Evaluating the Integration of AI-Risk Prediction Models in Breast Cancer Screening: Clinical & Systemic Effects

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Abstract

Breast Cancer (BC) detection programmes, demonstrating significant reduction in BC mortality. However, reliance on age alone fails to account for individual risk variation, which contributes to overdiagnosis, false positives and interval cancers. This review outlines the evolution from age-based to risk-stratified breast cancer screening, assessing the role of artificial intelligence and examining the evidence required for clinical implementation effectively.

Methods: Literature was identified by searching PubMed, Scopus, Web of Science Scopus, and Cochrane Library with relevant MeSH terms and keywords. Inclusion and exclusion criteria were applied, with title and abstract screening conducted to assess eligibility. Studies addressing breast cancer screening, AI based risk prediction, and frameworks published between 2007 and 2026 were prioritised, generating the articles used in this review.

Results: Advances in the understanding of breast cancer risk factors, including family history, genetic predisposition, lifestyle and mammographic breast density, have driven the evolution towards risk stratified screening, enabling greater consideration of individual variability in disease presentation. AI has recently emerged as a supplement to screening with applications in both computer aided detention and mammography derived risk prediction modelling. Evidence suggests that AI systems may enhance cancer detection, improve accuracy of risk stratification and perform consistently among diverse populations. However, many barriers exist before AI can be incorporated into existing screening programmes, including the need for strong prospective evaluation and demonstration of consistent performance among different subgroups.

Conclusion: AI driven risk prediction has the potential to refine breast cancer screening beyond age based approaches. The clinical implementation however, will require rigorous validation, attention to equity among the population and development of appropriate ethical frameworks.

Age-Based Screening

Breast Cancer (BC) screening is a fundamental public health intervention that integrates clinical practice as a secondary prevention method. It has progressed immensely from being an age-based model to being risk-based, depending on individual risks. Recently, within research settings, Artificial Intelligence (AI) has been considered as a tool for risk stratification to enhance cancer detection and individualized risk prediction (1). These advances have the potential to refine screened populations, time intervals and the intensity of screening in an attempt to move toward risk prediction. However, any replacement of established screening pathways requires addressing disparities, risks and ethical uncertainty.

BC screening was introduced in Ireland in the early 2000s by screening women for early detection between the ages of 50-69 biennially. The decision to stratify based on age is often utilized in health services as it is an indicator for 'need' when the primary risk factors are not fully identified (2). The National Cancer Registry of Ireland reports that 93% of women diagnosed through screening programs are diagnosed at stage I and II demonstrating a significant mortality reduction and survival benefit directly due to early screening (3).

Despite the demonstrable mortality reduction, dangers of screening stem from the very same reason the program is beneficial, the scalable nature of the program amplifies its harm and inefficiency and increases burden on the system. False positive results lead to an increase in recall imaging and benign biopsy, with associated anxiety and short-term morbidity (4). Furthermore, overdiagnosis can expose women to unnecessary surgery and adjuvant treatment for a disease that would not have become clinically significant. A feature of the age-based screening program are interval breast cancers; these are tumours that grow despite a negative mammogram and prior to the next biennial appointment (4). They are further subclassified into true intervals, minimal signs, and occult cancers (5). Any tumour that was missed due to a normal mammogram, or was dismissed for further assessment despite an underlying abnormality is the basis of the issue of only stratifying based on age.

Risk-Stratified Screening

Many programmes have started to recommend earlier surveillance based on risk stratification rather than age alone (6). Although advanced age is a strong predictor for breast cancer, reliance on this factor alone fails to account for other important determinants such as familial, genetic, environmental and lifestyle factors (7). Accordingly, screening strategies have shifted away from age only criteria towards risk stratified approaches, which have been shown to reduce overdiagnosis, while maintaining favourable benefit to harm and cost effectiveness rations (8).

Patients with a family history of breast cancer have been shown to have higher rates of imaging detected tumours, which are often smaller at the time of diagnosis in comparison to women without affected family members.

Individuals with strong family history are often referred to genetic counselling where they are managed through higher screening pathways. Guidelines recommend the use of familial risk assessment tools in women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer, with referral for genetic counselling and testing if the assessment is positive. Nonetheless, it is not recommended for women without these risk factors to receive routine genetic risk assessment for BRCA1/2 mutations, which reflects a reduced benefit (9). Genetic screening however, can also be determined, using polygenic risk scores (PRS), which measures the effect of multiple genetic variants. PRS can stratify breast cancer risk in women without a family history and can also be used to guide more individualised screening (6).

Furthermore, breast tissue density is an independent risk factor which results in undetected cancer during mammography screening. Women with dense breast tissue experience an increased likelihood of late diagnosis. Although this finding is reported in many screening programs, breast density has been inconsistently included in risk stratification (10).

Despite advances in risk prediction, the integration of risk based stratification into routine screening practice remains inconsistent. Limitations to genetic counselling and the variability in the incorporation of key risk factors contribute to the reliance on age-based screening methods (8). However, transitioning from age-based pathways or risk-stratification screening will require further analysis to optimize clinical benefit.

AI Detection and Prediction

AI has introduced numerous advancements in BC screening, as it aids in detecting signs of possible malignancies in mammograms and has the ability to predict a patient's future risk using AI risk models. Computed Aided Detection and AI risk models are examples of AI based tools that extrapolate existing information and pair it with patients' individual risk factors to predict the likelihood of developing BC.

In terms of detection, AI-assisted models have demonstrated higher specificity compared to radiologists, with some studies reporting specificity rates of 93% versus 77.6%. This suggests that AI may play a role in improving diagnosis accuracy and reducing false positive findings.

In addition to detection, AI has also been used for risk prediction, using machine learning to interpret imaging, eventually predicting future risk. The MIRAE model is an example of an advancement in technology that uses four mammography views in combination with patient risk factors to predict a patient's risk of developing breast cancer in the next 5 years. The model received an AUC of 0.79 in external validation indicating that it could reliably predict the likelihood of women developing breast cancer, even when other variables were involved (11).

One of the concerns with using AI in the medical field is its generalisability across populations. To assess this, ProFound AI Risk, a short-term risk prediction software, has been used to address this concern by identifying women with a high risk of being diagnosed with breast cancer within 2 years. The model incorporates age and imaging features including breast density, masses and microcalcifications.

External validation was evaluated in a cohort of American patients, demonstrating no statistically significant differences in performance among different racial and breast density categories, suggesting that the model is generalisable amongst diverse populations. When compared to the GAIL 5-year risk model, ProFound AI risk model demonstrated improved discrimination, outperforming in racial subgroup analyses and invasive cancer. Reported limitations included differential discrimination for some tumour characteristics such as in situ tumours and very small invasive cancers (12). This demonstrates that although AI has shown improvement in risk discrimination, further refinement is necessary to ensure consistent performance for varying tumour characteristics.

Another concern arises from the lack of studies focusing on the calibration of these models. Calibration measures how well the probabilities generated by the risk prediction model agree with the observed probabilities in the population of interest, reflecting the true incidence of BC. While the majority of studies focus on discrimination performance of the models, there is limited evaluation of calibration, despite the importance in risk factor prediction (13).

In addition to limitations in evaluation of models, there is also a significant lack of prospective studies assessing the use of AI performance in clinical settings. Prospective AI trials are important as they allow AI models to be evaluated in areas that are not in the cancer enriched databases, which provides an accurate assessment of their use. However, conducting these trials is time consuming and expensive, which limits the implementation and contributes to the current lack of evidence (14).

Overall, these findings suggest that AI-based risk prediction models can generalise across populations and key subgroups. However, their clinical performance depends on consistent performance across biologically and clinically important tumour phenotypes and demonstrated net benefit in prospective screening settings, both of which require further evaluation.

Policy, ethics, and equity

Over time, breast cancer screening has progressed from age-based screening to the inclusion of risk-based approaches, and now to the innovative involvement of AI-guided screening. With such progression, factors such as policy, ethicality, and equity are key considerations in determining the benefit of applying AI-screening methods into public health.

Previously, age-based screening methods were justified politically and ethically on the basis of simplicity, transparency, and ability for population-based coverage, despite overdiagnosis and elevated false positive rates (15). Implementation of risk based screening has improved ethical precision by enabling personalized risk stratification. However, these methods may introduce inequalities in access, including differences in how these risk models are applied across populations, as well as limited access and health literacy required for individual risk assessment (16).

The shift towards innovative AI-generated screening increases the idea of personalized care, but has equally raised concern regarding policy, ethics, and equity. AI utilizes ‘machine learning’ creating ethical concerns as any input of biased data could impose systematic bias. Systematic bias translates to limited generalisability of AI-screening in different settings (17).

Furthermore, sufficient AI systems would require 'training' accountability. However, accountability blurs with AI-provided results that are independent of human input. Unexplainable AI algorithms open the door to many issues, one of which is patient understanding creating a lack of trust in their healthcare team (17).

Although AI-enabled screening demonstrates promise of more personalized care, significant policy, ethical, and equitable issues exist and must be addressed through regulatory frameworks before successful implementation.

Evidence thresholds and Implementation

AI should not be fully incorporated until there is a net benefit reached enough to deescalate current screening. Any incorporation should help detect cancers at an earlier stage and reduce interval cancers in an attempt to equalise or perhaps outperform the current data. This is an important measure of how effective a screening programme is as detection of the cancer is not enough unless it results in earlier treatment and better health outcomes for patients (18).
Another aspect to consider are the programme's costs including its software, infrastructure, maintenance and training. Economic model studies suggest that AI risk stratification tools may be cost effective, with an annual net monetary benefit of approximately £60.4 million to £85.3 million within the NHS, while also improving quality-adjusted life years, compared to standard screening programmes (19).

Its impact on the healthcare workforce must also be considered, such as changes in radiologist workload and workflow efficiency (20). An immense amount of work would be required to enhance the sustainability of the system to ensure no additional strain placed on the system.

Implementation proposals recommend slow introduction in stages to ensure transparency within the healthcare system and toward patients (21). An example of such a proposal utilizes the US Food and Drug Administration clinical trials informed framework that highlights safety, efficacy, effectiveness and monitoring as key steps in integration that advocates for a structured approach that yields tangible outcomes while addressing any systemically crucial concerns that may arise (20). This implementation roadmap will require an evaluation of the programme's clinical effectiveness evaluation against the pre-existing standard-of-care. When the screening has solid prospective data, a clear clinical benefit, equitable performance and has demonstrated cost-effectiveness, it may be deemed suitable for implementation. Other readiness frameworks such as FAIR-AI and TEHAI enable systematic evaluation of AI systems across key domains, helping determine whether they are suitable for use or require additional evidence (22).

Conclusion

For AI to be effectively incorporated into BC screening programmes, rigorous evidence-based studies are required. Although AI demonstrates the potential to improve cancer detection and risk stratification, its implementation into clinical settings must be done with caution. Currently, AI should be considered as an adjunct to existing screening programmes, rather than replacing them as a whole. By using AI as a supporting tool, this will permit clinical decision making while further evidence of its efficacy is generated. Overall, careful integration of AI into screening programmes with supporting evidence of its effectiveness is essential to ensure improvement in mortality rates and equity amongst populations.

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