Computer modelling of the Swedish two county trial of mammographic screening and trade offs between participation and screening interval

M J Fett

Abstract

***Objectives*—A computerised model of the Swedish two county trial of mammographic screening was built to explore the applicability of deterministic group modelling for health policy analysis and to examine trade offs between screening interval and population coverage on breast cancer mortality.**

***Methods*—Powersim system dynamics modelling software running on a PC was used. Model inputs were published data on the populations and screening regimens used in the trial, a Swedish female population life table, incidence of breast cancer in Sweden, 95% confidence intervals (95% CIs) for mean sojourn time and screening sensitivity, and survival after diagnosis.**

***Results*—The model's output—cumulative mortality from breast cancer—agreed closely with trial results. This was robust to uncertainties in key input variables. Furthermore, with hypothetical screening regimes that had a fixed total number of mammograms over a fixed period a positive association was found between more even distribution of mammograms among a population and reduction in breast cancer mortality. For example, screening 50% of a hypothetical population annually produced a 33% reduction in breast cancer mortality, whereas screening 100% of the population every 2 years produced a 48% reduction.**

***Conclusions*—Deterministic group simulation modelling can be used to build reliable, evidence based quantitative models for policy analysis. This opens health policy simulation modelling to epidemiological researchers and will assist them in identifying important information needs—such as breast cancer survival according to sojourn time (the time between cancer being detectable by screening and becoming symptomatic). Scenarios examining reductions in mortality for a given number of mammograms showed that the more equitable the distribution of screening mammograms, the greater the reduction in deaths from breast cancer.**

(*J Med Screen* 2001;**8**:39–45)

Keywords: breast cancer screening; mammography; computer modelling

Division of Mathematical and Information Sciences, Commonwealth Scientific and Industrial Research Organisation, PO Box 664, Canberra, ACT 2601, Australia

Correspondence to:
Dr M J Fett
michael.fett@cmis.csiro.au

Accepted for publication
14 December 2000

Computer simulation modelling has long been recognised as a potentially important tool for analysing policy options in health services. An important issue in evaluating the usefulness of simulation models in health policy is their validity. To explore validity in health policy models, models of breast cancer screening with mammography were built with the system dynamics modelling package Powersim.

The ultimate goal was to build a model of the Australian breast cancer screening program known as BreastScreen[1] that could be used for policy analysis. As a first stage, a model was built with the intention of replicating the results of one of the major controlled trials of mammography, the Swedish two county trial.[2 3] This approach was undertaken on the grounds that it would be worthwhile proceeding to build a model of an ongoing screening programme only if it were possible to build a model that accurately replicated a major controlled trial which formed a key part of the evidence that was a basis for mammographic screening. If the results of a controlled trial could not be replicated, then the capacity of this modelling paradigm to simulate an ongoing mammographic screening programme would be called into question. Also, lessons from developing the model of the controlled trial would provide important input into modelling the screening programme. A similar approach has been used by several groups who used microsimulation models[4–6] or Markov models.[7] The modelling approach used here—deterministic group simulation—used simultaneous simulation of population groups rather than sequential simulation of individual life histories, and no stochastic phenomena were modelled.

This paper describes a computer model of the two county trial for those subjects aged 50–64 at entry to the trial. It also examines the mortality benefits of adjusting the balance between population coverage of screening and screening interval, as a means of examining the population health implications of uneven distributions of screening mammograms in eligible age groups. The paper concludes with a discussion of the implications of these findings for constructing a model of an ongoing screening programme specifically and for simulation modelling of health policy generally.

Methods

The model was built in Powersim Constructor version 2.51 (4009) (Powersim AS, Isdalsto,1998). Figure 1 shows the stocks and

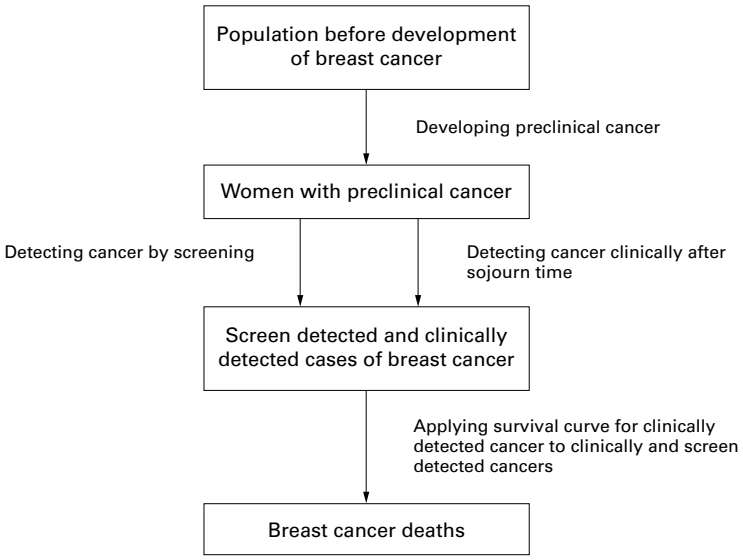

Figure 1 Breast cancer screening model stocks and flows.

flows in the model. Table 1 shows the sources or methods of calculation of these stocks and flows, from the initial population to death from breast cancer, and the calculation of cumulative breast cancer mortalities for the study and control groups. Disease stage has not been modelled because it is not required to simulate the mortality benefits of screening.

Estimates of tumour sojourn time (the duration of the time between cancer being detectable by screening and becoming symptomatic) in the preclinical but screen detectable phase and screening sensitivity (table 2) were obtained from a recent analysis of data from the Swedish two county trial.[10] The model used age specific sojourn time expressed as an integer number of years. The estimates of sojourn time in table 2 were converted into age specific integer values by assuming that the sojourn time for each 10 year age group applied to the midpoint of that group, applying linear interpolation and extrapolation to other ages and then rounding the value of the sojourn time for each age to the nearest integer (whole number of years). The estimates of sensitivity in table 2 were converted into age specific values by assuming that the sensitivity for each 10 year age group applied to the midpoint of that group and applying linear interpolation and extrapolation to other ages.

Table 2 Estimated mean sojourn time and sensitivity by age (95% CIs) from the two county trial

	Mean sojourn time (y)			*Sensitivity*		
Age (y)	*Point estimate*	*95% CI*		*Point estimate*	*95% CI*	
40–49	2.46	2.12	2.85	0.83	0.76	0.91
50–59	3.75	3.44	4.08	1	1	1
60–69	4.23	4.00	4.48	1	1	1

It was not possible to identify survival curves for breast cancer by mode of detection (screen or clinical). Instead, an estimated survival curve of clinically detected tumours was obtained from an analysis of the survival of women with breast cancer in South Australia.[12] This survival curve was derived from information on characteristics of breast cancer tumours of women with cancers that were diagnosed outside the South Australian breast radiography service. The data on tumour characteristics were combined with published information on survival by tumour characteristics from the Swedish two county trial[13 14] to

Table 1 Data stocks, data flows, and calculations to model transition from incidence of preclinical breast cancer to death from breast cancer and calculation of performance indicators

Stock or flow	*Sources of data and methods of calculation*
Stock: population before development of breast cancer	Study and control populations aged 50–64 y at randomisation,[8] by age. Women entered the study at ages 40–74 y. The model is restricted to those aged 50–64 y at entry because of the availability of a plot of the cumulative mortality for these women.[3] Women are divided into two groups (screened and not screened) within the study and control groups according to published participation rates in the study and control groups. Women in the screened and unscreened groups flow through the same processes within the model, except that unscreened women cannot have their cancers detected by screening. Estimated number of deaths each year due to non-breast cancer causes are removed from this and all subsequent stocks. The risk of non-breast cancer death by age is estimated from the 1985–9 Swedish all causes female life table (by age) and 1985 data on proportion of female deaths in Sweden due to breast cancer (by 10 y age group).
Flow: developing preclinical cancer	The incidence of preclinical cancer is assumed to be equal to the incidence of breast cancer before the introduction of mammography. Swedish breast cancer incidence in 1971–5[9] has been used. These years were chosen because data for the next periods (1978–82) and (1983–7) show progressively higher incidence, with the age standardised rates being 55.2, 60.7, and 62.5 respectively. This suggests that data for 1971–5 more closely represent the true underlying breast cancer incidence rate, with mammography increasing the observed breast cancer incidence from the mid-1970s, when the technology was being introduced.
Stock: women with preclinical cancer	The ages of the population of preclinical cases each year and the tumour's "age" each year (that is, the number of years since each preclinical cancer developed is recorded and advances each year for each cancer). Deaths each year due to non-breast cancer causes are removed.
Flow: detecting cancer by screening	Number of preclinical cases multiplied by screening rates after the start of screening[3] and screening sensitivity,[10] divided by screening interval.[11]
Flow: detecting cancer clinically after sojourn time	Preclinical cancers that reach the end of their age specific sojourn time and have not been screen detected, are detected clinically.
Stock: cases of screen detected and clinically detected breast cancer	Populations of screen and clinically detected cases age each year. Records number of years since each cancer was detected. Deaths each year due to non-breast cancer causes are removed.
Flow: applying survival curve for clinically detected cancer to clinically and screen detected cancers	Numbers of screen and clinically detected cancers diagnosed each year are multiplied by the proportions dying each year from breast cancer after time of diagnosis (from survival curve for clinically detected cancer[12]) to calculate number of breast cancer deaths each year. A linear interpolation of the clinically detected survival curve is used to reduce the death rate for screen detected cancers according to the point in the sojourn period at which they are detected. That is, the earlier in the sojourn period a cancer is detected by screening, the lower the death rate. Within each calendar year, numbers of breast cancer deaths are summed across all years of diagnosis.
Stock: Breast cancer deaths	Breast cancer deaths occurring each year are summed cumulatively over time and divided by initial study and control populations to calculate cumulative breast cancer death rates for the study and control groups.

Table 3 Relative risk of breast cancer mortality for screen detected cancers as a function of year of detection within the sojourn period compared with clinically detected cancers, for the point estimate of the mean sojourn time

Sojourn time (y)	Age (y)	Relative mortality according to year of detection				
		1	*2*	*3*	*4*	*5*
3	46–53	1/4	2/4	3/4	—	—
4	54–70	1/5	2/5	3/5	4/5	—
5	⩾71	1/6	2/6	3/6	4/6	5/6

construct the survival curve incorporated into the model.

This survival curve for clinically detected tumours was used to calculate breast cancer deaths in both the clinically detected and screen detected cancers. The curve was applied directly to clinically detected cancers. For screen detected cancers, a linear interpolation of the clinically detected survival curve was used to reduce the risk of death for screen detected cancers according to the point in the sojourn period at which they are detected. That is, the earlier in the sojourn period a cancer is detected by screening, the flatter the survival curve when compared with not being screen detected (table 3).

To model deaths from causes other than breast cancer, the 1985–9 Swedish female life table adjusted to exclude deaths from breast cancer was incorporated into the model to account for death from other causes. All subjects reaching the age of 90 were then lost to follow up. (The maximum age in this model is 80.)

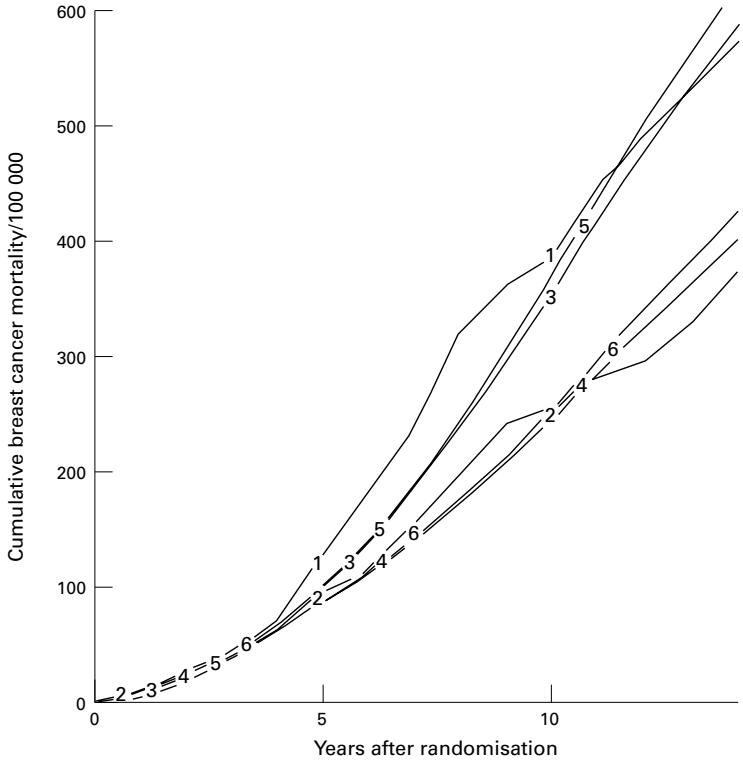

Figure 2 Observed and modelled cumulative breast cancer mortality for women aged 50–64 at randomisation with and without other causes of death. Lines 1 and 2 are observed control and study cumulative breast cancer mortality. Lines 3–6 are modelled control and study cumulative breast cancer mortality: lines 3 and 4 are with other causes of death; and lines 5 and 6 are without other causes of death.

The effects of moving from the upper to lower bounds of the 95% confidence intervals (95% CIs) of mean sojourn time and sensitivity on the cumulative mortality curves were examined. Long sojourn time and high sensitivity were examined simultaneously, as were short sojourn time and low sensitivity. These combinations were used because higher sensitivity of a screening test leads to earlier detection of the disease, thereby increasing the sojourn time.

To examine the impact of lack of published information on screening rates in the two county trial after 8 years of follow up, the effects on modelled mortality of large changes in screening rates after 8 years of follow up in both the study and control groups were examined. These changes had very little effect on the modelled mortality curves, suggesting that the lack of screening information after 8 years has had little impact on the modelled results.

An important but unexplored issue relative to breast cancer screening is the potential trade off between screening interval for individual women and the proportion of women in the target age range who are screened. This was examined with the current model in women aged 50–64 at the start of screening by comparing cumulative breast cancer mortality at 14 years after the start of screening in women offered screening with a group of unscreened women. In the group offered screening, women either participated in screening at the designated interval or were not screened at all. This allowed examination of the effect on reduction of breast cancer mortality of screens being confined to only a proportion of women offered screening, and the effect of different screening intervals among these women.

Results

The modelled cumulative mortality curves for breast cancer are close to and have similar forms to the observed patterns of cumulative breast cancer mortality (fig 2). The main differences in the magnitudes and shapes of the observed and modelled curves are the slightly lower cumulative breast cancer mortalities in years 5–9 in the modelled curves, the slightly higher cumulative breast cancer mortalities in years 13 and 14 in the modelled curves, and the absence from the modelled curves of the downturn at around 8 years in mortality seen in both the study and control groups. This downturn may be due to random variation, as it was not found in the 65–74 age group in the two county trial.[3] Among the modelled curves, the curves with and without other causes of death are close together for the study and control groups.

The modelled breast cancer relative cumulative mortality with and without other causes of death are above but close to the observed pattern of cumulative relative breast cancer mortality over the period of the trial (fig 3). At the end of the follow up period, the modelled mortality rate ratio is close to the midpoint of the 95% CI of the observed mortality rate ratio.

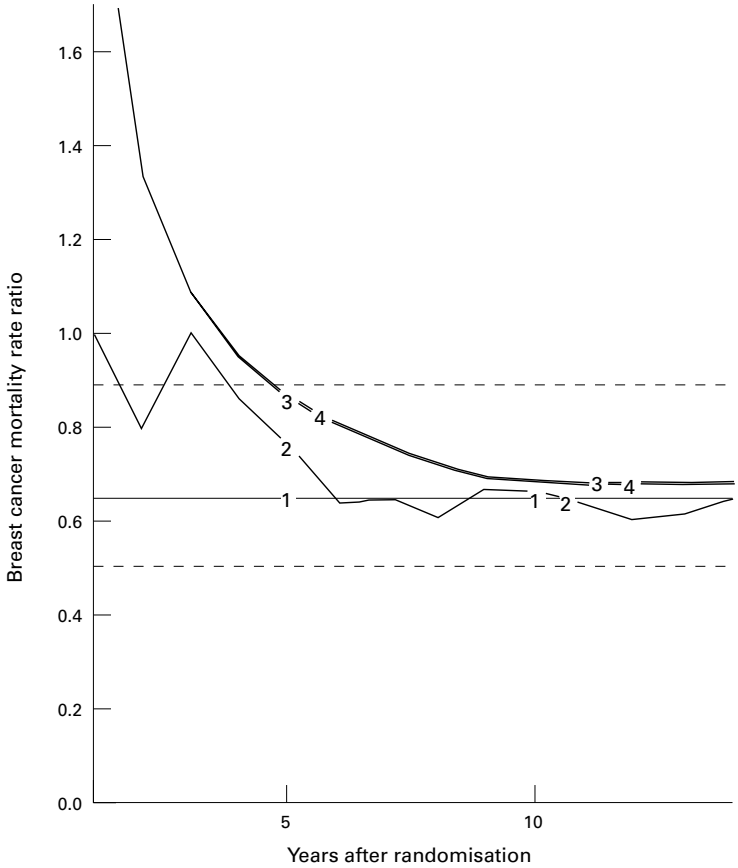

Figure 3 Observed and modelled relative cumulative breast cancer mortality rate ratio for women aged 50–64 at randomisation with and without other causes of death. Line 1 is the published mortality rate ratio at year 14; line 2 is the ratio of published cumulative breast cancer mortality. Lines 3 and 4 are the ratios of modelled cumulative breast cancer mortality: line 3 with other causes of death, and line 4 without other causes of death: –=the 95% CIs of the published mortality rate ratio at year 14.

Little significance can be attributed to the divergence between observed and modelled relative cumulative breast cancer mortality in the first few years after randomisation because of the relatively few events in the numerator and denominator of the mortality ratio, giving unstable and imprecise estimates. As with cumulative mortality, there is little difference in modelled relative cumulative mortality with and without modelling of other causes of death.

Changing the mean sojourn time and sensitivity from their mean values to the upper and lower bounds of their 95% CIs had little effect on the modelled cumulative mortality curves (fig 4) and the modelled relative cumulative mortality curves (both including deaths from other causes, fig 5). For all three sets of data, the modelled mortality rate ratio is close to the middle of the 95% CI of the observed mortality rate ratio.

As anticipated, the shorter the screening interval, the greater the modelled reduction in breast cancer mortality. With 100% participation, a screening interval of 5 years gives a 26% reduction in breast cancer mortality (compared with no screening) and a 1 year interval gives a 66% reduction (fig 6). As the participation rate in the group offered screening declines, the mortality reduction also declines. The question remains, however, as to the impact on mortality of different distributions of mammograms within a population. That is, does screening half the population twice as often produce the same reduction in mortality?

Analysis with the current model suggests that, for a given number of screens, the higher the population participation rate and the longer the screening interval, the greater the reduction in breast cancer mortality (table 4). The left column in table 4 presents the number of screens provided compared with screening all women annually. To illustrate, the screening regimens in the top two rows of data in the table involve delivery of 50% of the number of screens that would be provided if all women were screened annually. Here, screening 50% of the population annually produces a 33% reduction in breast cancer mortality, whereas screening 100% of the population every 2 years produces a 48% reduction.

Discussion

Developing a model that replicates the results of one or more major clinical trials of a health intervention may be an important preliminary step in constructing health policy models of that intervention, for several reasons. It tests understanding of the biological and behavioural mechanisms underlying the effect of the intervention. It provides a framework for building health programme policy models derived from the clinical trial model.

It provides a framework for assessing the availability of relevant data for populating the model. It provides a tool for conducting preliminary sensitivity analysis of different methods of modelling particular parts of the system and different values of important input variables. Finally, it provides a tool for experimentation and analysis while constructing and validating subsequent health programme policy models.

The modelling paradigm used—deterministic group simulation implemented with the software package Powersim—was successfully applied to building a simulation model that replicated to a substantial degree the cumulative breast cancer mortality found in the Swedish two county trial of mammographic screening.

Differences were found between the observed and modelled cumulative mortality curves. These differences may arise from differences between the actual circumstances of the trial and the data and the methods of data analysis used in the model. The most important potential differences are as follows:

A single fixed set of age specific incidences was used as the underlying incidence of breast cancer. It is possible that the true underlying incidence of breast cancer differed from the rate used and that the true rate varied over time. No data were available that could improve on the fixed incidences used, although an estimate has been made for the United Kingdom of a 1.6% annual increase in age adjusted incidence of breast cancer before the introduction of mass screening.[15] It is possible that the increase in incidence found in that

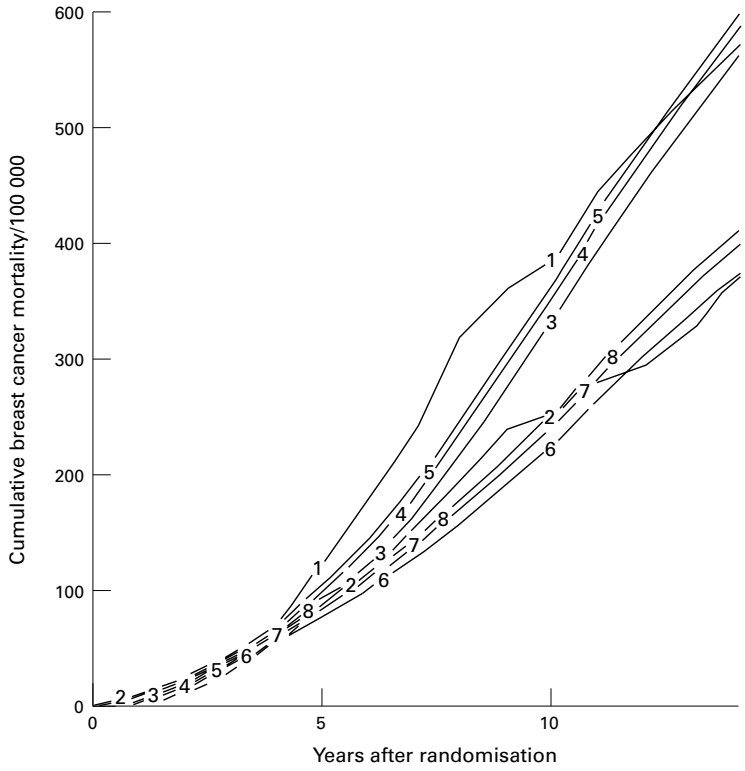

Figure 4 Observed and modelled cumulative breast cancer mortality for women aged 50–64 at randomisation using point estimates (95% CIs) for mean sojourn time and sensitivity for modelled mortality. Lines 1 and 2 are observed control and study cumulative breast cancer mortalities. Lines 3–8 are modelled control and study cumulative breast cancer mortalities: lines 3 and 6 sojourn time long and sensitivity high; lines 4 and 7 sojourn time and sensitivity both medium; and lines 5 and 8 sojourn time short and sensitivity low.

study was due to small scale screening before the introduction of the national screening programme.

It is possible that the relation between earlier detection within the sojourn period and reduced mortality may not be linear, and may vary among different types of breast cancer. However, given the close correspondence between observed and simulated mortality, and in the absence of data on the relation between time of diagnosis within the sojourn period and survival for individual cancers, this assumption seems reasonable.

No data were available on screening among the study and the control groups from the time screening started in the control group, 8 years after randomisation. In the absence of these data, it has been assumed that participation rates and screening intervals from that time in both the study and control groups were the same as the participation rates and screening intervals in the study group in the first 8 years. Model runs that varied this assumption produced no appreciable difference in model output, indicating that the model is insensitive to this assumption.

Similarly, in the absence of published data, it has been assumed that screening intervals and participation rates were uniform within the study and control groups, even though there would doubtless have been heterogeneity in screening interval for individual women. Lastly, modelled survival curves were used in the absence of published survival curves according to mode of cancer detection (clinically or by screening).

The absence of these data in the published literature is puzzling, given the many papers that have been published from the two county trial. Other authors have also commented on the lack of published data for modelling.[16] The absence of key data required for model building may arise from the publication of trial results being aimed solely at drawing conclusions on the efficacy of the intervention rather than further inference of mechanisms. Also, the disinclination of epidemiologists interested in screening to examine data based on time and mode of detection of disease (due to legitimate concerns about bias), as well as data on time of randomisation and study group, may contribute. This is probably exacerbated by trialists not being aware of the data needed for simulation modelling. Obtaining data for modelling shares some of the difficulties experienced in attempting to perform meta-analyses from trials, but with the additional difficulty that data are required for a range of phenomena, not just the measures of the effectiveness of a clinical trial and their uncertainty.

Given these assumptions and uncertainties, tests of model validity are required. One important and omnibus test of the validity of a simulation model is comparison of the output of the simulation model with comparable outcome data from the real world. The similarity between the modelled and observed patterns of breast cancer mortality found here suggests that the model input data and the structure of the model represent the real world of the trial with sufficient accuracy to permit the present model to be a useful tool for policy analysis.

Enhancing the model by including deaths from other causes and moving between upper and lower bounds of the 95% CIs of mean sojourn time and sensitivity had minimal effect on the modelled cumulative mortality and relative mortality. This suggests that the absence of a dynamic life table with different age specific death rates in each calendar year would have no appreciable effect on the utility of the model for policy analysis. Similarly, uncertainty in the estimates of sensitivity and sojourn time proved to be inconsequential.

Unlike the Markov[7] and microsimulation[5] models of breast cancer screening, one potentially significant limitation of this model is the absence of stochastic modelling of sojourn time and sensitivity. This should be apparent in the behaviour of the model when, for example, 100% of the population are screened at an interval less than the sojourn time: no interval cancers should be found, as no cancers remain undetected before the end of the sojourn period. However, clinically detected cancers are found under these circumstances because of the way screening intervals are implemented. One hundred per cent participation every second year is implemented as 50% of women are screened each year, under the assumption of the independent distribution of screening among the population in each year. As a result, clinically detected cancers do occur with 100% participation at intervals less than

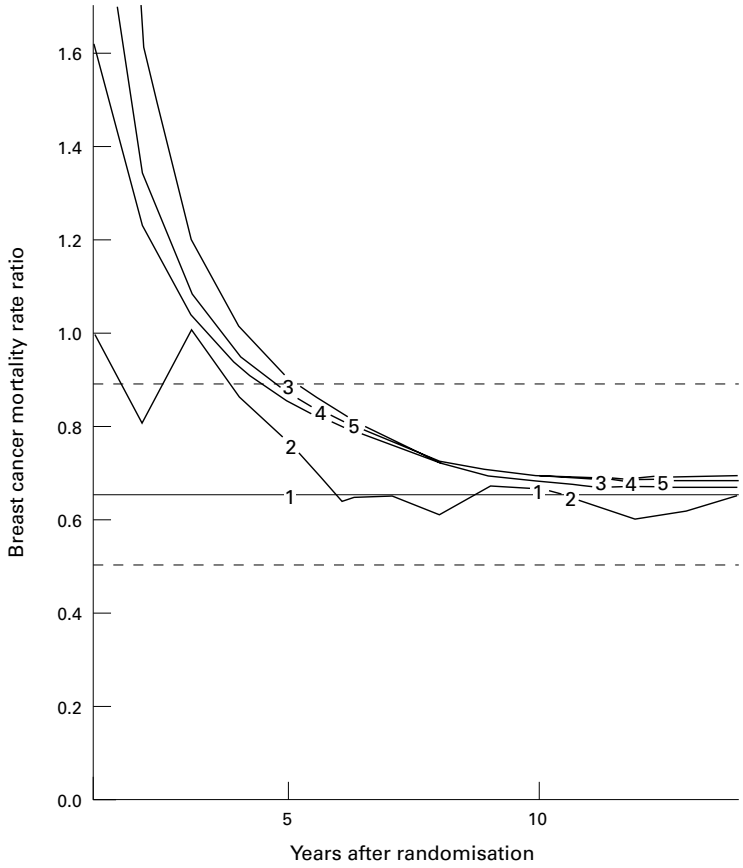

Figure 5 Observed and modelled relative cumulative breast cancer mortality rate ratio for women aged 50–64 at randomisation using point estimates (95% CIs) for mean sojourn time and sensitivity for modelled mortality. Line 1 is published mortality rate ratio at year 14; line 2 is ratio of published cumulative breast cancer mortality. Lines 3–5 are ratios of modelled cumulative breast cancer mortality: line 3 sojourn time long and sensitivity high; line 4 sojourn time and sensitivity both medium; and line 5 sojourn time short and sensitivity low.

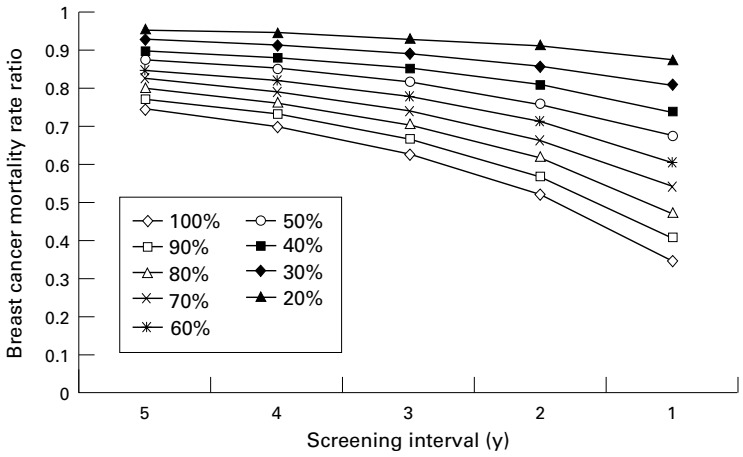

Figure 6 Relative breast cancer mortality with different screening intervals and participation rates, compared with no screening.

the sojourn time. The assumption of independent distribution of screening among the population is equivalent to the assumption used in the Markov model of mammographic screening[10] that screening tests are equally spaced.

All modelling requires assumptions. The model described here does not make the assumption of constant hazard rates for transitions between states that is made in both Markov and microsimulation models. Under this assumption, for an event that has not yet happened (such as the transition of cancer from preclinical to clinical), the probability of the event happening in the next period is the same as in all previous periods.[10] This seems intuitively implausible in the case of a preclinical cancer passing through its sojourn period before becoming clinically apparent. Even so, the inclusion of Markov processes in cancer screening models has not diminished their usefulness.

Ultimately, the empirical foundation of a model and the close correspondence of model output with the observed phenomenon being modelled should provide some confidence in the usefulness of the model for policy analysis. Relative to the model presented here, the minimal impact on simulated cumulative mortality of extreme values of mean sojourn time and sensitivity suggests that the lack of stochastic modelling has no effect on the usefulness of the model. Thus, it is concluded that deterministic group simulation modelling can be used to build reliable, evidence based quantitative models for policy analysis. This opens health policy simulation modelling to epidemiological researchers and will assist them in identifying important information needs, such as breast cancer survival according to time of diagnosis within the sojourn period.

Intuitively, it would be expected that population health gain from a cancer screening intervention would be greater the more evenly that intervention is distributed across the target population. This has been shown for Pap tests.[17] The protective effect of a Pap test in reducing incidence of cervical cancer has been found to be relatively insensitive to screening interval. For the Pap test, a 1 year interval reduces cervical cancer incidence by 93.5% and a 2 year interval reduces incidence by 92.5%, a minimal difference. This means that, for a given number of Pap tests (and hence, resource use), the greater the number of women screened and therefore the greater the screening interval, the greater the reduction in incidence of cervical cancer.

The relation between screening interval and reduction in mortality has been examined previously for mammographic screening in the Markov model already mentioned.[10] Published data allow direct comparison of the age group 50–59 in the Markov model[7] with the present model (50–64). (The Markov model showed little difference in reduction in mortality among different age groups.) For an assumed attendance rate of 90% and a 1 year screening interval, the Markov model gave a relative mortality of screened versus unscreened of 0.54, whereas the current model gives 0.40 (a 60% reduction in breast cancer mortality). For longer screening intervals, the difference between the modelled results is much less. For a 2 year interval, the relative mortalities are 0.61 and 0.57 respectively. For a 3 year interval, the relative mortalities are 0.66 and 0.67 respectively. Perhaps the 1 year time step of the current model makes estimates for shorter screening intervals progressively less accurate

Table 4 Breast cancer relative mortality with different screening intervals and participation rates, compared with no screening, grouped according to total number of screens provided (maximum possible screens taken to be 100% participation and 1 year interval)

Screens performed as a proportion of possible annual screens (%)	*Participation rate (%)*	*Screening interval (y)*	*Breast cancer mortality rate ratio*	*Breast cancer mortality reduction (%)*
50	50	1	0.67	33
50	100	2	0.52	48
40	40	1	0.74	26
40	80	2	0.62	38
30	30	1	0.80	20
30	60	2	0.71	29
30	90	3	0.67	33
20	20	1	0.87	13
20	40	2	0.81	19
20	60	3	0.78	22
20	80	4	0.76	24
20	100	5	0.75	25
10	20	2	0.91	9
10	30	3	0.89	11
10	40	4	0.88	12
10	50	5	0.87	13

than the Markov model, which used periods of 1 month. However, the implementation of screening interval as a proportion of women screened each time step should overcome this. Alternatively, assumptions in the Markov model, such as the assumption of constant hazard functions, may contribute to the discrepancies.

In any event, the results from the present model support the concept that the more even the distribution of mammograms in a population, the greater the reduction in breast cancer mortality. Thus the results of the model provide support to policies that seek to deploy resources available for mammographic screening most evenly across the target population.

This analysis represents just one of the many different kinds of policy analysis to which this and comparable models can be put. Subsequent papers will provide further analyses with this model.

The support of the Commonwealth Department of Health and Aged Care, the use of facilities of the Department of Civil Engineering, Australian Defence Force Academy, and the comments of Dr Ian Mathieson and anonymous referees are gratefully acknowledged. The views expressed are those of the author.

1 BreastScreen Australia. *BreastScreen Australia statistical report 1996.* Canberra: BreastScreen Australia, 1996.
2 Tabar L, Fagerberg CJG, Gad A, *et al*. Reduction in mortality from breast cancer after mass screening with mammography. *Lancet* 1985;i:829–32.
3 Chen HH, Tabar L, Fagerberg G, *et al*. Effect of breast cancer screening after age 65. *J Med Screen* 1995;**2**:10–14.
4 Connor RJ. Chu KC, Smart CR. Stage-shift cancer screening model. *J Clin Epidemiol* 1989;**42**:1083–95.
5 Boer R, de Koning H, Threlfall A, *et al*. Cost effectiveness of shortening screening interval or extending age range of NHS breast screening programme: computer simulation study. *BMJ* 1998;**317**:376–9.
6 Jansen J Th M, Zoetelief. Optimisation of mammographic breast cancer screening using a computer simulation model. *Eur J Radiol* 1997;**4**:137–44.
7 Duffy SW, Day NE, Tabar L, *et al*. Markov models of breast tumour progression: some age-specific results. *J Natl Cancer Inst Monogr* 1997;**2**:93–7.
8 Tabar L, Fagerberg G, Chen HH, *et al*. Screening for breast cancer in women aged under 50: mode of detection, incidence, fatality, and histology. *J Med Screen* 1995;**2**:94–8.
9 International Agency for Research on Cancer. *Cancer incidence in five continents volume IV*. Lyon: IARC, 1982.
10 Chen HH, Duffy SW, Tabar L. A Markov chain method to estimate the tumour progression rate from preclinical to clinical phase, sensitivity and positive predictive value for mammography in breast cancer screening. *Statistician* 1996;**45**:307–17.
11 Tabar L, Fagerberg G, Day NE, *et al*. What is the optimum interval between mammographic screening examinations?—An analysis based on the latest results of the Swedish two-county breast cancer screening trial. *Br J Cancer* 1987;**55**:547–51.
12 South Australian Cancer Registry. Prognostic features of breast cancers detected in mammographically screened women in South Australia: a pilot study. In: *Epidemiology of cancer in South Australia*. Adelaide: South Australian Health Commission, 1996.
13 Tabar L, Fagerberg G, Chen HH, *et al*. Efficacy of breast cancer screening by age. New results from the Swedish two-county trial. *Cancer* 1995;**75**:2507–17.
14 Day NE. Surrogate measures in the design of breast screening trials. In: Miller AB, Chamberlain J, Day NE, *et al*, eds. *Cancer screening*. Cambridge: Cambridge University Press, 1991:391–403.
15 Prior P, Woodman CBJ, Wilson S, *et al*. Reliability of underlying incidence rates for estimating the effect and efficiency of screening for breast cancer. *J Med Screen* 1996;**3**:19–22.
16 De Koning, Boer R, Warmerdam PG, *et al*. Quantitative interpretation of age-specific mortality reductions from the Swedish breast cancer-screening trials. *J Natl Cancer Inst* 1995;**87**:217–23.
17 Hakama M, Miller AB, Day N, eds. *Screening for cancer of the uterine cervix*. Lyon: International Agency for Research on Cancer, 1986.