Elevated breast density and overweight or obesity are well-established risk factors for breast cancer in both premenopausal and postmenopausal women. Breast density represents the amount of fibroglandular (dense) tissue relative to fatty (nondense) tissue on a mammogram. Furthermore, breast density and body mass index (BMI) are inversely related and act as confounders to each other’s effects. In the study by Tran et al, the authors sought to better elucidate the interactions between breast density and BMI in breast cancer risk using a population of millions of Korean women aged 40 years or older, who underwent mammography screening between 2009 and 2013. Tran and colleagues reported that breast density was an independent risk factor for breast cancer for premenopausal and postmenopausal women, but obesity was only associated with breast cancer risk in postmenopausal women. Moreover, when compared with underweight women categorized as Breast Imaging Reporting and Data System (BI-RADS) category 1 (breasts almost entirely fat), obese women with very dense breasts (BI-RADS category 4) showed the highest risk of breast cancer, with a 2-fold increase in risk for premenopausal women and a 6-fold increase for postmenopausal women. Furthermore, interactions in both the additive and multiplicative scales were considered, with the authors reporting a small or nonsignificant multiplicative interaction between BMI and breast density on breast cancer risk, but a positive additive interaction in both premenopausal and postmenopausal women. A positive additive interaction means that the combined effect size of the 2 risk factors is greater than the sum of each risk factor independently. Considering that additive interactions use the absolute risk they are more relevant for public health and clinical decision-making.

How do these results translate to a population that is not predominantly Asian? After all, Asian women are known for having heterogeneously dense (BI-RADS category 3) or very dense (BI-RADS category 4) breasts, which is not a characteristic of the Western population. Bissell et al showed that, across all races and ethnicities (including African American, Asian, Hispanic, and White women), breast density was a statistically significant risk factor for invasive breast cancer in premenopausal and postmenopausal women. However, premenopausal BMI was not associated with future breast cancer except for a small effect in White women; for postmenopausal women, BMI was a strong risk factor for all races studied. They pointed out that if all overweight or obese women achieved normal BMI, breast cancer incidence could be reduced by as much as 12% to 15% in Asian, Hispanic, and White women and by 28% in African American women. In addition, African American women are more likely to have dense breasts among overweight non-Hispanic populations, even after adjusting for all potential confounders. As BMI is a potentially modifiable risk factor, strategies for weight reduction in the affected populations are attractive and could reduce breast cancer risk substantially.

What are the implications of these results for breast cancer risk models? Most common models of breast cancer risk either use BMI (Tyrer-Cuzick model) or BI-RADS breast density (Breast Cancer Surveillance Consortium [BCSC] model) or do not use either (Gail model). In light of the findings by Tran et al that the interaction between BMI and breast density is additive, it suggests that perhaps these models are in fact underestimating breast cancer risk by not taking into account both factors.
What are the implications for breast cancer screening? To answer this question, we would need to consider 2 possibilities: (1) one-size-fits-all screening, most prevalent in today’s environment and (2) personalized screening, which is being advocated by many as a more efficient and effective strategy. In a one-size-fits-all screening scenario, the findings by Tran et al.³ suggest that, in addition to being informed of their breast density, women should also be informed about their BMI and the link between obesity and cancer, and encouraged to have discussions with their physicians about strategies for losing weight. In the case of personalized screening, the results of the study by Tran et al.³ suggest that, perhaps by using revised risk models (ie, models that accounted for both BMI and breast density), personalized decisions could be made about who were the women at higher risk of advanced breast cancer and may benefit the most from supplemental imaging, being that magnetic resonance imaging, ultrasonography, or digital breast tomosynthesis. The benefits of such a strategy are clear in studies such as that carried out by Kerlikowske et al.,⁸ who found that, in addition to breast density information, use of BCSC 5-year risk model was useful to identify women who would benefit the most from supplemental imaging. The authors reported that if supplemental imaging was offered to the 32.7% of women with highest risk, 54.7% of advanced breast cancers could potentially be prevented.⁸

The large study by Tran et al.³ included millions of Korean women and sought to identify the association between breast density, BMI, and breast cancer risk. In a surprising result, the authors found a positive additive interaction in both premenopausal and postmenopausal women, which suggests that BMI and breast density may act synergistically to increase breast cancer risk. This may have implications for breast cancer risk models, as most models do not use BMI and BI-RADS breast density in their risk estimations, as well as for both one-size-fits-all and personalized screening.

REFERENCES