



ABERDEEN BELFAST
EVIDENCE COLLABORATION

Risk stratification in breast cancer screening

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Relevant Stakeholders

UK National Screening Committee.

Background

Burden of breast cancer

Breast cancer remains the most common type of cancer in women and a leading cause of cancer-related mortality in most countries (157 of 185 globally). Although rare, breast cancer can also affect men, accounting for about 0.5 to 1% of cases. In 2022, 2.3 million women of all ages were newly diagnosed with breast cancer, representing 23.8% of all cancer cases, and there were approximately 670,000 breast cancer-related deaths. The World Health Organisation (WHO) launched the Global Breast Cancer Initiative (GBCI) to achieve a 2.5% annual reduction in breast cancer mortality between 2020 and 2040. This goal is underpinned by a three-pronged approach: promoting early detection through health promotion; ensuring a timely diagnosis; and delivering comprehensive breast cancer management.^{1,2}

In the UK, almost 1 in 3 (30%) of newly diagnosed cancers in women are breast cancer.³ Approximately 1 in 7 women will develop breast cancer in their lifetime, and 23% of breast cancer cases are considered preventable.⁴ Each year, there are around 56,800 new breast cancer diagnoses (2017-2019), with projections indicating this could increase to 69,900 annually by 2038-2040.⁵ Pre-pandemic incidence-based economic cost modelling (2019) has estimated the total economic burden of breast cancer in the UK, including both direct and societal costs, to be between £2.6 to 2.8 billion for 2024. Without further intervention strategies, this figure could rise to £3.6 billion by 2034.⁶ The 2019 UK NHS Long Term Plan states that the proportion of cancers diagnosed at an earlier stage (stages 1 and 2) will increase from around 50% in 2019 to 75% by 2028. A key priority for the NHS is to maximise the number of cancers identified through screening, including the implementation of personalised and risk-stratified screening approaches.⁷

Breast cancer screening

The UK National Health Service Breast Screening Programme (NHSBSP) routinely invites women aged 50 to 70 years who are registered with a general practitioner (GP) to attend breast screening every 3 years. This involves a breast mammogram (X-ray) to detect early signs of breast cancer. In addition to routine screening, the NHSBSP offers enhanced surveillance such as magnetic resonance imaging (MRI) or annual mammograms to women identified by genetics or oncology specialists as being at very high risk of developing breast cancer

compared to the general population.^{8,9} Women assessed as having moderate and high-risk are managed by local breast services per NICE guidance.¹⁰

Breast cancer screening provides significant benefits, including early detection and reduced breast cancer mortality.¹¹ However, it is also associated with potential harms. These include pain and discomfort during the mammogram procedure,¹² false positives that lead to unnecessary recalls,¹³ overdiagnosis,^{11,14} false negatives,¹⁵ and psychological distress.^{16,17} Therefore, any future changes to UK NHSBSP must carefully balance the goal of maximising reductions in breast cancer mortality and minimising associated harms whilst ensuring NHS affordability.¹⁸

The current population-based screening approach in the UK, albeit with age stratification, follows largely a 'one size fits all' model.¹⁹ This approach does not account for individual variations in breast cancer risk. Consequently, there is a growing interest in the potential benefits of personalised risk-based breast cancer screening, where women are categorised into risk groups.²⁰ Two large, international, multi-centre, randomised controlled trials are currently ongoing in Europe (My Personal Breast Screening – MyPeBS)²¹ and in the USA (Women Informed to Screen Depending on Measures of Risk - WISDOM).²² An individual's risk of developing breast cancer is influenced by a combination of modifiable and non-modifiable risk factors across several domains, including demographic, genetic, reproductive and hormonal, metabolic, medical history, lifestyle and environmental factors.²³

Various multifactorial breast cancer risk prediction models have been developed to estimate women's likelihood of developing breast cancer over a specified time frame (e.g., 5 or 10 years), accounting for additional risk factors, not just age.²⁴ These models have evolved over time,²⁵ and they differ in the range and type of risk factors included, the weight assigned to each factor and their predictive performance, which can vary according to characteristics of the population in which they were developed.²⁶ Increasingly, risk prediction models incorporate combinations of demographic, clinical, genetic and imaging-related parameters.^{25,27} There is also growing interest in the application of artificial intelligence (AI) to enhance the accuracy of breast cancer risk prediction.²⁶ However, a UK National Screening Committee (NSC) workshop held in London in 2022 emphasised that there are uncertainties about the effectiveness of some risk prediction models in certain populations, as well as how they can be operationalised in practice.¹⁸

Currently, the UK NHS endorses two validated risk prediction models:²⁸ the International Breast Cancer Intervention Study (IBIS)/Tyrer-Cuzick Model^{29, 30} and the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) Risk Model, available via the CanRisk web-based tool.³¹

Rationale for introducing risk-stratified breast screening

Breast cancer screening eligibility, frequency, intervals, and type of test may be tailored to an individual's risk level, allowing health service resources to be focused on those who are most likely to benefit while reducing potential harms for those at lower risk.³² A risk-stratified breast screening programme could, therefore, enhance resource management, improve efficiency, and offer a more cost-effective approach to healthcare delivery. However, there are still notable gaps in the current evidence base.¹⁸ To support effective, evidence-based screening, the European Collaborative on Personalised Early Detection and Prevention of Breast Cancer (ENVISION) network has emphasised the need for validated risk prediction models that account for genetic factors. Importantly, they have highlighted that the validity and clinical utility of these models must be established before they are adopted for routine use in clinical settings.²⁰ Understanding how existing risk prediction models are developed and how accurately they estimate breast cancer risk in women eligible for screening is, therefore, crucial. Evidence from risk prediction models, along with test accuracy studies and epidemiological data on disease risk and progression, can be synthesised using decision-analytic models to evaluate the potential impact of risk-stratified screening programmes and inform screening policy and practice.^{18, 33, 34} There is a need to evaluate the clinical and cost effectiveness of these approaches by comparing the outputs of existing decision-analytic models. This allows for the identification of high-quality models, both in terms of assumptions and underlying parameters, which can strengthen the evidence base. External validation of models is important to compare their performance directly, assess generalisability, and determine which outcomes are accurately estimated or subject to under- or over-estimation.¹⁸

Prior systematic reviews on breast cancer risk prediction and decision-analytic models

Several systematic reviews have evaluated breast cancer risk prediction models, with six published since 2022. These reviews differ considerably in scope and focus, including a wide range of studies that assess lifestyle-related factors,³⁵ questionnaire-based tools,²⁵ polygenic risk scores,³⁶ and the application of machine learning techniques.³⁷ Two systematic reviews published in 2021 found that risk-based screening is more cost-effective than age-based

methods. However, one review highlighted that the generalisability of findings is limited due to variations in population characteristics, screening protocols, and screening outcomes across countries.³⁸ The second review found that although risk-adapted strategies are still rare in Europe, they tend to be more effective and efficient than conventional screening methods.³⁹

In a recent overview of systematic reviews, Wolf et al. (2024)²⁴ examined eight reviews on breast cancer risk prediction models that were published up to March 2022. However, the most recent primary study included in their analysis was published in 2019, and more recent relevant studies were not considered. The overview found that existing models demonstrated limited accuracy for predicting breast cancer risk, and incorporating additional factors such as breast density and genetic data yielded only modest improvements. As a result, the authors concluded that current models remain insufficiently convincing for adoption in national screening programmes. This systematic review seeks to address this gap by synthesising the most recent evidence and offering deeper insight into emerging advancements in breast cancer risk prediction.

We are also aware of an ongoing PROSPERO-registered systematic review led by the University of Glasgow, which aims to examine modelling studies and cost-effectiveness analyses for cancer screening programmes in the UK, focusing on lung, breast, cervical, and bowel cancers.⁴⁰ While the Glasgow review has a broader scope, addressing multiple cancer types without considering subgroup analyses, our work focuses specifically on risk-stratified screening strategies for breast cancer.

Objectives

Key prerequisites for making evidence-based, informed decisions regarding potential implementation of risk-stratified breast cancer screening include:

- The identification of robust, validated, multivariable risk prediction models capable of accurately stratifying women according to their risk of breast cancer, and
- The availability of high-quality health economic evaluations assessing the costs and consequences of risk-stratified breast screening strategies relevant to the UK context.²⁷

To address these needs, we plan to conduct two complementary evidence summaries with the following objectives:

- i. To summarise and evaluate existing breast cancer risk prediction models used to stratify women eligible for breast screening into risk categories (Review 1) and
- ii. To summarise and evaluate existing decision-analytic model-based economic evaluations of risk-stratified breast cancer screening programmes (Review 2).

Although we recognise the importance of evaluating the feasibility and implementation of risk-stratified breast cancer screening, this falls outside the scope of the present review.

The proposed work will be undertaken in liaison with the UK NSC Evidence Team and will report to the UK NSC Adult Reference Group (RMG) when appropriate.

Methods

The two systematic reviews will be conducted following the Transparent Reporting of multivariable prediction models for Individual Prognosis or Diagnosis: checklist for Systematic Reviews and Meta-Analyses (TRIPOD-SRMA) for **Review 1**⁴¹ and in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) for **Review 2**.⁴²

The research protocol will be registered on the International Prospective Register of Systematic Reviews (PROSPERO) <https://www.crd.york.ac.uk/prospero/>.

Patient and public involvement (PPI)

Two PPI partners will be invited to join the Advisory Group for this evidence synthesis project, alongside academic and clinical experts, to ensure their perspectives are considered in project decisions. Specifically, the PPI partners will actively participate in regular Advisory Group meetings, contributing to discussions and making recommendations at each stage of the project.

Language and inclusivity statement

Most people who use the UK's breast screening programme identify as women, but not all. While exclusively using gender-neutral language can enhance inclusivity, it may also reduce clarity. To balance inclusivity and readability, we have chosen to use both 'women' and

gender-neutral language where appropriate. We acknowledge this is a compromise. When we refer to ‘women’, we ask readers to interpret this as including all individuals who use the breast screening service, regardless of gender identity.

Study eligibility criteria

The eligibility criteria for inclusion defined using the PICOTS (Population, Intervention, Comparator, Outcomes, Timing and Setting) and PICO (Population, Intervention, Comparator, Outcomes) (PICO) frameworks are presented in Table 1 and Table 2, respectively.

For Review 1, we will use the term ‘**risk prediction models**’ as an umbrella term to include synonymous concepts such as risk prediction tools, predictive models, prognostic models, risk assessment tools/ models, risk prediction algorithms, prediction index or rules, and risk scores. We will include studies of any design, published in English language, that report the development and/or validation of breast cancer risk prediction models for females eligible for breast cancer screening. Included models must use multiple predictor variables and report performance metrics. Literature reviews will be excluded; however, relevant reviews will be cross-referenced to identify additional primary studies.

For Review 2, we will include decision-analytic models, published in English language that compare at least two alternative strategies in terms of both costs and outcomes. We will consider all types of economic evaluations, including cost-effectiveness, cost-utility, cost-benefit and cost-consequence analyses. Reviews of economic evaluations identified through the literature searches or already known to the research team will be cross-referenced to identify additional relevant studies.

Table 1 PICOTS criteria for Review 1

Review Question	<i>What are the existing risk prediction models for estimating breast cancer risk in women eligible for screening, and how do they compare in terms of methodological quality and predictive performance?</i>
Population	All individuals who are eligible for breast cancer screening. Exclusions: Women who have already been diagnosed with breast cancer, women in high-risk screening pathways, and men.
Intervention	Breast cancer risk prediction models. Breast cancer risk prediction models that incorporate multiple risk factors to estimate an individual's risk of developing breast cancer, in women eligible for breast cancer screening. While not the central focus of this review, the inclusion of AI-based methodologies may be considered following input from the Advisory Group. Exclusion: Univariate breast cancer risk prediction models (i.e., models that rely on a single variable/risk factor).
Comparator	Not applicable.
Outcome of interest	Presence of breast cancer (including breast cancer subtypes). Exclusions: Models that aim to predict the recurrence of breast cancer in individuals with a prior history of the disease; breast cancer metastasis; breast cancer symptoms (e.g., vomiting, nausea); prognosis or survival related to breast cancer; and breast cancer treatment planning.
Timing	Time horizon for prediction as defined by the authors of included studies (e.g., risk diagnosis in 5 years, 10 years, or lifetime).
Setting	Breast cancer screening programme setting.

Note: Breast cancer risk prediction models that focus specifically on populations of high-risk or where the predicted outcome is a breast cancer sub-type will be eligible for inclusion but may be reported separately depending upon the overall number of eligible studies.

Table 2 PICOS criteria for Review 2

Review Question	<i>What are the existing decision-analytic models for breast cancer screening risk stratification, and how do they compare in terms of cost-effectiveness and recommendations?</i>
Population	All individuals who are eligible for breast cancer screening. Exclusions: Women who have already been diagnosed with breast cancer, women in high-risk screening pathways, and men.
Intervention	Risk-stratified breast cancer screening strategies that are based on multiple individual risk factors rather than relying on a single variable. For example, in addition to age, which is typically the primary variable considered, they should consider variables such as breast density, familial history of breast cancer, personal history of benign breast disease, and genomic profile. While not the central focus of this review, the inclusion of AI-based methodologies may be considered following input from the Advisory Group.
Comparator	Comparator strategies may include either no screening or the current national screening programme as defined by the authors of the included studies (i.e. based on the country of the screened population).
Outcomes	<ul style="list-style-type: none"> • Total cost, • Incremental cost, • Incremental life-years gained, • Gain in other clinical outcomes as defined by the study, • Quality-adjusted life years (QALYs), • Incremental cost-effectiveness ratio (ICER), • Any other economic outcome as outlined by the included studies, and • Characteristics of the risk prediction tool used in the model (e.g. name, source, risk factors included in the prediction model).
Setting	Breast cancer screening programme setting.

Search methods for identification of studies

An Information Specialist will develop comprehensive search strategies to identify relevant published studies. These will include relevant database index terms and free text keywords.

For Review 1, the following databases will be searched: MEDLINE (R) ALL (Ovid), Embase (Ovid), Web of Science Core Collection (Clarivate), the International Health Technology Assessment (INAHTA) Database and the Cochrane Database of Systematic Reviews (Wiley online). **For Review 2**, we will search: MEDLINE (R) ALL (Ovid), Embase (Ovid), EconLit (ProQuest), The Tufts Medical Center Cost Effectiveness Analysis (CEA) Registry, and the International Health Technology Assessment (INAHTA) Database; also websites of relevant professional organisations and health technology agencies such as the National Institute for Health and Care Excellence (NICE), Canada's Drug Agency (CDA-AMC), the ISPOR Presentations Database, and the Institute for Clinical and Economic Review (ICER) will also be searched for additional reports.

There will be no restriction on study type or language during the search phase, but search results will be limited to studies published in the last ten years, from 2015 onwards. Conference proceedings and abstracts without a corresponding full-text publication will not be considered eligible for inclusion. We do not plan to search the grey literature. The reference lists of included studies will be hand-searched to identify any additional relevant publications. All search results including full references, titles and abstracts will be imported into EndNote X9. For both reviews, examples of MEDLINE search strategies are presented in Appendix 1 and may be subject to further refinement.

Study selection and data extraction strategies

To increase efficiency, we may consider using existing software platforms (e.g., Covidence, EPPI Reviewer) that are designed to support and streamline the process of conducting systematic reviews and evidence syntheses, particularly the screening of search results.

Study selection

The titles and abstracts identified by the search strategies will be screened by one reviewer with a minimum of 20% checked by a second independent reviewer. Potentially relevant articles or uncertain articles will be retrieved in full. The full text of selected citations will be assessed in detail against the inclusion criteria by one reviewer with a minimum of 20% checked by a second reviewer. Reasons for the exclusion of full-text articles that do not meet the inclusion

criteria will be recorded. All studies identified for inclusion will be checked for retractions or withdrawals, and any affected papers will be excluded.

The results of the literature searches and the study selection process will be illustrated using the PRISMA 2020 flow diagram for systematic reviews.⁴²

Depending on available resources and agreed timelines, eligible studies may be prioritised based on factors such as their geographical location (relevance to the UK context) or the methodological approaches used in the models (e.g., cost-utility analyses in decision-analytic models).

Data extraction

Data will be extracted from each eligible study by one reviewer using a data extraction form specifically developed for this purpose and checked independently by a second reviewer. The data extraction form will undergo a pilot phase and will be modified as necessary to enhance its effectiveness. The authors of the included studies may be contacted for further clarification or additional data. The PRO-EDI initiative dataset will be incorporated into data extraction to ensure consideration of equality, diversity and inclusion in participant characteristics within evidence syntheses.⁴³

For review 1, we will extract data in accordance with the Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS).⁴⁴

Specifically, the following data items will be extracted:

- Study ID, year of publication, authors, country,
- Study design,
- Study aims/objectives,
- Source of data (e.g., cohort, case-control, randomised trial or registry data),
- Participants (e.g., description, including PRO-EDI data items),
- Outcomes to be predicted (e.g., definition and method used for measurement, time of outcome occurrence),
- Candidate predictors (e.g., number, type, definition and method of measurement),
- Sample size (number of participants and number of outcomes/events/events per variable),
- Missing data (e.g., number of participants with missing data, handling of missing data),

- Characteristics of model development (e.g., modelling method, assumptions, method for selection of predictors for inclusion),
- Model performance (e.g., statistical performance estimates such as calibration and discrimination measures with confidence intervals - performance indicators may include Expected/Observed (E/O) Ratio, Calibration Slope, Calibration Plot, C-Statistic/ Area Under the Receiver Operating Characteristic curve (AUROC), Decision Curve Analysis, Net Benefit, Brier Scores or Net Reclassification Index (NRI),
- Model evaluation (e.g., method used for testing model performance, including external validation),
- Key findings (e.g., final and other multivariable models presented),
- Conclusions (e.g., implications for clinical practice and research).

For review 2, the data extraction form will be developed based on an adapted version of the Philips et al. critical appraisal checklist for decision-analytic models. A selected subset of questions will be used, tailored to the specific objectives of our review and designed to address key elements related to risk of bias, as outlined in the ECOBIAS checklist,⁴⁵ rather than strictly adhering to the original Philips checklist in its entirety.⁴⁶

The following data will be extracted from the included studies:

- Study ID, year of publication, authors and country,
- Study aims/ objectives,
- Decision problem statement, context and perspective,
- Model strategies being compared,
- Risk-stratification models/tools,
- Structure and characteristic of the model: model type, reference population, risk factors used in stratification & tool if applicable, strategies being evaluated (number & details), time horizon, cycle length discount rates, cost categories considered, instrument for valuation of preference-based outcomes, assessment/ characterisation of uncertainty (e.g., natural history, test performance, treatment effectiveness),
- Key findings: total costs, incremental cost, life years, incremental life-years gained, gain in other clinical outcomes as defined by the study, quality-adjusted life years (QALYs), incremental cost-effectiveness ratio (ICER), any other economic outcome as outlined by the study authors, and
- Study limitations and conclusions.

For both reviews, depending on the volume of studies identified and the resources available, data extraction may be streamlined to focus on key data items.

Risk of bias (RoB) assessment

Two independent reviewers will assess the methodological quality of the included studies with methodological support from the wider research team when necessary.

The risk of bias (RoB) of studies included in **Review 1** will be assessed using the Prediction model Risk Of Bias Assessment tool (PROBAST).⁴⁷ PROBAST is organised into four domains, *i*) participants, *ii*) predictors, *iii*) outcome and *iv*) analysis. Each domain includes signalling questions to guide a structured evaluation of bias. Domains are rated as having a ‘low’, ‘high’ or ‘unclear’ risk of bias. An overall risk rating is then assigned to each study: ‘low’ (no relevant shortcomings) if no domain is rated as ‘high’ or ‘unclear’; ‘high’ if at least one domain is rated ‘high’; and ‘unclear’ if at least one domain is rated ‘unclear’ and none are rated ‘high’.

The RoB of studies included in **Review 2** will be assessed using the ECOBIAS checklist, which evaluates two main domains: overall bias in economic evaluation and model-specific biases.⁴⁵ The overall bias domain consists of 11 questions, while model-specific biases are divided into structural and data-related biases. Each item is rated as ‘yes’ (high RoB), ‘no’ (low RoB), ‘partly’, ‘unclear’ or ‘not applicable’. The results of the risk of bias assessment will be entered into a Microsoft Excel[®] spreadsheet.

Any disagreements during the screening of search results, study selection process, data extraction and risk of bias assessment will be resolved through discussion between reviewers or, if necessary, arbitration by a third reviewer.

Data synthesis

We will conduct a formal, structured narrative synthesis of findings complemented by tabular and graphical data presentation.

For review 1, results will be synthesised by individual risk prediction models and their key methodological characteristics. We will also consider the relevance of each model to the UK screening context.

For review 2, findings will be presented in a tabular format and summarised through a critical synthesis to provide a comprehensive overview of existing evidence. This will include an assessment of how risk-stratification has been incorporated into breast cancer screening programmes, with particular attention to the relevance of these approaches to the UK context. Methods used for risk estimation and stratification will be described.

Figure 1 in Appendix 2 outlines the main milestones and key activities associated with the delivery of Review 1 and Review 2.

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Appendix 1 Medline (R) ALL (Ovid) search strategies

Research Question Review 1: What are the existing risk prediction models for estimating breast cancer risk in women eligible for screening, and how do they compare in terms of methodological quality and predictive performance?

Ovid MEDLINE ® ALL

- 1 breast cancer.ti,kf.
- 2 (risk adj2 (score? or factor? or stratif* or predict* or individual* or personal* or "breast cancer")).tw,kf.
- 3 ((model* or tool? or algorithm?) adj3 (risk? or predict* or multifactorial or mathematical or clinical or "logistic regression" or "log-incidence" or empirical or prognos*)).tw,kf.
- 4 (Gail or Tyrer-Cuzick or BRCAPRO or "i-Care" or "iCARE-Lit" or BOADICEA or "Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm" or "Breast Cancer Risk Assessment Tool" or BCRAT or "Breast Cancer Surveillance Consortium" or BCSC or Rosner or "International Breast Cancer Intervention Study" or IBIS or "Asian American Breast Cancer Study" or AABCS or KREA or KRKR or KARMA or "Karolinska Mammography Project for Risk Prediction of Breast Cancer" or BRCAPRO or Barlow or Claus or ((original or empirical or genetic) adj3 model)).tw.
- 5 3 or 4
- 6 1 and 2 and 5
- 7 limit 6 to yr="2015 -Current"

Research Question Review 2: How have economic evaluations using decision-analytic models addressed risk-stratification for breast cancer screening programmes?

Ovid MEDLINE(R) ALL

1. *Breast Neoplasms/ or (breast adj3 (cancer? or neoplasm? or tumo?r?)).tw,kf.
2. "Early Detection of Cancer"/ or Mass Screening/
3. 1 and 2

4. Mammography/ or (breast adj3 screen*).tw,kf.
5. 3 or 4
6. (risk? adj2 (score? or factor? or "breast cancer?" or assessment or group? or stratif* or predict* or project* or individual* or personal* or classif*)).tw,kf.
7. ((risk or stratif* or classif* or individual* or personal*) adj5 (screen* or program* or regimen?)).tw,kf.
8. 6 or 7
9. Economics/
10. exp "Costs and Cost Analysis"/
11. Economics, Nursing/
12. Economics, Medical/
13. Economics, Pharmaceutical/
14. exp Economics, Hospital/
15. Economics, Dental/
16. exp "Fees and Charges"/
17. exp Budgets/
18. budget*.ti,ab,kf.
19. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf.
20. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2
21. (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.
22. (value adj2 (money or monetary)).ti,ab,kf.
23. exp models, economic/
24. economic model*.ab,kf.
25. markov chains/
26. markov.ti,ab,kf.
27. monte carlo method/
28. monte carlo.ti,ab,kf.
29. exp Decision Theory/

30. (decision* adj2 (tree* or analy* or model*).ti,ab,kf.
31. or/9-30
32. 5 and 8 and 31
33. limit 32 to yr="2015 -Current"

Appendix 2: Figure 1 Main milestones and key activities associated with the delivery of Review 1 and Review 2.

	February March 2025	April 2025	May 2025	June 2025	July 2025 [^]	August 2025 [^]	September 2025	October 2025	November 2025	December 2025	January 2026	February 2026
Stakeholders Meeting, Scoping Searches, Protocol Development												
Protocol Refinement and Registration												
Development of Search Strategies												
Screening of Search Results			*	*								
Full-text Assessment			*	*	*	*						
Data Extraction					*	*	*	*				
Quality Appraisal							*	*				
Data Synthesis								*	*	*		
Report Writing												
Preparation of Journal Manuscript												
Advisory Group Meetings												

*Will be dependent on the body of identified evidence; ^ Summer months may represent a period of reduced capacity due to staff annual leave

