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Global disparities in breast cancer outcomes: new perspectives, widening inequities, unanswered questions

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Breast cancer is the most common neoplastic disease and leading cause of cancer mortality in women.[1] Global estimates have recorded regional variations in the burden of breast cancer, but none have been disaggregated by menopausal status.[1] In *The Lancet Global Health*, Emily Heer and colleagues[2] contribute to the body of evidence on global disparities in outcomes, with particular reference to breast cancer incidence and survival by menopausal status and by a country's human development index (HDI). Heer and colleagues show that, although the incidence of postmenopausal breast cancer was much higher in countries with a very high HDI (age-standardised incidence 253·6 cases per 100 000, *vs* 91·5 cases per 100 000 in low HDI countries), countries with a low HDI had the highest burden of premature deaths from breast cancer (premenopausal age-standardised mortality 8·5 per 100 000, *vs* 2·8 per 100 000 in high HDI countries). Case fatalities from premenopausal and postmenopausal breast cancer were highest in low and medium HDI countries (>32% for premenopausal breast cancer and >54% for postmenopausal breast cancer). The widening mortality gap and growing inequities in access to affordable and quality treatment after a diagnosis of breast cancer in all regions of the world demand a global response.[3]

As shown by Heer and colleagues,[2] the increasing mortality gap within countries and across countries within the same region is striking. Key factors that are most likely contributing are population structure and differences in tumour biology and genomics among different populations, with the effect exacerbated by gaps in health systems and quality of care.[4] Although the genetic contributions of inherited mutations in cancer susceptibility genes such as *BRCA1* and *BRCA2* have been widely studied, most women with breast cancer have no identifiable genetic risk factor.[4] All global regions are recording increases in the incidence of premenopausal breast cancer, presumably linked to the epidemiological transition and changing reproductive patterns associated with increased risks of triple-negative breast cancer and human epidermal growth factor receptor 2 (*ERRB2*)-positive breast cancer. Unfortunately, both the looming epidemic of premenopausal breast cancer and presentation at advanced stages in low HDI countries have not received the attention deserved from the global scientific community. Conclusions on epidemiological and biological mechanisms should not be extrapolated from high HDI countries even though we also see a rising incidence of premenopausal breast cancer in these countries.[4] Compounding the paucity of locally relevant research are the health system gaps that will be further exacerbated by diversion of resources from chronic non-communicable diseases research to communicable diseases after the COVID-19 pandemic. Currently, there are neither effective screening nor therapeutic approaches optimised for women at risk of aggressive premenopausal breast cancer.[5] This absence underscores the need for large next-generation sequencing studies, clinical trials, and cancer control plans designed to provide optimal management of breast cancer in low HDI settings.

Thus, while acknowledging the novel insights that Heer and colleagues provide,[2] we assert that it is now necessary to critically explore unanswered questions with the aim of informing actions. First, some cancer registries have advanced to incorporation of molecular subtypes into their datasets. This move is important, in view of how breast cancer genomics clarify the differential epidemiological patterns.[6] However, most reporting countries still treat breast cancer as one disease entity, thus limiting the use of these data for efforts at improving precision cancer care. Obtaining data on breast tumour heterogeneity in diverse populations could inform actions to address this gap in breast cancer research. However, to obtain these data globally, systems for breast cancer genomic profiling need to be improved and collaborations and data sharing need to be increased within and across countries. Second, the rising burden of premenopausal breast cancer heightens the urgency around implementation of effective cancer risk assessment and genomic testing for population risk stratification. Although some countries are responding to the growing burden by providing opportunistic screening for breast cancer, no gains will be made in reducing mortality without a corresponding investment in accurate diagnosis of breast cancer subtypes and

modern treatment facilities. Third, the global estimation of the breast cancer burden hinges on the quality and completeness of cancer estimation at the national level. Data quality remains a challenge in low HDI countries because of underfunding and inadequate cancer registration. Better data present opportunities to monitor trends and variations of the disease and improve care and outcomes.[7]

Although the greatest burden of breast cancer now falls on low HDI countries, some countries with a high HDI continue to exacerbate inequities through inadequate service provision to underserved and understudied minority populations. Substantial inequities in access to radiotherapy, the underdeveloped interdisciplinary and interprofessional oncology workforce, and a paucity of access to affordable and effective cancer medicines have left women in low-resource settings in a veritable death trap.[8–10] There is an urgent need for health systems improvement and an environment that enables prioritising equal access to quality breast cancer care, not only as a public health issue but also as a human rights issue. Addressing structural racism and the widening health disparities are an exigency that require systems-level reforms to bring diagnostics and treatment to every region of the world. Global efforts to reduce inequities must prioritise building necessary infrastructure and promoting access to universal health insurance coverage for breast cancer treatment. Finally, to achieve the UN's Sustainable Development Goal 4 for prevention and control of non-communicable diseases, action on breast cancer must be at the top of national and women's health agendas.

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