

Risk stratification in breast screening: A word of caution

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A recent paper by Pashayan et al.¹ models a number of breast cancer screening scenarios and concludes that determination of eligibility using risk criteria such as single nucleotide polymorphism scores in addition to sex and age which are currently used could improve cost-effectiveness of the programme. While primary or secondary prevention is more cost-effective in groups at higher risk, two observations need to be made here: first, modelling exercises such as this necessarily depend on assumptions, which should be scrutinised carefully; second, there are other considerations in determining modes of healthcare delivery beyond using methods such as the cost per quality adjusted life-year (QALY).

To consider the first issue, one can see from the unnumbered table in the paper that age-based screening always prevents a greater number of breast cancer deaths than further risk stratification, and for risk thresholds up to the 32nd percentile, the overall estimated costs are very similar, indicating a greater effect of age-based screening on mortality, at little, if any, extra cost. There are larger numbers of QALY's in the regimens using further risk stratification, but this depends crucially on the assumed effect of breast cancer on quality of life, which is questionable.

From the supplemental material in Pashayan et al.,¹ it appears that the authors assumed the same loss of utility quality adjustment for all breast cancers regardless of stage or treatment. This will bias QALY results against screening which detects disease at a stage when less aggressive treatment is necessary. In particular, the same quality adjustment should not be made for overdiagnosed cancers as for 'true' cancers. The former are screen-detected by definition and are characterised by early stage, with a considerably lower chance of treatment with mastectomy or chemotherapy.² The assumption is also made that risk level does not affect overdiagnosis, but there is no assurance that increased risk will not increase the risk of overdiagnosed tumours.

As regards the prevention of breast cancer death, the paper aims to base the estimates on the results of the UK Independent review,³ but it is apparent from the supplemental material that a 20% relative reduction was assumed associated with regular screening. The UK review found this for *invitation* to screening. The effect of being

regularly screened is greater than this. This underestimate will in turn underestimate the effect of screening without risk stratification.

The second issue relates to the quality of screening programmes. Current practice is to offer breast screening on the basis of the two most important risk factors of all: sex and age. As can be seen from the table in Pashayan et al., unless one chose a very high risk threshold, addition of further risk criteria would make little difference to outcomes or costs. One has to consider whether the additional complexity of additional risk criteria may detract from the performance of the programme as a whole, while only possibly conferring some benefit in cost-effectiveness.

Risk stratification is itself a form of screening with its own potential false positives and false negatives. In relation to this, if risk estimation beyond age and sex is to be used to decide eligibility of an individual, the decision should be based on absolute risk rather than the percentile of the risk distribution on which the individual lies, as considered by Pashayan et al.¹ If an intervention is not to be offered on the basis of estimated risk, the population excluded must have confidence that their absolute risk is low. Public health interventions at population level need to have transparent and comprehensible protocols of eligibility and delivery.

The results of the modelling and risk stratification are therefore questionable. We would be prudent to wait for empirical results from trials such as MyPeBS⁴ before taking a view about the effectiveness, practicality and cost-effectiveness of risk stratification in determining eligibility for breast screening. As things stand at present, the need for further risk stratification is not established. The objections to this are not simply attitudinal: there are unresolved scientific and public health objections, as noted above.

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