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# Ethical Concerns Regarding Breast Cancer Screening

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## Abstract

The incidence and mortality of breast cancer are rising in the whole world in the past few decades, adding up to a total of around two million new cases and 620,000 deaths in 2018. Unlike what occurs in developed countries, most of the cases diagnosed in the developing world are already in advanced stages and also in women younger than 50 years old. As most screening programs suggest annual mammograms starting at the age of 50, we can infer that a considerable portion of the new breast cancer cases is missed with this strategy. Here, we will propose the adoption of an alternative hierarchical patient flow, with the creation of a diagnostic fast track with referral to timely treatment, promoting better resources reallocation favoring the least advantaged strata of the population, which is not only ethically acceptable but also a way of promoting social justice.

**Keywords:** breast cancer, screening, mammogram, public health, ethics

## 1. Introduction

According to data from the World Health Organization (WHO), the number of deaths due to cancer will increase up to 45% between 2008 and 2030 and 70% of those deaths will occur in developing countries [1]. To try and change this scenario, the WHO recommends the implementation of cancer control programs that must include cost-effective measures on healthy life style, vaccination programs and screening programs [2]. A screening program consists in a set of coordinated actions with the objective of reducing cancer mortality through early stage diagnosis in an asymptomatic population, with adequate referral to diagnostic and treatment facilities. These programs have four main components: the definition and recruitment of the target population, adequate offer of diagnostic tests with quality assurance, guaranteed offer of follow up exams and biopsies to confirm findings from the initial diagnostic tests, and referral to treatment facilities and timely navigation through the health system [3]. Although screening programs present the potential benefit of reducing mortality, they are not risk-free. The main risks of such a program are the false-positive and false-negative results, and also the occurrence of over diagnosis. All these can lead to clinical and psychological repercussions and, also, to the increase in the health care system expenditure. To address this issue, the Public Health Agency of Canada performed a study to estimate the harms

of the local breast cancer-screening program in 7 years, according to age, and the main results can be seen in **Table 1** [4].

In this text, we will use Brazil as a model to discuss screening programs in the developing countries. In the Brazilian setting, breast cancer is the most frequent type of cancer, responsible for 16,724 deaths in 2017 and with an estimate of 66,280 new cases in 2020 [5]. This scenario, however, has some peculiarities when compared to developed countries in the North America or Europe; 41.1% of all cases in Brazil happen in women younger than 50 years old and the majority of the operable cases is diagnosed in locally advanced stages, being 53.3% of the cases in stage II and 23.2% in stage III [6]. These characteristics are not typical of a country with a well-established breast cancer-screening program. The strategy adopted in Brazil states that women over 50 should get a mammogram every two years between 50 and 69 years old [7]. However, due to the early age of diagnosis that we observe in this developing country, we can argue that more than 40% of the diagnosed women are not eligible to the screening program in the first place. Moreover, the late presentation at diagnosis raises the hypothesis that the current screening program is not effective or that the patients do not have proper access to it. Added to that, the mortality due to breast cancer in Brazil has been increasing in the last decades [8]. All these issues taken together generate an ethical dilemma to be explored, once the investment of public resources in an ineffective program impacts negatively the whole society. This way, more effective resources reallocation strategies should be implemented to address this dilemma.

In this chapter we will discuss the breast cancer screening programs in developing countries and the main evidence regarding the barriers in the access to the healthcare system. Beyond that, we will address the main ethical questions related to breast cancer screening from the Rawls’s distributive justice [9] perspective, from the utilitarianism concepts [10, 11] and from the principles of autonomy and non-maleficence. Lastly, we will propose the support to an alternative approach to breast cancer in developing countries, maximizing the cost–benefit ratio in the use of public resources.

Age Range	40–49 years old	50 to 59 years old	60 to 69 years old	70 to 74 years old
Screening strategy	Annual mammogram	Mammogram every two years	Mammogram every two years	Mammogram every two years
Women that will not have cancer	993	988	979	968
Women that will have cancer	7	12	21	32
Unnecessary biopsies	43	37	35	30
False-positive results	294	294	256	219
Overdiagnosis	3	3	No reliable data	No reliable data
Deaths prevented by screening	<1	1	1	2
Number needed to screen to prevent one cancer-related death	1724	1333	1087	645

**Table 1.**  
*Benefits and harms of mammographic breast cancer screening [4].*

## **2. Recommendations to breast cancer screening around the world**

The U.S. Preventive Services Task Force (USPSTF) is an independent volunteer panel of American experts that develops recommendations regarding the efficacy of preventive services to asymptomatic patients. These recommendations are based on both benefits and harms that programs might cause, without consideration to the cost of the intervention. Current data about mammographic screening are solid regarding the benefits of this strategy when used in women over 50 years old and the USPSTF recommends a mammogram every two years, in women between 50 and 74; however, this same agency does not consider that there is enough evidence to support mammographic screening from 40 to 49 years old in asymptomatic patients without increased risk to breast cancer [12]. This recommendation is due to the fact that screening in this age range results in a smaller number of prevented deaths when compared to more advanced ages; also leads to a larger number of unnecessary biopsies; and to the possibility of psychological problems, like anxiety, because of the large number of false-positive results. While mammographic screening of 10,000 asymptomatic women between 50 and 59 years old can prevent 8 breast cancer deaths, the same strategy adopted in asymptomatic women between 40 and 49 years old would prevent only 3 breast cancer deaths [13, 14]. Another harm associated with mammographic screening of an asymptomatic population considered by the USPSTF when issuing their recommendation is the occurrence of over diagnosis. Although it is extremely complex to calculate the proportion of diagnosed cases that would never evolve to cancer, the best estimates from randomized clinical trials suggest the occurrence of over diagnosis in 20% of the cases due to mammographic screening [15].

Another agency that carefully evaluated the cost–benefit ratio of mammographic screening in asymptomatic women between 40 and 49 years old was the Ontario Health Technology Advisory Committee through a systematic review of the literature [16]. This work included an evaluation of the USPSTF report [17], the Canadian Preventive Services Task Force (CPSTF) report [18], a Cochrane systematic review [19], five health technology assessments and eight randomized clinical trials [20–27] with the objective to assess the reduction of the breast cancer mortality in this age range attributable to mammographic screening. This agency reached a similar conclusion as the USPSTF that the mammographic screening in an asymptomatic population between 40 and 49 years old is not effective in reducing breast cancer mortality and that the harms associated with this intervention, like exposure to radiation, high rate of false-negatives leading to delays in diagnosis and high rate of false-positives with associated psychological harmful effects should not be overlooked.

The Brazilian College of Radiology (BCR) and Brazilian Society of Mastology (BSM) however issued a different recommendation, based on different published articles of international literature and methodologically inferior to the ones evaluated and with a clear selection bias [25, 28, 29]. In these studies, it was demonstrated a breast cancer mortality reduction between 18% and 38% in the studied populations. The main point to justify the recommendation of mammographic screening for asymptomatic women between 40 and 49 years old is to emphasize that in this developing country there is a higher proportion of breast cancer patients in this age range when compared to developed countries [30]. Despite the fact that it is a recommendation for Brazil, it did not include a single Brazilian study in the analysis. This scenario is repeated throughout Latin America as it has been shown in a report by The Economist Intelligence unit. Cancer care registries are lacking in Latin America due to insufficient coverage of the population and also due to low quality [31]. Without local high-quality data, it is impossible to perform local health technology assessments and the decision-making process is jeopardized.



### 3. Ethical implications of mammographic screening

Carefully considering the recommendations of these three different countries with very diverse populations, we can conclude that although mammographic screening in women between 40 and 49 provide a modest benefit in reducing breast cancer mortality, the occurrence of adverse effects is more pronounced.

We can also note that the BCR and BSM adopt a paternalistic approach, reflecting the principle of beneficence. In the meantime, the USPSTF and the CPSTF advocate that the screening decision should be shared with the patient. This way, patients that are more risk averse could opt out of the screening program and patients that value more the potential benefits could opt in, following the principles of non-maleficence and autonomy. However, what we must ask is whether it is possible to convey important information regarding the risks associated with a screening program in a clear and, more important, neutral manner. In this sense, it is of utmost importance that the autonomy principle is respected and that patients are not manipulated to undergo tests or treatments which they do not agree with, due to the use of biased information.

Addressing this issue, Biddle introduced the concept of epistemic risk, defined as the risk of error that comes up at any moment in the process of knowledge production [32]. These errors can happen because of biases during the data collection step and also because of decisions made in scenarios of uncertainty. These decisions reflect the set of values of the involved researchers and have consequences to human health and to the definition of public policies. Rudner agrees with this argument and suggests that it's impossible to prove any hypothesis with full certainty, as there is always a possibility of error. This way, researchers must judge what is the necessary amount of data to accept or reject a hypothesis and this judgment depends on the set of values of the researcher and on the importance of the consequences an error can lead to [33]. Pramesh et al. discuss such a conflict in depth when they justify the necessity of a randomized clinical trial to prove a hypothesis raised by a cross-sectional study, as they believe the data gathered in the latter is not sufficient to support the decision-making process [34].

The reasoning to support a mammographic screening program for asymptomatic women below the age of 50 is not free of the risk of epistemic risks. One kind of epistemic risk associated with mammographic screening is the inductive risk, defined as the risk of incorrectly accept or reject a hypothesis based on the available evidence [35]. Breast surgeons must accept or reject that a patient has a disease, frequently a ductal carcinoma *in situ* (DCIS), that will evolve causing symptoms and death based on evidence that does not guarantee the veracity of this hypothesis. That happens mostly because of the lack of evidence to predict which cases of DCIS will evolve to become invasive carcinomas. Another epistemic risk, the one in the gathering of data of breast biopsies, occurs in the evaluation of the differential diagnosis between atypical hyperplasia and DCIS. While the first ones are treated with a small surgical procedure, the latter requires surgical excision followed by radiation therapy and, in some cases, endocrine therapy for 5 years. This way, an error committed by the pathologist might lead to an enormous impact in the treatment of the patients. As pathologists have different formations and different experience backgrounds, and as the biopsy evaluation is a subjective process, this is an epistemic risk that is hard to be assessed. In order to try and decrease the odds of such an error is the development of image analyses software. Mercan et al. evaluated 240 breast biopsies comparing the performance of three experienced pathologists and an automated image analysis method. In this study, the automated method performed better than the pathologists in differentiating atypical

hyperplasia and DCIS, becoming a promising alternative for the near future [36]. As we saw in these two examples, the information conveyed to the patients eligible to screening are not obtained in the absence of the researchers personal judgment and values. Thus, more than just respecting the autonomy principle in the shared decision-making process, healthcare workers must convey not only the necessary information but also their values and personal beliefs used by them to define their diagnostic and therapeutic decisions. As long as there is ambiguity in the results of mammographic screening studies in asymptomatic women below the age of 50, the priority should be debating the advantages and disadvantages of this strategy, instead of discrediting their opponents [37].

#### 4. Current situation of mammographic screening

In Brazil, as in many developing countries, there is no public policy to the implementation of an organized mammographic screening program. As mentioned previously, there is a recommendation from the Brazilian National Cancer Institute (INCA) for mammogram every two years for women between 50 and 69 years old [7] and the main medical societies recommend an annual mammogram for women starting at 40 years of age [30].

This difference in recommendations happens due to complex interactions between the country's decision makers' interests, beliefs, perspectives and personal values. In the present scenario, with this disparity of recommendations, patients present late stage diagnosis, worse than the ones observed in Norway before the implementation of the local mammographic screening program (**Table 2**) [38].

To evaluate the necessity to expand the INCA's recommendation to other age ranges, Brito et al. analyzed all breast cancer cases, all DCIS cases and all breast cancer related deaths in the city of Aracaju between 1998 and 2014, dividing pages according to age groups [39]. The breast cancer incidence trends remained stable over the studied period across all age groups. Both incidence and cancer-specific mortality in that municipality were similar to the ones observed in countries with the same human development index. The authors concluded that, as these rates remained stable in all age groups, including the ones in which screening is recommended, the investment of public resources to screen women below the age of 50 or over the age of 69 is not justifiable.

A broader study by Rodrigues et al. evaluated retrospective data regarding mammograms between 2008 and 2016 in the public health system [40]. Around nineteen million mammograms were performed in this period with an increase in coverage of 14.5% annually between 2008 and 2012 followed by a stable period

Stage	Brazil (n = 22,527)	Norway (n = 26,883)
I	21.3%	48.5%
II	35.2%	38.5%
III	25.2%	5.3%
IV	8.9%	6.5%
Unknown	1.6%	—

*Adapted from Tiezzi et al. [38].*

**Table 2.**  
*Prevalence of breast cancer according to stage in the state of São Paulo between 2000 and 2017, and in Norway before the implementation of mammographic screening.*

between 2012 and 2017. The population coverage of mammogram varied in the period from 14.4% to 24.2% of the target population. This number is far from the 70% coverage recommended by the WHO, necessary to effectively reduce breast cancer-specific mortality [41]. Rodrigues et al. also evaluated the number of mammogram machines available in the country, their geographical distribution and the total number of exams performed in 2016 [42]. In this study, it was demonstrated that Brazil has 4628 machines with a capacity of 14,279,654 exams per year. In 2016, however, only 4,073,079 exams were performed, 29% of the total capacity, displaying a clear under-use of the available infrastructure. The low coverage of the target population with the stable trend in the past few years associated with the under-use of the available infrastructure raises the hypothesis of the existence of barriers to access to the healthcare system.

The Barretos Cancer Hospital adopted an alternative to improve the coverage of the screening program with the use of mobile mammogram machines in trucks reaching 108 municipalities in the northeastern region of São Paulo, targeting women between 40 and 69 years old. Greenwald et al. evaluated the efficacy of this initiative from 2010 to 2015 [43] and, in this period, 122,634 women were evaluated with a coverage of 54.8% of the target population, referral of 12.25% of these women were referred for additional exams with a cancer detection rate of 3,63/1000 women. 92.51% of the referrals to treatment centers were successfully accepted. The results obtained by this program are very promising, showing the potential to be expanded to other regions and other countries.

## **5. Barriers to access the healthcare system**

Brazil is a developing country with a population of 209.3 million inhabitants with enormous social and economical disparities between its 5 regions [44]. Moreover, there are also inequalities in the distribution of human resources and health infrastructure with a significant variation in the number of hospital beds and physicians dedicated to oncological patients leading to significant differences in health outcomes [8]. Another source of outcome variability is the duality of access to the healthcare system. Every Brazilian citizen has unrestricted access to the public health system (PHS) and the richer portion of the population also has access to private healthcare providers through out-of-pocket direct expending or through healthcare insurance companies. This duality of the system is perverse in a way that it perpetuates the idea that a small portion of the population has access to state-of-the-art diagnostic and treatment facilities while the majority of the population, around 71%, depends exclusively on the PHS with all its limitations. When comparing this two scenarios, we observe a striking difference in the initial stage of the breast cancer patients; the majority of the patients seen in the private setting is diagnosed with early stage tumors, whereas the majority of patients that depend on the PHS is diagnosed with locally advanced tumors [45], a clear indication that difficulties to access the healthcare system are the main obstacles to early detection. 37% of the breast cancer cases diagnosed in the PHS are stage III or IV while in the private sector this number falls to 16.2% [46]. These data are corroborated by national studies that showed intervals of 75 to 185 days between initial symptom presentation and initial biopsy [45] and a median interval of 113.4 days between indication and initiation of radiation therapy [47]. For comparison purposes, patients seen in the private setting can have diagnostic tests and start treatment in less than 30 days.

To identify the main barriers to access to the PHS, Vieira et al. conducted a systematic review of the literature identifying 30 publications on this topic [48].



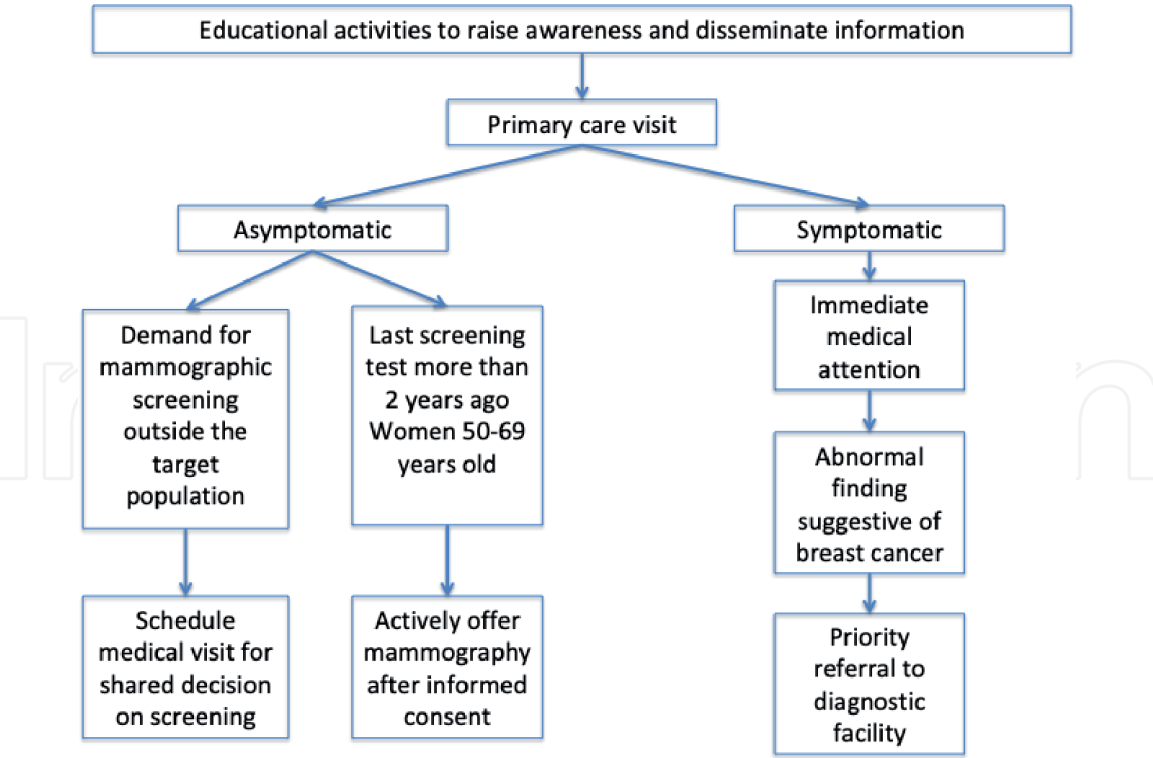
In a general analysis, it has been identified an underuse of mammogram machines on the north and northeast regions of the country and a mammogram coverage of only 35% of the Brazilian women, most of them in the private setting. The main issues related with not having a mammogram performed are non-white ethnicity, low educational level, low familiar income and not having health insurance. Another interesting finding of this study is that normally the treatment of breast cancer is performed in big cities and patients end up traveling more than 100 miles from their residences to the hospitals [49]. Even before the start of treatment, patients have to face delays of more than 60 days in 36.9% of the cases, because of inefficient referral and navigation. The main issues related with delays in the initiation of treatment were non-white ethnicity, not having a partner, low educational level, early stage breast cancer and dependence of the PHS [50]. Exclusive dependence on the PHS and non-white ethnicity were also associated with higher breast cancer-specific mortality [51].

## 6. Recommendation and discussion of the ethical dilemma

Considering the inefficacy of the screening programs in developing countries and the lack of solid evidence supporting screening of asymptomatic women below the age of 50 years old, we recommend resources reallocation to improve access to the healthcare system and the implementation of a fast track between diagnostic and treatment facilities to symptomatic patients, based on the hierarchical flow proposed by Migowski et al. (**Figure 1**) [52]. This algorithm proposes three different actions: educational activities in primary care facilities to raise awareness regarding breast cancer and also the potential benefits and harms of mammographic screening; to offer the option of screening mammogram to asymptomatic women aged 50 to 69 during their visit to the primary healthcare provider; and to promote priority access to symptomatic patients, without the need of prior scheduling, in which the ones with suspicious lesions will be referred to diagnostic facilities. This recommendation is supported by Rawls' two principles of justice [9]. The first principle governs that all persons have equal rights and freedoms. The second principle governs that the adoption of policies that generate social or economical inequalities is only acceptable if it favors the least advantaged portion of society. The promotion of educational activities proposed by Migowski et al. [52] is supported by Rawls' first principle since it standardizes the access to a basic right, education. The second part of the recommendation is justified by Rawls' second principle of justice. The adoption of a fast track to symptomatic patients, removing the need of a prior appointment or referral, promotes the reallocation of public resources to remove barriers in the access to care, reducing delays in diagnosis and treatment and, therefore, reducing inequalities in favor of the least advantaged part of the population that relies solely in the public health system. Although the recommendation favors a part of the population, it does not violate individual rights, as asymptomatic patients will still have access to screening mammogram in their routine visits to their primary healthcare providers. Moreover, the proposed recommendation promotes equal access to breast cancer diagnosis and treatment as it removes the age boundaries, starting to provide care to women below the age of 50 years old, an age range responsible for a large amount of new cases in developing countries and that were not previously included in the past recommendation [6].

Let us consider for a moment a hypothetical scenario in which the healthcare system works perfectly without any access barriers. Even in this setting, mammographic screening as it is currently suggested would not be ideal in developing countries. The current evidence that recommends mammographic screening is not





**Figure 1.** Hierarchical flow to promote early diagnosis and treatment of breast cancer. Adapted from Migowski et al. [52].

unanimous and large randomized clinical trials did not show a robust mortality reduction attributable to it [13, 53]. Moreover, even if these studies showed a significant mortality reduction attributable to screening mammogram, their results would hardly be applicable to the developing countries’ realities. Those studies were conducted in countries with high human development index (HDI) and in the context of organized screening. Brazil and most developing countries have lower HDIs and promote opportunistic screening due to the weak organizational structure of the healthcare system. This way, the international studies that assessed the effectiveness of mammographic screening lack the necessary external validity to be applied in developing countries. A recent article published by Vale et al. suggested, that the opportunistic screening program employed in the state of São Paulo, Brazil, promoted an increase in early stage diagnosis without, however, presenting data regarding mortality reduction [54]. Without data showing mortality reduction attributable to the screening program it is impossible to conclude whether this model is effective or not. Adding up to that data we have some concerning facts associated with screening women between the age of 40 and 49; we observe that less than one death from breast cancer is avoided for every one thousand screening mammograms performed; two hundred and ninety-four false-positive results (**Table 1**) generate additional diagnostic procedures leading to economical impact to the health system and also physical and psychological impacts to the patients. Based on everything that was exposed in this paragraph, we can conclude is not adequate from Bentham’s and Mill’s utilitarianism perspective [10, 11].

In this context, with the shortage of resources to invest in an organized mammo-graphic screening program and without solid data to justify its implementation, can we accept a sub-optimal program? On the one hand, the inexistence of a screening program can lead to the increase in the number of cases diagnosed in late stages, for which the treatment options might be inaccessible and, sometimes, ineffective. On the other hand, developing countries, such as Brazil, sometimes lack the necessary infrastructure to perform timely screening mammograms to the whole eligible

population and the consequent breast biopsies of lesions identified through screening [55]. In order to consider a screening program adequate, it must be acceptable, accessible, and sustainable, it must promote equity and it must be economically efficient to the target population [56]. As it has been demonstrated in this chapter, the Brazilian mammographic screening program is not accessible, since the coverage does not reach 30% of the target population [42]. This program is not sustainable either since there is a huge delay between the identification of an abnormal mammogram and the necessary biopsy to confirm the diagnostic. Due to the incapacity to adequately follow-up and refer patients with abnormal findings, the risk of a false-positive result must be considered clinically and ethically relevant. Finally, it's been demonstrated that mammographic screening in developing countries is not cost-effective when compared to the alternative of treating patients with palpable initial lesions [57, 58]. Contemplating all these issues, Sedhom et al. argued that clinical examination of the breast with fast referral to avoid delays in diagnosis and treatment, although not a screening program, must be considered a more pragmatic and adequate choice than screening mammogram in developing countries [59].

## **7. Conclusion**

When weighing the benefits and harms of a mammographic screening program in a developing country, in a context where breast cancer-specific mortality has been increasing in the past few decades, it is extremely hard to justify increasing the age range to women aged 40 to 49 years old from an utilitarian perspective, since the amount of resources to establish and make the system work adequately is prohibitive. An alternative strategy that promotes easy access and fast referral of symptomatic patients, relegating a secondary role to mammographic screening, favors a larger and more vulnerable part of the population that depends solely on the PHS. This reallocation of resources to favor the least advantaged members of society is not only ethically justifiable but also a way of promoting social justice.

## **Conflict of interest**

Rodrigo Goncalves has received consultation fees from EMS Pharmaceuticals in 2019 and 2020 and from Novartis in 2019, not related to the topics of this chapter. The remaining authors do not have any conflicts of interest to disclose.

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