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ORIGINAL ARTICLE

Estimation of the Cost-Effectiveness of Breast Cancer Screening Using Mammography in Mexico Through a Simulation

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ABSTRACT

Background: Currently, breast cancer is the most prevalent tumor among Mexican women. Screening methods such as mammography could potentially reduce the health and economic burden of breast cancer; however, its risk-benefit balance is still unclear. **Objective:** To estimate the cost-effectiveness of different breast cancer screening programs using mammography in Mexico and to contribute to the decision-making process on this preventive measure. **Methods:** A simulation study was performed using population data and incidence rates. Several screening programs were assessed using the cost-effectiveness methodology recommended by the World Health Organization. **Results:** The feasible recommended screening program has an examination schedule periodicity of every three years, with a population coverage of 0, 15, 18, 20, 25, 20, 18, and 0% for the age groups of 25-40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, and 70-75 years, respectively**. Conclusions**: Given the present coverage in Mexico, it is necessary to optimize our resource allocation to improve the country's breast cancer prevention policy. (REV INVES CLIN. 2016;68:184-91)

Key words: Cost-effectiveness. Breast cancer. Mammography.

INTRODUCTION

Breast cancer (BrCa) is the most prevalent tumor among women worldwide, being the first cause of death from cancer in this population group[1]. Detection programs addressed at receiving medical attention in early stages are of the utmost importance to reduce the global burden of this disease. However, the benefits of mammography as a screening method in asymptomatic people have been controversial.

In Mexico, mammography coverage is below that recommended by the World Health Organization (WHO) for an effective screening program[2]. According to the 2011 National Health and Nutrition Survey (ENSANUT)[3], 10.9 and 18.0% of women 40-49 and 50-69 years old, respectively, reported to have had a mammographic screening[4]. Additionally, it is estimated that 2,699,752 (95% CI: 2,503,582-2,895,922) mammography screenings were performed in Mexico in 2011. Of these, 1,694,230 were conducted in women over the age of 50, i.e. 15.24% of women

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over 50 years old in Mexico reported having a mammography during 2011. According to the ENSANUT 2012, mammography screening in Mexico was used during 2011 mostly for prevention rather than for diagnostic purposes; of all women who self-reported having a mammography, 18% had had symptoms before their screening, while the rest (82%) were asymptomatic. It is also estimated that in 2011, 28,700 (1.3%) of 2,142,618 asymptomatic women who had a mammographic screening received a positive result.

Within this context of scarce coverage due to the lack of an organized screening program, in addition to poor access to adequate diagnosis and treatment, as previously described[5], it is necessary to identify the scenario in which the application of mammography in the Mexican population could be more effective. In this paper, we attempted to estimate the cost-effectiveness of different possible scenarios of BrCa screening using the methodology proposed by the WHO[6]. We present results from different scenarios, depending on the female population structure in Mexico, program periodicity schedule, reached coverage, and mammography sensitivity adjusted for age group.

METHODS

Study design

We performed a cost-effectiveness analysis in line with the WHO-CHOICE methodology[6]. The analysis consisted of a comparison of all plausible screening programs compared to a scenario in which there is no early detection program, defined as the null scenario. Different screening programs were simulated using a population model for a period of 10 years beginning in 2016. Each scenario accounts for a specific screening coverage for women of ages 25-75, divided in age groups of five-year class intervals. Additionally, three possible screening frequencies were taken into account: yearly, every two years, and every three years.

The population model shown in figure 1 simulates the epidemiology of BrCa in the country, considering transitions from a healthy state to a disease state, death, or survival. Three stages were considered for BrCa pooling all four known clinical stages (Fig. 1). Each stage will have an observed distribution depending on the screening program, e.g. increasing coverage will decrease stage III and increase stage I prevalence. Demographic data were obtained from the Mexican National Population Council (CONAPO, for its acronym in Spanish, Consejo Nacional de Población), which also takes into account births and background mortality[7]. The incidence of BrCa was simulated using age group-adjusted annual incidence rates based on regional estimates[1,8] (Table 1).

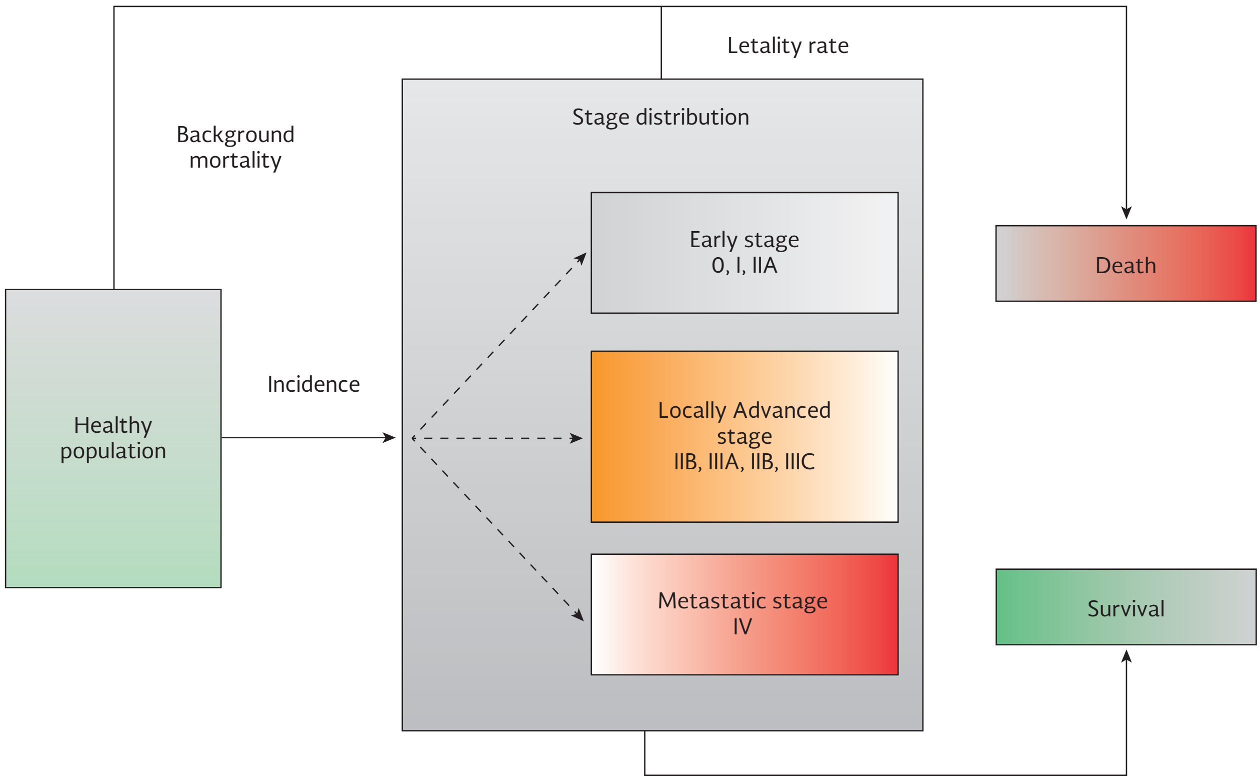
Transitions from BrCa to a death or survival state were simulated based on estimated BrCa stage-adjusted fatality rates derived from a patient cohort (n = 615) treated at the National Cancer Institute of Mexico (INCan, for its acronym in Spanish, Instituto Nacional de Cancerología), covered financially by the Catastrophic Expenditure Protection Fund (in Spanish, Fondo de Protección de Gastos Catastróficos, Seguro Popular), and followed up from 2007 to 2013[4]. The model assumes that a patient surviving more than five years will live to the age expectancy of 77.5 years, according to the Mexican National Institute of Statistics and Geography (INEGI, for its acronym in Spanish, Instituto Nacional de Estadística y Geografía)[9]. Additionally, women's age was estimated using the midpoint value of the five-year class interval (age) to which they belong.

Based on the described model, scenarios were simulated based on all possible combinations of coverage by age group and frequency shown in table 1. These scenarios were then compared to the null scenario to determine the most cost-efficient screening program.

Detection parameters

The mammography detection rate and proportion of screening-detected tumors were modeled following the method proposed by Duffy and Gabe[10]. According to Bray, et al.[8], these two variables depend on the mammogram's sensitivity and the BrCa latency period. The proportion of screen-detected tumors was estimated based on Tabar, et al.[11], who conducted a study of Swedish women between the ages of 40 and 74 (n = 133,000) with a follow-up period of 20 years. The mammogram's sensitivity was estimated based on Ohta, et al.[12], who carried out a detection program using mammography in Japanese women between 40-80 years old (n = 62,447). Finally, the latency

Figure 1. Population model used in the simulation. Arrows represent the transition from one state to another.



period of BrCa and the mammogram's sensitivity were linearly extrapolated for the 25-40 years age group[3]. Table 1 shows the latency period in years and the age group-adjusted mammogram's sensitivity.

Reproducibility

The analysis was performed using the R statistical software. Data analysis can be reproduced in its totality using the code, data sets, and markdown files[4,13].

Effectiveness

Following the WHO's methodology[6], the effectiveness of each detection scheme is measured in the number of disability-adjusted life years (DALY) averted in comparison to the null scenario. For each individual, a DALY is composed of years lost due to disability (YLD) and years of life lost (YLL) due to premature mortality[14]. The morbidity component (YLD) is computed as follows:

$$\mathrm{YLD} = \mathrm{DW} \times \int_{A}^{A+L} e^{-r(x-a)}\,dx$$

Where a is the age at which the disease was diagnosed (assigned); A and L are the age at onset and duration of the disease, respectively; r is the discount rate proposed by the WHO (6), and, finally, DW represents the disability weight which ranges between 0 and 1, where 0 represents a perfect health condition and 1 represents death. Disability weights corresponding to the three different cancer stages (Table 2) were obtained from the European Disability Weights Project[15]. Women who survived cancer were assigned a disability weight corresponding to mastectomy[16] until death. Each YLL is defined using the same equation setting DW = 1 and L accounts for the expected remaining years at the moment of death. The rest of the parameter definitions remain the same. The following equation was used for estimating DALY:

$$DALY = \tau\,(YLL) + (1-\tau)\,YLD,$$

where is the disease fatality rate.

Each DALY depends on the clinical stage of BrCa and the age of the individual. Table 2 shows the parameters used to estimate the effectiveness of each screening

Table 1. Input parameters for simulation

Age group	Incidence rate per 100,000 women[14]	BrCa latency period (in years)[9]	Mammogram's sensitivity[10]	Possible screening coverage
25-40	11.7	2.1	0.611	0, 1, 2%
40-45	58.7	2.4	0.698	0, 5, 10, 15%
45-50	84.3	2.4	0.698	0, 6, 12, 18%
50-55	106.5	3.7	0.667	0, 5, 10, 15, 20%
55-60	118.6	3.7	0.667	0, 5, 10, 15, 20, 25%
60-65	119.4	4.2	0.773	0, 5, 10, 15, 20%
65-70	116.6	4.2	0.773	0, 6, 12, 18%
70-75	108.8	4.0	0.838	0, 2%
Periodicity	–	–	–	Every 1, 2 or 3 years

For each age group stratified by groups of five years, columns 2 to 4 detail the population parameters used to estimate the detection rates from the mammography. Column 5 lists the possible coverage values assessed in the simulations.
BrCa: breast cancer.

Table 2. Estimated survival probabilities and disability weights

Estimated survival probabilities[3]	Early stage	Locally advanced	Metastatic
First year	0.99	0.97	0.69
Second year	0.97	0.88	0.41
Third year	0.93	0.74	0.20
Fourth year	0.88	0.58	0.08
Fifth year	0.82	0.43	0.02
Disability weights[13]	–	–	–
First year of disease	0.27	0.37	0.61
Second to fifth year	0.18	0.30	0.61
Death	1.0	1.0	1.0
Survival	0.05	0.05	0.05

Estimated survival probabilities and disability weights for each breast cancer clinical stage. These parameters were used to quantify the burden of disease for each breast cancer status.

scheme. Each program will have an amount of DALYs associated to it. According to the WHO method, the effectiveness of each screening program is defined as the difference of DALYs in comparison to the null scenario. That is, the number of DALYs averted is estimated as:

$$DALYS\ AVERTED_{Program\ j} = DALYS_{Null\ Scenario} - DALYS_{Program\ j}$$

Costs

In line with the WHO-CHOICE approach[4], patient and program treatment costs were identified. Stage-adjusted cancer treatment costs were obtained from the Reimbursement Tabulator of the INCan's Catastrophic Expenditures Protection Fund[17]. Mammography costs include a depreciation of the mammogram, use of electricity, use of building space, and radiologist wages according to the Costs Tabulator from the Office of Diagnostic and Treatment Ancillary Services of Mexico's National Cancer Institute. Transportation and opportunity costs were not taken into account. An inflation rate of 3% was assumed. Table 3 details the costs used in the model. The cost of a screening program is compared to the cost in the null scenario:

$$ADDITIONAL\ COST_{Program\ j} = TOTAL\ COST_{Program\ j} - TOTAL\ COST_{Null\ Scenario}$$

Cost-effectiveness analysis

Averages of the total costs and DALYs averted for the 10-year simulation period were calculated for every

Table 3. Costs associated with breast cancer screening in Mexican Pesos 2015

	Asymptomatic women	Early stage	Locally advanced stage	Metastatic stage
Treatment cost[15]	–	$176,733.30	$245,933.50	$264,355.80
Mammography cost[15]	$1,186.00	–	–	–

Costs of mammography and treatment used to estimate the costs of each screening program.

screening program to obtain the following average cost-effectiveness ratio (ACER):

$$ACER_{Program\ j} = \frac{AVERAGE\ OF\ ADDITIONAL\ COSTS_{Program\ j}}{AVERAGE\ OF\ DALYS\ AVERTED_{Program\ j}}$$

Having estimated the ACER for all possible interventions with respect to the null scenario, we defined the expansion route as a series of programs that could be potentially implemented by increasing the available budget. This expansion path is obtained calculating the ACER for all programs in comparison with the current intervention, and choosing the one with the lowest ratio. Starting from the null scenario on, this procedure results in the corresponding expansion path shown in figure 2[4].

Finally, in line with the WHO-CHOICE methodology[6], scenarios in which each DALY averted is strictly less than three-times the GDP per capita are defined as cost-effective, and those whose cost per DALY is strictly less than the GDP per capita as highly cost-effective. In the case of Mexico, these limits are $10,307 and $30,921 per DALY averted[18].

RESULTS

Estimation of DALYS averted by cancer stage and age group at an individual level is shown in table 4. Results of the analysis show that the current scenario is highly cost-effective, with an average of 10,741 DALYs averted per year. As shown in figure 2, the expansion path suggests implementing a feasible program with an ACER lower than that of the current program. As the best option, this screening program implies a frequency of once every three years with the coverage described in table 4; it increases the coverage in age groups between 40-70 years, specifically in the five-year class interval age group of 55-60 years, and would, additionally, result in average savings of 31 million dollars per year leading to 448 DALYs averted. Finally, if the annual budget were to increase 9 million dollars per year compared to the current intervention, the objective program shown in figure 2 would be feasible. Thus, the objective intervention consists of a periodic program schedule every two years with the coverage shown in table 4, which would result in 12,696 DALYs averted, representing an increase of 1,995 compared to the current program.

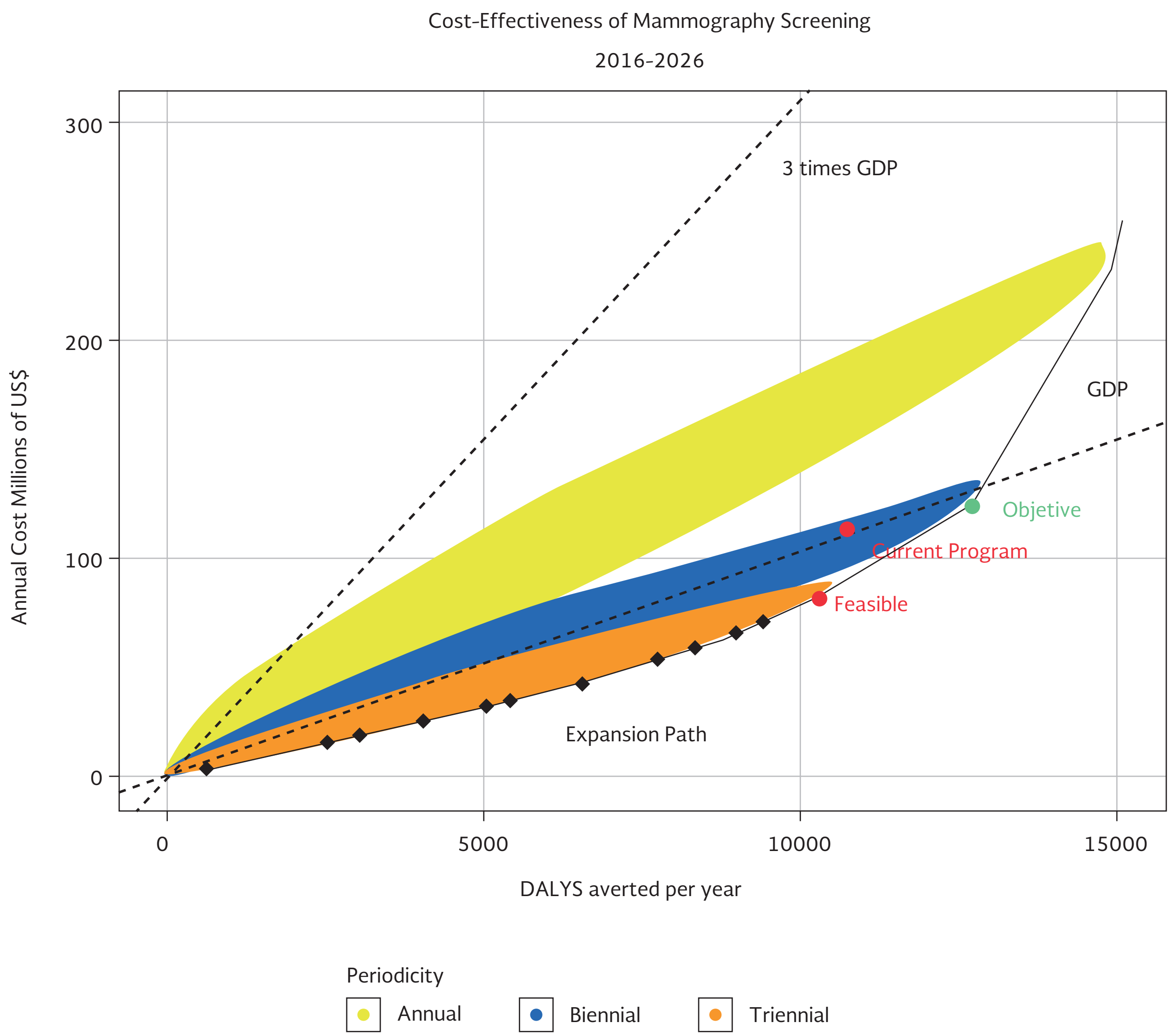
Sensitivity analysis

Following the WHO-CHOICE methodology, the discount rate was removed () for the estimation of DALYs averted per year. The feasible and objective programs were kept with the same coverage, but their frequency was changed to every two years and every year, respectively[4]. In a separate analysis, the latency period of BrCa and the mammography sensitivity were adjusted according to Taghipour, et al.[19], resulting in the same feasible and objective scenarios shown in figure 2, although the DALYs averted decreased considerably to 9,818 and 12,204, respectively[4]. In addition, the current program shifted from the region of highly cost-effective to cost-effective programs.

DISCUSSION

The WHO resolution on Cancer Prevention and Control (WHA58.22) recommends low- and middle-income countries to identify evidence-based, sustainable actions to improve cancer care and to make the best use of their resources to benefit the cancer-afflicted population[20]. Given Mexico's current resources, it is necessary to identify the best practices in prevention, early detection, and treatment for BrCa. According to Anderson, et al.[19], early detection efforts in low- and middle-income countries can be segmented according to the level of available resources. Mexico's current goal should be to reduce the proportion of the population with symptomatic disease through the use of

Figure 2. Results from the simulation; the x-axis shows the total disability-adjusted life years averted per year for each simulated program and the y-axis shows its approximate cost. Any program between the 3 x GDP and GDP threshold is considered to be cost-effective. The highly cost-effectiveness region is under the GDP dotted-line threshold. The expansion path is shown in grey and includes the most highly cost-effective feasible screening program in orange and the optimal program in green. The current screening program is shown in red.



mammography as an early screening method in target groups, along with an improvement in the quality of the imaging techniques and interpretation, appropriate monitoring of the population to identify the current incidence of interval breast cancers, and, of course, ensuring access to timely and appropriate treatment.

Nevertheless, the Mexican Official Standard[21] for breast cancer prevention, diagnosis, treatment, control, and epidemiological surveillance states that all women over the age of 50 should have a mammography once a year, and that women between 40-49 years old with two or more risk factors should have a mammography every two years, corresponding to an enhanced level of resources according to the guideline for breast healthcare in low- and middle-income countries[20]. This suggests that Mexico should adjust its current Official Standard to more realistic goals.

Table 4. Results from simulation

Age Group	DALYs adjusted for BrCa stage and age group			Screening programs		
	DALYs Early	DALYs Locally advanced	DALYs Metastatic	Current program*	Feasible program	Objective program
25-40	5.52	13.84	23.42	1.9%	0%	0%
40-45	4.86	12.05	20.46	9.6%	15%	15%
45-50	4.44	10.93	18.61	14.5%	18%	18%
50-55	3.95	9.64	16.45	19.6%	20%	20%
55-60	3.39	8.13	13.95	18.9%	25%	25%
60-65	2.74	6.38	11.05	17.9%	20%	20%
65-70	1.98	4.34	7.68	14.5%	18%	18%
70-75	1.09	1.98	3.76	7.3%	0%	0%
Frequency	–	–	–	Every two years	Every three years	Every two years
DALYs averted per year	–	–	–	10,741	10,293	12,696

Results obtained from the simulations. For each age group stratified by groups of five years, columns 2 to 4 show the estimated DALYs for each breast cancer clinical stage. Column 5 provides an estimate of the DALYs averted by the current screening program in Mexico based on the National Health and Nutrition Survey2. Column 6 details the optimal economically feasible screening coverage and the total of DALYs averted. Column 7 displays the optimal screening program in the highly cost effective region.
*Estimated based on the National Health and Nutrition Survey 2012 (Instituto Nacional de Salud Pública)[2]
DALY: disability-adjusted life year.

Our findings suggest that in Mexico, the use of mammography as a screening method for women is highly cost-effective only when the periodicity program schedule is every three or every two years for particular programs, and when coverage includes only women from the age group of 40-70 years, resulting in fewer unnecessary biopsies and a decrease in overdiagnosis and false positives (mainly in women under the age of 50 for whom the test is less sensitive and reliable). A frequency of every three years has also been defined as cost-effective in studies from Australia and New Zealand in women aged between 50-70 years[22], and countries with similar conditions to those in Mexico, such as Peru[23]. According to the International Agency for Research on Cancer[24], there is sufficient evidence that mammography can be cost-effective for women aged 50-75 in countries with high incidence rates, yet there is limited evidence to demonstrate that mammography is cost-effective in low- and middle-income countries. Notwithstanding, studies from Valencia-Mendoza, et al.[25] and Niëns, et al.[26] support the idea that screening interventions in Mexico using mammography are cost-effective according to the WHO-CHOICE criteria. The expansion path in figure 2 suggests that as the budget increases, priority should be given to the age group of 60-70 years. Clinical breast examination was not taken into consideration, but is known to shift the stage distribution to a lower stage and could be less expensive[24]. The probably underestimated prices of mammography and treatment, and the assumptions that the detection parameters are valid in Mexican women even though the studies were conducted abroad, may be additional study limitations. However, these variables were applied equally to all simulated scenarios. A lack of literature regarding the mammogram's sensitivity and the estimation of the latency period of BrCa in Mexican women suggests the need for further studies in this area. Since the model is population-based, it does not take into account additional risk factors such as physical activity, weight control, and hormone therapy. Furthermore, the population model does not account for over-diagnosis or false positives that are known to lead to psychological consequences[25]. One of the strengths of the simulation is its relatively low population coverage levels, which are close to the percentages reported for the current screening[3]. If they were to be implemented, this restriction allows a relative feasibility of the programs.

In conclusion, from a health policy perspective, it is necessary to optimize the scarce resources available for prevention, implementing an organized prevention program targeting a specific population age group, preferably women between 40-70 years of age, with regular monitoring every three years. However, this intervention would only be truly useful if diagnostic, referral, treatment, and basic palliative services were simultaneously improved, and access to such services was improved by reducing existing barriers.

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