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Breast cancer control policies in Brazil: where to go from here?

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In three articles published in this issue, Migowski et al. introduce the new national guidelines for breast cancer control in Brazil ^{1,2,3}. This update is timely as it addresses long-held misconceptions, recent controversies, and new developments. The authors should be commended for having formulated these guidelines on the basis of an independent, transparent, and methodologically sound review of the published scientific evidence.

Breast cancer is a potentially curable disease if diagnosed and treated early. There are two different, but rather complementary, approaches to achieving this: (i) downstaging, i.e. by ensuring clinically detectable disease is diagnosed at an early stage and (ii) screening, i.e. through early detection of clinically occult disease, that is, before it causes symptoms or can be felt in a clinical examination (i.e. when tumor size is < 2cm).

Much of the updated national guidelines focuses on screening. Mammography is far from a perfect screening tool, being associated with benefits as well as harms (e.g. false-positives, overdiagnosis and overtreatment, and radiation-induced cancers). Nevertheless, the review of the published evidence by Migowski et al. confirmed that, despite recent controversies, the overall scientific evidence is consistent with mammographic screening reducing mortality from breast cancer by 20-25% among women invited to attend organized screening programs every two years between 50 and 69 years of age, with the benefits outweighing potential harms. These findings are in line with those from the International Agency for Research on Cancer (IARC) Working Group on breast cancer screening ⁴.

Mammographic screening programs have been established in many high-income countries (HICs) since the late 1980s, when findings from the earliest randomized trials were published. Since then there has been increasing pressure from national and international advocacy groups for healthcare systems in low/middle-income countries (LMICs) to emulate HICs. Such demand is, however, ill-judged because what works in HICs does not necessarily work in LMICs. Organized mammographic screening programs are complex, multi-disciplinary undertakings which, to be effective, require access to high-quality mammography, high coverage of the target population (at least 70% ⁵) with a call-recall system, timely access of women with screen-detected suspicious abnormalities to appropriate diagnostic and treatment services, as well as comprehensive built-in quality assurance mechanisms (e.g. trained healthcare workforce, standardized protocols, well-defined performance targets,

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and regular auditing procedures). Unfortunately, health systems in LMICs are too weak, lacking the infrastructure and human and financial resources to implement such large-scale programs. Thus, attempts to implement mammographic screening in these settings have resulted in opportunistic initiatives which are inequitable and much less effective than organized screening. Brazil is no exception – its 2004 national guidelines recommended that all women aged 50-69 years should undergo mammographic screening every two years ⁶ but, more than a decade later, the coverage in the target age group remains low (ranging from 27%, based on data from the Brazilian Unified National Health System or SUS ⁷, to 51%, based on self-reports from the *Brazilian National Health Survey* ⁸), with poor follow-up of suspicious radiological findings (27% at ages 50-59 and 63% at ages 60-69, based on SUS data ⁷). At the same time, due to increasing demand from advocacy and professional groups, resources are being diverted to screen women outside the target age group, particularly those under 50 years ^{7,9}, and to shorten the screening interval below the recommended two years ⁹, despite the fact that there is no evidence base demonstrating that these are associated with a favorable benefits:harms ratio. Similar experiences have been observed in other LMICs, leading the IARC Working Group to conclude that there is currently limited evidence that mammographic screening is cost-effective in such settings ⁴.

In HICs, organized screening programs were introduced at a time when symptomatic disease had already been successfully downstaged. For instance, in Norway only 20% of breast cancers were late-stage (TNM ¹⁰ stages III/IV) at diagnosis by the 1970s ¹¹, that is, almost two decades prior to the introduction of organized screening in this country. This contrasts markedly with the current situation in Brazil, where about 40% of breast cancer patients are diagnosed at a late stage, with this proportion having changed little since 2004, when the national screening guidelines were enacted ¹². Most women diagnosed with late-stage disease would have had symptoms for a considerable time. In HICs, the time interval from symptom recognition to diagnosis is usually < 30 days ^{13,14}, but in Brazil this interval is much longer (median: ~7-8 months) ¹⁵. Delays ≥ 3 months are associated not only with late stage at diagnosis but also with poorer survival ¹⁶.

The large proportion of women being diagnosed at an advanced stage in Brazil, when treatment options are more limited and less effective, calls for downstaging to be regarded as the priority for breast cancer control policies. Ensuring that symptomatic breast cancer is diagnosed early markedly increases survival from the disease – e.g. 5-year survival in São Paulo State rises from 30% if the disease is diagnosed at stage IV to 82% if diagnosed at stage IIB ¹⁷. Downstaging is also likely to be more cost-effective than screening, for several reasons. First, resources will be concentrated on the small group of women with breast symptoms rather than on the much larger population of asymptomatic participants in a screening program, the large majority of whom will never develop breast cancer. Second, the health care requirements necessary for the diagnosis of clinically detectable disease are far less complex than those required to diagnose asymptomatic disease. Third, it is early treatment, not early detection per se, that saves lives. Thus, for mammographic screening to be effective, women who are found to have suspicious lesions must be promptly investigated (e.g. by undergoing repeat mammography, ultrasound, and/or biopsy), and if a breast cancer diagnosis is confirmed, they must be properly treated. Only a strong, well-organized cancer care system that can deal appropriately with symptomatic disease is able to cope with the additional burden associated with the management of a large volume of women with screen-detected suspicious lesions.

Migowski et al. acknowledge that the 2004 national guidelines⁶ focused unduly on mammographic screening. Their updated guidelines offer a welcome, and rather overdue, departure from this by recognizing for the first time the importance of downstaging symptomatic disease, and by reviewing strategies to achieve this. However, successful strategies in Brazil may differ from those used elsewhere; indeed, different strategies may be required across such a vast and ethnically and socioeconomically diverse country. Studies mapping a woman's journey from symptom recognition to breast cancer diagnosis and treatment in different settings will identify the reasons for delays and key modifiable barriers in access to cancer diagnosis and treatment. Such investigations will provide the basis for the development, evaluation, and implementation of locally appropriate and culturally sensitive approaches to downstaging breast cancer in Brazil.

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