VALUE IN HEALTH 16 (2013) 932–941

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

Program-Specific Cost-Effectiveness Analysis: Breast Cancer Screening Policies for a Safety-Net Program

Joy Melnikow, MD, MPH[1,], Daniel J. Tancredi, PhD[1], Zhuo Yang, MSc[1], Dominique Ritley, MPH[1], Yun Jiang, MS[1], Christina Slee, MPH[1], Svetlana Popova, MD, MPH[2], Phillip Rylett, BSc (Hons), RN[2], Kirsten Knutson, MPH[2], Sherie Smalley, MD[2]*

[1]*Center for Healthcare Policy and Research, University of California, Davis, Sacramento, CA, USA;* [2]*Every Woman Counts Program, Cancer Detection Section, California Department of Public Health, Sacramento, CA, USA*

ABSTRACT

Background: *Every Woman Counts* (EWC), a California breast cancer screening program, faced challenging budget cutbacks and policy choices. **Methods:** A microsimulation model evaluated costs, outcomes, and cost-effectiveness of EWC program mammography policy options on coverage for digital mammography (which has a higher cost than film mammography but recent legislation allowed reimbursement at the lower film rate); screening eligibility age; and screening frequency. Model inputs were based on analyses of program claims data linked to California Cancer Registry data, Surveillance, Epidemiology, and End Results data, and the Medi-Cal literature. Outcomes included number of procedures, cancers, cancer deaths, costs, and incremental cost per life-year. **Results:** Projected model outcomes matched program data closely. With restrictions on the number of clients screened, strategies starting screening at age 40 years were dominated (not cost-effective). This finding was highly robust in sensitivity analyses. Compared with no screening, biennial film mammography for women aged 50 to 64 years was projected to reduce 15-year breast cancer mortality by nearly 7.8% at $18,999 per additional life-year, annual film mammography was $106,428 per additional life-year, and digital mammography $180,333 per additional life-year. This more effective, more expensive strategy was projected to reduce breast cancer mortality by 8.6%. Under equal mammography reimbursement, biennial digital mammography beginning at age 50 years was projected to decrease 15-year breast cancer mortality by 8.6% at an incremental cost per additional life-year of $17,050. **Conclusions:** For the EWC program, biennial screening mammography starting at age 50 years was the most cost-effective strategy. The impact of digital mammography on life expectancy was small. Program-specific cost-effectiveness analysis can be completed in a policy-relevant time frame to assist policymakers faced with difficult program choices.

Keywords: breast cancer screening, cost-effectiveness analysis, health policy, safety net programs.

Introduction

Cost-effectiveness analysis (CEA) allows policymakers and others to consider the potential impacts of alternative policies on future program outcomes and costs. As demands escalate on the health care system to provide more services within constrained budgets, CEA is a technique that can enable policymakers to examine the value of health care services [1]. Although well established for providing guidance to policymakers in many arenas, CEA has been slow to take hold in United States health policy [2]. Health care resources, particularly those for safety net programs, are increasingly limited, and carefully constructed CEA models can inform resource allocation decisions.

While CEA has considerable potential to assist makers of health policy, a number of challenges confront its application to health policy formulation. Models often take the perspective of society in accounting for program impacts, but for public health programs, the perspective of the payer is also highly relevant [3]. The generalizability of models is often curtailed by assumptions embedded within the model that may not be relevant to public health program or policy needs [4]. Timeliness is another challenge confronting the adoption of CEA; historically, cost-effectiveness results have been published too late to influence health policy decisions [5].

To use CEA more effectively to inform health policy, we worked with a state safety net breast cancer screening program to conduct a program-specific CEA, based on program data and addressing policy questions posed by program administrators. California's *Cancer Detection Programs: Every Woman Counts* (EWC) was administered through the state Department of Public Health Cancer Detection Section. It is funded jointly by state tobacco tax dollars and federal funds administered through the Centers for Disease Control and Prevention National Breast and Cervical Cancer Early Detection Program. One of the largest of all 68 Centers for Disease Control and Prevention–funded programs, EWC reimburses public and private providers at Medi-Cal rates for screening and diagnostic services for breast and cervical cancers. Medi-Cal is the California version of Medicaid, a joint

* *Address correspondence to*: Joy Melnikow, Center for Healthcare Policy and Research, University of California, Davis, 2103 Stockton Boulevard, Ste 2226, Sacramento, CA 95817.

E-mail: jamelnikow@ucdavis.edu.

1098-3015/$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2013.06.013

state-federal program providing health insurance to very low-income individuals who meet eligibility criteria. California women not eligible for Medi-Cal whose income is less than 200% of the federal poverty threshold who also lack adequate coverage for breast and cervical cancer screening are eligible to enroll in the EWC program.

Our study focused exclusively on the breast cancer screening program, which largely served women aged 40 to 64 years with both screening and diagnostic evaluations. Like many public health programs, the program budget was limited. Program staff estimated that the program served approximately 40% of low-income, uninsured women 40 years and older. Declining tax revenues combined with increased demand for services created intense budgetary pressure on the program. At the same time, digital mammography, not included in the program because of higher cost, was diffusing throughout the state. Program staff were concerned that EWC program clients might have reduced access to screening in some areas because of rapid provider adoption of this newer technology. Digital mammography requires a large initial investment in equipment, but eliminates the need for film storage and enables the digital manipulation of images. It is reimbursed by Medi-Cal at a rate about double that of film mammography. A large US trial evaluating the diagnostic accuracy of digital compared with film mammography found overall similar performance for the two modalities; however, digital mammography performed slightly better in women younger than 50 years [6]. After the project began, Assembly Bill 359 permitted digital mammography providers to bill the EWC program and be reimbursed at the Medi-Cal film mammography rate beginning January 1, 2010. This legislation will expire in 2014, and if it is not renewed, the program will then be required to pay the higher rate for digital mammograms or limit EWC program clients to film mammography only.

The age to begin regular screening mammography and the interval for screening were additional areas of program policy concern, due to limited resources and scientific controversy [7–13]. Randomized trials have demonstrated a relative reduction of about 15% in breast cancer mortality from screening mammography among women aged 40 to 59 years, but women aged 40 to 49 years have a lower absolute risk reduction due to a lower incidence of breast cancer [14]. This age group also has a higher rate of false-positive mammograms [13,14]. Interpretations of the evidence and resulting recommendations for the age to start screening differ across countries and between guidelines [15–20]. Recommended screening intervals are another area in which evidence is uncertain and recommendations differ [21,22].

Our analysis, based on conversations with program personnel, focused on three key policy questions:

1. What would be the projected program costs and outcomes should the EWC program begin reimbursing for digital mammography?
2. What would be the effect on projected program costs and outcomes of starting screening at age 50 years in place of age 40 years?
3. What would be the effects on costs and outcomes of screening every 2 years in place of the current annual screening policy?

Methods

Model Structure

A microsimulation model was developed in TreeAge Pro (TreeAge Software, Williamstown, MA) to estimate population-level effects associated with breast cancer screening and diagnosis for women enrolled in the EWC program, while at the same time accounting for individual variation in age-related mammography diagnostic characteristics and breast cancer risk, as well as allowing tracking of women in the cohort with undiagnosed breast cancer. Analysis of EWC program claims data provided model inputs including client age and race-ethnicity distributions, status-specific transition probabilities between follow-up diagnostic procedures, and costs for screening and diagnosis.

The model structure is illustrated in Figure 1. EWC clients entering the model included women with no cancer and those whose cancer was undiagnosed. Women with abnormal screening test results received follow-up diagnostic testing. Women began treatment when breast cancer was confirmed by either core needle biopsy or open biopsy. New incident cancer cases and those missed by the previous screening or follow-up diagnostic tests presented clinically as interval cancers between screening rounds or were detected at the subsequent screen.

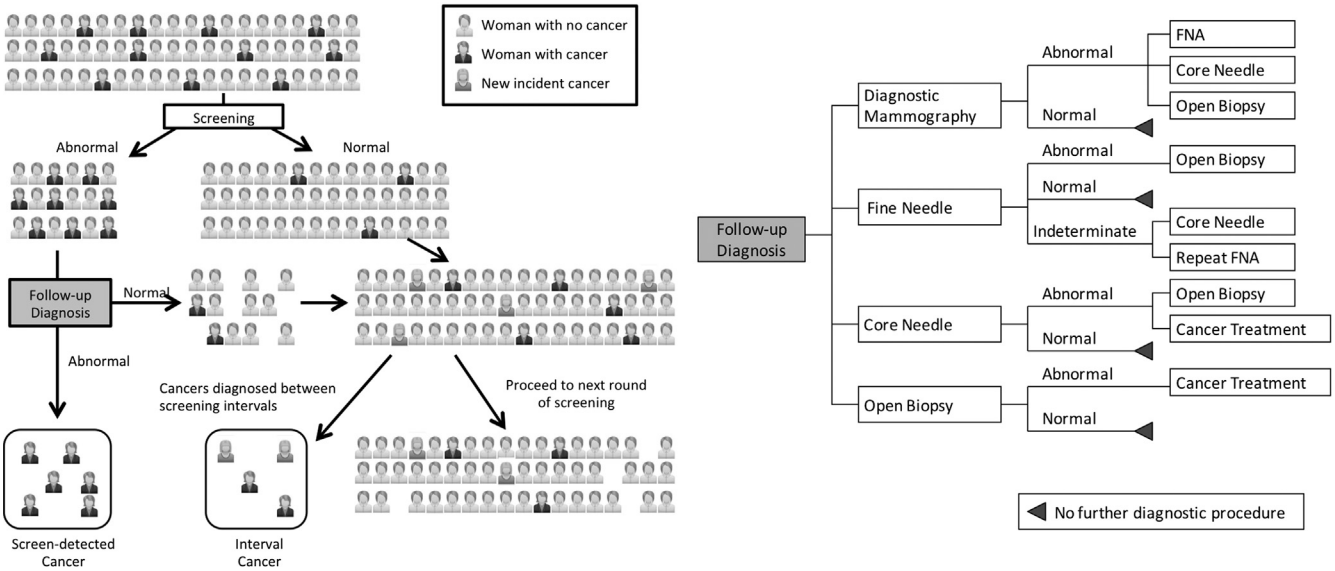

Fig. 1 – Micro-simulation model overview. (Proportions of undiagnosed cancer and incident cancer exaggerated for demonstration.)

Eight screening strategies were evaluated on the basis of policy choices related to three factors: 1) mammography type (film mammography vs. digital), 2) age of screening initiation (40 vs. 50 years), and 3) screening frequency (annual vs. biennial). All strategies were evaluated under the assumption of 1) equal reimbursement for film and digital mammography (currently allowed by legislation) and 2) standard Medi-Cal (higher) reimbursement for digital mammography anticipated for 2014. The reference standard for the model was no screening because women eligible for this safety net program lack insurance coverage or sufficient income to pay for breast cancer screening. The model simulated a 5-year program; outcomes and related costs were analyzed over a 15-year time horizon. We chose the 5-year implementation period for its relevance to public policy planning. The 15-year period for screening outcomes was chosen to better evaluate the long-term effects of the short-term policy decision because effects of mammography on breast cancer mortality were shown after median follow-up of 12 to 16 years in randomized controlled trials [23].

A hypothetical cohort of 100,000 women with an age distribution based on EWC program clients was followed over 15 years in each simulation. The model simulated the history of each cohort member during this period, based on age-specific breast cancer incidence and mortality rates, using age- and strategy-specific input parameters for the sensitivity and specificity of mammography. To address the challenge of a limited program budget, we assumed that the same number of women in the cohort could undergo screening mammography whether the strategy began screening at age 40 years or age 50 years. For strategies beginning at age 50 years, all 50- to 64-year-olds (56% of the cohort) underwent screening during the program period, while the 40- to 49-year-olds had no screening. For strategies beginning screening at age 40 years, 56% of all cohort members underwent screening, while 44% of cohort members did not. An unrestricted version of the model was run for comparison. Age-specific breast cancer incidence was weighted on the basis of race-ethnicity distribution of EWC program clients. Transition probabilities for diagnostic testing to evaluate abnormal screening results were derived from the analysis of EWC program claims data.

To assess first-order uncertainty, 60 simulations were run to calculate means and standard errors of model output values. Eight strategies were run in parallel each time, which meant that same sampled input values were used across strategies to ensure counterfactual comparison. Costs and outcomes were discounted annually at 3%. The incremental cost-effectiveness ratios (ICERs) were calculated by using the "ratio of means" approach [24].

Model Parameters

Model parameters were obtained from analyses of EWC program claims, California Cancer Registry data linked to the EWC program, Surveillance, Epidemiology and End Results data, and the published literature. Model parameters are shown in Table 1.

Parameters derived from EWC Program Claims Data Analysis

We analyzed EWC program claims from 2006 to 2009 linked with California Cancer Registry data to inform model input parameters for age and race-ethnicity distributions of EWC program clients, screening and diagnosis costs, the relative frequency of abnormal results from screening mammography, and transition probabilities between possible options for subsequent diagnostic procedures. A total of 336,115 women aged 40 years and older enrolled in the EWC program in the period 2006 to 2009 underwent screening mammography at least once. The mean age of women screened was 52 years. During this period, the program provided 519,846 screening mammograms, 131,494 diagnostic mammograms, and 15,496 biopsies (1,377 fine needle biopsies, 10,725 core needle biopsies, and 3,394 open biopsies). In the 1-year follow-up period following screening, cancer detection rates were 278 cases/100,000 woman-years in women aged 40 to 64 years and 326 cases/100,000 woman-years in women aged 50 to 64 years.

Other Model Parameters

Other model parameters, including those describing screening and diagnostic test characteristics, are listed in Table 1. Prevalence rates of breast cancer in the hypothetical cohort (defined as the proportion of women with breast cancer present at the initial time point of the policy implementation period) were derived from the linked EWC program claims-California Cancer Registry data, and adjusted for the estimated undetected proportion of breast cancer (based on the age-specific sensitivity of digital or film mammography). Age-specific breast cancer incidence rates and mortality by year since diagnosis were estimated on the basis of Surveillance, Epidemiology, and End Results (SEER 17 Registries database) data [30] adjusted for the race-ethnicity distribution of EWC program clients.

Breast cancers were categorized into three groups depending on cancer detection: screen-detected cancer, interval breast cancer, and cancer detected in the absence of a screening program. Interval breast cancers were defined as histologically proven breast cancers detected in women with a previous negative screening test result, during the interval between screening rounds. Interval cancers have been reported to be more aggressive and to have a worse prognosis compared with the overall behavior of cancers detected in the absence of screening [31–33]. Relative to screen-detected cancer, we assigned 1.39 as the relative mortality risk for interval breast cancer and 1.30 as the relative risk for cancers detected in the absence of a screening program [23]. Longer screening intervals lead to a higher probability for breast cancer to be detected because of presentation with symptoms rather than by mammographic detection at an asymptomatic phase. Biennial screening has a higher interval cancer incidence rate between 13 and 24 months after a previous mammogram than during the first 12 months [32,34]. Proportions of interval cancer cases were adjusted on the basis of the screening interval.

Age group–specific sensitivity and specificity for digital and film mammography were derived from the largest comparative study of digital and film mammography conducted in the United States [6]. The age distribution of that study population differed from the age distribution in the EWC program, and subgroup analysis of the trial suggested that digital mammography performs differently in different age groups [26]. To assess the impact of digital mammography's sensitivity and specificity in age groups conforming to the EWC program, age group–specific estimates of sensitivity and specificity were derived. The sensitivity and specificity of fine needle biopsy and core needle biopsy were based on the medical literature [27,28]; open biopsies were assumed to be the reference standard.

Costs

We included direct costs to the screening program for screening mammography and professional interpretation, follow-up diagnosis costs incurred by abnormal test outcomes, and, for women diagnosed with breast cancer, costs of treatment (surgeries and medical costs in the following years). Treatment costs accrue to a separate breast cancer treatment program, not the EWC program, but treatment access is required for screening to be effective, and the treatment program is also funded by state and federal revenues. Indirect costs were not included. Program costs for film mammography and diagnostic procedures including diagnostic mammography, ultrasound, fine needle aspiration, core needle biopsy, and open breast biopsy were based on average claims payments by the EWC program for these procedures. Payments for associated charges (e.g., core needle biopsy and pathology)

Table 1 – Breast cancer screening program model parameters.

Parameters	Values		Source
Population characteristics of breast cancer			
Age distribution (%)			EWC program claims data
40–44 y	20.7		
45–49 y	22.9		
50–54 y	22.7		
55–59 y	19.4		
60–64 y	14.3		
Breast cancer prevalence rate (%)			EWC program claims data
40–49 y	0.2301		
50–64 y	0.3568		
Breast cancer incidence rate (%)			SEER-AJCC weighted by EWC program race-ethnicity proportions
40–44 y	0.099		
45–49 y	0.152		
50–54 y	0.184		
55–59 y	0.226		
60–64 y	0.264		
	Age group (y)		
Breast cancer mortality rate (%)	**40–49**	**50–64**	SEER-AJCC mortality rates over 10 y weighted by EWC program cancer stage and age distributions
Year 1	1.05	1.26	
Year 2	1.82	2.23	
Year 3	1.52	2.02	
Year 4	1.48	1.76	
Year 5	1.28	1.51	
Year 6	0.92	1.38	
Year 7	0.91	1.14	
Year 8	0.75	1.03	
Year 9	0.38	1.05	
Year 10	0.78	1.01	
Relative risks of breast cancer death			
Interval cancer vs. screen-detected cancer		1.39	[23]
Cancer in the absence of screening vs. screen-detected cancer		1.30	[23,25]
Accuracy of screening and diagnostic procedures			
	Age group (y)		
Screening mammography (%)	**40–49**	**50–64**	[26] weighted average of subgroup estimates
Sensitivity, digital	68.1	52.7	
Sensitivity, film	44.5	49.7	
Specificity, digital	90.2	92.5	
Specificity, film	90.1	92.3	
Diagnostic mammography			[6]*
Ratio of sensitivity relative to screening mammography		1.15	
Ratio of specificity relative to screening mammography		0.98	
FNA result, given having cancer (%)			[27]
Normal		2.6	
Suspicious		17.0	
Abnormal		80.4	
FNA result, given not having cancer (%)			[27]
Normal		77.7	
Suspicious		20.8	
Abnormal		1.5	
Core needle biopsy (%)			[28]
Sensitivity		90.2	
Specificity		1000.0	
Open biopsy (%)			Reference standard
Sensitivity		100.0	
Specificity		100.0	

Table 1 – *continued*

Parameters	Values		Source
Transition probabilities between procedures			
	Age group (y)		
	40–49	50–64	
From abnormal screening mammography to:			EWC program claims data
Open biopsy	0.93	0.70	
Core needle biopsy	2.04	1.74	
Fine needle aspirate	0.49	0.26	
Diagnostic mammography	96.53	97.29	
From abnormal diagnostic mammography to:			
Open biopsy	15.07	11.74	
Core needle biopsy	77.42	82.03	
Fine needle aspirate	7.50	6.24	
From suspicious fine needle aspirate to:			
Open biopsy	86.24	97.83	
Additional fine needle aspirate	13.75	2.17	
From abnormal core needle biopsy to:			
Open biopsy	40.60	26.17	
Costs for screening, diagnosis, and treatment of breast cancer[†]			
Routine screening ($)			
Routine mammogram (digital)		127.2	Medi-Cal
Routine mammogram (film)		66.8	EWC program claims data
Follow-up procedures ($)			
Diagnostic mammogram (digital)		133.0	Medi-Cal
Diagnostic mammogram (film)		99.4	
Open biopsy		444.0	EWC program claims data
Core needle		471.8	
Fine needle aspirate		188.2	
Breast cancer treatment by year from diagnosis[‡]			Medicare Reimbursement [29]
Year 1		19,000.5	
Year 2		1,238.8	
Year 3		983.0	
Years 4–10 cost per year		933.2	

EWC, Every Woman Counts; FNA, fine needle biopsy; SEER-AJCC, Surveillance, Epidemiology and End Results-American Joint Committee on Cancer.
* Sensitivity-specificity based on mammography receiver operator curves (Fig. 1A of Pisano et al. [6]).
† Bundled costs include professional and facility claims.
‡ Bundled cost based on EWC program stage distribution

were bundled to obtain an average payment for all elements in that care episode. Costs of digital and film mammography were based on Medi-Cal reimbursement rates used by the EWC program. Costs for breast cancer treatment by year since diagnosis were based on previously developed clinical pathways using Medicare reimbursement rates [29]. In two separate analytical models, costs for digital mammography screening were set (under current law) as equivalent to the average claim paid for screening film mammography ($67) and as the Medi-Cal reimbursement rate for digital mammography ($127), respectively. All cost units were adjusted to 2007 dollars.

Model Calibration

The model was calibrated by comparing predicted numbers of screening mammograms, procedures, and cancer detection rates for a hypothetical cohort of 100,000 women screened annually for 2 years to actual findings in the claims data for 40- to 64-year-old and 50- to 64-year-old age groups during 2006 to 2008. Projected values corresponded closely to actual values.

Sensitivity Analysis

To analyze the effect of underlying uncertainty of values for key parameters used in the model, we conducted one-way sensitivity analyses by varying a single parameter or bundle of parameters (the cancer-year–specific mortality rates and treatment costs from year 1 to year 10). We considered a range for underlying breast cancer incidence, prevalence, and mortality, prognosis of non–screen detected cancers, mammography test sensitivity and specificity, costs of mammography, and costs of breast cancer treatment. We also varied the discount rate from 1% to 5%. The change in ICERs based on 60 simulation rounds was calculated by using the ratio of means approach [24]. If both mean costs and mean life-year gains were not statistically different (based on two-tailed t test, with $\alpha = 5\%$] from the base-case values, the differences were considered to be due to random variation and the base-case ICERs were reported. A scenario analysis was used to evaluate lack of adherence to mammography screening. Probabilistic sensitivity analysis was not feasible in this microsimulation model because of very high computational intensity.

Model Assumptions

All models are based on underlying assumptions that determine how the model is structured. The EWC program model was based on four key assumptions:

1. In the base-case model, the limited program budget enabled only a fixed number of women to be screened in each year no

matter what age range policy was specified. The same number of women was screened in the 40- to 64-year screening strategy and in the 50- to 64-year screening strategy. While not fixing costs for the program, this assumption addressed the often difficult budgetary realities of public health programs. This assumption was removed in the comparison model.
2. EWC program clients in the hypothetical cohort were adherent to the screening schedule specified in that particular scenario. It is extremely difficult to document the actual screening adherence in this program because many women leave the program when they become eligible for Medi-Cal or gain private insurance; hence, lack of return for a scheduled repeat mammogram cannot be interpreted as lack of adherence. We conducted a sensitivity analysis to evaluate the impact of this assumption.
3. Digital and film mammography were equally accessible to EWC program clients.
4. No changes in outcomes or costs of breast cancer treatment were projected for the time period of the model.

Results

Base-Case Model

During the 15-year cohort follow-up, the simulation model projected between 1000 and 1100 total breast cancers. Projected screen-detected breast cancer rates were higher when screening was limited to the 50- to 64-year-old age group. Digital mammography modestly increased screen-detected cancers than did film mammography, with larger differences when women in the 40- to 49-year age group were screened. The 5-year program costs for screening and diagnosis in the cohort of 100,000 women ranged from $13 million to $21 million under the scenario of equal reimbursement for film and digital mammography, and increased to between $23 million and $37 million for digital mammography reimbursed at the standard Medi-Cal rate. Appendix Table A1 (in Supplemental Materials found at: http://dx.doi.org/10.1016/j.jval.2013.06.013) shows the projected procedures, cancers, and total costs for a 5-year program period. Table 2 shows the per-person total costs (including screening, diagnosis, and treatment), life expectancy, incremental costs, incremental life expectancy, and incremental cost-effectiveness ratios of alternative screening strategies for film and digital mammography compared with no screening. These outcomes were projected over a 15-year period to capture the effects of screening on breast cancer mortality. We chose no screening as a comparison because if no safety net program were available, this population would have little or no access to screening. In the model restricted to a fixed number of clients, all strategies initiating screening at age 40 years were dominated (more costly and less effective, or more costly for the same effectiveness). In the unrestricted model, which assumed that program funds were available to screen all eligible clients in the cohort, under standard differential reimbursement for digital and film mammography, biennial film mammography beginning at age 50 years was the least expensive cost-effective option, at $18,999 per additional life-year. Screening strategies beginning at age 40 years also had ICERs that could be considered cost-effective, at $84,607 per additional life-year for biennial digital mammography and $95,068 per additional life-year for annual digital mammography (see Appendix Table A2 in Supplemental Materials found at: http://dx.doi.org/10.1016/j.jval.2013.06.013).

When digital and film mammography were reimbursed at the same rate, film mammography strategies were dominated. Biennial digital mammography screening for women in the age 50 to 64 years cohort was projected to reduce cancer mortality by 8.6% and had an incremental cost per additional life-year of $17,050. Annual screening added to mean life expectancy (0.0069 life-years) at higher costs, with an incremental cost per additional life-year of $81,666. Under the assumption of standard Medi-Cal (higher) reimbursement for digital mammography, biennial film mammography for women aged 50 to 64 years was projected to reduce breast cancer mortality by nearly 7.8%, at $18,999 per additional life-year. Annual film mammography added to mean life expectancy at $106,428 incremental cost per additional life-year, and annual digital mammography incremental cost per additional life-year was $180,333. The corresponding cost-effectiveness scatter plots for all strategies under equal reimbursement and standard reimbursement rate for digital mammography are shown in Figure 2.

Sensitivity Analyses

In one-way sensitivity analyses, compared with starting screening at age 40 years, initiating screening for women at age 50 years was always a dominant strategy (less costly and more effective, or less costly for the same effectiveness) in the restricted model. Hence, the finding of greater cost-effectiveness if the EWC program limited screening to this age group was highly robust. We did encounter variability in whether digital or film mammography was an optimal strategy. Assuming equal mammography costs to the program, decreasing specificity of digital mammography by 5%, or increasing specificity of film mammography by 5% reversed the advantage of digital mammography over film. Considering the intrinsic uncertainty of the differences in specificity between film and digital mammography, results regarding the optimal mammography modality should be interpreted with caution.

We examined the effect of lack of adherence to screening mammography by modeling an annual dropout rate of 10%, 30%, and 50%, assuming no further mammography screening in the program period. As the dropout rate increased, the ICER for biennial screening using digital mammography from age 50 years (as compared with no screening) decreased (from $17,050 to $9,788 per additional life-year), suggesting higher cost-effectiveness of any screening compared with no screening at lower adherence rates. In contrast, the ICER for annual screening with digital mammography from age 50 years (as compared with biennial screening using digital mammography from age 50 years) increased (from $81,666 to $121,465 per additional life-year), suggesting that annual screening became less cost-effective as compared with biennial screening when the adherence rate dropped. Results of sensitivity analyses are shown in Table 3.

Discussion

This program-based cost-effectiveness model illustrated the potential consequences of policy choices for the EWC program. Unless funding is available to screen the full population of eligible women beginning at age 40 years, starting routine screening at age 50 years is strongly supported by the model results. This policy maximized the cost-effectiveness of mammography screening for this budget-constrained program. This finding is not surprising, given that women aged 50 years and older have a higher incidence and prevalence of breast cancer; hence, screening in this group will yield more early stage cancers and fewer false-positive results. Because of limited program resources, full coverage of eligible women has not been achieved for any age group. Using available resources to maximize access for women aged 50 to 64 years would have the greatest impact on breast cancer early detection and breast cancer mortality. Screening every 2 years captures most of the benefit of annual screening and could allow more eligible women to be served. This finding is consistent with that of other models of breast cancer screening using different approaches and assumptions [35,36].

The impact of digital mammography on life expectancy is small and cannot be precisely estimated, but there is likely

Table 2 – Costs, life expectancy, incremental costs, incremental life expectancy, incremental cost-effectiveness ratios, and cancer mortality reduction for alternative screening strategies, compared with no screening (reference strategy).

	15-y cost* per person (2007 $)	15-y life expectancy (y)	Incremental costs (2007 $)	Incremental life- years gained (y)	Incremental CE ratio ($ per additional life-year)	Projected reduction in breast cancer mortality† (%)
Equal reimbursement for digital and film mammography						
No screening	283.9 (±16.1)	11.6783 (±0.0010)				
Biennial, 40–64, film	383.7 (±20.6)	11.6813 (±0.0012)	99.8 (±8.6)	0.0030 (±0.0005)	–	6.2 (±1.3)
Biennial, 50–64, film	384.6 (±22.2)	11.6836 (±0.0011)	100.7 (±7.7)	0.0053 (±0.0004)	–	7.8 (±1.3)
Biennial, 50–64, digital	386.2 (±22.8)	11.6843 (±0.0010)	102.3 (±8.5)	0.0060 (±0.0005)	$17,050	8.6 (±1.4)
Biennial, 40–64, digital	391.4 (±23.3)	11.6828 (±0.0009)	107.5 (±7.8)	0.0045 (±0.0006)	–	7.8 (±1.5)
Annual, 40–64, film	458.7 (±21.7)	11.6819 (±0.0010)	174.8 (±8.2)	0.0036 (±0.0004)	–	6.5 (±1.0)
Annual, 50–64, film	459.1 (±22.3)	11.6843 (±0.0011)	175.2 (±8.0)	0.0060 (±0.0006)	–	9.0 (±1.1)
Annual, 50–64, digital	459.7 (±22.5)	11.6852 (±0.0009)	175.8 (±7.4)	0.0069 (±0.0005)	$81,666	10.5 (±1.2)
Annual, 40–64, digital	470.2 (±23.0)	11.6847 (±0.0011)	186.3 (±8.6)	0.0064 (±0.0006)	–	10.3 (±1.3)
Standard reimbursement for digital and film mammography						
No screening, 40–64	283.9 (±16.1)	11.6783 (±0.0010)				
Biennial, 40–64, film	383.7 (±20.6)	11.6813 (±0.0012)	99.8 (±8.6)	0.0030 (±0.0005)	–	6.2 (±1.3)
Biennial, 50–64, film	384.6 (±22.2)	11.6836 (±0.0011)	100.7 (±7.7)	0.0053 (±0.0004)	$18,999	7.8 (±1.3)
Annual, 40–64, film	458.7 (±21.7)	11.6819 (±0.0010)	174.8 (±8.2)	0.0036 (±0.0004)	–	6.5 (±1.0)
Annual, 50–64, film	459.1 (±22.3)	11.6843 (±0.0011)	175.2 (±8.0)	0.0060 (±0.0006)	$106,428	9.0 (±1.1)
Biennial, 40–64, digital	474.4 (±21.9)	11.6828 (±0.0009)	190.5 (±8.6)	0.0045 (±0.0006)	–	8.6 (±1.4)
Biennial, 50–64, digital	476.0 (±23.6)	11.6843 (±0.0010)	192.1 (±8.7)	0.0060 (±0.0005)	–	7.8 (±1.5)
Annual, 50–64, digital	621.4 (±21.7)	11.6852 (±0.0009)	337.5 (±8.6)	0.0069 (±0.0005)	$180,333	10.5 (±1.2)
Annual, 40–64, digital	629.9 (±20.9)	11.6847 (±0.0011)	346.0 (±8.8)	0.0064 (±0.0006)	–	10.3 (±1.3)

Notes. All screening strategies are compared on the basis that an equal number of women (56%‡ of the cohort) receive screening in every strategy. Results shown for equal and standard Medi-Cal reimbursement rates for digital and film mammography (±standard error of 60 simulation rounds).

CE, cost-effectiveness.

* Fifteen-year costs include screening, diagnosis, and treatment costs for the initial 5 y, and additional treatment costs extending beyond 5 y for cancers diagnosed during the 5-y program.

† Mortality reduction over 15 y for the breast cancers diagnosed during the 5-y program.

‡ Fifty-six percent is the proportion of women aged 50 to 64 y derived from the program claims data. In strategies starting screening from age 50 y, all women aged 50 to 64 y are assumed to receive screening service, and women aged 40 to 49 y receive none; in strategies starting screening from age 40 y, 56% of the women aged 40 to 64 y receive screening and the remaining 44% receive none.

some benefit to EWC program clients because it seems to perform slightly better in younger women [6]. Digital mammography adds less than a million dollars to 5-year program costs when reimbursed at the Medi-Cal film mammography rate, because of additional diagnostic testing resulting from its higher sensitivity. In 2014, after AB 359 expires, coverage of digital mammography at the standard Medi-Cal reimbursement rate would require a substantial budget increase or a reduction in the number of women screened. The cost per additional life-year gained for digital mammography under standard reimbursement is well above the range generally considered cost-effective, and our findings are consistent with those of a US population-based microsimulation model [37].

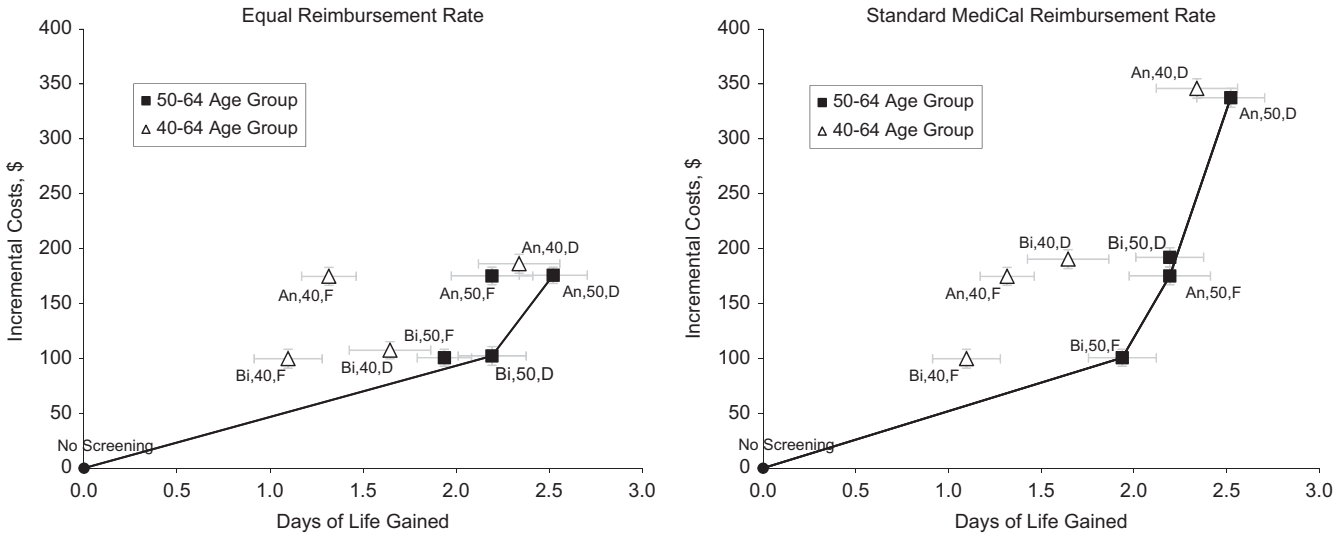

Fig. 2 – Incremental days of life gained and incremental costs for all evaluated screening strategies in the base-case analysis under equal and standard Medi-Cal reimbursement for digital mammography. An, annual; Bi, biennial; D, digital; F, film.

Our analysis was limited by simplifying assumptions and the nature of the data used to inform the model. We assumed that women in the cohort were beginning screening mammography and continued in the program throughout the 5-year period that the policy was modeled. In reality, women are constantly gaining and losing eligibility for the program and may not follow screening recommendations. However, sensitivity analyses supported the relative cost-effectiveness of providing biennial screening even in situations of poor adherence. The average screening interval for women in the EWC program was 17 months, falling between the intervals in the model. Similarly, the comparison of adopting either purely digital mammography or purely film mammography does not reflect reality because the accessibility of mammography technology varies geographically. Nevertheless, comparing two pure strategies is useful in distinguishing their potential overall costs and effects on breast cancer outcomes. Modeling these variables to more closely match the real world would have required a much more complex model and a longer time frame, reducing the policy relevance of the findings. Because of a lack of utility data specific to the program clients or to the multiple health states in the model, we opted to report unadjusted life-years as the main outcome. This meant that the impact of false-positive results (more common in women aged 40-49 years) on quality of life in terms of both physical harms of testing and psychological harms of false positives was not considered. Life-years are also a relatively straightforward metric for policymakers. Analysis of the EWC program claims data added greatly to the specificity of our model but was also limited by the lack of data on diagnostic test outcomes. Despite these limitations, the model calibrated remarkably well to program breast cancer outcomes.

How did our findings inform EWC program policy? The time elapsed from the inception of project funding to project completion was 18 months. Although this seemed a short time in the academic environment, events overtook our work and required changes to the model. Some program policy decisions were made before the final results of the model were available. At the project's inception in 2009, women 40 years and older who met the EWC program criteria were eligible to enroll. Major cuts in the program were made at the end of 2009 because of increased demand for services and declining state revenues. Legislation proposed to restore program funding was vetoed by Governor Schwarzenegger. The California Department of Public Health suspended "all new enrollments for breast cancer screening services … and change[d] the eligibility age for breast cancer screening services to 50 years of age or older" [38]. This change in eligibility age was confirmed by our analysis as a cost-effective strategy. Because of concerns by state legislators about the program policy changes, funding was subsequently increased and after some restructuring, the program reopened to new clients and restored eligibility at age 40 years for mammography screening. Because of budget limitations, the program has continued to reach only a portion of the eligible population.

The contrasting findings of our model with restrictions on the number of eligible women screened by the program with those of the conventional model in which no limits were imposed illustrate the challenge for public health programs in applying the results of conventional CEA to policy. The objective of conventional CEA to maximize the health benefit obtained based on the cost per individual does not account for the limited budgets of public programs and the need to consider the opportunity cost of each policy decision [39,40].

Timeliness is an important issue limiting the application of CEA. Historically, cost-effectiveness models have been published too late to influence health policy decisions [5]. Policy options that were feasible and sensible when an analysis was designed may become unworkable under shifting political or budgetary contexts. Furthermore, models constructed for one policy context or health care system may not be applicable to another. Program cost-effectiveness is only one consideration of many in the policy arena. Despite the barriers to implementing CEA, researchers and policy analysts continue to advocate for its integration into health care policy formulation [41]. These challenges underscore the importance of flexibility, speed, and dissemination to increase the relevance and usefulness of CEA models to inform health policy.

The ongoing state budget shortfall in California continues to challenge public health safety net programs. Simultaneously, the number of women eligible for the EWC program has increased over time consequent to increased unemployment and loss of insurance coverage [42]. Implementation of mandatory coverage for preventive services under the Affordable Care Act may reduce the demand for EWC program services among underinsured

Table 3 – One-way sensitivity analysis of base-case model, with assumption of equal reimbursement for film and digital mammography.

Variables	Base-case values	Range	ICER* ($ per life-year gain)	
			Biennial, 50–64, digital	Annual, 50–64, digital
Base case			17,050	81,666
Cost of screening mammography ($)	66.8	53.4	12,596	59,423
		80.2	32,611	122,950
Costs of breast cancer years 1–10	Year-specific	0.8 × baseline	16,412	75,958
		1.2 × baseline	22,314	103,879
Prevalence of breast cancer, 40–49 y (%)	0.302	0.242	17,050	81,666
		0.362	17,050	81,666
Prevalence of breast cancer, 50–64 y (%)	0.357	0.286	37,143	145,433
		0.428	10,913	65,333
Breast cancer incidence rate	Age-specific	0.8 × baseline	23,122	133,734
		1.2 ×baseline	13,295	68,333
Sensitivity of digital mammography, 50–64 y (%)	52.70	47.43	Dominated by "Bi, 50, F"†	Dominated by "An, 50, F"†
		57.97	12,212	62.734
Specificity of digital mammography, 50–64 y (%)	92.50	87.88	Dominated by "Bi, 50, F"†	118,800
		97.13	8,714	46,634
Sensitivity of film mammography, 50–64 y (%)	49.70	44.73	17,050	81,666
		55.67	Dominated by "Bi, 50, F"†	Dominated by "An, 50, F"†
Specificity of film mammography, 50–64 y (%)	92.30	87.69	17,050	81,666
		96.92	Dominated by "Bi, 50, F"†	Dominated by "An, 50, F"†
Annual discount rate (%)	3.0	1.0	13,232	75,484
		5.0	25,687	102,302
Mortality rate of breast cancer	Year-specific	0.8 × baseline	27,483	106,900
		1.2 ×baseline	11,233	59,544
Adherence rate of screened subjects	Perfectly adherent			
	10% annual dropout		15,188	92,183
	30% annual dropout		11,577	108,976
	50% annual dropout		9,788	121,465

Note. Parameters are varied ±20%, except for sensitivities (±10%), specificities (±5%), and discount rate (1%–5%).
An, annual; Bi, biennial; D, digital; F, film; ICER, incremental cost-effectiveness ratio.
* In case both mean cost and mean life year gains were not statistically different (α=5%) with the base-case values, the basecase ICERs were reported
† Dominance under certain scenarios indicates its moving away from the efficiency frontier. Strategy "An, 50, D" was compared with the adjacent cost-effective but less-costly strategy on the efficiency frontier, which is "Bi, 50, D" or the strategy replacing "Bi, 50, D" if "Dominated by" was stated.

women and shift their costs of breast cancer screening to private and public insurance programs; however, some women in California will not be affected by the Affordable Care Act and will continue to require safety net assistance for access to breast cancer screening. The challenges of allocating limited resources to health care programs are widespread, and modeling the potential outcomes and costs of alternative policy choices provides important information to inform decision making. Engaging policymakers in structuring models, selecting inputs, defining relevant model outcomes, and viewing results will make CEA more relevant to health care policy decision making, and may ultimately result in more effective utilization of safety net and other health care resources. Source of financial support: Funding was provided by the California Program on Access to Care (CPAC), School of Public Health, UC Berkeley, in cooperation with the University of California, Office of the President. CPAC had no influence on the design and conduct of the study or the content of the manuscript. The authors' views and recommendations do not necessarily represent those of the CPAC, the School of Public Health, UC Berkeley, the Regents of the University of California, or the California Department of Public Health.

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.

jval.2013.06.013 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

REFERENCES

[1] Weinstein MC, Stason WB. Foundations of cost-effectiveness analysis for health and Medi-Cal practices. N Engl J Med 1977;296:716–21.
[2] Neumann PJ. Why don't Americans use cost-effectiveness analysis? Am J Manag Care 2004;10:308–12.
[3] Russell LB, Fryback DG, Sonnenberg FA. Is the societal perspective in cost-effectiveness analysis useful for decision makers? Jt Comm J Qual Improv 1999;25:447–54.
[4] Detsky AS, Laupacis A. Relevance of cost-effectiveness analysis to clinicians and policy makers. JAMA 2007;298:221–4.
[5] Prosser LA, Koplan JP, Neumann PJ, et al. Barriers to using cost-effectiveness analysis in managed care decision making. Am J Manag Care 2000;6:173–9.
[6] Pisano ED, Gatsonis C, Hendrick E, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. N Engl J Med 2005;353:1773–83.
[7] Armstrong K, Moye E, Williams S, et al. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. Ann Intern Med 2007;146:516–26.
[8] Brewer NT, Salz T, Lillie SE. Systematic review: the long-term effects of false-positive mammograms. Ann Intern Med 2007;146:502–10.
[9] Elmore JG, Choe JH. Breast cancer screening for women in their 40s: moving from controversy about data to helping individual women. Ann Intern Med 2007;146:529–31.
[10] Gregory KD, Sawaya GF. Updated recommendations for breast cancer screening. Curr Opin Obstet Gyn 2010;22:498–505.
[11] Health Quality Ontario. Screening mammography for women aged 40 to 49 years at average risk for breast cancer: an evidence-based analysis. Ont Health Technol Assess Ser 2007;7:1–32.
[12] Moss S. Should women under 50 be screened for breast cancer? Br J Cancer 2004;91:413–7.
[13] Salas D, Ibanez J, Roman R, et al. Effect of start age of breast cancer screening mammography on the risk of false-positive results. Prev Med 2011;53:76–81.
[14] Nelson HD, Tyne K, Naik A, et al. Screening for Breast Cancer: Systematic Evidence Review Update for the US Preventive Services Task Force. Rockville, MD, 2009.
[15] Albert US, Schulz KD. German Association of the Scientific Medi-Cal Societies GAfQiM. Short version of the Guideline: Early Detection of Breast Cancer in Germany. An evidence-, consensus-, and outcome-based guideline according to the German Association of the Scientific Medi-Cal Societies (AWMF) and the German Agency for Quality in Medicine (AeZQ). J Cancer Res Clin Oncol 2004;130:527–36.
[16] American College of Obstetrics and Gynecology. Practice bulletin no. 122: breast cancer screening. Obstet Gynecol 2011;118:372–82.
[17] Bevers TB, Anderson BO, Bonaccio E, et al. Breast cancer screening and diagnosis. J Natl Compr Canc Ne 2009;7:1060–96.
[18] Dickinson J, Singh H, Birtwhistle R, et al. Recommendations on screening for breast cancer in average-risk women aged 40-74 years. Can Med Assoc J 2011;183:1991–2001.
[19] Qaseem A, Snow V, Sherif K, et al. Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2007;146:511–5.
[20] Smith RA, Saslow D, Sawyer KA, et al. American Cancer Society guidelines for breast cancer screening: update 2003. Ca-Cancer J Clin 2003;53:141–69.
[21] White E, Miglioretti DL, Yankaskas BC, et al. Biennial versus annual mammography and the risk of late-stage breast cancer. J Natl Cancer Inst 2004;96:1832–9.
[22] Braithwaite D, Zhu W, Hubbard RA, et al. Screening outcomes in older US women undergoing multiple mammograms in community practice: does interval, age or comorbidity score affect tumor characteristics or false positive rates? J Natl Cancer Inst 2013;105:334–41.
[23] Shen Y, Yang Y, Inoue LYT, et al. Role of detection method in predicting breast cancer survival: analysis of randomized screening trials. J Natl Cancer Inst 2005;97:1195–203.
[24] Stinnett AA, Paltiel AD. Estimating CE ratios under second-order uncertainty: the mean ratio versus the ratio of means. Medi-Cal Decision Making 1997;17:483–9.
[25] Fryback DG, Stout NK, Rosenberg MA, et al. The Wisconsin Breast Cancer Epidemiology Simulation Model. J Natl Cancer Inst Monogr 2006;36:37–47.
[26] Pisano ED, Hendrick RE, Yaffe MJ, et al. Diagnostic accuracy of digital versus film mammography: exploratory analysis of selected population subgroups in DMIST. Radiology 2008;246:376–83.
[27] O'Neil S, Castelli M, Gattuso P, et al. Fine-needle aspiration of 697 palpable breast lesions with histopathologic correlation. Surgery 1997;122:824–8.
[28] Bukhari MH, Akhtar ZM. Comparison of accuracy of diagnostic modalities for evaluation of breast cancer with review of literature. Diagn Cytopathol 2009;37:416–24.
[29] Melnikow J, Kuenneth C, Helms LJ, et al. Chemoprevention: drug pricing and mortality: the case of tamoxifen. Cancer 2006;107:950–8.
[30] SEER 17 registries database. Available from: http://seer.cancer.gov/data/index.html. [Accessed December 10, 2010].
[31] Tornberg S, Kemetli L, Ascunce N, et al. A pooled analysis of interval cancer rates in six European countries. Eur J Cancer Prev 19:87–93.
[32] Fracheboud J, de Koning HJ, Beemsterboer PM, et al. Interval cancers in the Dutch breast cancer screening programme. Br J Cancer 1999;81:912–7.
[33] Shapiro S, Strax P, Venet L. Evaluation of periodic breast cancer screening with mammography: methodology and early observations. JAMA 1966;195:731–8.
[34] Hofvind S, Vacek PM, Skelly J, et al. Comparing screening mammography for early breast cancer detection in Vermont and Norway. J Natl Cancer Inst 2008;100:1082–91.
[35] Ahern CH, Shen Y. Cost-effectiveness analysis of mammography and clinical breast examination strategies: a comparison with current guidelines. Cancer Epidemiol Biomarkers Prev 2009;18:718–25.
[36] Stout NK, Rosenberg MA, Trentham-Dietz A, et al. Retrospective cost-effectiveness analysis of screening mammography. J Natl Cancer Inst 2006;98:774–82.
[37] Tosteson AN, Stout NK, Fryback DG, et al. Cost-effectiveness of digital mammography breast cancer screening. Ann Intern Med 2008;148:1–10.
[38] Horton M, Director of California Department of Public Health. Statement in 2009. Available from: http://www.cdph.ca.gov/Pages/NR09-115.aspx. [Accessed June 17, 2013].
[39] Birch S, Gafni A. The biggest bang for the buck or bigger bucks for the bang: the fallacy of the cost-effectiveness threshold. J Health Serv Res Policy 2006;11:46–51.
[40] Birch S, Gafni A. Information created to evade reality (ICER): things we should not look to for answers. Pharmacoeconomics 2006;24:1121–31.
[41] Jacobson PD, Kanna ML. Cost-effectiveness analysis in the courts: recent trends and future prospects. J Health Polit Policy Law 2001;26:291–326.
[42] Shana L, Chia Y, Cabezas L, et al. California's uninsured by county: nearly one-third of residents in Los Angeles County, the San Joaquin Valley, and the Northern/Sierra Counties lacked health insurance in 2009. 2010. Available from: http://www.healthpolicy.ucla.edu/pubs/files/County_Uninsured_FS_CORRECTION.pdf.