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ORIGINAL ARTICLE

Breast cancer methodology for maximization of resources currently used in Mexican centers

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Abstract

Background: *Breast cancer is worldwide the leading cause of death from neoplasia. Therefore, health-care centers must be prepared for assessing the most optimal management of resources while seeking the best clinical outcome.* **Objective:** *To present a currently applied model for quantification and informed decision-making by a breast cancer service in Mexico.* **Method:** *The primary information necessary to calibrate this methodology's model was provided by the Breast Tumors Service of the National Cancer Institute of Mexico City and the Centennial Hospital Miguel Hidalgo in the city of Aguascalientes. The data analysis was carried out for each one of the health institutions because the treatment algorithm, the number of patients, and the distribution of patients by stage with breast cancer differ between both institutions.* **Results:** *The methodology allowed the assessment of the cost of the current management of breast cancer in each institution, as well as the clinical and economic impact generated by the inclusion of new innovative drugs to the current treatment algorithm.* **Conclusion:** *The proposed methodology allows the allocation of resources to be optimized, as well as estimating potential scenarios for the inclusion of new health technologies.*

Keywords: *Breast cancer. Resource maximization. Mexico.*

Metodología de cáncer de mama para la maximización de recursos utilizada actualmente en México

Resumen

Antecedentes: *El cáncer de mama es la principal causa mundial de muerte por neoplasias. Por lo tanto, los centros médicos deben estar preparados para evaluar la gestión óptima de sus recursos, buscando el mejor resultado clínico.* **Objetivo:** *Presentar un modelo aplicado para la cuantificación y toma de decisiones informadas por parte de un servicio de cáncer de mama en México.* **Método:** *La información primaria necesaria para calibrar el modelo de esta metodología fue proporcionada por el Servicio de Tumores de Mama del Instituto Nacional de Cancerología de la Ciudad de México y el Hospital Centenario Miguel Hidalgo de la ciudad de Aguascalientes. El análisis de datos se realizó para cada una de las instituciones de salud debido a que el algoritmo de tratamiento, el número de pacientes y la distribución de pacientes por estadio con cáncer de mama difieren entre ambas instituciones.* **Resultados:** *La metodología permitió evaluar el costo del manejo actual del cáncer de mama en cada institución, así como el impacto clínico y económico que genera la inclusión de nuevos fármacos innovadores al algoritmo de tratamiento actual.* **Conclusión:** *La metodología propuesta permite optimizar la asignación de recursos, así como estimar escenarios potenciales para la inclusión de nuevas tecnologías en salud.*

Palabras clave: *Cáncer de mama. Maximización de recursos. México.*

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Introduction

The United Nations has declared cancer as a non-communicable disease that threatens global development due to its worldwide impact on social and economic development[1]. In the world, one in six women will develop breast cancer and one in eleven will die from it, being the worldwide leading cause of death from neoplasia[2]. The death rate from breast cancer is expected to increase in Mexico in the coming years[3]. According to the World Health Organization, breast cancer is the second cause of cancer mortality in Mexico and has the highest incidence among women, with 27,283 new cases per year[4].

Since 2007 in Mexico, the Health Protection System's (Seguro Popular) coverage of breast cancer was provided by the Protection Fund against Catastrophic Expenses (FPGC)[5]. The high prevalence of the disease has prompted the creation of new treatments that have been a watershed in disease management and have expanded the possibilities of clinical practice. These innovative treatments have significantly increased the patients' life expectancy; however, the cost of new innovative resources is high[6].

This work is motivated by the difficulty that represents for a director of a clinical cancer service, in this case of breast tumors, to make reasoned and justified decisions regarding the modification of treatment procedures used for the care of patients. The decision-maker must take into consideration the introduction of new health-care technologies and the adjustments in clinical activities, always under tight budget constraints. These changes normally affect a subgroup of patients and it is difficult for the service line directors to estimate the total clinical and economic impact of such changes on the entire attended population in their hospitals. For example, deciding between a targeted therapy in stage IV for the second line, at a certain budget impact knowing its impact on a 5-year survival over the weighted total of patients with breast cancer, and investing in the impact generated by breast reconstruction, is not always easy for a manager to compare (Fig. 1).

The objective of this work is to present a model for quantification and informed decision-making by a breast cancer service. Specifically, it is sought to present a practical methodology to contrast the clinical impact against the economic impact of patient service management in their different stages in the line of treatment. In recent years, models regarding the cost-effectiveness of breast cancer individual treatments have been made[7-13] as well as reviews analyzing new therapies' cost-efficiency[14-16]. However, during open research, only the study made by Wong *et al.*[16] was found to be like ours. This publication presents a model to optimize the allocation of resources for the prevention and treatment of breast cancer in Hong Kong. Wong *et al.* used a Markov model to evaluate different interventions through simulations. Nevertheless, its primary objective was to influence public policies, while the main purpose of this publication is to support informed decision-making at the hospital level. Therefore, to our knowledge, this is the first study to provide a practical methodology for quantifying and evaluating the clinical versus economic impact of a breast cancer treatment algorithm.

Materials and methods

The primary information necessary to calibrate this methodology's model was provided by the Breast Tumors Service of the National Cancer Institute (INCAN) of Mexico City and the Centennial Hospital Miguel Hidalgo (CHMH) in the city of Aguascalientes. The data analysis was carried out for each one of the health institutions because the treatment algorithm, the number of patients, and the distribution of patients by stage with breast cancer differ between both institutions.

The economical and clinical data provided by both institutions was from 2019 since it was the year of the methodology and model implementation for decision-making in both centers. All economic variables were adjusted for inflation and converted into US dollars. The primary clinical results of all tables presented were adjusted by the clinical centers taking into consideration the literature and its specific center's results of response to treatments. It is worth mentioning that treatment algorithms could change over time based on evolving scientific evidence; therefore, the proposed model would need to be readjusted. The calculation of the model's variables will be described along with a matrix to evaluate the clinical impact of the increase in treatment schemes' costs.

Average duration

The average duration of a procedure is calculated with a weighted average. Hence, to calculate the average duration of treatment for a group of patients using procedure X, we must do a weighted average (Eq. 1).

Equation 1. Average duration of use of a procedure, used by N patients of stage K $D_x = \frac{\sum_{i=1}^{n} t_i p_i}{N}$, where

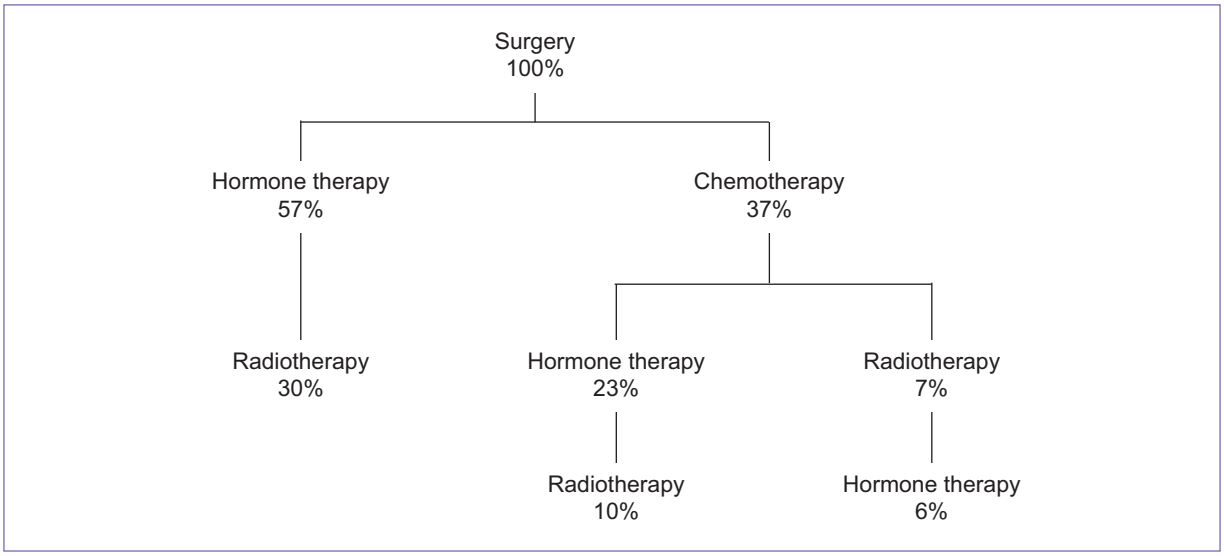

Figure 1. Example of a treatment regimen for early-stage breast cancer patients.

D_x is the average duration of a specific procedure, t_i is the duration of group i, p_i is the number of patients in that group and N is the total number of patients.

Total procedure cost

Procedure cost is calculated by multiplying the procedure's average duration by the number of patients using it and by the cost per time unit and patient (Eq. 2). It is important to note that the monthly cost was used because the average duration is given in months.

Equation 2. Total procedure cost per stage $C_x = P_x D_x N$; where P_x is the price per time unit of the procedure, D_x is the average duration per unit of time at that stage, and N is the number of patients using that procedure at that stage. The unit of time must be predefined and be the same in all variables.

Annualized procedure cost

To calculate it, we multiply the monthly cost by the number of people who use it and by 12 (the number of months in a year). In addition, the annualized cost per treatment scheme can be calculated by adding the annualized cost per procedure for all the procedures and treatments included in a scheme.

Annualized breast cancer cost by stage

For treatment regimens where the duration exceeds 1 year, the annualized cost can be used. This is calculated by multiplying the monthly cost, by the number of people who use it and then by 12. This is for the case where all patients receive the treatment for at least a year, if that is not the case, we would need to consider this patient(s) as a proportion of the corresponding treatment duration with respect to the year (e.g., 9 months tx patient = 9 months/12 months = 0.75).

Then, we must calculate the annualized cost of all the procedures used in the stage in question and add them (Eq. 3).

Equation 3. Annualized breast cancer cost by stage L: $C_L = \sum_{i=1}^{n} C_{Xi}$, Where n is the number of procedures used in the given stage.

After obtaining the annualized breast cancer cost of each of the stages, we can calculate the total annual breast cancer cost (Eq. 4).

Equation 4. Total annual cost of treating breast cancer: $Cost_T = \sum_{i=1}^{e} C_{Li}$, where e is the number of considered stages.

Survival

To calculate the survival generated at 5 years in a stage, given different treatment schemes, the literature has to be reviewed and the expected survival is obtained for each treatment scheme. A weighted average is obtained based on the number of patients in each treatment scheme (Eq. 5).

Equation 5. Survival in one stage, given different treatment schemes with different survival data reported in the literature:

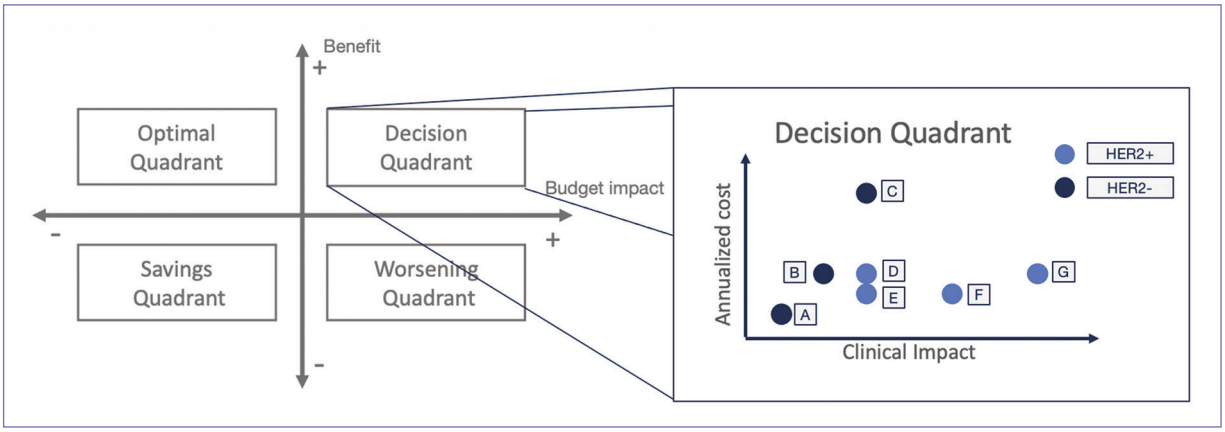

Figure 2. Decision matrix and Resource optimization quadrant.

$S_T = \frac{\sum_{i=1}^{T} S_i p_i}{N}$; where N is the number of patients in the stage, S_i is survival given a treatment scheme reported in the literature and p_i the number of patients in such scheme.

The survival times reported in the literature are not always reported at 5 years and for those reported survival times, a standardization with an exponential distribution was employed (Eq. 6). The data reported in the literature was used to calculate λ, extrapolate, and standardize the clinical results to normalize this survival time.

Equation 6. Survival exponential distribution for normalization: $S(t)=e^{-\lambda t}$

Decision matrix and efficiency index

With the previous variable consideration, a decision matrix can be used to graphically locate and classify the clinical and economic impact of new treatments, relative to the average survival and cost of currently used treatments, as can be observed in figure 2. While the optimal, savings, and worsening quadrant scenarios do not involve decision-making struggle for a manager, the decision quadrant helps him/her to evaluate competing regiments in its treatment lines.

The intention is to find innovative treatments that maximize survival, with respect to their impact on costs. Figure 2 also shows a close up to the decision quadrant of the decision matrix. In the example presented, the budget impact of innovative treatments was located with its clinical impact and differentiated in color by molecular subtype. Note that these are compared using the annualized cost and survival of current disease management as a starting point. While for human epidermal growth factor receptor 2 positive (HER2+) patients, for example, the best treatment option would be the "G" treatment, since it is the most affordable as well as the one with the best clinical impact on the patient. However, while in HER2+ the optimal decision is clear, for human epidermal growth factor receptor 2 negative (HER2–) is not. Therefore, the efficiency ratio between treatments must be evaluated to solve this issue.

Efficiency ratio

The efficiency index allows us to assess and compare different scenarios in the decision quadrant by showing us how much the better clinical benefit is against its price. The greater the efficiency ratio, the better and is calculated as follows:

Equation 7. Efficiency ratio: $E_{ratio} = \frac{S_{T,I} - S_{T,C}}{C_{T,I} - C_{T,C}}$; S_T refers to survival rate and C_T is the annualized cost of the treatment where the subscript I stands for innovative treatment and the C for the comparator.

Results

The information shared by the INCAN and the CHMH shows the number of annual patients and the distribution by stage and molecular subtype in each institution (Table 1).

In addition, 5-year survival was estimated by stage and patient type in each institution (Table 2). The cost of each procedure was obtained through secondary research considering prices from 2019 and adjusted for inflation, with which the total cost per stage and type of

Table 1. Distribution of patients by stage and molecular subtype at the National Cancer Institute and the Centennial Hospital Miguel Hidalgo

Institution	Molecular subtype	Number of patients by stage			Number of patients by subtype (%)
		Early stage (%)	Locally advanced stage (%)	Metastatic stage (%)	
INCAN	HR–/HER2–	32 (5)	71 (12)	7 (1)	110 (18)
	HR+/HER2–	182 (30)	171 (28)	20 (3)	373 (62)
	HR+/HER2+	15 (2)	36 (6)	0 (0)	51 (9)
	HR–/HER2+	10 (2)	54 (9)	2 (0)	66 (11)
	Total (%)	239 (40)	332 (55)	29 (5)	600 (100)
CHMH	HR–/HER2–	8 (7)	14 (11)	3 (2)	25 (20)
	HR+/HER2–	27 (22)	44 (37)	8 (7)	79 (65)
	HR+/HER2+	2 (2)	4 (3)	1 (1)	7 (6)
	HR–/HER2+	3 (3)	5 (5)	1 (1)	9 (8)
	Total (%)	40 (34)	67 (56)	13 (10)	120 (100)

INCAN: National Cancer Institute; CHMH: Centennial Hospital Miguel Hidalgo; HR: hormone receptor; HER: human epidermal growth factor receptor.

Table 2. Estimated 5-year survival with current management by type of patient at the National Cancer Institute and the Centennial Hospital Miguel Hidalgo

Institution	Molecular subtype	5-year estimated survival by breast cancer stage			5-year estimated survival by subtype (%)
		Early stage (%)	Locally advanced stage (%)	Metastatic stage (%)	
INCAN	HR–/HER2–	89	77	13	76
	HR+/HER2–	91	79	17	82
	HR+/HER2+	89	86	24	87
	HR–/HER2+	87	84	24	83
	Total	90	81	17	81
CHMH	HR–/HER2–	89	77	14	75
	HR+/HER2–	92	79	17	77
	HR+/HER2+	89	85	32	81
	HR–/HER2+	88	86	32	81
	Total	91	79	19	77

INCAN: National Cancer Institute; CHMH: Centennial Hospital Miguel Hidalgo; HR: hormone receptor; HER: human epidermal growth factor receptor.

patient was estimated, as well as the total cost of breast cancer management in both institutions (Table 3).

Moreover, an analysis of the clinical and economic impact was carried out to measure the inclusion of six innovative treatments in each institution. The clinical impact was measured considering the difference between the survival time of the innovative treatment and the comparator, while the budgetary impact measured the relative increase over the total cost of breast cancer management. Both calculations were segmented by stage and molecular subtype and were used to estimate the efficiency ratio (Tables 4 and 5).

It is noteworthy to mention that each letter represents a current treatment regimen under consideration by

Table 3. Current annualized cost of breast cancer management by stage at the National Cancer Institute and the Centennial Hospital Miguel Hidalgo

Institution	Molecular subtype	Current annualized cost of breast cancer management by stage (USD)			Current cost of breast cancer management by molecular subtype (USD)*
		Early stage	Locally advanced stage	Metastatic stage	
INCAN	HR–/HER2–	$ 0.20 M USD	$ 0.43 M USD	$ 0.04 M USD	$ 0.67 M USD
	HR+/HER2–	$ 0.78 M USD	$ 1.19 M USD	$ 0.13 M USD	$ 2.09 M USD
	HR+/HER2+	$ 0.37 M USD	$ 1.62 M USD	-	$ 1.99 M USD
	HR–/HER2+	$ 0.34 M USD	$ 2.16 M USD	$ 1.7 K USD	$ 2.49 M USD
	Total	$ 1.69 M USD	$ 5.41 M USD	$ 0.17 M USD	$ 7.25 M USD
CHMH	HR–/HER2–	$ 0.05 M USD	$ 0.10 M US	$ 0.01 M USD	$ 0.17 M USD
	HR+/HER2–	$ 0.15 M USD	$ 0.27 M USD	$ 0.17 M USD	$ 0.59 M USD
	HR+/HER2+	$ 0.07 M USD	$ 0.16 M USD	$ 0.05 M USD	$ 0.29 M USD
	HR–/HER2+	$ 0.09 M USD	$ 0.29 M USD	$ 0.07 M USD	$ 0.46 M USD
	Total	$ 0.37 M USD	$ 0.83 M USD	$ 0.30 M USD	$ 1.51 M USD

INCAN: National Cancer Institute; CHMH: Centennial Hospital Miguel Hidalgo; HR: hormone receptor; HER: human epidermal growth factor receptor. *Original figures in Mexican Pesos, 20.2032 MXN=1 USD.

Table 4. Clinical and economic impact of the inclusion of innovative treatments in the National Cancer Institute

Subtype and disease stage	Analyzed treatment**	Indicated Patients	Absolute impact on 5-year survival in patient subtype	Additional budgetary impact (USD)*	Efficiency ratio
HER2+/HR–in early stage	A	8	+ 5%	+ $ 0.40 M USD	0.126
HER2+in locally advanced stage	A	82	+ 1%	+ $ 2.71 M USD	0.004
	B+C	82	+ 1%	+ $ 0.40 M USD	0.025
HER2+in metastatic stage	A	3	+ 23%	+ $ 0.28 M USD	0.813
	B+C	0	+ 2%	+ $ 0.06 M USD	0.318
HER2–/HR+in metastatic stage	D+E	20	+ 6%	+ $ 0.44 M USD	0.136
	D+F	17	+ 4.7%	+ $ 0.23 M USD	0.200
	F	20	+ 1.3%	+ $ 0.17 M USD	0.080
	G	2	+ 0.4%	+ $ 0.04 M USD	0.100

*Original figures in Mexican Pesos, 20.2032 MXN=1 USD, **Each letter represents a current treatment regimen under consideration by INCAN. However, their specific names have been withheld since the primary objective of this paper is to provide an assessment methodology (oppositely to a direct comparison of specific oncological treatments) and to avoid any possible conflict of interest. Furthermore, this information was obtained directly from each health-care center database since due to a variety of reasons, each had access to different kinds of treatments, however, both treatment offerings were based on national clinical guidelines for the public sector.
HR: hormone receptor; HER: human epidermal growth factor receptor.

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As can be observed, figures 3 and 4 are the result of the methodology.

Table 5. Clinical and economic impact of the inclusion of innovative treatments in the Centennial Hospital Miguel Hidalgo*

Subtype and disease stage	Analyzed treatment***	Indicated patients	Absolute impact on 5-year survival in patient subtype	Additional budgetary impact (USD)**	Efficiency ratio
HER2+/HR–in early stage	A	3	+ 3%	+ $ 0.15 M USD	0.205
HER2+in locally advanced stage	A	7	+ 0.3%	+ $ 0.22 M USD	0.014
HER2+in metastatic stage	A	2	+ 6%	+ $ 0.08 M USD	0.716
HER2–/HR+in metastatic stage	B+C	2	+ 1.1%	+ $ 0.04 M USD	0.263
	D	6	+ 0.8%	+ $ 0.05 M USD	0.153
	E	1	+ 0.3%	+ $ 0.02 M USD	0.143

*The results of worst clinical outcomes of alternative treatments compared to the current algorithm or those which do not have candidate patients are not shown, **Original figures in Mexican Pesos, 20.2032 MXN=1 USD, ***Each letter represents a current treatment regimen under consideration by CHMH. However, their specific names have been withheld since the primary objective of this paper is to provide an assessment methodology (oppositely to a direct comparison of specific oncological treatments) and to avoid any possible conflict of interest. Furthermore, this information was obtained directly from each health-care center data base, since due to a variety of reasons, each had access to different kinds of treatments, however, both treatment offerings were based on national clinical guidelines for the public sector. HR: hormone receptor; HER: human epidermal growth factor receptor.

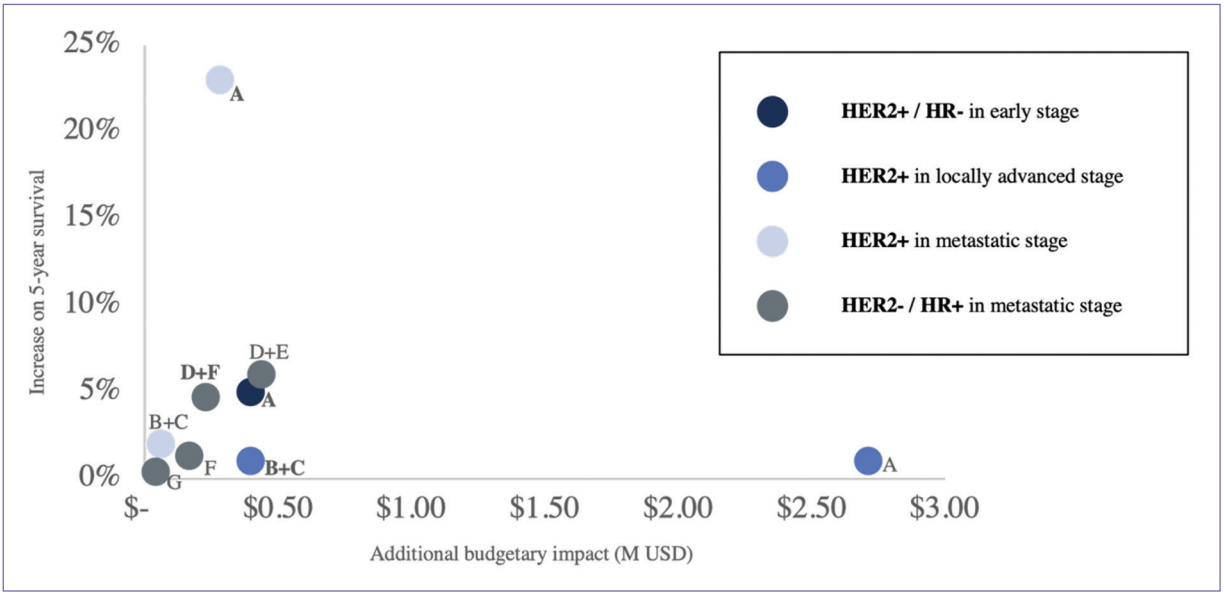

Figure 3. Decision quadrant for INCAN considering the increase in 5-year survival and additional budgetary impact due to the change in breast cancer treatment by molecular subtype and stage. INCAN: Instituto Nacional de Cancerología.

Discussion

Given the increasing prevalence of breast cancer, it is essential to have methodologies that help optimize the management of resources allocated for this disease. The priority, of course, is access to treatment with the best possible clinical impact; however, the budget is limited, so it is essential to have an objective tool to support informed decision-making by the service providers.

In the case of INCAN and patients with HER2–/hormone receptor-positive (HR+) in metastatic stage breast cancer, the treatment that has the greatest clinical benefit is D + E, however, it is not the most cost-efficient, that would be D + F by the efficiency index. In the same health-care center but with HER2+ in metastatic stage patients, the visual representation of the decision matrix allows a clear result that A is more cost-efficient by far compared to the B + C regimen. With the INCAN model, the decision-maker can assess not only the

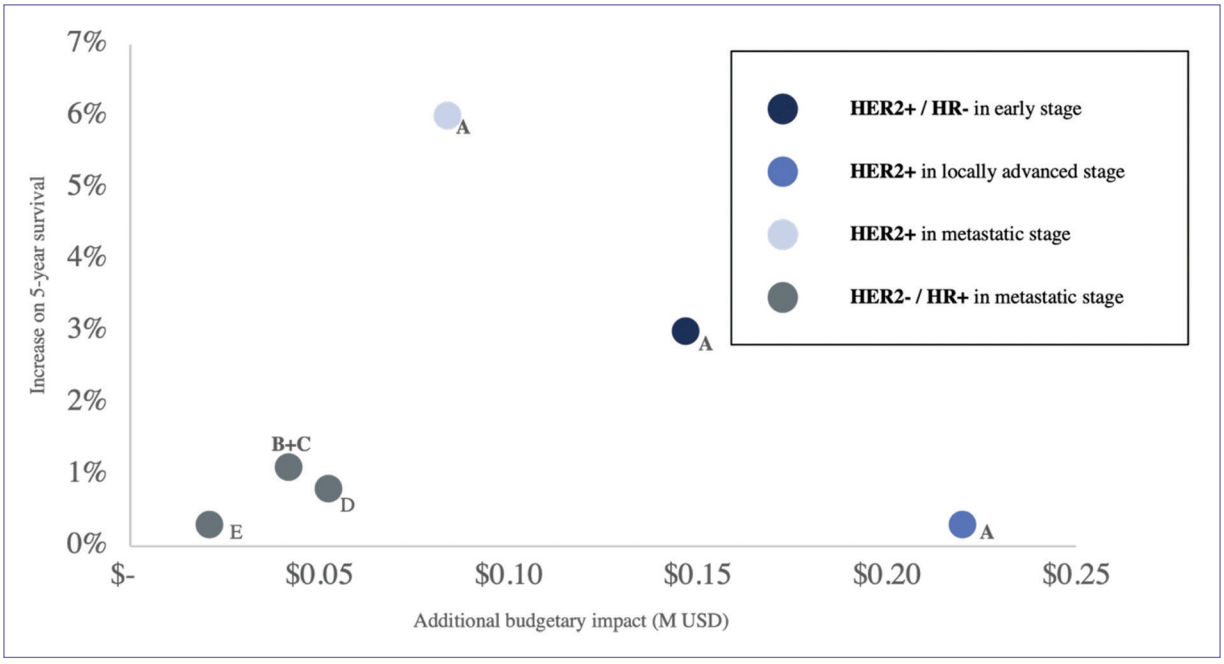

Figure 4. Decision quadrant for CHMH considering the increase in 5-year survival and additional budgetary impact due to the change in breast cancer treatment by molecular subtype and stage. CHMH: Centennial Hospital Miguel Hidalgo.

most cost-efficient treatment but also the budget impact of the increased benefit with the efficiency coefficient. This is useful for the case when there is not any other comparator, as in the case of HER2+/hormone receptor-negative (HR–) in early-stage patients where A is the only available treatment that increases the 5-year survival.

For the analysis of the CHMH, it can be observed in figure 4 that for HER2+/HR– in early stage, HER2+ in locally advanced stage, and HER2+ in metastatic stage patients, there is only one treatment that provides increased clinical benefit. Furthermore, it is noteworthy the difference in clinical benefit of treatment A depending on the specific patient characteristics. That's why is important to consider every stage separately because for some stages, it may make sense the investment and for others not. This depends on the willingness to pay for the increased benefit of every player or health-care provider. The only patients with several options for treatment improvement are the HER2–/HR+ in metastatic stage, and in this case, the most efficient treatment is also the one that brings the most clinical benefit.

It is important to notice that while in this real-world data analysis of Mexican institutions, we used data from 2019, this exercise was only to illustrate its usefulness as a decision-making tool in real-world health-care centers that is currently used. All interested centers are welcome to use this methodology to evaluate its expenditure in a specific subset of patients, a certain stage, or its complete line of treatment for breast cancer as well as other areas where it may apply. Another noteworthy observation is that while in this case, we used as clinical benefit the absolute impact on 5-year survival, any other clinical benefit of the most interest for the health-care center could be used for assessing its cost-benefit analysis with the methodology proposed.

Furthermore, it is important to address the effects that the incidence of each cancer subtype may present on the decision model presented. While the model does not consider as input the incidence or prevalence of the studied population, only the molecular types presented at the healthcare center, the incidence of any center is not relevant to the calculation of the efficacy of capital allocation in each center. However, it can clearly evaluate the most efficient course of action regarding the best budget allocation option of each type of cancer. With this in mind, the financial decision maker now has the optimal option for its treatment expenditure. If the budget is not enough for the affordability of the recommended treatment options by the model, then the decision maker must assess a course of action taking into consideration the prevalence/incidence of its health-care choosing to maximize overall coverage among its

patients or aggregated clinical benefit. While the solution of this decision is out of scope for this model, now, the decision maker has a framework for which the most efficient expenditure could be made for each cancer subtype and available treatments on its center.

A possible limitation of this article could be found in the estimation of the clinical impact, which is measured purely by survival time. As previously mentioned, it can be arguable that there are other indicators to measure this impact, which are more related to health-related quality of life.

While in this real-world evidence and data analysis, we only considered drug treatments for the methodology, other variables or interventions may be taken into consideration to increase the efficiency of the resources at the disposal of a health-care center.

Conclusion

In conclusion, we presented a methodology already used in two health-care centers in Mexico as an evaluation tool for making decisions about adjustments in current treatments or the acquisition of new innovative pharmacological treatments by stage and molecular subtype (HER2 and HR) of breast cancer patients or adjustments in treatment procedures (surgeries, genetic diagnoses, etc.) The proposed methodology allows the allocation of resources to be optimized, considering the current epidemiological and economic situation of each payer, as well as estimating potential scenarios for the inclusion of new health technologies in current treatment schemes.

The improvement in the clinical impact, with budgetary impact control, is a challenging problem that must be solved by requiring strategies from various areas of management. This methodology provides one for health-care centers, specifically for key decision-makers such as managers or service line directors in charge of assessing the investment cost-efficiency of new treatments against its budget impact.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that for this research, they have not been performed experiments on humans or animals.

Data confidentiality. The authors declare that in this article, there is no data on patients.

Right to privacy and informed consent. The authors declare that in this article, there is no patient data appears.

Use of artificial intelligence to generate texts. The authors declare that they have not used any type of generative artificial intelligence in the writing of this manuscript nor for the creation of figures, graphics, tables, or their corresponding captions or legends.

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