heartbreak. Certainly, research has shown that prevention and early detection of disease can be effective, To mention just a few effective prevention programs, for example, decreasing the speed on our highways saves lives and limbs, as well as property; decreasing smoking and weight lowers general mortality; immunization prevents illness and death; and fluoride treatment decreases dental caries. Belloc and Breslow (2) have shown that moderate changes in basic lifestyle are associated with lower overall mortality. In addition, over the past century, there has been overwhelming evidence that much of the success in limiting disease and extending life is attributable to basic preventive activities.

Nevertheless, the vast majority of health dollars are spent on acute medical care that produces little change in overall mortality or morbidity rates, and there is every reason to believe that the future promises more of the same *(26),* Why does the health care sector persist in remaining wedded to the treatment mode of medical care to the near exclusion of the preventive mode? We know prevention can be effective, but can it be cost effective?

One reason for the neglect of preventive care may have to do with the manner in which the costs of health promotion/disease prevention programs are incurred and the benefits are accrued. The costs are usually certain, incurred in the present, and not borne by the recipient of many of the benefits. The benefits, on the other hand, are ordinarily uncertain and are generally accrued in the future.

Suppose, for example, that a health insurer such as Blue Cross is considering whether to include hypertension screening in its insurance package. Part of its decision will be based on a determination of whether such a program is efficient, i.e., whether the savings (benefits) due to the future decreased cardiovascular disease will be equal to or greater than the costs of the screening program. Most of the costs of the program can be estimated rather accurately, will be incurred in the present, and will be borne only by Blue Cross. However, the benefits of screening will accrue to: 1) the individual, in terms of more earnings, less morbidity, and longer life; 2) the life insurer, in terms of postponed death benefit payments and more premium payments; 3) the employer, in terms of a healthier, more productive work force, lower employee turnover, and lower disability payments; 4) the government at all levels, in terms of lower medical costs (for those "saved" individuals who do not have heart disease while on medicare), higher tax revenues and fewer unemployment benefits; *5)* society in general, in terms of higher general prosperity; and, finally, 6) Blue Cross, in terms of lower future medical costs due to heart disease.1 Furthermore, many of the benefits that might otherwise accrue to Blue Cross will be lessened because some individuals who participate in the initial screening programs will not continue treatment and others will change insurance plans owing to dissatisfaction, job change, or advanced age leading to medicare eligibility. The medical care cost savings which accrue to Blue Cross will do so over many years and consequently must be discounted at a substantial rate (probably 10 percent). The net effect of all these factors may make the hypertension screening program financially unattractive to Blue Cross.

Most other health promotion/disease prevention programs can be analyzed in a similar manner, with the analysis producing similar results. Consequently, health insurers such as Blue Cross and medicare tend not to include health promotion/disease prevention coverage in their plans, irrespective of whether the benefits in their aggregate outweigh (or justify) the costs in their aggregate,

Nevertheless, many health promotion/disease prevention programs do exist outside of the country's mainstream—private fee-for-service, third-party reimbursed—health care system. The military, for instance, strongly encourages

[1]This` enumeration of benefits Includes much double counting,

preventive measures such as regularly scheduled physical examinations and immunizations, as well as programs in weight control, exercise, drug counseling, venereal disease control, and safety. Unlike Blue Cross, the military has many natural incentives to maintain a healthy population, becuase although the military incurs the costs of the aforementioned programs, it also accrues many of the benefits.

We also observe an increasing number of health promotion programs in the private sector with industry's exercise activities, antismoking clinics, alcoholism programs, etc., and a proliferation of independent, health-oriented organizations such as Weight Watchers, Smokenders, Alcoholics Anonymous, health spas, and organic food stores. The thriving existence of these organizations indicates that some employers and many individuals believe that sufficient benefits accrue to them to justify their paying for particular preventive programs.

Essentially, then, many different private parties are evaluating health programs independently and are allocating resources on the basis of their own perception of the programs' value. Since the benefits are often accrued by other and unrelated parties, however, society may be able to further the public welfare by encouraging those programs whose total benefits to society are proven to exceed total ***costs*** to society. Thus, evaluation methods need to be developed and used to help society determine which programs should be encouraged, for whom, and at what level.

This study attempts to shed light on some of the economic and other policy issues related to health promotion and disease prevention. A basic cost-effectiveness methodology for cervical cancer screening is developed, and various costs and benefits are gathered in different combinations to simulate the objective functions of the many potential financiers of this particular disease prevention program. We ask: For whom is cervical cancer screening cost effective, under what conditions, and at what screening intensity?

BACKGROUND: CERVICAL CANCER

Disease Etiology

The etiology of cervical cancer has been difficult to trace with precision, because the evidence confirming the presence of this disease interrupts its natural course. Nevertheless, there is considerable circumstantial and epidemiological evidence that suggests the pathway that cervical cancer takes.

A recent and important long-term study was done and reported by a Canadian task force appointed by the Conference of Deputy Ministers of Health **(38).** After many years of data gathering and a 1ong history of cervical screening, the task force concluded that the progressiveness of the disease is suggested, as indicated in table 1. (See app. A for definitions of technical medical terms.) The Canadian task force reported the following *(38):*

1. Dysplasia:
   a. The annual progression rate from dysplasia to cancer is *5* to *6.4* percent.
   b. The incidence of carcinoma in situ (CIS) in a population with dysplastic changes is *49/1,000* but is only *0.04/1,000* in a population without them.
   c. The spontaneous regression rate from dysplasia to normal is 30 to **40 percent,** but dysplastic lesions are more apt to return in a reverted normal population than they would be in a completely nor-

Table 1 .—Progressive Stages of Cervical Cancer

Disease stage	Mean age at diagnosis
Dysplasia	24.0
Carcinoma in situ *(CIS)*	34.0
CIS with microinvasion	43.7
Occult carcinoma of cervix	48.6
Clinical carcinoma of cervix	52.0

mal population. Also, the greater the degree of dysplasia, the better the chance CIS and invasive carcinoma will develop.

2. Carcinoma in situ:
   - **a.** Progression rates from CIS to invasive carcinoma have been reported as ranging from *25* to *70* percent, but the progression rate is very difficult to observe because CIS is generally treated when discovered.
   - b. The phase lasts from 1 to 20 years, depending on the study cited.
   - c. The disease regresses in *o* to *25* percent of cases, depending on the study cited.
   - d. It is believed that, except in rare cases, CIS precedes invasive carcinoma. [2]

The task force also reported that there is some evidence which shows that the incidence of clinical cancer of the cervix began declining prior to the screening program **(38).** Although it is not possible to prove that screening has had an effect on this decline in incidence, data the task force examined do tend to indicate that screening has had a significant effect on the decline in mortality from carcinoma of the uterus, a finding confirmed by many others *(4,8,28).* In contrast to these investigators, Dickenson, et al. (12) claim that the incidence of clinical carcinoma of the cervix is increasing, and Boyes (3) claims it is remaining constant; and both report their data as showing an increasing incidence of CIS.

A study from Finland (18) found results with respect to the progression of the disease that somewhat resembled the results of the Canadian task force. It reported that the probability of a preinvasive lesion's progressing to invasive cancer was 0.28 to 0.39, while the probability that an invasive cancer was either not preceded by a preinvasive stage or was preceded by a preinvasive stage of less than 5 years was O to 0.38. The latter finding is not surprising when one considers that other studies have also demonstrated that the preinvasive stages of older women are of relatively short duration. Dunn (14), for example, estimated the duration of CIS to be approximately 16 years for 20- to 30-year-old women but less than 5 years for postmenopausal women. This finding may be due to the fact that the site of the lesions on the cervix in older women is not as exposed as it is in younger women and is consequently less available for scraping.

Incidence

Although much research has been conducted in an attempt to determine the true incidence of cervical cancer, the findings reported in the literature are not consistent. Nevertheless, there is general agreement that the incidence of cervical cancer is, at least secondarily, highly correlated with age and socioeconomic status. Because of this correlation, much of the work using a single incidence/prevalence rate for a demographically diverse population is not very helpful.[3]

Tables 2 and 3 are presented below to demonstrate the variability of CIS and invasive carcinoma incidence rates reported in the literature (some of the data have been combined or interpolated for purposes of comparison). The rates vary enormously across categories of age and socioeconomic status and across studies. However, the trends seem to be more consistent. Note that the incidence of CIS is highest in the middle years, whereas the incidence of invasive carcinoma rises continuously with age until well after menopause. Note also that CIS, not invasive disease, accounts for most of the variability and high frequency. When cultural lines **are** compared, the incidence of CIS is seen to be significantly higher in blacks than in whites, in non-Latins than in Latins, and in poor than nonpoor.

The reason for the extreme variability of CIS incidence rates within categories and across studies is unknown. However, some of the variation may be due to test error and to the timing of incidence rate calculations. For instance, if the false-negative rate is very high, any subsequent screening will be "contaminated" by the "leftover prevalence" cases. One theoretical

[2] It should be noted that other studies not cited i n the task force's report have pointed to a small percentage of cases in which either no preinvasive lesion or one of very short duration preceded invasive carcinoma **(18).**

[3] Incidence refers to new cases; prevalence refers to existing cases.

Table 2.—Annual Incidence of Carcinoma in Situ[a] (cases per 100,000 population)

Age	Mayo Clinic (12)	Alameda Co., Calif. (13) (white)	Alameda Co., Calif. (13) (black)	Connecticut (13)	Nevada (13)	El Paso (13) (Latin)	El Paso (13) (non-Latin)	British Columbia (38) 1966-70	Miami (2) (indigent)	Miami (2) (private)
15 to 19.	0	**4**	**176**	*2*	0	0	o	–	1,880	0
20 to 24.	94	121	838	42	297	0	55	200		
									2,024	165
25 to 29.	194	390	1,240	131	860	197	294	350		
30 to 34.	163	729	1,308	176	903	310	600	285		
									1,020	100
35 to 39.	163	704	590	197	992	316	499	200		
40 to 44.	57	557	609	171	736	229	528	150		
									790	310
45 to 54.	78	287	144	88	443	180	285	80		
									1,772	312
									597	187
55 to 64.	17	183	117	36	183	153	190	45		
65+	10	83	129	21	83	30	71	43		

[a] Numbers in parentheses refer to the references in the list at the end of this case study

Table 3.—Annual Incidence of Invasive Carcinoma' (cases per 100,000 population)

Age	Mayo Clinic (12)	Alameda Co., Calif. (13) (white)	Alameda Co., Calif. (13) (black)	Connecticut (13)	Nevada (13)	El Paso (13) (Latin)	El Paso (13) (non-Latin)	Alameda Co. (28) 1968-69	British Columbia (38) 1966-70	Mean
15 to 19. ., ...	0	0	0	0	0	0	o	–	–	0
20 to 24.	5		5	1	5	0	0		5	2
25 to 29. ., ...	0		o	7	24	13	8		20	9
30 to 34.	0	30	23	10	44	35	10	26	28	23
35 to 39.	18	42	46	18	51	61	20	15	50	36
40 to 44.	26	34	45	22	55	86	33	43	68	46
45 to 54.	36	34	85	24	55	105	40	31	65	53
55 to 64.	26	50	109	26	71	92	55	38	103	63
65+	27	45	85	29	59	113	89	44	73	63

[a] Numbers in parentheses refer to the references in the list at the end of this case study

model has been developed (7) which demonstrates that subsequent tests will asymptotically approach the true incidence. Therefore, if the study in question is calculating an incidence rate using second or even third test screening data and its test errors are high, the reported incidence will be proportionally overstated. It is also probably safe to speculate that the studies reporting very high incidence rates are unwittingly including many prevalence cases, especially in light of the much lesser variation in invasive incidence.

In light of the discussion above, it is interesting to note that Dickenson's study at the Mayo Clinic (12) reported both a low incidence rate (see table 2) and a low false-negative rate (3.3 percent). The clinic has been screening since 1947, so presumably the asymptote had been reached by the time the incidence was calculated on the respective cohorts.

Detection

Decision Tree Analysis

With minor variations, most authors agree on the general decision strategy for the appropriate method of cervical cancer diagnosis (23,27,34, 41). The consensus is that an atypical or abnormal Pap test should be followed by colposcopy. Kuptsow **(23)** suggests two positive Paps for mild dysplasia prior to examination of the patient by colposcopy. Nyirjesy *(27)* recommends that anti-infectious treatment be given to all patients with atypical Pap smears before a second Pap, whose positive finding would then lead to colposcopy. He reports that 84 percent

of those with atypical Pap smears are presented as normal after anti-infectious treatment.

In any case, most authors (23,34,41) suggest that biopsy should follow colposcopy when indicated. Nyirjesy *(27)* recommends immediate biopsy under colposcopic control. Yates, et al. (41) and Stafl, et al. (34) agree that an unsatisfactory colposcopic examination should be followed by a diagnostic cone biopsy.

Appropriate treatment for confirmed diagnosis is indicated in figure **1.** An expanded form of the Stafl, et al. (34) decision tree will be used as the appropriate course of action in this study.

Pap Test Error Rates

There has been a considerable amount of disagreement concerning the precise magnitude of Pap test error rates. Part of the reported variation is due to definitional problems, part to the nature of Pap testing itself, and the rest to the fact that, for ethical reasons, the error rates can never be proven empirically.

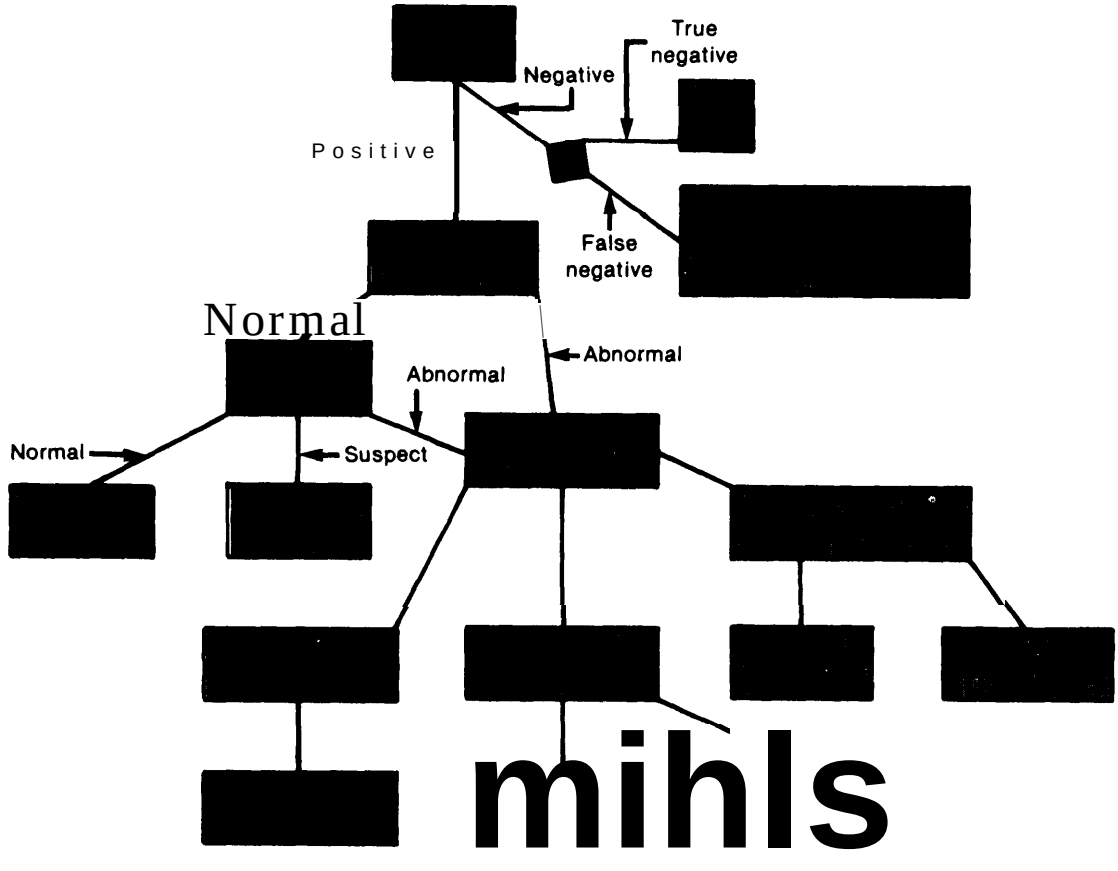
DEFINITIONAL PROBLEMS

The first definitional problem is the category into which Pap test results must be placed. The classification of Pap test results is generally regarded as consisting of the following (27):

Class 1	Negative
Class II	Atypical
Class 111	Suspicious
Class IV	Strongly suggestive of malignancy
Class V	Conclusive for malignancy

The few researchers who state where they distinguish the negative from the positive pole make the distinction between classes II and III—

Figure 1 .- Decision Tree for Cervical Cancer Screening and Treatment"



*See app. A for deflnitionsof medical terms that appear in this figure

but the subjective nature of those classifications hints at the obscurity of the Pap test result. The Pap test result is not clearly positive or negative, but is regarded as an intermediate step leading to more conclusive results. As was previously mentioned, Nyirjesy **(27)** reported that in his study **84** percent of class 11s (atypicals) reverted to negative after anti-infectious treatment; 10 percent were confirmed positive by biopsy. Nyirjesy further reported that **84** percent of class 111s (suspicious) were confirmed positive by biopsy. Although the specific results differ from study to study, it is clear that a significant proportion of class 11s will be positive and a significant proportion of class 111s will be negative.

Since the purpose of the Pap test is to discover true positives, and since the purpose of calculating the false-negative rate is to estimate the true number of missed positives, it is wise to consider the findings of the class 11s and 111s before calculating the sensitivity and specificity of the test. As was indicated previously, both findings are ordinarily followed up by either anti-infectious treatment (class 11s) and then retesting, or by biopsy (class 111s). Therefore, true positives and true negatives are much more likely to surface, and error rates can be calculated which better reflect their conceptual meaning.

The next major definitional problem is the category—positive or negative—into which confirmed biopsy results must be placed. Biopsy results are often classified as follows:

- Negative
- Dysplasia
  - Mild
  - Moderate
  - Severe
- Carcinoma in situ (CIS)
- CIS with microinvasion
- Invasive carcinoma

At which point is a result considered to be **positive? As** May (25) pointed out, if the purpose of the Pap test is to detect carcinoma of the cervix, only CIS and the more serious categories must be considered as positive. If one considers that the purpose of the test is to detect a precursor to cancer, however, then dysplasia must also be considered positive. Some researchers seem to draw the line between positive and negative results within the dysplasia category, which further complicates the analysis of the literature. The biggest problem in all of these definitional difficulties is that many authors fail to state their assumptions, thereby making it hazardous to compare data. May **(25)** partially avoided the difficulty by doing his calculations twice—considering dysplasia once as negative and once as positive.

THE NATURE OF THE TEST

False Negatives. —Since there is much human involvement in scraping the cervix, preparing the slide, and reading the microscopic results of the Pap test, as well as in clerical work, it is not surprising that different organizations report different errors. The false-negative rates reported range from **2.8** to **45** percent (1,7,12,19, 22,23,25,27,29,32,33,34,35,37,38,41,42). Watchel (37) estimates that the false-negative rate is **6** to 10 percent in specialized labs and **20** to **25** percent in mass screening centers. The literature appears to bear this out, with many average labs reporting figures somewhere in the middle, i.e., false-negative rates of 10 to **20** percent. However, Coppleson, et al. **(7),** using an analytical technique for assessing multiple screens and using various sources of data, have estimated false-negative rates of the Pap test to be *40* percent for dysplasia, **20** to 45 percent for CIS, and **24** percent for preclinical invasive carcinoma.

False Positives. —For several reasons, false positives do not raise the concern that false negatives do. First of all, the false-positive rate appears to be low except in the class 111 category (suspicious) which, as discussed previously, probably should not be considered until after further workup. Second, colposcopy and subsequent biopsy are accurate and not terribly expensive in terms of dollars or morbidity. Finally, the disease is so life threatening that to suspect a nonexistent cancer pales into insignificance compared to missing cancerous tissue. In any case, there seldom are estimates of the false-positive rate in the literature. Those few studies which either estimate a false-positive rate or provide sufficient data for the reader to estimate

one **(25,32)** suggest that the rate is less than 2 percent.

Cost-Effective Detection

Clearly, if one is to formulate a rational re-screening strategy, it must be tailored to the various risk categories. Several researchers have developed screening schedules tailored to risk categories, but few have employed economics in **a** cost-effective approach. Anderson and Gunn (1) developed a family of incidence curves corresponding to age and socioeconomic variables, but their rescreening criteria were based on an arbitrary incidence level (the overall reported national average). Walton, et al. (38) recommended a similar schedule based on risk factors, but did not indicate how they determined the screening interval length.

Knox (21) has used a comprehensive and complex computer simulation model which adjusts disease progression transition probabilities until the model predicts reported incidence, prevalence, and mortality rates. A simplified variation is described in a later article **(20).** The output of this model is the determination of the "optimal" ages for screening. Economic factors are implied only by considering the number of screening tests per lives saved.

Galliher (17) has applied benefit-cost analysis to a somewhat simplified disease etiology to determine optimal ages for screening. He and Knox both use a cohort design, simulating a group of individuals through an entire lifetime. Studies on the cost effectiveness of cervical cancer screening have also been published by Coppleson and Brown **(5,6).** Their model, using Markov chains to simulate a disease process, like Knox's model "correctly" predicts reported prevalence data. However, the problem with this approach is that it ignores the effect of previous screening efforts which "purifies" the population, resulting in an understatement of the prevalence of invasive cervical cancer. Knox attempts to correct for this by including screening and treatment effects in the model. Eddy (15) similarly has used mathematical modeling to analyze lifetime screening strategies and to compare screening programs across different cancer sites.

Other studies have analyzed the cost effectiveness of one strategy over another (9,11,32), but these studies have used overall incidence rates rather than risk-related ones, and they have often omitted critical variables such as discounting factors or error rates. In none of the aforementioned studies has there been an appropriate or complete economic analysis: None of the studies has concerned itself with joint production effects (e.g., a visit for a Pap test usually includes other examinations as well), emigration rates (e. g., disenrollment from an insurance plan), the value of time costs, nor even with an estimation of the cost effectiveness of employing nonphysician personnel to perform routine procedures. Neither has anyone attempted to determine who actually incurs the different costs involved in cervical cancer screening and who accrues the many benefits. Our CEA presented below considers all of the aforementioned factors.

METHODOLOGY

The nature of cervical cancer and the state of medical ethics preclude our determining the cost effectiveness of alternative screening strategies through a true experimental situation: Once CIS is detected, it is imperative that medical intervention take place; and such intervention prevents observations over a longer period.

Therefore, using our model, we simulate screening the population twice (see app. B), aging it for 11 years while simulating screening at various intervals, and calculating the costs and benefits for each screening policy tested. Ten possible screening policies are examined—from screening every year to screening only in the loth year. All costs of screening and of treating disease associated with cervical cancer are totaled for each policy. Benefits are calculated by comparing lives and years of life saved for each policy compared to no screening for the 11 years. Finally, many different cost-effectiveness ratios are devised for society's interested parties

(e.g., a philanthropic organization, a health insurer, society itself).

Disease Transition Probabilities

A mathematical modeling technique known as a Markov chain process is used to simulate the aging of a population at risk for cervical cancer, so that a population is "exposed" to a disease process over a number of periods and undergoes changes in health status according to a set of disease transition probabilities, each of which is the probability of changing from a particular health state to another in one period.

For purposes of our analysis, 13 health states are defined as folIows:

- H_1 Normal
- H_2 Reverted normal—having regressed from a previous state of dysplasia
- H_3 Dysplasia
- H_4 *CIS*
- H_5 Invasive carcinoma of the cervix
- H_6 High-risk, disease-free
- H_7 High-risk, dysplasia
- H_8 High-risk, CIS
- H_9 High-risk, invasive carcinoma
- H_{10} Hysterectomy
- H_{11} Emigration
- H_{12} Death due to cervical cancer
- H_{13} Death due to all other causes

The probability of annual progression and regression from one state to another is shown in the disease progression chart in table *4.* According to that matrix, a 30- to 39-year-old woman who is normal (Hi) in one period has a 0.00110 probability of developing dysplasia within 1 year, a probability of 0.00116 of dying from causes other than cervical cancer, and a probability of 0.99718 of remaining disease free. A woman who is disease free but who previously had dysplasia (H,) has a much higher probability, 0.32000, of contracting dysplasia again. Most of the transition probabilities presented in table 4 are estimates from various sources, but these probabilities are actually variables themselves. We have chosen many of the particular values shown because their use corresponds to published prevalence and mortality rates (1,32,36).

The high-risk states, H_6, H_7, H_8, and H_9, are included for accounting purposes only; that is, once a woman is identified as high risk, she will automatically be placed on a more intensive Pap testing sequence than those women not so identified, as discussed further below. Transition probabilities for the high-risk states H_6, H_7, H_8, and H_9 are assumed to be the same as those for H_2, H_3, H_4, and H_5, respectively. States H_{10} through H_{13} serve as collecting states and essentially do not allow outward transition. The hysterectomy state (H10) is included, because a hysterectomy ordinarily ensures that the patient is no longer at risk for cancer of the cervix. Emigration (Hi,) simulates women who have left the program[4] and approximates the position of a health insurer who incurs screening expenses without deriving future benefits; the health insurer's position is opposed to that of society, because society would accrue the benefits of screening regardless of migration patterns. Initially, we assume no emigration, but we subsequently test several migration rates to analyze the effects which enrollee loss has on the cost-effective solution for different parties. Our model accepts the feature of emigration by accumulating in the emigration state (Hll) a fixed proportion of individuals from each alive state, sending away, for example, 10 percent per year (depending on the migration rate) and acting as though the health status of those persons does not change—and from the health insurer's perspective, that is exactly what happens. The feature of emigration is ignored in calculating society's cost-effectiveness ratios.

Screening Policies

Ten different policies are analyzed, beginning with the policy of screening every ***year*** and ending with the policy of screening only in the l0th year. The costs and benefits of the entire Ii-year period are totaled and compared. A simplified decision tree for screening and treating preclinical disease (see figure 2) is used in our model. Each time a screen is simulated, lesions (H_3, H_4) are detected (minus error) and treated, and the cases are placed in the high-risk, disease-free health state (H,), which has defined probabilities of transition according to the matrix in

[4]Emigration is used here in the broad sense, with any movement out of an enrollment considered emigration.

able 4.—Sample Disease Progress on Chart

Women, Aged 30 to 39: Estimated Annual Rate

Period t		H	H	H	H	H	H	H	H	H_9	H_{10}	H_{11}	H_{12}	H_{13}
	Period t + 1													
H_1	Normal[a]	.99. .8	[illegible]	[illegible]	[illegible]	[illegible]	0.00000	0.00000	0.00000	0.00000	0.00050	0.00000	0.00000	0.00116
H_2	Reverted normal[a]	0.00000	0.66724	0.33000	0.00100	0.00010	0.00000	0.00000	0.00000	0.00000	0.00050	0.00000	0.00000	0.00116
H_3	Dysplasia[a]	0.00000	0.32000	0.62533	0.04900	0.00400	0.00000	0.00000	0.00000	0.00000	0.00050	0.00000	0.00001	0.00116
H_4	CIS[b]	0.00000	0.00000	0.00000	0.94824	0.05000	0.00000	0.00000	0.00000	0.00000	0.00050	0.00000	0.00010	0.00116
H_5	Invasive car a[c]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00050	0.00000	0.00010	0.00116
H_6	High-risk, [d]	0.00000	0.00000	0.00000	0.00000	0.00000	0.66724	0.33000	0.00100	0.00010	0.00050	0.00000	0.00000	0.00116
H_7	High-risk,	0.00000	0.32000	0.00000	0.00000	0.00000	0.00000	0.62533	0.04900	0.00400	0.00050	0.00000	0.00001	0.00116
H_8	High-risk,	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.94824	0.05000	0.00050	0.00000	0.00010	0.00116
H_9	High-risk, invasive carcinoma[c]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.49884	0.00000	0.50000	0.00116
H_{10}	Hysterectomy	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.49884	0.00000	0.50000	0.00116
H_{11}	Emigration	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.99884	0.00000	0.00000	0.00116
H_{12}	Death due to cervical cancer	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	1.00000	0.00000	0.00000
H_{13}	Death due to all other causes[e]	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	1.00000

[a]See E. Stern (36); see Knox (21) [illegible] not associated with cervical cancer.

[b]The assumptions are that: 1) there is a linear progression to invasive cancer spanning 10 years, and 2) 0.5 ultimately will progress to invasive cancer.

[c]See Schneider and Twiggs (32). Note that the matrix assumes hysterectomy will be performed for clinically apparent invasives.

[d]Transition rates for the high-risk states H_6, H_7, H_8, and H_9 are assumed to be the same as those for H_2, H_3, H_4, and H_5, respectively.

[e]See Life Table, *Vital Statistics* (1976); the 10-year period was averaged.

Figure 2.— Decision Tree for Cervical Cancer Screening and Treatment (simplified for analysis)

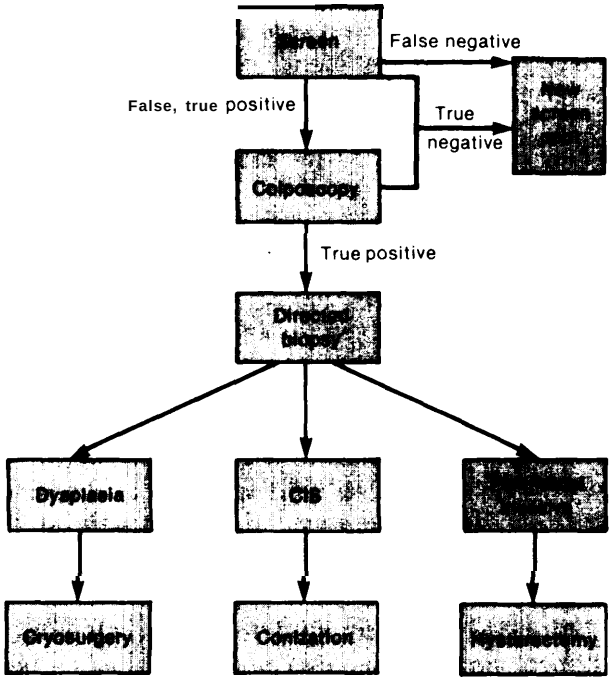


table 4. Invasive cases (H_5) discovered by screening are treated and placed in the hysterectomy state (H_{10}). The undetected lesions remain in their previous health state continuing to age, also **as** defined by the matrix.

Note that the matrix indicates that one period later, half of the remaining invasive cases will have received a hysterectomy and will be "saved;" the other half will also receive a hysterectomy but will not survive. The literature confirms this survival rate **(32).**

The assumption is made that all this will occur within 1 year. That assumption is an oversimplification, but adopting it makes calculation easier; furthermore it results in erring on the medically conservative side, making more frequent screening more attractive.

By using the high-risk states, we are able to age high- and regular-risk groups simultaneously and to differentiate between the two, simulating separate screening policies. This differentiation between high- and regular-risk groups is important, since women who have experienced precursors to cancer and who have been treated, as well as women who have had noncancerous but atypical Pap smears, are usually scheduled for repeat smears at short, regular intervals of time. Since our model has this feature, costs can be appropriately calculated.

costs

Costs are accumulated by screening, diagnostic, and treatment categories in order to assign them to the appropriate parties, For discounting purposes, all costs are calculated at the time they are incurred, which requires calculation of the screening and treatment costs only when screening is performed, and calculation of the costs of treating invasive cancer as it occurs (i.e., yearly).

Two basic cost formulations are applied: a low-cost model and a high-cost model (see app. C for further details). The low-cost model is a hypothetical health clinic in which licensed vocational nurses (L. V.N. S) perform the Pap testing, a registered nurse practitioner (R. N. P.) performs the colposcopic examinations and biopsies, and a part-time physician who is on call for professional staff support performs all cryosurgeries. This model uses a reputable cytology laboratory, which bills the clinic periodically, thus taking advantage of economies of ***scale.*** Conservative treatment with the costs calculated from a composite of treatments as described by Lacey and Townsend **(24),** is assumed for all CIS discovered: **$10** percent cryosurgery and 10 percent ionization. Costs of hospitalization are as described in the Third National Cancer Survey (10). The high-cost model is **a** hypothetical private, fee-for-service practice in a university teaching hospital that has physicians take Pap smears and perform colposcopic examinations and biopsies. This model uses a university hospital laboratory that bills each ***pa***tient individually. More radical treatment for CIS is assumed: 10 percent cryosurgery and **90** percent ionization. All hospitalization costs are calculated in the same way as that described for the low-cost model.

In order to simulate joint production effects of the high-cost model, the cost of the Pap smear

procedure is systematicall[y] reduced as the screening interval Lengthens. s This feature is included because other evaluations are also being performed when a woman has a Pap smear. If she were to have an annual smear, for instance, it would be assumed that since the main purpose of the visit would be for the Pap test, the total physician charge should be allocated only to the Pap. However, if the policy were for women to wait 4 to 5 years for a "checkup," at which point a Pap would also be administered, perhaps only a small fraction of the physician's charge should be allocated to the screening procedure, since the probability of such visits' taking place—even without a procedure as a Pap smear—would be high. One may, in fact, assume that a significant proportion of women with gynecological symptoms will visit a physician within some specified time and that the Paps that would be taken would not be primarily a screening measure at all; consequently, the proportion of the cost allocated to cervical cancer screening is further diminished.

We assume an inverse linear relationship between the amount of cost allocated to the smear and the length of interval between smears (i. e., the longer the interval, the lower the cost). Since the low-cost clinic operates for the sole purpose of Pap testing, this joint production feature is not included. However, its omission is not necessary because the L.V.N. S can be adequatel[y] trained to perform pelvic and breast examinations, take general history, as well as to do numerous other health promotion/disease prevention activities (30),

Actual costs can and do vary between the two extreme models suggested here, and other estimates will affect the cost-effective solution, depending on the system employed and assumptions made.

Our simulation model also has other features. One is its capability of including high case-finding costs for high-risk women who are difficult to reach. Another is its capability of including estimates of time opportunity costs for women to undergo not only the Pap test but also the other diagnostic and treatment procedures.

[5]The cost of the lab is not included,

As stated previously, costs are calculated and discounted as they occur; therefore, the population is screened, and costs are calculated according to the screening policy (i. e., screenin[g] every year, every second year, every third year, etc.). Those cases identified as high-risk are screened annually, and costs are assigned as they occur. Likewise, clinically detected invasives accrue costs as the disease becomes clinically apparent.

Benefits

Number of Lives Saved.—To calculate the number of lives saved for each screening policy compared to no screening, the number of deaths incurred in each year for each of the 10 policies is subtracted from the number of deaths in the respective years when no screening occurs for 11 years. Each life saved is discounted at the time accrued. This latter calculation weighs the state of health in which each policy leaves its population after 11 years, [b]

Number of Years of Life Saved.—It is assumed that each woman saved will live to her average life span as indicated by standard life tables. Next, the stream of benefits is discounted as if it were an annuity of 1 life-year for x years. Although this simulation process is not as accurate as using a life table process whereb[y] the life saved has a probability of loss of life associated with each year of life (as opposed to our method which assumes that the survivor will live until the average life span and then die), it is much easier to calculate and results in a higher (i.e., more conservative) estimate of benefits.

Policy Analysis

The prevention and the financing of preventive programs are social decisions as well as a series of private decisions, and costs are incurred and benefits are accrued in different mixes depending on the perspective of the parties involved. Therefore, the cervical cancer screening program is analyzed to determine

[6]This is necessary because each screening policy leaves the population with differing degrees of morbidity. For instance, a policy which last screened women at age **36** will result in many more precancerous and cancerous lesions a t age **41** than would a policy which last screened women at age **39 or 40.**

whether a private party must be subsidized by society in order to induce the party to carry out social policy. If benefits to the private party are already greater than zero, a pareto solution (i.e., a solution whereby no one can be made better off without making someone worse off) can be reached by society's subsidization.

Another policy explored is that of financing a case-finding effort for a high-risk but isolated population, the cost effectiveness of which is compared to more inexpensive programs for a normal-risk population.

A third policy option is embodied in the low- and high-cost models that are presented. If all other factors are the same, the low-cost model must be more cost effective, but the sensitivity of different possible error rates (i. e., a differential in quality) must be examined.

Sensitivity Analysis

Each of the major variables is estimated at all reasonable levels, ranging from minimum to maximum values, in order to provide an interval of confidence. The specific variables that are tested include: 1) error rates, 2) transition probabilities, 3) emigration rates, 4) costs, 5) discount rates, and 6) prevalence rates.

RESULTS

Except where noted, the results presented below are calculated from our "base case" set of parameters (see app. D). Every comparison consists of 10 data points, each one representing a different screening policy (i. e., screening every year, every second year, etc.).

Benefits and Costs

Benefits and costs, discounted at the same rate (40), clearly indicate the declining function of both as the interval between screens lengthens (see table 5). Although benefits decline rather rapidly in near linear fashion (see figure 3), costs decline at a decreasing rate (see figure 4). This is an expected phenomenon, because a change from policy 1 (screening every year) to that of policy 2 (screening *every* second year) results in 50-percent fewer screens, whereas a change from policy 7 to policy 8 results in simply post-

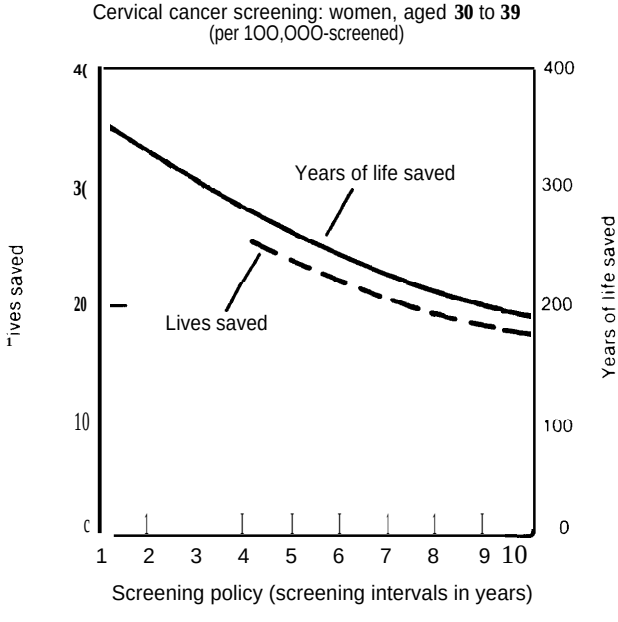
Table 5.—Benefits and Costs"

Cervical cancer screening: women, aged 30 to 39 (per 100,000 screened)

Policy (screening intervals in years)	Lives saved	Years of life saved	Total costs (screening, diagnosis & treatment)
1	32	348	$34,006,000
2	30	323	13,397,000
3	27	295	8,423,000
4	25	269	5,919,000
5	**24**	**257**	5,330,000
6	21	223	3,394,000
7	20	218	3,185,000
8	19	210	2,993,000
9	18	199	2,819,000
10	17	186	2,662,000

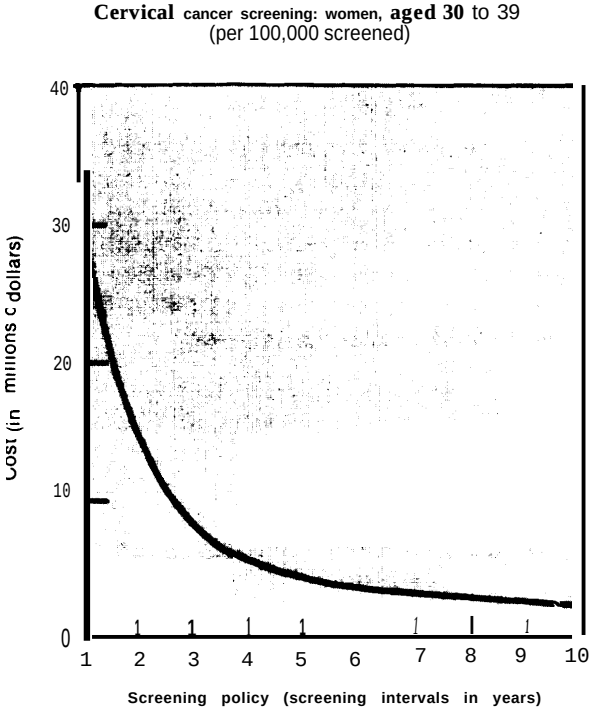
[a]Base case, discount rate = 10%

Figure 3.—Benefits: Lives Saved and Years of Life Saved"



[a]Base Case, discount rate = 10%

Figure 4.—Total Costs (screening, diagnosis, and treatment



[a] Base case; discount rate = 10%.

poning screening for 1 year. The different shapes of the benefit and cost curves, as well as their decreasing functions, form the basis of the changing natures of the calculated cost-effectiveness ratios.

Society's cost-effectiveness curve (see table 6 and figure 5) indicates that the cost effectiveness increases markedly as the interval lengthens but increases at a decreasing rate. The final upward break of the curve suggests that the minimum screening policy for society under these conditions and assumptions is to screen once in the ninth year. That is, although it is more cost effective to postpone cervical cancer screening until the ninth year, postponing screening an additional year increases societal costs.

A health insurer's curve, simulated by total medical costs (see figure 4), however, never breaks upward. This curve indicates that it is always financially beneficial to postpone screening. The reason is that although more serious

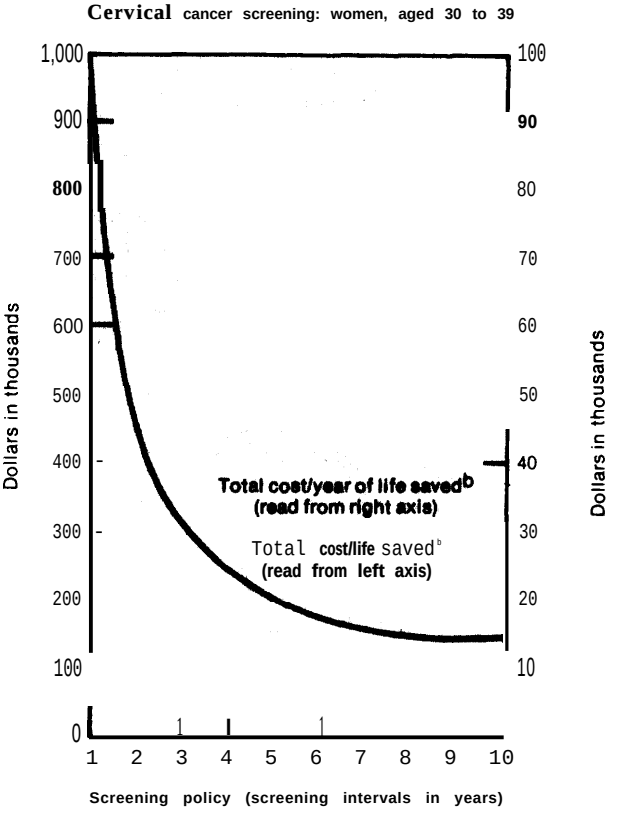
Table 6.—Cost.Effectiveness Ratios for Society[a]

Cervical cancer screening: women, aged 30 to 39

Policy (screening intervals in years)	Total cost per life saved [b]	Total cost per year of life saved [b]
1	$1,064,800	$97,600
2	452,600	41,500
3	311,100	28,600
4	239,600	22,000
5	224,900	20,700
6	164,900	15,200
7	158,300	14,600
8	154,400	14,300
9	153,100	14,200
10	153,900	14,300

[a] Base; discount rate = 10%.
[b] Total cost is the cost of screening, diagnosis, and treatment

Figure 5.—Cost-Effectiveness Ratios for Society



[a] Base case; discount rate = 10%.
Total cost is the cost of screening, diagnosis, and treatment.

disease must be treated as screening is postponed, the resulting costs never become so large that funding a screening program at any level becomes financially advantageous to the organization.

Unlike health insurers, patient-education-oriented philanthropic organizations such as the American Cancer Society seek to reduce lives or years of life lost due to cancer, without bearing any of the costs of doing so. The benefit curve (see figure 3 and table 7) is continually falling, indicating that the optimal screening strategy from this perspective is to screen annually (or even more frequently).

Discount Rate Sensitivity

A discount rate of 10 percent was selected as appropriate for our analysis, because it is approximately the present rate of return on investments in the private market. Table 8 and figure 6 indicate that the sensitivity of our results to small changes in the discount rate is minimal and decreases rapidly for policies less frequent than annual screening. As expected, however, the significantly lower cost-effectiveness values for very low discount rates (i. e., O or 5 percent) reflect the facts that costs tend to be incurred in the present and benefits tend to be accrued in the future.

Table 7.- Cost= Effectiveness Ratios for Philanthropic Organizations'

Cervical cancer screening: women, aged 30 to 39

Policy (screening intervals in years)	Initial screening cost per life saved	Initial screening cost per year of life saved
1	$850,000	$77,957
2	386,000	34,463
3	251,000	23,101
4	182,000	16,757
5	166,000	15,282
6	108,000	9,911
	100,000	9,215
	94,000	8,694
9	90,000	8,322
10	87,000	8,068

[a] Basecase; discount rate = 10%

Pap Test Error Rate Sensitivity

False-negative rates are reported over a wide range of values. For our base case analysis, we chose an overall false-negative rate of 0.2, a compromise between the frequently reported rate of 0.1 and the analytically derived rates of 0.4 for dysplasia, 0.3 for CIS, *0.24* for invasive disease (7). Sensitivity analysis (see table 9, columns 1 through 3) indicates that the results are affected little by varying the error rates over this range.

False-positive rates are rarely reported (16) but are often thought to be no higher than 0.10 *(25,32).* Our analysis (table 9, columns 4 through 6), indicates little sensitivity to the precise error rate used.

Joint Production Effects

The proportion of the cost of a gynecological visit which should be allocated to the Pap test is

Table 8.—Discount Rate Sensitivity: Total Cost per Year of Life Saved" [b]

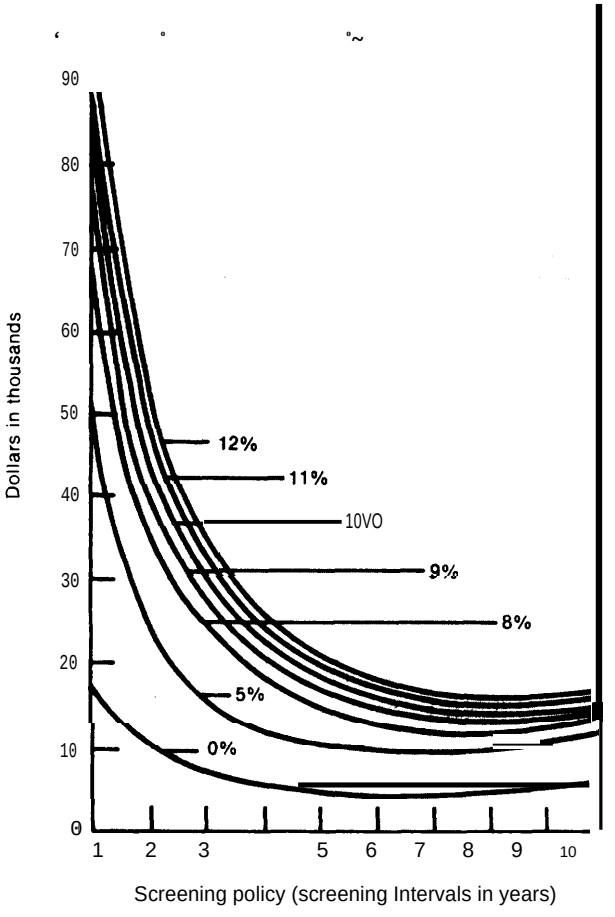
Cervical cancer screening: women, aged 30 to 39

Policy (screening intervals in years)	O%	50/0	80/0	9 %	10%	11%`	120/0
	$18,473	$51,928	$78,530	$87,985	$97,632	$107,424	$117,323
	8,598	23,039	33,971	37,746	41,537	45,321	49,081
3	6,049	15,971	23,436	26,003	28,574	31,131	33,662
4	4,770	12,404	18,116	20,073	22,028	23,968	25,880
5	5,309	12,575	17,524	19,136	20,706	22,220	23,673
6	3,447	8,683	12,561	13,884	15,201	16,501	17,777
7	3,655	8,718	12,276	13,454	14,609	15,730	16,811
8	3,987	8,946	12,220	13,267	14,273	15,230	16,134
9	4,506	9,409	12,402	13,318	14,176	14,973	15,705
10	5,349	10,190	12,847	13,610	14,302	14,921	15,468

[a] Base case except for discount rates as indicated.
[b] Total cost is the cost of screening, diagnosis, and treatment

Figure 6.—Discount Rate Sensitivity: Total Cost per Year of Life Saved" [ab]

Cervical cancer screening: women, aged **30 to 39**



[a]Base case, except for discount rates as indicated
[b]Total cost is the cost of screening, diagnosis, **and treatment**

not known, but it is hypothesized here that the proportion must decline as the screening interval lengthens. With the assumption of a IO-percent linear reduction in cost as the screening interval increases by 1 year, both cost per life saved and total cost stabilize at about half the value of the cost when no joint production effects are considered (see table 10 and figure **7).**

Migration Effects

When the effects of migration are simulated (see table 11), we again note the familiar pattern of highest sensitivity for the most frequent screening policies and little difference as the interval lengthens. As was expected, higher migration rates result in each screening policy's being less cost effective.

Low=Cost Model

When minimum cost estimates are assigned for screening, diagnostic workups, and minor treatment procedures, all cost-effective indicators improve dramatically (see tables 12 and 13). Cost per year of life saved drops below $10,000 by policy *2* (screening every second year) and quickly stabilizes between **$4,000** and $5,000 (see table 12). The optimum screening interval is policy 7 (screening only in the seventh year), since screening either more or less often saves less money.

An evaluation of cost-effectiveness ratios for philanthropic organizations (see table 13) yields the familiar continually declining function, because no savings are associated with lower cancer morbidity, although relatively low costs per year of life saved are quickly reached.

High= Risk, High= Case-Finding=Cost Population

The women who are at highest risk for cervical cancer are often both the most difficult to find and the most reluctant to participate in a screening program. To evaluate the cost effectiveness of screening this special population, we modify our variables in the following manner:

1. All transition probabilities from the disease-free state (H_1) to dysplasia (H_3), CIS (Hal), and invasive carcinoma of the cervix ($H_,$) are doubled.
2. Disease prevalence of the initial population vector is doubled for disease states H_2, H_3, H_4, and $H_,$.
3. The low-cost model is used, except that an additional **$20,** which is intended to simulate a case-finding cost, is assigned for the Pap.

Results with this high-risk model are compared to those of the high- and low-cost, regular-risk models (see table 14). At every screening level, the cost per year of life saved is less

Table 9.—Pap Test Error Rate Sensitivity: Total Cost per Year of Life Saved a b

Cervical cancer screening: women, aged 30 to 39

Policy (screening intervals in years)	Test error rates [c]					
	$e = 0.1$ $e_2 = 0.1$ $e_3 = 0.1$ $e_4 = 0.05$	$e_1 = 0.2$ $e_2 = \mathbf{0.2}$ $e_3 = 0.2$ $e4 = 0.05$	$e_1 = 0.4$ $e_2 = \mathbf{0.3}$ $e_3 = 0.24$ $e_4 = 0.05$	$e_1 = \mathbf{0.2}$ $e_2 = \mathbf{0.2}$ $e_3 = 0.2$ $e4 = 0.01$	$e_1 = \mathbf{0.2}$ $e_2 = \mathbf{0.2}$ $e_3 = 0.2$ $e4 = 0.05$	$e_1 = \mathbf{0.2}$ $e_2 = 0.2$ $e_3 = 0.2$ $e_4 = 0.10$
	$113,800	$113,300	$113,500	$108,600	$113,300	$119,100
	40,900	41,500	43,300	39,700	41,500	43,800
3	27,600	28,600	30,800	27,400	28,600	30,100
4	21,000	22,000	24,400	21,200	22,000	23,100
5	19,600	20,800	23,100	20,000	20,800	21,700
6	14,200	15,200	17,500	14,700	15,200	15,900
	13,600	14,600	16,900	14,100	14,600	15,200
	13,300	14,300	16,500	13,800	14,300	14,900
9	13,200	14,200	16,500	13,700	14,200	14,700
10	13,300	14,300	16,700	13,900	14,300	14,900

[a] Base case, **except** for error values **as** indicated.

[b] **Total cost is the** cost **of screening, diagnosis, and treatment.**

[c] E_{rror} **rates: e, = false-negative rate for dysplasia; = false-negative rate for CIS; e, = false-negative rate for preclinical invasive carcinoma; e_4 = false-positive rate.**

Table 10.—Joint Production Effects"

Cervical cancer screening: women, aged **30** to **39**

Policy (screening intervals in years)	Total cost per year of life saved [b]		Total cost per 100,000 screened [b]	
	No joint production	Joint production	No joint production	Joint product ion
1	$97,600	$97,600	$34,006,000	$34,006,000
2	41,500	30,600	13,397,000	9,861,000
3	28,600	17,000	8,423,000	5,004,000
4	22,000	11,400	5,919,000	3,064,000
5	20,700	9,600	5,330,000	2,460,000
6	15,200	7,400	3,394,000	1,647,000
7	14,600	7,100	3,185,000	1,537,000
	14,300	7,000	2,993,000	1,472,000
	14,200	7,200	2,819,000	1,424,000
10	14,300	7,400	2,662,000	1,387,000

[a] Base case; discount rate= 10%; and the cost **of the Pap test for the** joint production columns **was decreased by 10% for each yearly increase of screening internal.**

b Total cost is the cost of screening, diagnosis, and treatment.

than half that of the high-cost, regular-risk model and is only slightly higher than that of the low-cost model.

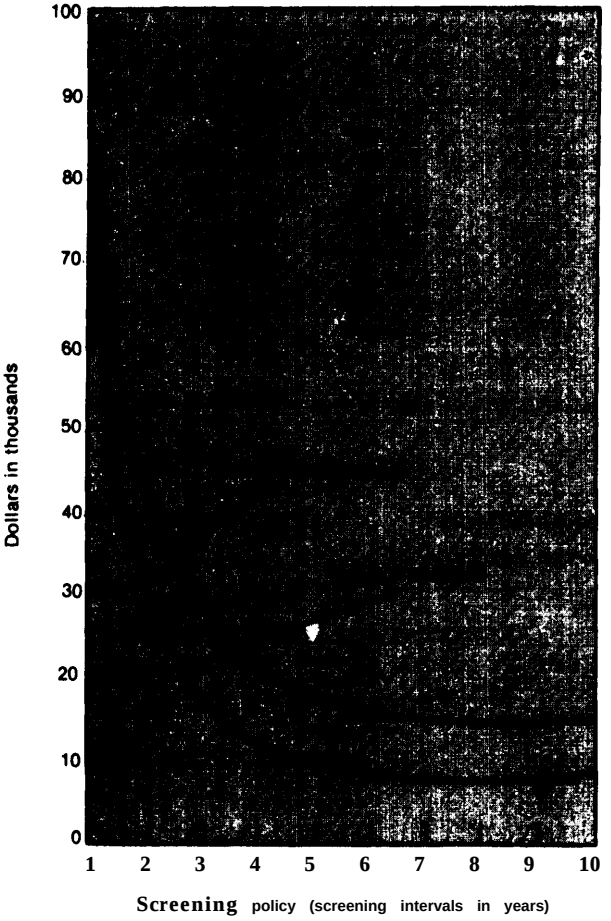
Discussion

The worth of cervical cancer screening is affected far more by the method of analysis and the point of view taken than by the sensitivity of disputed values such as the precise discount rate or the correct error rates. Traditionally, the latter two parameters are the principal ones considered if, indeed, any sensitivity analysis is performed at all.

The results of our study are affected most by varying the costs. This finding is not necessarily unexpected for a couple of reasons. First, only the costs of cervical cancer screening and the more simple diagnostic and treatment procedures are varied–as opposed to the costs of treating invasive carcinoma. This approach seems appropriate, since one can more easily employ less costly personnel and resources for

Figure 7.- Joint Production Effects: Total Cost per Year.of Life Saveda b

Cervical cancer screening: women, **aged 30 to** *39*



● Base case; discount rate = 10%; and the cost of the Pap test for joint production was decreased by 10% for each yearly increase of screening interval.
total coat is the cost of screening, diagnosis, and treatment.

the former than for the latter. Second, the disease is not very common; consequently, many women must be screened in order to discover a single **case.** Although most screening in this country is not performed the way depicted in the low-cost model, the proper method of analyzing the cost effectiveness of any procedure is by using the most efficient possible method.

Nevertheless, efficiency of operation is only one of many aspects to consider when evaluating the cost effectiveness of health programs. Another consideration is the effect of joint production, since clearly the entire cost of a gynecological visit should not be allocated to the Pap test. In fact, our results show that as the yearly interval increases, a cost reduction of only 10 percent makes screening more than twice as cost effective as it would be if joint production were not taken into account.

Furthermore, analyzing the worth of a health program solely from the point of view of society is insufficient, because the decisionmakers in this country are very often private parties or private individuals. A health insurer, for instance, is apt to make policy decisions primarily on a financial basis. **A** consideration of only the financial aspects of this problem indicates that it is good policy for all private parties to put screening off an additional year, regardless of the model or assumptions used. Consequently, if society wants certain segments of the private sector to have incentives to screen, it may have to subsidize cervical cancer screening programs. This conclusion is further substantiated when migration effects are considered, since the financial rewards of reduced cancer morbidity are lost when screened members move away or change insurance plans.

Finally, simulation of high case-finding costs for a high-risk population of women indicates that such a program is indeed cost effective if it employs the low-cost option. The increased cost assigned to case-finding is apparently offset by the increased morbidity which is discovered and cured. This finding is particularly interesting, since the same high case-finding cost is assigned to all Pap testing, even for policies in which the women receive multiple tests over the Ii-year period.

The results of our study demonstrate that there are many ways to evaluate a health program, even when using basic cost-effectiveness techniques. The interpretation of the results depends on which benefits and costs are germane to the evaluator and how the program is organized and financed.

Table 11 .—Migration Effects"

Cervical cancer screening: women, aged *30* to *39*

Policy (screening intervals in years)	Total cost per year of life saved b			Total cost per 100,000 screened[b]		
	No migration	10% migration/yr	30 %migration/yr	No migration	1O% migration/yr	*30%* migration/yr
1	$97,600	$148,500	$383,900	$34,006,000	$23,231,000	$13,378,000
2	41,500	57,100	107,800	13,397,000	8,053,000	3,123,000
3	28,600	38,900	69,200	8,423,000	4,931,000	1,710,000
4	22,000	29,600	49,200	5,919,000	3,384,000	1,063,000
5	20,700	25,670	37,600	5,330,000	2,753,000	734,000
6	15,200	19,900	29,500	3,394,000	1,873,000	520,000
7 : : : : : : : :	14,600	18,139	24,900	3,185,000	1,638,000	413,000
8	14,300	16,818	21,900	2,993,000	1,444,000	344,000
9	14,200	15,825	19,800	2,819,000	1,284,000	299,000
10	14,300	15,079	18,500	2,662,000	1,153,000	271,000

aBase case, discount rate = 10O%.
bTotal cost is the cost of screening, diagnosis, and treatment

Table 12.—Cost"Effectiveness Ratios for Society: Low"Cost Model'

Cervical cancer screening: women, aged *30* to *39*

Policy (screening intervals in years)	Total cost per life saved b	Total cost per year of life savedb
1	$298,000	$27,300
2	101,700	9,300
3	72,800	6,700
4	59,000	5,400
5	57,000	5,200
6	46,500	4,300
7	45,800	4,200
8	46,000	4,200
9	47,100	4,400
10	49,300	4,600

aBaSe Case With low.cost screening and treatment procedures, discount rate = 10%
bTotal cost is the cost of screening, diagnosis. and treatment

Table 13.—Cost-Effectiveness Ratios for Philanthropic Organizations: Low-Cost Model'

Cervical cancer screening: women, aged *30* to *39*

Policy (screening intervals in years)	Screening cost per life saved	Screening cost per year of life saved
1	$175,700	$16,110
2	77,300	7,090
3 : : : : : : : : : : : : : : : :	50,300	4,620
4	36,400	3,350
5	33,200	3,060
6	21,500	1,980
7	20,000	1,840
8 : : : : : ; : : : : : : : : :	18,800	1,740
9	18,000	1,670
10 : : : : : : : : : : : : : : : :	17,400	1,610

aBaSe Case with low.COSt screening and treatment procedures, discount rate = 10%.

Table 14.—Cost"Effectiveness Comparisons: High-Cost, Low"Cost, and High.Risk Models
(total cost per year of life saved)"

Cervical cancer screening: women, aged 30 to 39

Policy	High-cost model b	Low-cost model	High-risk, low-cost model
1	$97,600	$27,300	$36,600
2, ...	41,500	9,300	14,600
3	28,600	6,700	10,300
4	22,000	5,400	8,200
5	20,700	5,200	7,800
**6 . . . . . **	15,200	4,300	6,200
**7 . . . . . **	14,600	4,200	6,000
**8, ... **	14,300	4,200	6,000
9	14,200	4,400	6,100
10 : : : : : : : :	14,300	4,600	6,200

aTotal COSt is the cost of screening, diagnosls, and treatment
b The high.co5t model is **the** base case model, discount rate = 1O%

LIMITATIONS

There are numerous limitations to a study such as ours, most of them related to the inability to examine and control variables as one could in a true experimental design. This problem is most clear when one realizes that neither has it been proved that dysplasia and CIS are precursors to cancer, nor has it been proved that screening for and treating of these conditions have led to decreased cervical cancer mortality. Sufficient inferential evidence is available to warrant screening at some level, but sufficient uncertainty is present to question the optimal periodicity. Therefore, in simulating the disease process and its diagnosing, the best we can do is test the various estimates of prevalence, incidence, screening, error, and death rates reported by clinicians and researchers in order to produce results that seem reasonable.

Disease Transition

One of the more severe limitations of our study stems from the model's inherent assumptions. For instance, the transition probabilities from one disease state to another, regardless of a woman's prior medical history, are assumed to be constant, which almost certainly is not the case. In fact, logic alone would dictate that time in certain disease states be positively correlated with the probability of transition to the next higher state. To overcome this restriction, high-risk categories have been included which allow for higher transition rates for selected groups of individuals who are at higher risk. Also, the Markov technique does not allow for the possibility of a threshold effect (i.e., the disease's having a zero probability of progressing to the next state in one period), whereas it does allow for the nonzero probability of progressing within two, three, or more periods.

Since apparently not every disease progresses to invasive cancer, there is a distinct possibility that this phenomenon is not a random procedure, but rather the result of two or more separate disease processes—one which progresses and one which does not, and possibly even a third which regresses. Obviously, this is not so much a limitation of the modeling process as it is a statement of the lack of understanding of the disease process itself.

Other simplifying assumptions also are made regarding transition probabilities. The literature, for instance, suggests that treatment of clinically invasive carcinoma results in about a 50-percent overall survival rate (24), which is ordinarily couched in terms of 1, 2, or 5 years. Our model assumes that clinically invasive cases transit directly, within the single period of 1 year, to the permanent states of either hysterectomy or death. To mitigate this oversimplification, the simulated screening process identifies a given proportion of invasive cases and transfers them directly to the hysterectomy category, thus mimicking the discovery of microinvasive cases and simulating a higher survival rate.

Screening and Treatment

A simplifying assumption in our model is that a single algorithm is available to practitioners for screening and treatment of preclinical disease. Actual practitioners, though, may use several different possible treatments for the same diagnosis. For example, although the model assumes treatment of early dysplasia by cryosurgery, actual practitioners may in some instances not treat this condition immediately, in some treat it by laser carbon dioxide, and in others treat it by only the biopsy itself. Actual practitioners may also use the same treatment for very different diagnoses. Although medical authorities currently recommend hysterectomy for only the more severe cases, practitioners actually perform this surgery based on factors such as the woman's interest in bearing children (24) or the availability of beds (31). We attempt to account for these possibilities by simulating conservative therapy for the low-cost model and more radical therapy for the high-cost model. Thus, actual costs should lie somewhere in between these extremes.

Another possibility which our analysis ignores altogether is that of medical complications following therapy, Although complications

may be expensive, produce illness, and result in deaths, they are relatively rare. In addition, they are only associated with the radical forms of treatment, and their exclusion is not expected to affect this study's conclusions.

Finally, since there is considerable uncertainty regarding error rates, the results were calculated with a wide range of rates. Such a sensitivity analysis requires the reader to interpret the findings with appropriate caution, although the model is not very sensitive to the rates used.

costs

Assigning costs to any production process is usually a difficult task and often results in arbitrary allocation decisions. In that regard, our study is no exception. For instance, since a fee is not recovered for- each service performed in the low-cost clinic model, we decided that all fixed and variable costs, with the exception of **25** percent of the physician's and *50* percent of the R.N. 's time, would be allocated to the Pap procedure. This decision was reached after many hours of discussion with health clinic personnel. The practitioners' remaining times are allocated to colposcopy and cryosurgery; for the purpose of simplicity, an average "fee" was assigned to these treatments, resulting in slightly overestimated costs for- some policies and underestimated costs for others.

The joint production phenomenon is a related cost allocation problem. Joint production should be considered, because multiple activi ties occur during any patient/practitioner contact. When a Pap smear is administered during a visit, the Pap may or may not be the primary reason for the visit; the patient may also be formally or informally "screened" for problems such as cervicitis, hypertension, breast cancer, anemia, and wife battering. Whatever the case, we at tempted to account for this phenomenon by assuming an inverse linear relationship between the cost allocated to the screening program and the length of interval between screens, a relationship which appears to be as reasonable an assumption as any other without the benefit of a very careful study of the activities involved. Such a study was clearly beyond the scope of this research. The inverse relationship probably holds more strongly for the shorter intervals and becomes weaker as the interval lengthens. Nevertheless, this assumption certainly approximates reality more closely than do most other cost-effectiveness studies, which seldom even consider the phenomenon of joint production.

Benefits

Benefits are even more difficult to estimate and allocate than are costs. As stated several times previously, there is no irrefutable evidence that any benefits associate positively with cervical cancer screening, not to mention the lack of consensus regarding the magnitude of benefits attributable to different levels of screening.

Nevertheless, one of our principal tasks was to quantify estimated benefits as expressed in terms of: 1) number of lives saved, 2) years of life saved, and 3) related economic consequences for each screening policy. The first problem with this method is that it considers only saving lives, although there are many *lesser* benefits such as the prevention of pain, suffering, and mourning, as well as the psychological and physical consequences of losing one's childbearing ability. Most of these other effects are too difficult to measure adequately, and we fared no better in this effort than other investigators.

The second major problem with this approach, that of comparing benefits of each screening policy with no screening for 10 years, arises because the purpose of our analysis is to measure and compare both costs and benefits from the perspective of the potential financier who does not ordinarily finance preventive health care (the few major exceptions being prepaid group practice plans, military health systems, and individuals paying for screening out-of-pocket). Therefore, comparing one screening policy with no screening seems to be the most appropriate choice. One could argue that it is reasonable to compare a given screening policy with the annual screening often recommended by cancer control organizations

and cancer specialists. We suspect, however, that the final ratios would be substantially the same. A related concern is that benefits from the last screen for each of the policies continue past the llth year, because each policy leaves its population in a unique health status mix; as a result, future benefits will accrue differentially for each policy. We chose to stop at the llth year partly for convenience, but with the expectation that it would still be possible to obtain a reasonably accurate picture of the relative merits of one policy over another and with the realization that the discounting mechanism significantly dilutes benefits which accrue far into the future.

Summary

As must be evident by now, there are numerous limitations to this study's simulation process (the more important ones have been discussed). However, reality never can be—nor need be—perfectly duplicated, even if all elements are known. The value of a simulation model is measured by determining both its usefulness in gaining new insights into a complex process and its ability to successfully predict events, and simplifying assumptions are permitted so long as they do not unduly bias the results.

CONCLUSIONS

Regardless of the assumptions made or measures used, the cost effectiveness of cervical cancer screening increases as the screening interval length increases until some maximum value is reached, This function is largely due to the effect of discounting, since costs are incurred in the present and benefits are delayed, accruing in the future. As indicated in figure **6**, the higher the discount rate, the more advantageous it is to postpone screening. However, since the functions observed are nonlinear, decreasing at a decreasing rate, it is much more cost effective to postpone screening 1 additional year when the intervals are frequent than it is when the intervals are infrequent. For example, at a 10-percent discount rate, if the established policy were to screen biennially, then changing to a policy of screening every year would cost an extra $56,000 per year of life saved; however, changing from a policy of screening every 8 years to a policy of screening every 7 years would cost only an extra **$300** per year of life saved. Cervical cancer screening is already an accepted practice, so the most pertinent issue is the appropriate screening interval length. The most useful way to address this would be a marginal analysis such as that just described. A CEA does not provide the desirable level of screening, because there is no information regarding the value of life. Once one assigns a value, one can easily read the interval from the appropriate table.

The analysis does indicate that the results are not very sensitive to error rates or to small changes in the discount rate, as long as one accepts the premise that the true discount rate currently lies somewhere near 10 percent. However, much more attention must be paid to the true costs of operating a screening program. For instance, when costs are decreased in recognition of the effects of joint production and in recognition of the obvious fact that benefits (other than averting death due to cervical cancer) are accrued, the cost effectiveness of the program increases approximately twofold throughout most of the interval range under consideration (see table 10). Likewise, when we simulate a minimal cost screening program, still maintaining acceptable standards of care, we note a tremendous difference in cost effectiveness, making every screening level more than three times more attractive. If the effects of joint production were evaluated in the low-cost model, as they were in the base case (high-cost) model, cervical cancer screening would be even more appealing.

One of the purposes of this study was to examine the cost effectiveness of cervical cancer screening in light of the perspectives of different individuals and institutions within society, since, ordinarily, cost-effectiveness studies are performed with only society's objectives in mind. The results of our analysis show a continuous decline in total medical costs as the screening interval lengthens (see table 5 and figure 4), indicating that an institution whose primary objective is financial will always benefit from postponing screening. To a health insurer, for example, cervical cancer screening always costs more than it saves, which may explain why preventive benefits are often not covered by insurance policies. But at least one other thing that makes cervical cancer screening even less attractive to a private insurer is the fact that subscribers leave the plan. Table 11 indicates that as emigration rates increase, screening becomes less attractive, particularly if the screenings are frequent. The combined effects of screening costs being larger than medical cost savings and the loss of subscribers (and with them, future benefits) may help explain the reluctance of the private sector to finance screening.

This study has also demonstrated the offsetting costs and benefits associated with outreach programs designed to increase access to health care for a high-risk population. Although the cost of finding these women was substantial (an additional *$20* for each visit), their increased risk for cervical cancer (twice the risk) was sufficient to keep the cost-effective function nearly identical to that for the low-cost, normal-risk group. This finding implies that the increased costs of outreach programs can be justified on the basis of decreased cervical cancer mortality alone. If these high-risk women are also assumed to be at high risk for diseases other than cervical cancer, one can hypothesize that significant additional dividends can be gained from the gynecological visit. These additional benefits have been labeled "joint production effects. " The added costs of performing other tests and evaluations will not be large, but the additional health benefits could be substantial. Owing to the way costs and benefits are evaluated, though, an outreach program will probably not be undertaken. Where a private party may place emphasis on the increased screening and induced treatment costs, a public party **may** be interested only in the cost per woman screened. Thus, an outreach program may be attractive to neither party. If all costs and all benefits are taken into account, however, it may become very appealing, particularly from a societal point of view.

Policy Considerations.—We conclude from our study that simple totaling and comparing all benefits and all costs of disease prevention/ health promotion programs will not provide sufficient information for society to allocate its resources efficiently. This is because many of the decisions are made by individuals in the private sector rather than by those in the public sector, and because the key decisionmaker **may** not be personally affected by the benefits.

Nevertheless, as medical costs continue to escalate, more and more private parties are considering different types of health promotion/ disease prevention programs as potential ways to save money. Rather than by governmental exhortations, these programs could be encouraged by carefully planned subsidies that function as transfer payments. Such subsidies could be in the form of assistance to either suppliers or consumers, e.g., tax incentives, direct financial assistance to defray program costs, or redeemable health promotion coupons similar to food stamps.

A second potentially effective method of promoting these programs might be to encourage private employers to accept more direct liability for the health and welfare of their work force, thus creating health promotion incentives similar to those found in the military (see introduction). Employers could be given tax incentives to contract with specific organizations for the provision of health care and possibly to provide life insurance and increased disability insurance coverage (39).

By combining these two suggestions, powerful incentives could be created within the private sector to establish effective programs throughout the country. Programs such as weight control, smoking cessation, and hypertension control, as well as more medically oriented programs such as Pap testing and glaucoma screen-

ing, could be more accessible to the general public and could become an accepted part of the daily working environment.

Such an approach to promoting health would be feasible, because it would capitalize on natural incentives and it would combine public and private resources. Without this partnership, health promotion/disease prevention programs are often too expensive for either the public or private sector to undertake independently.

APPENDIX A.—GLOSSARY OF TERMS

Biopsy .—Removal and examination (usually microscopic) of tissue from the living body, performed to establish precise diagnosis.

Carcinoma in situ (CIS).—A neoplastic (cancerous) lesion wherein the tumor cells lie only within the epitheliums or origin (i. e., preinvasive carcinoma).

Clinical carcinoma .—Carcinoma (cancer) which has developed to such an extent as to be diagnosed by overt signs and symptoms. Clinical carcinoma is normally invasive carcinoma.

Colposcopy.—Visual examination of the vagina and cervix by means of a colposcope (i. e., a speculum or instrument inserted into the vagina for the examination of tissues by means of a magnifying lens).

Ionization.—A large, cone-shaped biopsy which can be performed for both diagnostic and therapeutic purposes.

Cryosurgery .—Surgery performed by freezing a portion of the cervix.

Directed biopsy.—A biopsy using a colposcope to "direct" the procedure.

Dysplasia. —A lesion which is thought to be precancerous when found on the cervix.

False-negative rate,—The number of persons with disease but not identified by the test (i.e., false negatives), divided by the total number of persons with the disease.

False-positive rate.—The number of persons without disease but not classified by the test as being without disease (i. e., false positives), divided by the total number of persons who are disease free.

Invasive carcinoma.—A mass of cancerous cells which has "invaded" the surrounding tissue (i. e., not confined to the epitheliums, as is carcinoma in situ).

Occult carcinoma.—A preclinical stage of invasive carcinoma.

Pap test.—An exfoliative cytological staining procedure for the detection and diagnosis of various conditions, particularly malignant and premalignant conditions of the femal genital tract (e. g., cancer of the cervix), in which cells from the genital epitheliums are obtained by smears, fixed and stained, and examined under a microscope for evidence of pathologic changes.

Precancerous lesion.—Cell abnormality (lesion) that is thought to be a precursor to cancer. Dysplasia is considered to be a precancerous lesion.

Preclinical invasive carcinoma. —invasive carcinoma which has not yet **developed to** such an extent as to be diagnosed by overt signs and symptoms.

APPENDIX B.–HEALTH STATE VECTORS FOR SCREENING POLICIES

		Initial vector'	Vector after first screening	Vector after second screening
H1	Normal.	0.986000	0.986000	0.986000
H2	Reverted normal.	0.003000	0.003000	0.003000
H3	Dysplasia	0.005000	0.001000	0.000200
H4	CIS	0.004000	0.000800	0.000160
H5	Invasive	0,002000	0.001840	0.001693
H6	High-risk, disease free	0.000000	0.007200	0.003640
H7	High-risk, dysplasia . . . . . ,	0.000000	0.000000	0.000000
H8	High-risk, CIS	0.000000	0.000000	0.000000
H9	High-risk, invasive.	0.000000	0.000000	0.000000
H10	Hysterectomy	0.000000	0.000160	0.000307
H11	Emigration	0.000000	0.000000	0.000000
H12	Death due to cervical cancer . .	0.000000	0.000000	0,000000
H13	Death due to all other causes . ,	0.000000	0.000000	0.000000

[a] The Initial vector is screened twice More aging begins

[b] The vector after the second screening is subequently aged according to the disease progression chart in table 4

APPENDIX C.–COST FORMULATIONS

Low=Cost Model[1]

The low-cost model is not based on fee-for-service, so costs were assigned by estimating resources required for a hypothetical patient load and by estimating allocation schedules. Listed below are staffing requirements, rent and utility expenses, and furniture and equipment costs. All expenses other than those specifically noted are allocated to Pap testing.

Pap Test Cost Calculations

	Cost per day
1 physician (10% time @ $20/hr)[2]	$ 4
1 registered nurse practitioner (100% time @ $12/hr)[3]	72
2 licensed vocational nurses (100% time @ $6.50/hr)	104
1 receptionist/clerk (100% time @ $3.49 /hr)	28
Rent: 1,200 sq ft (@ $1/sq ft/mo) (3 examination rooms, office, waiting area, lounge, bath)	57
Phone and utilities	5
Furniture and equipment (see list and prices below) ($18,000 amortized @ *570* for 10 years)	9
Supplies, expendable	33
Total	$312
Assuming each L.V.N. sees 1 patient every 15 minutes, then 64 patients are seen each day: 312 -64 =	$5 Pap test

Furniture and Equipment Costs

	Cost per item	*Total cost*
Weight scale (1)	*$ 177*	*$ 177*
Exam table with stirrups (3)	*256*	*768*
Supply cart (1)	*85*	*85*
Equipment/supply table (3)	*224*	*672*
Lamps, exam (3)	*34*	*102*
Stools, exam (3)	*72*	*216*
Cabinet, instrument (I)	*310*	*310*
Punch, biopsy, uterine (4)	*138*	*552*
Forceps, uterine (4)	*75*	*300*
Curette, endocervical (4)	*28*	*112*
Speculum, endocervical (4)	100	*400*
Colposcope (2)	3,650	*7,300*
Unit, cryosurgery (1)	695	*695*
Tank, NO	110	110
Sphygmomanometer (4)	*33*	132
Stethoscope (4)	*5*	20
Wastebasket with cover (3)	*80*	240
Desk (4)	*156*	624
Chair, desk (4)	*90*	360
Typewriter,	*890*	890
Cabinet, filing, 4 drawer (2)	*75*	150
Cabinet, filing, 1 drawer (1)	*25*	25
Bookcase (1)	*35*	35
Boards, bulletin (2)	*50*	100
Roller deck (1)	*10*	10
Chair, comfort/lounge & waiting room (10)	*60*	600
Dictionary (4)	*15*	60
Dictionary, medical (4)	*30*	120
Couch (1)	*350*	350
Table, typewriter (1)	*25*	25
Table, small (4)	*65*	260
Refrigerator, small (1)	*150*	150
Stove, small (1)	*200*	200
Sinks, installed (5)	*200*	1,000
Wastebasket (3)	*10*	30
Miscellaneous	*500*	500
Total		$17,680

Summary of Low-Cost Model[4]

	Practitioner	*Lab*	*Hospital*	*Total*
Pap	$ 5	$3	—	*$ 8*
Coloscopy	20	—	—	*20*
Biopsy	10	12	—	*22*
Cryosurgery	*20*	—		
Ionization	400	–	*$2760*	*220*
Hysterectomy	2,000		*5,900'*	*7,9005*

High-Cost Model[6]

	Practitioner	*Lab*	*Hospital*	*Total*
Pap	$ 2 0	$10	—	*$ 30*
Coloscopy	50	—	—	*50*
Biopsy	*25*	*55*	—	*80*
Cryosurgery	55	—		*55*
Ionization	400	—	*$2,360*	*2,760*
Hysterectomy	2,000	—	*5,900*	*7,900*

[1] Except as noted, all items were Identified and priced in consultation with Reyes (3o). Equipment was priced through standard catalogs.

[2] Assuming 25 percent of time allocated to Pap test backup.

[3] Assuming 75 percent of time to Pap test backup, which includes patient health education actvities.

[4] Assuming a patient load of 15,360/year (i.e., 2 L, V.N. S, each seeing one patient every 15 minutes for 48 weeks of the year).

[5] Total hospitalization charges for diagnosis of CIS and invasive cervical cancer, respectively, includin multiple admissions. Source: *Hospitalizations and Payments to Hospitals,* Third National Cancer Survey, HEW publication No. 76-1094, March 1976 (costs adjusted to 1979).

[6] The high-cost model is used in the base case (see app. D).

APPENDIX D.–VALUES FOR BASE CASE ANALYSIS

To establish a base against which to make comparisons of the effects of assigning alternative values to variables, a base case is established in which the study's variables are assigned the following initial values.

1. The initial disease transition matrix is **as shown** in table 4.
2. The initial population vector (i.e., the state of health of the initial population) is as defined in appendix B.
3. The population is screened twice before aging begins.
4. Error rates:
   —False-negative rates for the Pap test: 0.2 for dysplasia, CIS, and preclinical invasive disease.
   —False-positive rate: 0.05.
5. The proportion of invasives which are preclinical and therefore are eligible for detection by Pap test = 0.1.
6. Discount rate = 10 percent.
7. Costs (high-cost model):

Pap test	$ 20
Pap cytology	10
Colposcopy	50
Biopsy	80
Cryosurgery	55
Ionization	2,500
Hysterectomy	7,900

Sensitivity analysis is used to compare the effect of assigning other values.

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