Screening for osteoporosis: protocol for an evidence map and umbrella review

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Abbreviations

BMD	Bone mineral density
BMI	Body mass index
CI	Confidence interval
CDR	Centre for Reviews and Dissemination
DARE	Database of Abstract of Reviews of Effects
DALYs	Disability-adjusted life years
DXA	Dual-Energy X-ray Absorptiometry
FRAX	Fracture Risk Assessment Tool
HR	Hazard ratio
ICER	Incremental Cost-Effectiveness Ratio
N/A	Not applicable
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NOGG	National Osteoporosis Guideline Group
PPI	Patient and Public Involvement
PPV	Positive predictive value
QALY	Quality-adjusted life year
QoL	Quality of life
RCT	Randomised controlled trial
SF-36	Short Form-36 Health Survey
RoB2	Cochrane Risk-of-Bias tool for randomized trials 2
ROBINS-I	Risk Of Bias In Non-randomised Studies - of Interventions
SERMs	Selective oestrogen receptor modulators
UK NSC	UK National Screening Committee
WHO	World Health Organization

1. Background

1.1. Condition

Osteoporosis is a systemic metabolic bone disorder characterized by reduced bone mass and deterioration of bone microarchitecture (1, 2). These changes increase bone fragility and, consequently, the risk of fractures (3). The most severe consequence of osteoporosis is the occurrence of osteoporotic or fragility fractures. In 2019, the global incidence of osteoporosis was estimated at 41.5 million cases, with projections suggesting 263.2 million cases between 2030 and 2034 (4). Within the European Union, approximately 5.5 million men and 22 million women are affected, resulting in about 3.5 million fractures annually (5, 6). Globally, 158 million individuals aged ≥50 years were at risk of osteoporotic fractures in 2010, a figure expected to double by 2040 (7). Osteoporosis is a major health concern in postmenopausal women, with fracture risk increasing sharply with age. Bone mass peaks in early adulthood before gradually declining, with loss accelerating after menopause. Epidemiological data show prevalence nearly doubling every five years, from 3.3% at ages 45–49 to 50.3% in women aged ≥85 years (8). Most cases in postmenopausal women are linked to oestrogen deficiency, where rapid bone loss results from increased turnover and an imbalance between resorption and formation (9).

Fragility fractures, particularly hip fractures, represent a major public health concern due to their association with significant disability and mortality (10). It is estimated that mortality from hip fractures ranges between 18 and 33% per year (5) with the mortality risk highest immediately after the fracture event and then decreasing with time (11). In 2010, osteoporosis was responsible for 5.8 million disability-adjusted life years (DALYs) lost in Europe, representing 0.83% of the global burden of non-communicable diseases (5). The DALY loss and associated mortality from osteoporosis-related fractures exceeded that of hypertensive heart disease, rheumatoid arthritis, and all cancers except lung cancer (5, 12).

The economic burden of fragility fractures is also substantial, affecting both patients and healthcare systems (13). A 2020 review reported that the cost of osteoporosis-related fracture is approximately $17.9 and £4 billion per annum in the USA and UK respectively (14). In a 2023 study of women aged ≥50 years in Australia, Germany, South Korea, Spain, and the USA, those with osteoporotic fractures had significantly higher inpatient admission rates, longer hospital stays, and greater healthcare costs compared with a matched cohort of women without previous evidence of osteoporotic fractures (13). Across all countries, the adjusted cost ratios for pharmacy, inpatient, emergency, and outpatient care were consistently higher in the osteoporotic fractures cohort.

Fragility fractures can be largely prevented through the early detection, diagnosis, and treatment of osteoporosis. Implementing an effective early screening programme might help prevent fractures while reducing the clinical, humanistic, and economic burden of the disease.

1.2. Screening strategies

Screening for osteoporosis aims to find people who could benefit from treatment to prevent fragility fractures and their complications. Early identification and timely referral has the potential to improve

outcomes and prognosis, while good frontline diagnostic capability promotes equity and shortens waits for specialist care. Diagnosing osteoporosis early can also reduce public health costs by preventing fractures and avoiding expensive surgeries and hospital stays.

People with suspected osteoporosis are commonly evaluated using risk assessment tools that estimate the 10-year probability of a fragility fracture. The most widely used tools include the Fracture Risk Assessment Tool (FRAX) (15) and QFracture (16). These tests are used to identify individuals who require further tests such as measurement of bone mineral density (BMD) using Dual-Energy X-ray Absorptiometry (DXA).

FRAX is a computer-based algorithm (http://www.shef.ac.uk/FRAX) designed to estimate the 10-year probability of a major osteoporotic fracture (hip, clinical spine, humerus, or wrist) as well as the 10-year probability of hip fracture. It calculates risk based on age, body mass index, and a set of well-validated dichotomous clinical risk factors, with the option to include femoral neck BMD for improved accuracy (17). The FRAX algorithm was developed from a series of meta-analyses incorporating data from 12 independent fracture studies conducted across North America, Europe, Asia, and Australia (18-23). Together, these studies included 60,000 men and women, with more than 250,000 person-years of follow-up, and documented over 1,100 hip fractures and 3,300 osteoporotic fractures (24). Because fracture probability varies considerably across regions, FRAX is calibrated to the local epidemiology of fracture and mortality in countries where such data are available (currently 64 countries). Since its launch in 2008, following eight years of development, FRAX has been widely adopted worldwide, with approximately 6 million calculations performed each year in 173 countries (17). Today, it serves as an important tool in clinical practice and guidelines, helping clinicians identify high-risk individuals and guide treatment decisions for osteoporosis.

QFracture (www.qfracture.org), developed in 2009, is a risk assessment tool based on routinely collected electronic health record data and validated in large UK primary care populations (25). It estimates the 10-year risk of hip and major osteoporotic fractures (hip, spine, wrist) in individuals aged 30 to 85 years, without requiring BMD measurement. The algorithm incorporates a broad range of clinical risk factors, including age, sex, BMI, smoking, alcohol intake, glucocorticoid use, asthma, cardiovascular disease, history of falls, chronic liver disease, rheumatoid arthritis, type 2 diabetes, and tricyclic antidepressant use, with additional female-specific variables such as hormone replacement therapy, menopausal symptoms, parental hip fracture, gastrointestinal malabsorption, and other endocrine disorders (26). QFracture was derived from a UK prospective open cohort study of over 2 million men and women from 357 general practices (26). External validation studies report that QFracture has relatively low PPVs, with PPVs for hip fracture of approximately 4.0% at a 3% 10-year risk threshold (i.e., ≥3% predicted risk of hip fracture over 10 years) and 4.6% at a 5% threshold in women, while negative predictive values consistently exceeded 90% (27).

Both FRAX and QFracture estimate 10-year fracture risk using common clinical risk factors such as smoking, alcohol use, corticosteroid exposure, and parental history of fracture, but they differ in key aspects. Unlike FRAX, QFracture includes a history of falls and a wider range of clinical variables, though it does not incorporate BMD, which FRAX allows, and which remains an important predictor of fracture

risk (28). QFracture has been extensively validated in UK populations and shown to be more accurate for predicting fractures in this setting, but it is reported to be more cumbersome to use and not calibrated for other countries (16). In contrast, FRAX is widely calibrated internationally and integrated into guideline-based treatment thresholds, such as those of the National Osteoporosis Guideline Group (NOGG) in England and Wales (29). Clinical use of either tool depends on local guidelines and patient context, with caution advised in interpreting 10-year risk estimates in the very elderly, where short-term risk may be underestimated.

1.3. Treatment

When osteoporosis is diagnosed it can be managed by a combination of lifestyle measures (weight control, exercise, smoking and alcohol avoidance, and calcium/vitamin D supplementation) with pharmacological therapy (30). First-line treatments are usually antiresorptive agents such as bisphosphonates (alendronic acid or risedronate sodium), zoledronic acid or denosumab, which reduce bone turnover and fracture risk, while anabolic or dual-action therapies (for example, teriparatide, abaloparatide, romosozumab) stimulate new bone formation and are reserved for severe or high-risk cases (31). In post-menopausal women oestrogen or elective oestrogen receptor modulators (SERMs), can be used (32). Both classes increase BMD and reduce fractures, though bone-forming therapies are generally more effective in severe disease and are often followed by antiresorptives to sustain benefits (31). Long-term, individualised treatment strategies may include switching or combining agents if side effects or treatment failure occur (31). Both NICE and NOGG (29, 33, 34) recommends a comprehensive strategy that includes fracture risk assessment, lifestyle modifications, and pharmacological intervention based on risk level. Bisphosphonates are the foundation of treatment, with newer anabolic agents like romosozumab and abaloparatide reserved for those at very high risk or who cannot use first-line agents. Regular reassessment and attention to adherence ensure long-term effectiveness.

1.4. Current UK NSC recommendation on screening for osteoporosis

The UK NSC currently does not recommend screening for osteoporosis in postmenopausal women (35).

1.5. Previous UK NSC reviews

In 2019, the UK NSC commissioned a review to assess whether systematic population screening for osteoporosis in postmenopausal women should be introduced (36). The review, covering evidence published between 2011 and 2018, addressed four key questions: How accurate are screening tests? How effective are the interventions? Do randomised controlled trials demonstrate a clinical benefit of screening? Do UK-based evaluations show screening to be cost-effective? For screening accuracy, the focus was on strategies combining risk assessment tools (such as FRAX) with DXA.

The review incorporated new evidence from two RCTs, SCOOP and ROSE (37, 38), since the previous review in 2013 (39), which directly compared screening with usual care. Results showed no significant reduction in osteoporotic fractures among systematically screened women compared to those receiving usual care. Although a variety of screening approaches were identified in the wider literature, few met

the inclusion criteria, and all of the review's key questions (the accuracy of screening tests, the effectiveness of interventions, whether RCTs demonstrate a clinical benefit, and whether UK-based evaluations show cost-effectiveness) could not be fully addressed by the evidence identified (36).

Overall, the report concluded that important uncertainties and evidence gaps remained. On this basis, the UK NSC maintained its recommendation against introducing a national osteoporosis screening programme for postmenopausal women.

In 2024, the UK NSC commissioned an evidence map (40) to assess the volume and type of evidence on key issues in osteoporosis screening since the 2019 review (36). The map addressed three questions: what is (1a) the volume and type of evidence exploring the clinical benefit of whole population screening in women over 65, in reducing osteoporotic fractures compared to standard care? (1b) the volume and type of evidence exploring the clinical benefit of targeted screening of women aged under 65 with risk factors for osteoporosis, in reducing osteoporotic fractures compared to standard care? and (2) the volume and type of evidence exploring the cost-effectiveness of screening (whole population and targeted) for osteoporosis?

Nineteen articles were included: three RCTs (SCOOP (38), ROSE (37) SALT/SOS (41)), one nonconcurrent cohort study (42), six reviews (41, 43-47), five sibling papers related to SCOOP (48-52), and four related to ROSE (53-56). The RCTs and cohort study examined whole-population screening in women over 65, while all six reviews also addressed this question to some degree. However, conclusions as to whether screening was significantly beneficial and the recommendations whether to implement it were mixed across studies.

The 2024 evidence map found mixed results from systematic reviews on osteoporosis screening in women over 65 (41, 43-47). Although the reviews had similar criteria and used largely the same primary trials, their conclusions differed: some reported small but meaningful reductions in fractures, while others found little-to-no benefit. To understand these disparities and identify evidence gaps relevant to policy, the UK NSC has commissioned the current review. While early detection of osteoporosis may be valuable, if existing evidence does not support the implementation of a screening programme, the review aims to highlight priorities for future research.

2. Overall approach

This review will consist of two components

1. Evidence map
   Conduct an updated literature search to identify any new primary studies or reviews reporting on the efficacy of population screening for osteoporosis in women published since the 2024 evidence map.

2. Assessment of reviews
   Conduct an assessment of reviews to examine the included primary studies and reviews (identified in both the previous UK NSC reviews and the update (Q1)) in detail and investigate what factors (methodological or otherwise) could account for differences in conclusions between the reviews.

3. Methods: Evidence map

The review will be undertaken using the UK NSC assessment approach for an Evidence Map (57).

3.1. Decision questions

Decision questions for the evidence map are presented below:

Question 1a. What is the volume and type of evidence exploring the clinical benefit of whole population screening in women over 65, in reducing osteoporotic fractures compared to standard care?

Question 1b. What is the volume and type of evidence exploring the clinical benefit of targeted screening of women aged under 65 with risk factors for osteoporosis, in reducing osteoporotic fractures compared to standard care?

Question 2. What is the volume of evidence exploring the cost-effectiveness of screening (whole population and targeted) for osteoporosis?

3.2. Identification and selection of studies

3.2.1 Search strategy

Systematic literature searches will be undertaken using terms for the condition which will identify evidence for all review questions. The search strategies from the 2024 evidence map will be rerun to find studies published since the last search date (12th November 2024). A date restriction from the start of November 2024 was added to the search for this purpose. The searches will be conducted in the same 11 databases:

- Medline (1946-current) and Embase (1974-current) via Ovid,
- The Cochrane Database of Systematic Reviews (CDSR) (Cochrane),

- Epistemonikos (https://www.epistemonikos.org/en/),
- CEA Registry (https://cevr.tuftsmedicalcenter.org/databases/cea-registry),
- CINAHL Ultimate (1937- current) via EBSCO host,
- Google Scholar (https://scholar.google.co.U K/),
- Science Citation Index (SCI) (1900-current) and,
- Social Sciences Citation Index (SSCI) (1900-current) via Clarivate's Web of Science.

The retrieved papers will be imported into Endnote and deduplicated.

3.2.2. Study eligibility criteria

Studies that satisfy the inclusion criteria listed in Table 1 will be included.

Table 1. Inclusion and exclusion criteria for the key questions

Key question	Inclusion criteria							Exclusion criteria
	Population	Target condition	Intervention	Comparator	Outcome	Study type	Geographic focus	

1a. What is the volume and type of evidence exploring the clinical benefit of whole population screening in women over 65, in reducing osteoporotic fractures compared to standard care?	Women > 65 years	Osteoporosis	• Any population or targeted screening[a] intervention that involves any combination of risk assessment and DXA designed to identify women that have, or are at risk of, developing osteoporosis.	Standard care/ no screening	Prevention of osteoporosis:
					• Osteoporotic fracture:
					  ○ Vertebral
					  ○ Non vertebral
					  ○ Hip
					• All cause fracture
					• Mortality
					Possible harms of screening / treatment, e.g.
					• Overdiagnosis/overtreatment
					• False positive results
					• Anxiety
					• Thromboembolic event
					• Osteonecrosis of the jaw
					• Gastrointestinal problems
						• Systematic reviews
						• Rapid reviews
						• RCTs
						• Non-RCTs
						• Quasi-RCTs
							No restriction	• Male or mixed-gender samples (unless female sample data can be separated)
								• Samples of women under 65
								• Samples where either risk factors or a mean age of 65 at study entry is not explicit
								• Letters, reviews, editorials, communications, commentaries, conference abstracts and other grey literature, studies that have been retracted
								• Studies where it cannot be established if the inclusion criteria are met

1b. What is the volume and type of evidence exploring the clinical benefit of targeted screening of women aged under	Women < 65 years with risk factors for osteoporosis:
	• Previous fragility fracture
	• Current use or frequent use of
		Osteoporosis	• Any population or targeted screening[a] intervention that involves any combination of risk assessment and dual energy x-ray scan (DXA) designed to	Standard care/ no screening	Prevention of osteoporosis:
					• Osteoporotic fracture:
					  ○ Vertebral
					  ○ Non vertebral
					  ○ Hip
					• All cause fracture
						• Systematic reviews
						• Rapid reviews
						• RCTs
						• Non-RCTs
						• Quasi-RCTs
							No restriction	• Male or mixed-gender samples (unless female sample data can be separated)
								• Samples of women under 65 where risk

Key question	Inclusion criteria Population	Target condition	Intervention	Comparator	Outcome	Study type	Geographic focus	Exclusion criteria
65 with risk factors for osteoporosis, in reducing osteoporotic fractures compared to standard care?	oral or systemic glucocorticoids • History of falls • Family history of hip fracture • Other causes of secondary osteoporosis[b] • Smoking • Alcohol intake of more than 14 units per week • Menopause		identify women that have, or are at risk of, developing osteoporosis.		• Mortality Possible harms of screening / treatment, e.g. • Overdiagnosis/overtreatment • False positive results • Anxiety • Thromboembolic event • Osteonecrosis of the jaw • Gastrointestinal problems			factors are not explicit • Samples where either risk factors or a mean age of 65 at study entry is not explicit • Letters, reviews, editorials, communications, commentaries, conference abstracts and other grey literature, studies that have been retracted • Studies where it cannot be established if the inclusion criteria are met
2. What is the volume of evidence exploring the cost-effectiveness of screening (whole population and targeted) for osteoporosis?	Adults	Osteoporosis	• Any population or targeted screening[a] intervention that involves any combination of risk assessment and dual energy x-ray scan (DXA) designed to identify adults that have, or are at risk of, developing osteoporosis.	Any comparator	• Incremental cost-effectiveness ratio (ICER) • Quality-adjusted life years (QALYs), • Cost per life-year gained • Cost per quality-adjusted life years (DALYs) averted • Net health or monetary benefit	• Cost-effectiveness Analysis • Cost-utility analysis • Cost-minimisation analysis/ cost comparison • Cost-consequence analysis	No restriction	• Studies not reporting cost effectiveness in population screening

Key question	Inclusion criteria Population	Target condition	Intervention	Comparator	Outcome	Study type	Geographic focus	Exclusion criteria
					• Overall costs from a healthcare and/or societal perspective, • Health-related quality of life (e.g. EQ-5D, SF-36)	• Cost-of-Illness • Cost-benefit analysis • Budget impact		

DALY, Disability-adjusted life year; DXA, Dual-energy X-ray absorptiometry; EQ-5D, EuroQol 5-Dimensions; ICER, Incremental cost-effectiveness ratio; QALY, Quality-adjusted life year; RCT, Randomised controlled trial; SF-36, Short Form (36) Health Survey.

[a]UK NSC definitions of targeted and population screening were used:

- Population screening: A nationally delivered (in England, Scotland, Wales and Northern Ireland), proactive (individuals are actively invited for screening) screening programme which aims to improve health outcomes in people with the condition being screened for and/or offer information to enable informed choices. It is offered to a group of people identified from the whole population and defined demographically such as by age or sex.
- Targeted screening: A nationally delivered, proactive screening programme which aims to improve health outcomes in people with the condition being screened for, among groups of people identified as being at elevated/above average risk of a specific condition. Compared to the general population, the people targeted may have higher risk because of lifestyle factors, genetic variants or having another health condition. Targeted screening differs from population screening as it aims to identify groups of people with a higher risk of a specific condition beyond demographics such as age or sex. For example, individuals who smoke are at a higher risk of developing lung cancer regardless of their age or sex.

[b]Causes of secondary osteoporosis include endocrine (hypogonadism in either sex including untreated premature menopause and treatment with aromatase inhibitors or androgen deprivation therapy; hyperthyroidism; hyperparathyroidism; hyperprolactinaemia; Cushing's disease; diabetes), gastrointestinal (coeliac disease; inflammatory bowel disease; chronic liver disease; chronic pancreatitis; other causes of malabsorption), rheumatological (rheumatoid arthritis; other inflammatory arthropathies), haematological (multiple myeloma; haemoglobinopathies; systemic mastocytosis), respiratory (cystic fibrosis; chronic obstructive pulmonary disease), metabolic (homocystinuria), chronic renal disease and immobility (due for example to neurological injury or disease.

3.3. Review strategy

Titles and abstracts of records identified by the searches will be assessed against the eligibility criteria by one reviewer.

We will note the number of unclear studies by question following title and abstract assessment and consult with UK NSC partners to determine whether full text assessment is necessary, taking into account the volume of included studies for each review question. If full text review of unclear studies is agreed on, full text articles will be assessed by one reviewer. If full text assessment is not required, we will report the number of unclear records as potential additional studies.

3.4. Data extraction strategy

Data will be extracted by a single reviewer. The following data will be extracted (but not limited to): citation details, study details including country, study design, population details, intervention, comparator, outcomes including osteoporotic fracture rates (vertebral, non-vertebral, hip), all cause fracture, mortality and possible harms of screening / treatment (for example overdiagnosis/overtreatment, false positive results, anxiety, thromboembolic event etc). Outcomes will be stratified by age, sex, ethnicity and other population or targeted characteristics where available.

3.5. Assessment of study quality

No assessment of study quality will be undertaken.

4. Methods: Assessment of reviews

4.1. Decision question

What methodological factors could explain the mixed conclusions across existing reviews on the effectiveness of screening for osteoporosis in women, considering:

- women aged over 65 (whole population)
- women with identifiable risk factors (targeted screening)?

4.2. Identification and selection of studies

Any new publications identified in the updated evidence map will be added to the six relevant reviews (41, 43-47) identified in the 2024 Osteoporosis Evidence Map (40):

- Auais *et al*. The effectiveness and cost-effectiveness of clinical fracture-risk assessment tools in reducing future osteoporotic fractures among older adults: a structured scoping review (43)

- Gates *et al*. Screening for the primary prevention of fragility fractures among adults aged 40 years and older in primary care: systematic reviews of the effects and acceptability of screening and treatment, and the accuracy of risk prediction tools (45)
- Johnell et al. What evidence is there for the prevention and screening of osteoporosis? (6).
- Merlijn *et al*. Fracture prevention by screening for high fracture risk: a systematic review and meta-analysis (41)
- Viswanathan *et al*. Screening to Prevent Osteoporotic Fractures: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force (47)
- EUnetHTAOTCA19 Assessment Team. Screening for osteoporosis in the general population. Collaborative Assessment (44).

4.3. Data extraction strategy

Data extraction will be performed independently by two reviewers. Data will be collected in Excel; however, only key information necessary to support the findings will be presented in tables in the final report. The full Excel dataset will be provided as a supplementary file to ensure transparency and completeness.

The following data will be extracted from the reviews[1]:

- Study design
    - Product (systematic review/rapid review etc)
    - Objectives
    - Search dates
    - Databases
    - Additional searches
    - Inclusion criteria
        - Study designs
        - Population (and details of those relevant to the decision question)
        - Intervention
        - Comparator
        - Outcomes (to include definitions)
    - Risk of bias tool
- Statistical methods (meta-analysis)
    - Software
    - Methods (random vs fixed effect etc)
    - Details of sensitivity analyses
    - Details of trials included and data inputs for the analysis of each outcome
- Included studies
    - To include citation details for the source of data

[1] Where publications consider multiple research questions, extraction will be limited to only those relevant to the decision question (Section 4.1)

- Quantitative results for outcomes reported in at least two of the included reviews
  - Meta-analysis results
  - Trial level data presented
- Author reported conclusions of results
- Author reported methodological issues

For all primary trials included in the reviews the following data will be extracted[2]:

- Study design
- Primary outcome
- Inclusion/exclusion criteria
- Intervention
- Comparison
- Outcomes (restricted to those included in the reviews/meta-analyses)
  - Definitions
  - Data reported (i.e. counts or hazard ratios)

4.4. Assessment of study quality

Quality assessment will be undertaken for each systematic review using ROBIS (58) and for each primary study included in the reviews using an appropriate tool (Cochrane Risk-of-Bias tool for randomised trials (RoB 2)(59) or the Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) (60). The studies will be assessed by one reviewer and checked by a second. Discrepancies will be resolved by consensus or a third reviewer.

We will compare the risk of bias reported in the reviews with our judgement and flag only major discrepancies (e.g. different overall rating). Where major discrepancies occur, we will note likely reasons (e.g. different tool/version or signalling questions, missing information).

4.5. Approach to assessment

We will assess the included reviews using a structured framework focusing on four key domains:

- Review objectives and key questions
  - Identify and compare the stated aims of each review to determine alignment or divergence in scope.
- Primary studies included
  - Compare reviews in terms of search dates, search strategies, and inclusion criteria, and assess how these factors contributed to variations in the set of primary studies included.

[2] That are relevant to the decision question

    - Explain differences across the primary trials included in the meta-analyses in terms of study designs, populations, and outcome data reported.

- Meta-analyses/numerical data
    - Compare the statistical approaches (for example, effect measures, models, software) used in the meta-analyses.
    - Cross-check the data inputs from each review (for the meta-analysis or as presented in reviews where no meta-analysis is conducted) against the original trial publications to validate them. Explain any differences between trial data inputs across the reviews.
    - Sense check the results of each meta-analysis based on data input.
    - Compare the meta-analysis results across studies for each outcome and highlight any instances where there are key differences such as opposite direction of treatment effects and differences in statistical significance (i.e. the 95% CI does or doesn't include the null value).
- Author conclusions/interpretation
    - Validate the author reported conclusions of the meta-analysis results. In cases where a review has not conducted a meta-analysis, but reports trial level estimates validate these against the reported author conclusions.

Using this framework, we will draw out the underlying reasons for any differences in conclusions across reviews. Potential explanatory factors may include:

- Timing of the review (for example, earlier reviews may have omitted later trials)
- Methods of the review and included studies (for example, RCTs only versus the inclusion of broader designs)
- Statistical methodology applied (for example, random-effects vs fixed-effect meta-analysis)
- Trial data included (for example, adjusted vs unadjusted hazard ratios)
- Interpretation of numerical data by review authors (for example, considering a hazard ratio statistically significant when the upper 95% CI = 1)
- Authors/purpose of the review (i.e. for the United States Preventive Services Task Force)

5. Methods for reporting

Results from the updated evidence map and assessment of reviews will be presented in a single report comprising the following sections:

- Introduction (background on osteoporosis, screening, treatment, current UK recommendations and previous reviews)
- Evidence map (methods, results (including PRISMA flow diagram), summary of results)

- Assessment of Reviews (methods, results (including tables of key data), discussion of results, future considerations)[3]
- Overall conclusions

6. Patient and Public Involvement

No PPI activity will be undertaken as part of this evidence review.

7. Timescale

The proposed timeline for the evidence map is presented in Table 2 and for the assessment of reviews in Table 3.

[3] The assessment of reviews will be guided by best-practice methods for overviews of reviews (45)

Table 2. Project timeline for evidence map

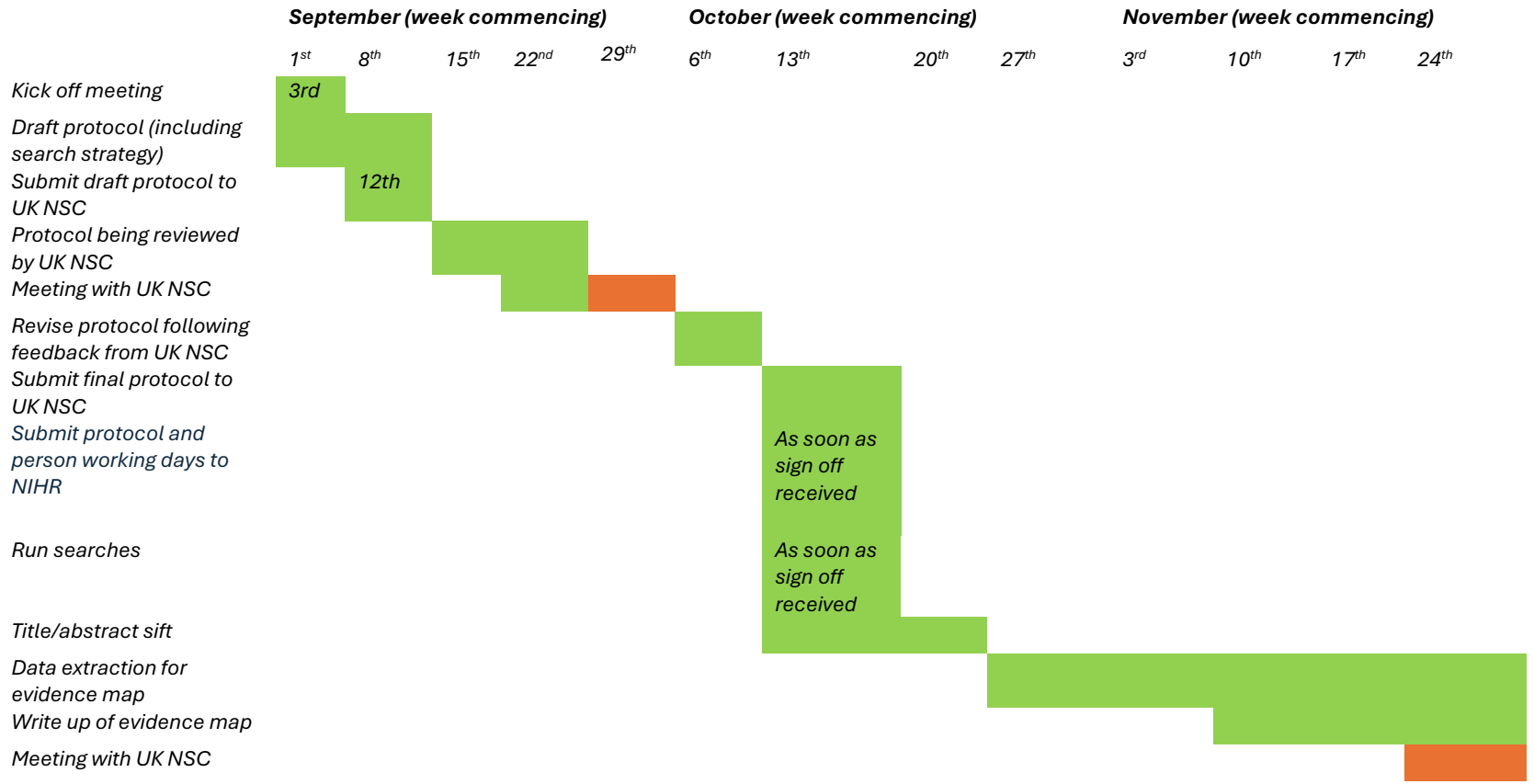
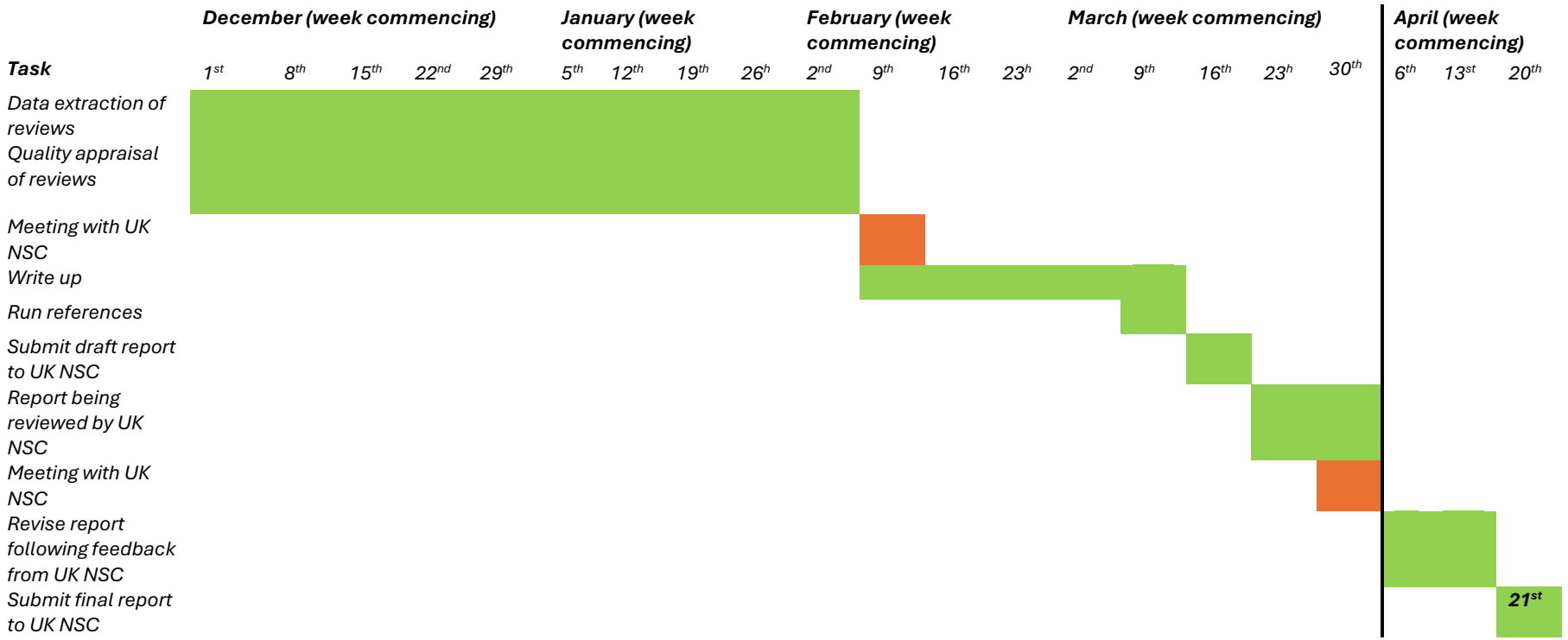


Table 3. Project timeline for assessment of reviews



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9. Competing interest of authors

Chris Stinton is a member of the UK NSC's Adult Reference Group. None of the other authors declared any competing interests for the project.

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Appendix A: Search strategies

Searches run: 12.09.25
Ovid MEDLINE(R) ALL <1946 to September 11, 2025>

#	Searches	Results
1	exp *osteoporosis/ or exp osteoporosis, postmenopausal/	53707
2	*Bone Density/	30221
3	*fractures, bone/ or osteoporotic fractures/	67160
4	(osteoporo* or osteopenia).tw.	106803
5	((densit* or loss or mass or strength*) adj2 bone*).tw.	118533
6	fractur*.ti.	186236
7	1 or 2 or 3 or 4 or 5 or 6	366196
8	*Mass Screening/	60324
9	(screen or screening or screened or prescreen*).ti.	239599
10	8 or 9	257245
11	7 and 10	1953
12	(screen or screening or screened or prescreen*).tw.	1114588
13	(fractur* or bone* or osteop*).tw.	1194534
14	((screen or screening or screened or prescreen*) adj2 (fractur* or bone* or osteop*)).tw.	2516
15	11 or 14	3539
16	((dexa or dxa) adj2 scan*).tw.	3511
17	dual energy x ray absorptiomet*.tw.	26673
18	(fracture* adj2 risk* adj2 assessment*).tw.	1891
19	FRAX.tw.	1981
20	16 or 17 or 18 or 19	30391
21	osteop*.tw.	147141
22	((((dexa or dxa) adj2 scan*) or dual energy x ray absorptiomet* or (fracture* adj2 risk* adj2 as-sessment*) or FRAX) adj2 osteop*).tw.	382
23	15 or 22	3856
24	*Absorptiometry, Photon/	4948
25	osteopor*.ti.	42298
26	24 and 25	563
27	23 or 26	4280
28	(scan* and osteop*).ti.	163
29	27 or 28	4389
30	limit 29 to dt=20241101-20250912	317
31	limit 29 to ed=20241101-20250912	234
32	**30 or 31**	**353**