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Cost-effectiveness of Cervical Cancer Prevention

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Abstract: Cost-effectiveness analyses are an important tool for the evaluation and modification of many health care services. Given the variety of screening tests and treatments available for cervical cancer screening and prevention, the costs associated with these options and with their alternatives, and the differences in resources and settings in which these tests are applied worldwide, cost-effectiveness analyses evaluation can be very useful to help determine best practices.
Key words: cost-effectiveness, cervical cancer screening, cervical cancer prevention

Introduction

Cost-effectiveness analyses (CEA) are an important tool for the evaluation and modification of many health care services. In particular, for programs and services for which the options are complicated, and both the costs and the benefits can be highly variable, CEA may be helpful at clarifying the best alternatives. Given the variety of screening tests and treatments available for cervical cancer screening and prevention, the costs associated with these options and with their alternatives, and the differences in resources and settings in which these tests are applied worldwide, CEA evaluation can be very useful to help determine best practices.

Over the last 60 years, the incidence of cervical cancer in the United States has decreased by 82.5% (http://seer.cancer.gov/csr/1975_2009_pops09/results_single/sect_01_table.01.pdf), mostly because of cytology screening, also known as "the Pap test."

In 2012, it is estimated that there will be 12,170 new cases of cervical cancer and 4220 deaths in the United States (http://seer.cancer.gov/csr/1975_2009_pops09/results_single/sect_01_table.01.pdf). Internationally, cervical cancer is the second leading cause of cancer-related deaths in women. In 2008, there were an estimated 529,828 new cases of cervical cancer and 275,128 deaths (http://www.who.int/hpvcentre/statistics/en/). Innovative research and development continue to lead to

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improved screening capabilities with technology, including liquid-based cytology (LBC), human papilloma virus (HPV) testing, and the HPV vaccine. All of this technology has the potential to improve cervical cancer detection and prevention even further, but these services add additional cost, and variable increased value, depending on how they are used. With the burgeoning health care economic crisis, it is essential to consider both efficacy and cost implications of this new technology in the creation of screening guidelines. Today, screening and treatment of HPV-related diseases in the United States alone is estimated to cost 4.6 billion dollars.[1] In resource-poor nations, there are limited screening programs if any at all and access to the treatment of cervical cancer with radiation, chemotherapy, or surgical expertise is very limited. Thus, the potential impact of screening programs is immense. However, the challenges associated with building screening programs in these settings are innumerable, including creation of infrastructure, training programs, and follow-up. Furthermore, limited resources remain a great constraint. Thus, considerations of effectiveness and cost are also essential in this setting in the creation of cervical cancer screening programs.

CEA are decision analytic tools generated from complex mathematical models built with the best available clinical data to compare health interventions on both efficacy and cost criteria. With growing economic constraints, CEA are becoming increasingly relied upon as public health policy decisions are made. Thus, this chapter will educate the reader regarding the elements of CEA and then will further review the existing literature of cost-effectiveness and cervical cancer screening in the United States and in the developing world.

CEA

CEA compare 2 or more health care interventions with unique health outcomes and costs. The intention of a CEA is not to find a unique answer to a question but rather to take a complex problem and generate information that can help guide clinical decision making and health care policy. Population-based screening programs are an excellent example of a complex problem that a CEA may address. There are a number of CEA that specifically address cervical cancer screening and the use of cervical cytology, HPV testing, and the role of HPV vaccination. However, before we review the literature, we should clearly define what comprises a CEA.

It is important to remember "cost-effective" does not equal "cost-savings." A CEA attempts to address the question of whether or not the additional cost of a health care intervention is worthwhile or adds value. To do this with any validity, there must be an adequate amount of data available with regard to the natural course of a disease, probability of events, health outcomes, and associated costs. These data are used to generate a model that incorporates disease states, health outcomes, and costs, to allow comparison of 2 or more health interventions.

In 1993, the Panel on Cost-Effectiveness in Health and Medicine was convened by the US Public Health Service in 1993 to provide guidelines for CEA. After deliberations, the Panel laid out several important principles that should be included in all CEA.[2,3] They recommended that a CEA model must encompass an adequate amount of time over that health benefits and costs accrue to measure the full economic and health benefits of each intervention. Models should be developed on the basis of the best available data. This includes data from randomized controlled trials, observational trials if randomized data are not available, public health statistics, and expert opinion. In addition, a clear statement of the perspective of the analysis must be made. In our complex health care

system, the societal perspective is very different from the patient, the managed care organization, or the payer perspective. Thus, a CEA should clearly define the perspective from which it is framed.

Sophisticated CEA are built with complex mathematical models that describe a disease process or health states associated with a condition, including all possible treatments, complications, and outcomes. There are several types of mathematical models that were used in the CEA reviewed later in this chapter. The Markov model reproduces disease progression for a particular cohort of patients over an expected lifetime. It follows a linear pattern of disease progression using probabilities of moving between states of disease that are derived from well-established data. In the case of cervical dysplasia and cancer, a Markov model will assign a probability of progression and regression between each of the classifications of dysplasia and invasive cancer. The transmission dynamic model follows an entire population over a period of time. In this model, the subjects are the entire population as opposed to a discrete cohort of patients, which allows for evaluation of the impact of herd immunity in the population, which might be important when considering impact of a cervical cancer vaccine.[4] Finally, there are hybrid models which incorporate elements of both the Markov and transmission models.[5]

Costs can be estimated from any number of sources but those sources should be clearly documented. A wide variety of costs are included in most CEA and what is included may directly speak to what the perspective of the analysis is. The Panel on Cost-Effectiveness in Health in Medicine recommended that in the interest of uniformity, a societal perspective should be adopted. These analyses would include costs associated with direct medical care, patient time and travel costs, and intangible costs of pain and suffering and lost productivity. Estimates of direct medical care can be made from medical charges, reimbursements, or actual resources used. By examining the costs included in a CEA analysis, the perspective should be clear. For example, inclusion of costs of lost productivity of patients must be included to encompass a societal perspective, yet are not essential for analyses built from a payer perspective. Finally, the Panel on Cost-Effectiveness in Health and Medicine recommends that all costs be discounted to present value at the same rate of 3%.

The most commonly used measurements of health outcomes are life-years saved (LYS), and quality-adjusted life-years (QALY), although simpler measures such as hospital days saved or number of health events (ie, heart attacks, cases detected) can also be used. LYS is the outcome unit used to compare differences in survival. Meanwhile, a QALY is a slightly more complex unit that allows for comparison of both improved survival and the quality of life associated with different health states. QALYs are generated by assigning a utility to the various health states within the model. Classically, a utility score of 0 is equal to death and a score of 1 is equal to perfect health. Utility scores are derived on the basis of the best available quality-of-life data and expert opinion. The Panel on Cost-Effectiveness in Health and Medicine recommends that analogous to its recommendation on costs, all health outcomes should be discounted to present value at a rate of 3%. Similar to the way inflation changes actual dollar values over time, patients value different health states differently over the course of a lifetime or disease process.

All CEA should present a baseline scenario, either the standard of care or no intervention, then generate subsequent incremental cost-effectiveness ratio (ICER) to compare the new health intervention. The ICER is an equation that enables comparison of a health intervention to

the base case or the comparison of 2 different health interventions. In the numerator are the costs associated with the health care intervention and the denominator represents the units of effectiveness. Another way to describe the ratio is resource impact divided by health outcomes impact.

found that the median intervention cost \$42,000 per LYS.[6] In the United States, a generally agreed upon range for cost-effectiveness is anything $<$ \$50,000 per LYS or QALY is cost-effective, although a range of \$50,000 to \$100,000 per LYS or QALY is generally accepted as a reasonably cost-effective intervention.

$$\text{ICER} = \frac{\text{Cost of intervention(A)} - \text{Cost of intervention(B)}}{\text{Effect of intervention(A)} - \text{Effect of intervention(B)}}$$

As described above, a compelling CEA will be built upon a model that incorporates the best available data about the natural history of a disease and its associated health states. That model will generate different health outcomes (QALY, LYS, number of hospital days, etc.) and costs depending on the health interventions utilized. This will enable generation of the ICER between 2 different health interventions. Although a conclusion of relative value can now be made between 2 health interventions, it is only as valid as the assumptions with which the model was built. Thus, a robust CEA must perform sensitivity analyses to test these assumptions. This is achieved by varying the inputs in the model and evaluating how that might change the ICER. In the case of cervical cancer screening tests, an important model assumption to vary are the sensitivity and specificity of each test, in addition to the prevalence of HPV and the costs associated with all interventions. The sensitivity analyses are essential to address the uncertainty inherent within all CEA, yet they can also generate interesting data. For example, by varying the cost of a test, you might find at what price-point that test becomes "cost-effective."

There is no absolute consensus regarding what is "cost-effective." A 1995 review of all CEA in the United States, looking at 587 life-saving interventions

Internationally, different thresholds are used to reflect what is cost-effective for that particular nation. Interventions are often compared with the per capita gross domestic product (GDP) of that country. A well-accepted standard for cost-effective care in low-resource setting is if the cost per life-year saved is >3 times the per capita GDP, that intervention is considered cost-effective and anything less than the absolute per capita GDP is highly cost-effective.

CEA and Cervical Cancer Screening in the United States

There are numerous CEA addressing various changes to cervical cancer screening within the United States. In March of 2012, the American Society for Colposcopy and Cervical Pathology, the American Cancer Society, and the American Society for Clinical Pathology published new cervical cancer screening guidelines. These guidelines were generated by a collaborative group of experts organized into working groups convened from 2009 to 2011 to systematically review the evidence to determine optimal cytology screening intervals, screening strategies for women older than 30, management of discordant cytology and HPV testing, optimal age to exit screening, impact of HPV vaccination on screening strategies, and potential

utility of molecular HPV screening.[7] Much of the literature reviewed to generate the cervical cancer screening guidelines were decision analytic models including many cost-effectiveness models.

In March of 2011, Kulasingam et al[8] published their work for the US Preventative Services Task Force that utilized a decision model to address at what ages screening should commence and end, in addition to the optimal screening intervals and how to best test HPV DNA in conjunction with cytology. This decision model chose not to use cost as an endpoint but rather measured outcomes in units of colposcopies per life-year gained. Other estimated outcomes measured were number of colposcopies, expected false-positives, CIN2-3 cases, cancer cases, and cancer deaths. This metric was chosen by the US Preventative Services Task Force because it was felt to best represent a reasonable trade-off between the burden and benefits of screening. Although cost is not the endpoint, the creation of the decision model is analagous to that of a cost-effectiveness model. To perform this analysis, Kulasingam and colleagues utilized the well-established Duke Cervical Cancer model, which is a modified Markov model simulating the natural progression of HPV infection in a cohort of unvaccinated girls beginning at age 12, followed until death or 100 years of age. Screening strategies were compared with one another to generate incremental ratios comparing colposcopies per life-year gained. Four specific strategies were investigated: (1) cytology with repeat cytology at 6 and 12 months for Atypical Squamous Cells of Undetermined Significance (ASCUS); (2) cytology with HPV triage for ASCUS; (3) cotesting with cytology and HPV; and (4) HPV testing with cytology triage. All strategies were tested over screening intervals of 1, 2, 3, and 5 years. Efficient strategies were those that demonstrated the greatest effectiveness with the fewest number of colposcopies performed. They found that a strategy commencing screening with cytology only at age 21 every 3 years was efficient. With regard to exiting screening, they found that women who were well screened could exit at age 65 and those who had never been screened could be screened every 2 to 5 years stopping in their mid-70s.

Finally, incorporation of HPV testing into screening demonstrated that it was sensitive to how the burden of screening was measured. Utilizing their main outcome, colposcopies per life-year gained demonstrated that cotesting every 3 to 5 years for women older than 30 was highly efficient. When the burden of screening was measured in number of tests, however, cytology only every 3 years was shown to be the efficient strategy. Interestingly, this analysis validated many of the screening guidelines at the time it was published in 2011, moreover, generating important evidence for some of the modifications reflected in the updated screening guidelines released in March of 2012.

The working groups who generated the March 2012 cervical cancer screening guidelines also reviewed many other more traditional CEA. To understand the history of cervical cancer CEA, several well-designed CEA will be reviewed below to highlight the greater body of literature on the subject. The analyses presented in (Supplementary Digital Content Table 1: http://links.lww.com/GRF/A8)[9–14] addresses different and important questions about screening for cervical cancer. The topics of the CEA range from use of screening in different demographic groups, incorporation of HPV testing, and comparisons of different cytologic technology (Supplementary Digital Content Table 1: http://links.lww.com/GRF/A8). A great majority of recent CEA publications have focused on the impact of the HPV vaccine and its implications for screening programs (Supplementary Digital Content Table 2: http://links.lww.com/GRF/A8)[15–18] and

those will be discussed in the next section.

Mandelblatt and Fahs[9] queried whether or not it was cost-effective to screen low-income elderly women. They built a Markov model with incidence of dysplasia and cancer seen in low-income elderly women visiting the Medical Primary Care Unit, New York, a municipal hospital outpatient medical clinic. All women older than 65 visiting the clinic were offered a screening exam including a Pap smear and 816 of 1542 agreed to be screened. Data from these women were used then to build their CEA model in addition to a review of the best available literature on cervical cancer in elderly women. In 11 of the 816 women, the Pap test was abnormal. After inputting all the variables into their model, they actually found that screening this population was not only cost-effective but also cost-saving, given that both sides of the cost-effectiveness ratio generated savings.

Several of the studies presented in (Supplementary Digital Content Table 1: http://links.lww.com/GRF/A8) address what type of testing for cervical cancer screening is cost-effective. Brown and Garber[10] looked at a very specific question regarding what the impact of 3 different and new Pap smear technologies (ThinPrep, AutoPap, Papnet) was in comparison with traditional Pap testing. Utilizing 8 published studies that met their criteria, they generated a model accounting for the differences in sensitivity and cost among the 3 technologies. They found that the AutoPap increased survival at the lowest cost for a variety of different screening intervals studied and that at the triennial screening interval, all 3 technologies produced more life-years than convential Pap smears every 2 years. AutoPap generated an ICER of $7777 per LYS at quadriennial screening compared with conventional Pap smear every 4 years. This study was funded by the Technology Evaluation Center of Blue Cross Blue Shield Association, but was designed from the societal perspective including all costs paid either by the patient, the insurer, or other parties.[10]

Myers et al[11] asked a general question about the impact of changing the sensitivity and specificity of new screening methods. They used a Markov model to map the natural history of cervical cancer and examined the effects of changing the sensitivity and specificity of an unspecified screening test. What they found was that increasing the sensitivity of a triennial screening test from 51% to 99% while holding specificity constant did improve life expectancy and generated an ICER of $7206 per LYS when the cost of the screening test was held constant. Interestingly, they looked at screening intervals of 1 to 5 years and found that at every interval, increased sensitivity resulted in increased cost even when the cost of the test was held constant. This was attributed to the increased cost of evaluation and treatment of low-grade lesions that were identified in greater numbers with increased sensitivity.[11]

The final 3 analyses included in (Supplementary Digital Content Table 1: http://links.lww.com/GRF/A8) address the use of HPV testing or genotyping. Mandelblatt et al[12] built a Markov model to study the different screening strategies of Pap smear and HPV testing, Pap smear alone, and HPV alone at 2- and 3-year screening intervals. They found that maximal life expectancy savings were achieved using Pap and HPV testing at 2-year intervals until death generating an ICER of $76,183 per QALY. Interestingly, by adjusting the age of screening cessation to 75 years, they maintained 97.8% of the benefits of lifetime screening but decreased the ICER to $70,347 per QALY. In this analysis, they looked at all 3 strategies at 2 different screening intervals and 3 different ages (death, 75 and 65 y) at which screening ceases. The range of ICERs generated was $11,830 per QALY for a strategy of Pap smears every 3 years to age 75 up to the most life-saving

intervention of Pap smear plus HPV testing every 2 years at $76,183 per QALY. By performing sensitivity analyses around the costs associated with the various tests, they also found that Pap smears alone are more cost-effective unless an HPV test cost only $5. Finally, they showed that a screening strategy of cotesting with Pap and HPV every 3 years until age 75 was highly cost-effective at $38,699 per QALY.[12]

The analysis by Kim et al[13] investigating the use of HPV testing, specifically addressed the question of management around the ASCUS. This is a significant public health problem as they estimate approximately 2 million women undergoing routine screening will have this equivocal result annually. The authors queried what the most efficient management strategy for these patients was by looking at 4 different strategies (ASCUS = negative result, immediate colposcopy, repeat Pap smears at 6 and 12 mo, and reflexive HPV testing). When they compared LBC with reflexive HPV testing for patients with ASCUS Pap smears screened every 3 years compared with the same strategy every 5 years, they found an ICER of $59,600 per LYS and was less costly and more effective than conventional cytology with either repeat cytology or immediate colposcopy performed every 2 years.[13]

Finally, Vijayaraghavan et al[14] queried whether or not HPV 16, 18 genotype triage in cervical cancer screening was cost-effective. Of all the studies included in (Supplementary Digital Content Table 1: http://links.lww.com/GRF/A8), this is the only one not performed from the societal perspective. The study was funded by a grant from Roche Molecular Systems and was built from a payer perspective. They used a Markov model in which all women were screened with biennial LBC testing until age 30 and then entered one of 6 different screening strategies. Strategies ranged from LBC only to coscreening to regimens including HPV genotyping. They found that HPV genotyping to triage women with positive high-risk HPV testing was a cost-effective strategy with an ICER of $34,074 per QALY when compared with HPV and LBC coscreening without genotyping. They also found that adding HPV genotyping triage to coscreening regimens was even more effective and had an ICER of $33,807 per QALY when compared with reflexive HPV genotyping for all high-risk positive HPV women.[14]

These examples of United States-based CEA of cervical cancer screening beginning in the late 1980s follow the controversies in screening and challenges associated with incorporation of new technology. The most recent analyses including the Kulasingam and colleagues decision model described in detail at the beginning of the chapter have all generated important evidence for the optimal screening ages, screening intervals, and use of HPV testing and unsurprisingly, these analyses have directly impacted the generation of the latest generation of cervical cancer screening guidelines released in March 2012.

HPV Vaccination and CEA

The US Food and Drug Administration (FDA) approved the first HPV vaccine in 2006, Gardasil for use in females ageing 9 to 26 years. Gardasil is a quadrivalent vaccine active against HPV subtypes 16, 18, 6, and 11. It protects against approximately 70% of all cervical cancers thought to be related to HPV subtypes 16, 18, and genital warts caused by 6 and 11. In 2009, the FDA approved a second cervical cancer vaccine, Cervarix, which protects against HPV type 16, 18 for females ageing 10 to 25 years. In the years surrounding the FDA approval, many CEA were undertaken to investigate the impact of the vaccine on cervical cancer screening. In the development of these CEA models, several assumptions about the vaccine had to be made including its efficacy, duration of effect, and cost. The

analyses included below assigned an efficacy of 90% to 100%, a vaccine duration of protection from 10 years to lifetime and vaccine cost ranged from $200 to $500. Each CEA tested these assumptions with sensitivity analyses. In addition, many of the analyses below sought to answer questions surrounding how screening guidelines might change with the advent of the vaccine. All analyses are from the societal perspective and used 3% discounting.

In 2010, Armstrong[19] published a comprehensive review of the literature on the cost-effectiveness of the HPV vaccination, which included many of the analyses in (Supplementary Digital Content Table 2: http://links.lww.com/GRF/A8). They found that HPV vaccination was cost-effective in preadolescent girls with ICERs of $\leq$$100,000, but these catch-up programs often increase the cost per QALY to more than $100,000. Of note, some of the models including Kulasingam and Myers[15] preceded the actual use of the HPV vaccine. In reality, costs are higher and efficacy is lower in actual practice, and duration of effect is not yet known. Nonetheless, their review highlights that varying the actual characteristics of the vaccine efficacy, duration of protection, and cost can have a significant impact on the cost-effectiveness ratios. Further, similar to the first series of analyses presented in (Supplementary Digital Content Table 1: http://links.lww.com/GRF/A8), these CEA lend further evidence that alterations in screening guidelines from age of population screened, type of screening tests utilized, and frequency of screening also significantly impact the cost-effectiveness ratios.

CEA and Cervical Cancer Screening in Low-resource International Settings

Cervical cancer remains a leading cause of death for women in developing nations. The high incidence of cervical cancer is a tragedy given the availability of excellent screening tests available in more developed countries. The potential impact of cervical cancer screening programs in these settings is immense, yet great challenges to implementation exist including limited resources and access to services. Careful consideration to the efficacy of screening, type of tests, and associated costs must be undertaken to determine what the best strategies are. Thus, CEA are again a very useful tool in this setting. A selection of well-designed CEA in low-resource settings is reviewed below and is presented in (Supplementary Digital Content Table 3: http://links.lww.com/GRF/A8).[20–23]

Goldie et al[18] developed a Markov model to look at different screening strategies in unscreened black South African women. They compared 3 strategies over different screening intervals including direct visual inspection (DVI), cytology, and HPV testing. All strategies in a single lifetime screen were compared with no screening and it was found that HPV testing at age 35 with a single repeat visit for treatment (cryotherapy) cost $39 per LYS with a 27% reduction in cervical cancer, whereas DVI with immediate treatment was cost-saving with a 26% reduction in cervical cancer. Meanwhile, cytology followed by a second visit for treatment was least effective at 19% reduction in incidence of cervical cancer and more costly $81 per LYS. Furthermore, this study demonstrated that increasing the number of visits or using conventional cytology are less cost-effective than single-visit DVI or HPV testing in this setting.[20]

Goldie et al[21] broadened their analyses to include 5 developing countries—India, Kenya, Peru, Thailand, and South Africa. They used the same model to test screening models of visual inspection with acetic acid (VIA), Pap smear, and HPV testing in 1 or 2 visits in each country. They found

similar rates of reduction in cervical cancer incidence as above ranging from 25% to 36% reduction for VIA and HPV testing in 1 and 2 visit strategies. Again, the Pap smear was the least effective strategy with reductions in cervical cancer incidence of 18% to 22%. Cost per LYS for a single lifetime screen with either single-visit VIA or 2-visit HPV testing ranged from $10 to $467 per LYS for all countries. Although the absolute international dollar values did vary slightly from country to country and there were slight differences in which strategy was most cost-effective by country, once lifetime screening strategy remains highly cost-effective in all 5 the countries. Interestingly, they also found that if they increased screening to twice per lifetime at age 35 and 40 in each country, the cost per LYS remained less than the per capita GDP in each country for visual inspection or HPV testing depending on the country.[21]

Vijayaraghavan et al[22] investigated HPV testing as a screening strategy in South African women. Using a Markov model following 100,000 women beginning at age 30, they tested 5 different screening strategies from no screening to coscreening with cytology and HPV. Cost-effectiveness ratios were generated in South African Rand and the study was funded by Roche Molecular Systems. They found that conventional screening, a Pap smear every 10 years beginning at age 30, with the addition of HPV triage cost 13,270 Rand compared with no screening. Thus, they felt that the addition of HPV testing to cervical cancer screening in South Africa was a cost-effective strategy.[22]

Ginsberg et al[23] authored an extensive WHO-CHOICE analysis of screening strategies against breast, colorectal, and cervical cancer in sub-Saharan Africa and southeast Asia. WHO-CHOICE is a world health organization (WHO) initiative started in 1998 that aims to provide evidence to policy makers about what health interventions are cost-effective. In this analysis, they tested 52 different cervical cancer screening strategies in these 2 regions. Screening interventions included Pap smears and VIA at varying ages and screening intervals with and without the HPV vaccination. The HPV vaccination was assumed to cost $0.60 and was administered at different ages. They found that the single most cost-effective strategy in both regions, assuming that 50% population is screened, was a single lifetime screen with Pap smear including lesion removal and treatment [$Int 307 per DALY (a disability-adjusted life-year is a unit measure of effectiveness often employed in international CEAs) sub-Saharan Africa and $Int 142 per disability-adjusted life-year southeast Asia]. They found that the vaccine was cost-effective in sub-Saharan Africa if it costs $0.60 US dollars in conjunction with a single lifetime Pap smear at age 40, but was not cost-effective in southeast Asia. Of note, this analysis did not consider HPV testing as the currently available tests are so expensive. It does clearly show, again, that some level of cervical cancer screening is cost-effective in these resource-poor regions. It also demonstrates that the HPV vaccine is not cost-effective at current prices.[23]

All of these analyses suggest that cervical cancer screening is cost-effective even in resource-poor nations with the potential to reduce cervical cancer incidence by at least 25% to 30%. The models described above were created with assumptions based upon the best available data about the natural history of HPV in the region and expert opinion on the costs to support proposed screening programs. This may account for the differences seen among these analyses with regard to what the most effective strategies are. Nonetheless, development of screening programs is a worthwhile use of limited resources and careful consideration to each region's existing infrastructure and unique cultural environment should be undertaken in the creation of the screening program.

Conclusions/Summary

CEA are a useful tool for synthesizing complicated information about effectiveness, cost, and for comparing alternative approaches, in a variety of circumstances and from different perspectives. These analyses, when applied thoughtfully, may be very useful for determining the best approaches to cervical cancer screening and prevention. However, their usefulness is limited by the quality of the data, the underlying assumptions of the model, and the viewpoint of the analysis and may change as new information or options emerge.

References

1. Fleurence RL, Dixon JM, Milanova TF, et al. Review of the economic and quality-of-life burden of cervical human papillomavirus disease. *Am J Obstet Gynecol*. 2007;196:206–212.
2. Russell LB, Gold MR, Siegel JE, et al. The role of cost-effectiveness analysis in health and medicine. *JAMA*. 1996;276:1172–1177.
3. Weinstein MC, Siegel JE, Gold MR, et al. Recommendations of the panel on cost-effectiveness in health and medicine. *JAMA*. 1996;276:1253–1258.
4. Dasbach EJ. Mathematical models for predicting the epidemiologic and economic impact of vaccination against human papillomavirus infection and disease. *Epidemiol Rev*. 2006;28:88–100.
5. Goldhaber-Fiebert JD, Stout NK, Ortendahl J, et al. Modeling human papillomavirus and cervical cancer in the United States for analyses of screening and vaccination. *Popul Health Metr*. 2007; 5:11. Available at: http://www.pophealthmetrics.com/content/5/1/11. Accessed January 2, 2013.
6. Tengs TO, Adama ME, Pliskin JS, et al. Five-hundred life-saving interventions and their cost-effectiveness. *Risk Anal*. 1995;15:369–390.
7. Saslow D, Solomon D, Lawson HW, et al. American cancer society, American society for colposcopy and cervical pathology and American society for clinical pathology screening guidelines for the prevention and early detection of cervical cancer. *CA Cancer J Clin*. 2012;62:147–172.
8. Kulasingam S, Havrilesky L, Ghebre R, et al. *Screening for Cervical Cancer: A Decision Analysis for the US Preventative Services Task Force*. Rockville, MD: Agency for Healthcare Research and Quality.
9. Mandelblatt JS, Fahs MC. The cost-effectiveness of cervical cancer screening for low-income elderly women. *JAMA*. 1988;259:2409–2413.
10. Brown AD, Garber AM. Cost-effectiveness of 3 methods to enhance the sensitivity of papnicolau testing. *JAMA*. 1999;281:347–353.
11. Myers ER, McCrory DC, Subramanian S, et al. Setting the target for a better cervical screening test: characteristics of a cost-effective test for cervical neoplasia screening. *Obstet Gynecol*. 2000;96:645–652.
12. Mandelblatt JS, Lawrence WF, Womack SM, et al. Benefits and costs of using HPV testing to screen for cervical cancer. *JAMA*. 2002;287:2372–2381.
13. Kim JJ, Thomas TC, Goldie SJ. Cost-effectiveness of alternative triage strategies for atypical squamous cells of undetermined significance. *JAMA*. 2002;287:2382–2390.
14. Vijayaraghavan A, Efrusy MB, Goodman KA, et al. Cost-effectiveness of using human papillomavirus 16/18 genotype triage in cervical cancer screening. *Gynecol Oncol*. 2010;119:237–242.
15. Kulasingam SL, Myers ER. Potential health and economic impact of adding a human papillomavirus vaccine to screening programs. *JAMA*. 2003;290:781–789.
16. Goldhaber-Fiebert JD, Stout NK, Salomon JA, et al. Cost-effectiveness of cervical cancer screening with human papillomavirus DNA testing and HPV-16, 18 vaccination. *J Natl Cancer Inst*. 2008;100:308–320.
17. Kim JJ, Ortendahl BS, Goldie SJ. Cost-effectiveness of human papillomavirus vaccination and cervical cancer screening in women older than 30 years in the united states. *Ann Intern Med*. 2009;151:538–545.
18. Kim JJ, Goldie SJ. Health and economic implications of HPV vaccination in the United States. *N Engl J Med*. 2008;359:821–832.
19. Armstrong EP. Prophylaxis of cervical cancer and related cervical disease: a review of the cost-effectiveness of vaccination against oncogenic HPV types. *J Manag Care Pharm*. 2010;16:217–230.
20. Goldie SJ, Kuhn L, Denny L, et al. Policy analysis of cervical cancer screening strategies in low-resource settings clinical benefits and cost-effectiveness. *JAMA*. 2001;285:3107–3115.
21. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, et al. For the alliance for cervical cancer prevention cost working group cost effectiveness of cervical cancer screening in five developing countries. *N Engl J Med*. 2005;353:2158–2168.
22. Vijayaraghavan A, Efrusy M, Lindeque G, et al. Cost-effectiveness of high-risk HPV DNA testing for cervical cancer screening in South Africa. *Gynecol Oncol*. 2009;112:377–383.
23. Ginsberg GM, Lauer JA, Zelle S, et al. Cost effectiveness of strategies to combat breast, cervical and colorectal cancer in sub-Saharan Africa and South East Asia: mathematical modeling study. *BMJ*. 2012;344:e614.