Risk-based algorithms are increasingly recognized as a valuable strategy to maximize the effectiveness and minimize harms of breast cancer screening. In the US and elsewhere, age has long been the primary risk factor considered in screening guidelines. Although experts increasingly recommend that considerations such as family history, breast density, and other breast cancer risk factors inform screening decisions, this approach is not yet formally integrated into US national guidelines such as the US Preventive Service Task Force screening recommendations.1 The study by Zheng et al2 examines data from more than 1.5 million women participating in a population-based breast cancer screening program in China. The authors used available data on select breast cancer risk factors in the cohort (including family history, reproductive history, and benign breast disease) and incident cancers.2 Using a multivariable Cox proportional hazards model, they assigned risk scores to individuals in the cohort who were then grouped into 3 risk categories: low (hazard ratio [HR], 1 [reference]), medium (HR, 1.32 [95% CI, 1.24-1.41]), or high (HR, 1.75 [95% CI, 1.53-1.99]). Zheng et al3 then examined age-specific 10-year cumulative risks of developing breast cancer among individuals at each risk level. The authors suggest that the 10-year cumulative risk of a 50-year-old individual at average risk serves as a reasonable standard for screening initiation, and they propose that individuals in China should initiate screening at the age when they face the equivalent 10-year risk. For women in the cohort at high risk, this would mean screening initiation at 43 years.

Because of a dearth of studies that prospectively compare different screening initiation ages and intervals, most data to support risk-stratified algorithms to date have come from modeling studies or large cohort studies such as this one, although prospective data are anticipated from ongoing trials of risk-stratified screening (eg, the WISDOM trial in the US).3 However, most studies of risk-stratified screening come from countries with well-established screening programs, such as the US and Sweden.4,5

There is a pressing need to identify optimal screening algorithms in low- and middle-income countries, including China, where the incidence of and mortality from breast cancer is increasing rapidly and where resources for early detection are variable. Because the age structure of the population, the peak age of breast cancer incidence, and the distribution of risk factors are country or region specific, the appropriate age of screening initiation should ideally be based on local data. The work by Zheng et al2 represents an important effort to inform evidence-based algorithms for individualized early detection in an upper-middle-income country.

Of note, China's 2021 breast cancer screening guideline includes some risk stratification of screening initiation beyond age alone, proposing that screening should start at 45 years for women at average risk but at 40 years for women at high risk.6 The guideline defines women at high risk as those having any one of a notably broad variety of risk factors, ranging from having 1 first-degree relative with breast cancer to carrying a \textit{BRCA1/2} pathogenic variant. As Zheng et al2 point out, China's current approach to risk-adapted initiation of screening was not derived from empirical data, so efforts such as their study could inform the evolution of breast cancer screening guidelines.

Another important feature of the Chinese guideline is that it permits screening with either ultrasound or mammography for women at average risk of breast cancer and both ultrasound and mammography for individuals at high risk or with dense breasts. This recommendation may partially reflect limited access to mammography in more rural regions of China, but it is also supported by evidence from a randomized trial that suggested that in Chinese women aged 30 to 65 years who were identified as being at high risk of breast cancer, screening breast ultrasound had favorable test
characteristics (and lower cost) compared with mammography.\textsuperscript{7} Longer-term evaluation of the effect of ultrasound screening will be essential to support this approach.

There are important limitations to the work by Zheng et al.\textsuperscript{2} First, the researchers had a limited set of risk factors available. Moreover, risk factors for the development of breast cancer in the Chinese population are less well studied than they are for the US population, for example. More research will be essential to validate the risk scores developed in this study and to understand how well they and other risk factors estimate breast cancer risk in the broader Chinese population. In addition, Zheng et al\textsuperscript{2} did not examine risk factors that have a greater association with breast cancer, such as \textit{BRCA1/2} mutation, a family history suggestive of such a mutation, or a history of chest irradiation. The presence of these risk factors would merit a more aggressive screening approach. Second, as the authors acknowledge, whether age 50 years should be the reference standard for screening in the Chinese population is not a given. Finally, although this study uses a real-world population to estimate cancer risk, it does not evaluate the benefits, downsides, feasibility, and both individual and health system costs of risk-adapted approaches to breast cancer screening in the Chinese population, and further study will be important to continually inform China’s evolving policies.

Despite its limitations, the study by Zheng et al\textsuperscript{2} is remarkable because of the size of its community-based cohort and the wealth of data collected. It represents an important effort to identify risk-based screening strategies in a country where breast cancer screening is newly unfolding. Most new breast cancer cases and deaths occur in low- and middle-income countries, where a much higher proportion of individuals with breast cancer are diagnosed with late-stage disease compared with high-income countries and where feasible approaches to screening and/or early detection are urgently needed. In addition to optimizing the benefits and harms of breast cancer screening for individuals, risk-stratified approaches can help direct limited health care resources to those likely to benefit the most. Research to evaluate the effects of a risk-based screening strategy in China could help advance understanding of the role of individualized early cancer detection in other countries with emerging approaches to breast cancer control.

ARTICLE INFORMATION

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