Evaluation of a Stratified National Breast Screening Program in the United Kingdom: An Early Model-Based Cost-Effectiveness Analysis

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A B S T R A C T

Objectives: To identify the incremental costs and consequences of stratified national breast screening programs (stratified NBSPs) and drivers of relative cost-effectiveness. Methods: A decision-analytic model (discrete event simulation) was conceptualized to represent four stratified NBSPs (risk 1, risk 2, masking [supplemental screening for women with higher breast density], and masking and risk 1) compared with the current UK NBSP and no screening. The model assumed a lifetime horizon, the health service perspective to identify costs (£, 2015), and measured consequences in quality-adjusted life-years (QALYs). Multiple data sources were used: systematic reviews of effectiveness and utility, published studies reporting costs, and cohort studies embedded in existing NBSPs. Model parameter uncertainty was assessed using probabilistic sensitivity analysis and one-way sensitivity analysis. Results: The base-case analysis, supported by probabilistic sensitivity analysis, suggested that the risk stratified NBSPs (risk 1 and risk-2) were relatively cost-effective when compared with the current UK NBSP, with incremental cost-effectiveness ratios of £16,689 per QALY and £25,924 per QALY, respectively. Stratified NBSP including masking approaches (supplemental screening for women with higher breast density) was not a cost-effective alternative, with incremental cost-effectiveness ratios of £212,947 per QALY (masking) and £75,254 per QALY (risk 1 and masking). When compared with no screening, all stratified NBSPs could be considered cost-effective. Key drivers of cost-effectiveness were discount rate, natural history model parameters, mammographic sensitivity, and biopsy rates for recalled cases. A key assumption was that the risk model used in the stratification process was perfectly calibrated to the population. Conclusions: This early model-based cost-effectiveness analysis provides indicative evidence for decision makers to understand the key drivers of costs and QALYs for exemplar stratified NBSP.

Keywords: breast cancer, cost-effectiveness analysis, discrete event simulation, screening.

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Introduction

National breast screening programs (NBSPs) have emerged as important public health interventions that aim to reduce deaths from breast cancer through early detection [1]. NBSPs in different jurisdictions differ in terms of the age at which screening is first offered to women in the population (start of NBSP), the interval between screens (screening interval), and the age at which screening is stopped. In the United Kingdom, the current NBSP is targeted at women within the first 3 years of their 50th birthday until the age of 70 years with a 3-yearly screening interval [2]. In some areas of the United Kingdom, the age range has been extended to women aged 47 to 49 years and 71 to 73 years as part of an age extension trial [3]. The current UK NBSP is a standard program with the same screening modality (mammography) offered at the same screening interval to all women regardless of their risk of developing breast cancer.

A new concept called "stratified screening," also known as personalized screening, is being considered to replace the existing standard, or "one-size-fits-all" UK NBSP, with the aim of improving the predictive value of cancer detection and, therefore, the relative cost-effectiveness of the program [4]. Risks of breast cancer may vary across a wide range because of familial risk, mammographic density, and modifiable risk factors. The potential for improved clinical and relative cost-effectiveness is achieved by modifying the screening protocol depending on an...
individual’s characteristics such as breast cancer risk factors or the performance of the screening modality for that individual. The introduction of, or any modification to, an NBSP has an opportunity cost. It is therefore important for decision makers deciding how to allocate finite budgets for screening programs to understand the added value of any additions or changes to an NBSP.

A substantial, but heterogeneous, economic evidence base has been developed to quantify the potential added value of an NBSP. A systematic review, conducted in 2014, identified 71 economic evaluations of relevance to breast screening in a general population of women. Of these, 52 were model-based evaluations [5]. There were three studies identified that conducted model-based analyses of a stratified screening strategy. Two of these studies were based in the United States [6,7] with no relevance to health care systems outside that setting. One study was UK-based [8] but provided no detail on the study perspective, time horizon, nature, and source of model inputs or method of analysis, which meant it is not possible to critique the relevance and quality of the results. Given the lack of an existing evidence base, it was timely to design an early model-based cost-effectiveness analysis (CEA) to identify the potential impact of introducing stratified NBSP in the UK setting and key drivers of the relative cost-effectiveness of different types of stratified NBSPs.

### Methods

An early model-based CEA was developed to address the key criteria as presented in Table 1 and reported in line with published criteria [9]. The concept of an early model-based economic evaluation is used in keeping with the definition offered by Annemans et al. [10]. Using an early model-based economic evaluation is in keeping with the recommendation by Sculpher et al. [11] to use an iterative approach to developing economic evidence to inform the introduction of new health care interventions.

### Interventions

Four potential approaches (hereafter called risk 1, risk 2, masking, and masking and risk 1) to stratified NBSP (see Table 1) were developed as part of a European collaborative project called Adapting Breast Cancer Screening Strategy Using Personalised Risk Estimation (ASSURE) [4].

### Comparators

The identified relevant comparator was the current UK NBSP (see Table 1). “No screening” was also identified as a comparator of interest. A pragmatic approach was taken to define no screening (see Table 1).

### Model Conceptualization and Structure

A systematic review of economic evaluations of breast screening programs identified no relevant existing models that could be used without extensive modification [5]. A de novo model structure was conceptualized, in line with published recommendations [12], and developed with input from key clinical members in the ASSURE team (n = 5) and external experts (n = 15). The conceptualization process identified that the model required three components to represent: the stratification approach, breast cancer natural history with screening, and the diagnosis and treatment process after a cancer detected by screening. A discrete event simulation (DES) model was used to represent these three components. Appendix 1 in Supplemental Materials found at [http://dx.doi.org/10.1016/j.jval.2017.04.012](http://dx.doi.org/10.1016/j.jval.2017.04.012) shows the model structures and descriptions in detail. The model codes, created in R statistical package (R Foundation for Statistical Computing, Vienna, Austria), are available on request.
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