Cost-effectiveness of risk-stratified screening for breast cancer

**Key findings**
- A risk-stratified screening strategy, informed by polygenic risk scores (PRS) for breast cancer, would improve the quality of life of women and save resources.
- As the threshold risk was lowered in a hypothetical cohort, a larger proportion of women would be offered screening, so the cost of the screening program increased while the gain in quality-adjusted life years (QALYs) flattened out.
- The risk-stratified screening program had the highest net monetary benefit when screening was targeted to the 30% of women with the highest risk scores, at a willingness-to-pay of $26,800 per QALY gained. However, screening offered to approximately 70% of the risk-stratified population had a more favorable trade-off between benefits and cost, being still cost-effective and reducing overdiagnoses while maintaining the benefits of screening.

**Background**
In the United Kingdom (UK), women aged 50 to 69 years are invited for mammography screening for breast cancer every 3 years. However, the risk of developing breast cancer varies among individuals, and this age-based, “one-size-fits-all” screening approach does not take into account the variation in individual risk. Several recent studies have reported that tailoring screening to an individual's risk level could improve the efficiency of the screening program and reduce adverse consequences. While screening reduces deaths from cancer, overdiagnosis and overtreatment can also occur.

Among other things, genetic factors affect a person’s risk for breast cancer. As of 2018, genome-wide association (GWAS) studies had identified 310 breast cancer susceptibility loci. Using these loci (and others as they are discovered), polygenic risk scores can be generated for all individuals, and a more efficient, cost-effective, risk-stratified approach to screening can be implemented.
Case study

Approach: Pashayan et al. [1] set out to assess the benefit-to-harm ratio and the cost-effectiveness of risk-stratified breast screening programs compared with a standard age-based screening program and no screening. To do this, they created a life-table model of a hypothetical cohort of 364,500 women in the UK, aged 50 years, with follow-up to age 85 years, using risk distribution based on polygenic risk score.

Strategies compared: (1) No screening, (2) age-based screening (mammography screening every 3 years from age 50 to 69), and (3) risk-stratified screening in which women at age 50 with a risk score above a threshold were offered screening every 3 years until age 69 years.

Key metrics: QALYs gained, overdiagnoses, breast cancer deaths averted, costs, and net monetary benefit.

Example finding: Compared with an age-based screening program, risk-based screening in a population of 10,000 in which screening is targeted to the 70% with the highest risk scores would cost the screening program $26,800 less, yield ~450 more QALYs, and result in ~27% fewer overdiagnoses, at a cost of ~3% fewer deaths averted.

“Targeting screening to women at higher risk of breast cancer is associated with reduced overdiagnosis and reduced cost of screening without compromising QALYs gained.” [1]

Conclusion

A PRS-informed, risk-stratified screening strategy could improve the cost-effectiveness and benefit-to-harm ratio of a breast cancer screening program. The optimal risk threshold for risk-stratified screening depends on the acceptable trade-off between lowering costs and maximizing the benefit-to-harm ratio. Based on their overall analysis (data not shown here), the authors conclude that risk-stratified screening offered to approximately 70% of the relevant population would be cost-effective and reduce overdiagnosis while maintaining the benefits of screening (Figure 1).

Reference


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