National Institute for Health and Care Excellence

Draft for consultation

Osteoporosis: risk assessment

[F] Diagnostic accuracy and effectiveness of vertebral fracture clinical decision tool (Vfrac)

NICE guideline <number>

Evidence reviews underpinning recommendation for research in the NICE guideline

January 2026

Draft for Consultation

This evidence review was developed by NICE

1

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ISBN:

Contents

1

1. Diagnostic accuracy of vertebral fracture clinical decision tool (Vfrac)

1.1. Review question: What is the diagnostic accuracy of the vertebral fracture clinical decision tool (Vfrac) for determining who needs imaging to identify people with a suspected vertebral fracture?

1.1.1. Introduction

The use of clinical tools to aid decision making for managing health conditions is increasing in the UK health services. Vfrac is a recently developed clinical tool, which can be performed by a practice nurse, for assessing risk of osteoporotic vertebral fractures and need for spinal radiography. This review question assesses what its diagnostic accuracy is in older adults with recent back pain and at risk of fracture.

1.1.2. Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Older adults (65 years and older) who are at risk of fragility fracture and have had back pain in the last 4 months.
Target condition	Vertebral fractures
Index test	The vertebral fracture clinical decision tool (Vfrac)
Reference standard	Vertebral fracture found by standard imaging procedures (X-ray, CT, and MRI).
Statistical measures	All outcomes are considered equally important for decision making and therefore have all been rated as critical: Accuracy of estimation of vertebral fracture: • Sensitivity/ specificity • Likelihood ratio • Positive predictive value/ negative predictive value • Area under the curve (AUC)
Study design	Diagnostic: cross-sectional studies will be included If cross-sectional studies are not found diagnostic cohort studies will be included

1.1.3. Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4. Diagnostic evidence

1.1.5. Included studies

One study (Khera 2022) was included in the review and summarised in **Table 2**. Evidence from this study is summarised in the clinical evidence summary below in **Table 3**. This study developed the Vfrac clinical tool using self-completed questionnaires and physical examination to determine the model parameters and cut-off threshold. The study included an internal validation.

The assessment of the evidence quality was conducted with emphasis on sensitivity and specificity as this was identified by the committee as the primary measure in guiding decision making. The committee set clinical decision thresholds for sensitivity/specificity at 0.7 above which a test would be recommended and 0.5 below which a test is of no clinical use.

See also the study selection flow chart in Appendix C, study evidence tables in Appendix D and sensitivity and specificity forest plots in Appendix E

1.1.6. Excluded studies

See the excluded studies list in Appendix I.

1.1.7. Summary of studies included in the diagnostic accuracy evidence

Table 2: Summary of studies included in the evidence review

Study	Population	Target condition	Index test	Reference standard	Outcomes
Khera 2022 Cohort study UK	Women aged 65 years or above with a self-reported episode of back pain in the previous 4 months were recruited from general practices. Age: 73.9 (5.6) years. N=1635	Osteoporotic vertebral fractures	Vfrac clinical tool Derivation/internal validation study to develop the Vfrac clinical tool using self-completed questionnaires and physical examination to determine the model parameters and cut-off threshold.	Lateral thoracic and lumbar radiographs	• Sensitivity • Specificity • Area under the curve (AUC) • Likelihood ratios • Positive predictive ratio • Negative predictive ratio

1.1.8. Summary of the diagnostic accuracy evidence

Table 3: Clinical evidence summary: sensitivity and specificity for Vfrac

Studies	N	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect size (95%CI)	GRADE certainty
Vfrac (all predictors) to detect who needs imaging to identify people with a suspected vertebral fracture							
1 cohort study	1337	Very serious[a]	Not serious[b]	Not serious	Serious[c]	Sensitivity=0.73 (0.65 to 0.79)	VERY LOW
		Very serious[a]	Not serious[b]	Not serious	Serious[c]	Specificity= 0.73 (0.70 to 0.75)	VERY LOW

a. Downgraded by 2 increments for risk of bias due to patient flow and patient selection.
b. Not applicable as outcome is from 1 study.

c. Downgraded by 1 increment for imprecision because the 95% CI crossed 1 MID line (0.5, 0.7 for sensitivity and specificity).

Table 4: Summary of diagnostic accuracy: AUC

Studies	N	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect size (95%CI)	Certainty
Vfrac (all predictors) to detect who needs imaging to identify people with a suspected vertebral fracture							
1 cohort study	1337	Very serious[a]	Not serious[b]	Not serious	Not serious	0.802 (0.764 to 0.840)	LOW

a. Downgraded by 2 increments for risk of bias due to patient flow and patient selection.
b. Not applicable as outcome is from 1 study.

1.1.9. Economic evidence

Economic evidence related to Vfrac is considered as part of the evidence review in Section 1.2 below.

1.2. Review question: What is the clinical and cost-effectiveness of vertebral fracture clinical decision tool (Vfrac) to identify people with a suspected vertebral fracture?

1.2.1. Introduction

The use of clinical tools to aid decision making for managing health conditions is increasing in the UK health services. Vfrac is a recently developed clinical tool, which can be performed by a practice nurse, for assessing risk of osteoporotic vertebral fractures and need for spinal radiography. This review question assesses what its effectiveness and cost effectiveness in identifying suspected vertebral fractures is in older adults with recent back pain and at risk of fracture.

1.2.2. Summary of the protocol

Table 5: PICO characteristics of review question

Population	Older adults (65 years and older) who have had back pain the last 4 months
Risk assessment tool	Vfrac Followed by imaging and then appropriate treatment. Treatments: • Alendronate • Ibandronate • Risedronate • Abaloparatide • Denosumab • Raloxifene • Romosozumab • Teriparatide • Strontium ranelate • HRT (newer forms)
Comparison	Usual care / no Vfrac Followed by imaging and then appropriate treatment. Treatments: • Alendronate • Ibandronate • Risedronate • Abaloparatide • Denosumab • Raloxifene • Romosozumab • Teriparatide • Strontium ranelate • HRT (Newer forms)
Outcomes	All outcomes are considered equally important for decision making and therefore have all been rated as critical:

	• Vertebral fracture
	• Generic health-related quality of life (continuous outcomes will be prioritised [validated measures]). The hierarchy for extracting will be as follows, if measures higher on higher on hierarchy are reported others will not be:
	  ○ EQ-5D
	  ○ SF-6D
	  ○ SF-36
	  ○ SF-12
	  ○ Other utility measures (AQOL, HUI, 15D, QWB)
	• Health-related quality of life measure for vertebral fractures (QUALEFFO-41)
	• Change in management.

Study design	• Diagnostic randomised controlled trials (RCTs). • Published NMAs and IPDs will be considered for inclusion. Systematic reviews of randomised controlled trials

1.2.3. Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.2.4. Effectiveness evidence

1.2.5. Included studies

No studies were identified from searching. For study selection, see flow chart in Appendix C.

1.2.6. Excluded studies

See the excluded studies listed in Appendix I.

1.2.7. Summary of studies included in the effectiveness evidence

No studies were identified.

1.2.8. Summary of the effectiveness evidence

No studies were identified.

1.2.9. Economic evidence

For methods, see the health economic review protocol in Appendix A.

1.2.10. Included studies

One health economic study with relevant comparisons was included in this review (Khera 2022). This was a cost-effectiveness analysis that compared the use of the Vfrac tool to selectively refer patients for a spinal radiograph to standard care.

This is summarised in the health economic evidence profile below (Table 6) and the health economic evidence table in Appendix G.

See also the health economic study selection flow chart in Appendix F.

1.2.11. Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations, as detailed in Appendix I.

1.2.12. Summary of included economic evidence

Table 6: Health economic evidence profile: Vfrac compared to standard care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	ICER	Uncertainty
Khera 2022 (UK)	Partially applicable[a]	Potentially serious limitations[b]	• Cost-utility analysis (QALYs) • Decision tree capturing numbers referred for radiograph, diagnosed with OVF, and treated, with lifetime costs and QALYs estimated using a published DES model. • Population: women aged 65+ years from primary care with self-reported back pain in the previous 4 months • Comparators: 1. Standard care: All patients had a GP consultation, the outcomes of which were: • with OVF and referred for radiograph (2.5%), • with OVF but not referred for radiograph (10%) • without OVF but referred for radiograph (19%) • Without OVF and not referred for radiograph (68.5%) 2. Vfrac: informed by cohort study included in diagnostic review, with the following outcomes: • with OVF and referred for radiograph (9.1%),	£7.28[c]	0.00044	£16,545 per QALY gained	Probability Intervention 2 cost effective versus Intervention 1 (£20K threshold): 49.4% No one way or scenario analyses were reported. EVPI analysis indicated there would be value in pursuing further research. The primary focus of the research would be the analysis of Vfrac against an appropriate comparator in a RCT setting.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	ICER	Uncertainty
			• with OVF but not referred for radiograph (3.4%) • without OVF but referred for radiograph (25%) • Without OVF and not referred for radiograph (62.5%) ○ All patients with OVF and who were referred for radiograph were then assumed to initiate treatment with alendronate. • Time horizon: lifetime				

Abbreviations: DES= discrete event simulation; EVPI= expected value of perfect information; GP= general practitioner; ICER= incremental cost-effectiveness ratio; OVF= osteoporotic vertebral fracture; QALYs= quality-adjusted life years; RCT= randomised-controlled trial

(a) The cost year for the radiograph was not reported. The published model used to estimate long-term costs applied a 2018 cost year, and no updates were stated – therefore, these values may not reflect the current NHS cost context.

(b) Resource-use estimates for the standard care arm were derived from a clinician- and patient-led committee. Population characteristics informing the DES model for treated and untreated OVF were taken from the 118 patients in the associated cohort study with a positive Vfrac score and confirmed OVF; comparison with the 2011 UK Census indicated under-representation of non-white groups. No one-way or scenario analyses were conducted.

(c) 2020 UK pounds (£). Cost components included: radiograph to diagnose OVF, treatment costs (alendronate), fracture costs, residential care following hip fracture.

1.2.13. Economic model

This area was not prioritised for new cost-effectiveness analysis.

1.2.14. Unit costs

Vfrac is used to assess the need for spinal radiography. Current unit costs of spinal radiography are included to support cost-effectiveness considerations. The committee assumed that spinal radiography would be performed using a plain film (x-ray).

Table 7. Unit costs associated with diagnostic imaging

Resource	Unit costs	Source
Plain film (x-ray)	£43.72[(a)]	NHS National Cost Collection 2023/24

(a) Weighted average cost of plain film.

1.2.15. Evidence statements

- One cost-utility analysis (with a lifetime horizon) found that, among women aged 65 and older in primary care who had self-reported back pain within the previous four months, using the Vfrac tool to support clinician decisions on spinal radiograph referrals was cost effective (ICER: £16,545 per QALY) compared to standard care at a threshold of £20,000 per QALY gained, with a 49% probability of being cost effective. This analysis was assessed as partially applicable with potentially serious limitations.

1.3. The committee's discussion and interpretation of the evidence

1.3.1. The outcomes that matter most

1.3.1.1. Diagnostic accuracy

Diagnostic accuracy of the vertebral fracture clinical decision tool (Vfrac) was the outcome prioritised for this review. The following accuracy outcomes were prioritised for decision making: sensitivity, specificity, likelihood ratio, positive predictive value, negative predictive value, and area under the curve (AUC). The guideline committee considered sensitivity the most important measure for this tool to minimise the risk of false negative results. False negative results would mean that people with vertebral fractures would be missed and not receive appropriate treatment that could reduce the risk of subsequent fractures. Specificity was also considered important to prevent a high number of false positive results which would mean unnecessary imaging which has health and cost implications. The evidence for the diagnostic accuracy of Vfrac was identified in one study. The study presented area under the curve, sensitivity, specificity, positive predictive values, and negative predictive values. Likelihood ratios and confidence intervals for sensitivity and specificity were calculated from the information presented in the study.

1.3.1.2. Diagnostic clinical effectiveness

Vertebral fracture, generic health related quality of life, health related quality of life measures for vertebral fractures and change in management were considered by the guideline committee to be equally important for decision making and were therefore all rated as critical. No evidence was identified for any of the outcomes.

1.3.2. The quality of the evidence

1.3.3. Diagnostic accuracy

Evidence was found from one cohort study that developed the Vfrac tool from a group of women over 65 years old with self-reported back pain in the last 4 months. Subsequent internal validation using bootstrapping methods was conducted in the same population. The Vfrac tool was used to identify the people who should have a spinal radiograph to assess for vertebral fractures.

The identified evidence ranged from low to very low certainty. The area under the curve value was downgraded for very serious risk of bias. Sensitivity and specificity were downgraded due to high risk of bias and imprecision. The high risk of bias was due to bias of patient flow (unclear interval between the radiographs and the Vfrac and some patients were missing from the analysis) and patient selection (unclear if Vfrac results were interpreted without knowledge form the radiograph findings). There was serious imprecision due to confidence intervals that crossed the threshold for high sensitivity (70%).

The committee considered the limitations of the evidence from this single study and acknowledged the difficulty in making recommendations before further studies had been completed.

1.3.4. Diagnostic clinical effectiveness

No evidence was identified.

1.3.5. Benefits and harms

The Vfrac findings presented AUC of 0.802 (95%CI 0.764 to 0.840), which indicates moderate discrimination.

The sensitivity and specificity of Vfrac were 72% and 73% respectively, which were above the prespecified clinical decision threshold of 0.7 above which a test could be recommended. These outcomes were reported using a cut-point of the model's linear predictor of -2.0 that weighed false positives and false negatives equally, maximising sensitivity and specificity. However, it was noted that the evidence was from a single preliminary study that had yet to be validated in different populations.

1.3.6. Committee discussion and conclusions

The committee discussed that the Vfrac decision tool appeared to have promising discrimination between people with and without vertebral fractures. The committee agreed it could be a useful tool to support GPs decision whether to order imaging in the future. However, it was noted that the one included study was a preliminary development study with internal validation and further evidence would be needed to support a recommendation within this guideline.

Further studies would be necessary to support the tool's use in different populations as the current evidence only included women aged 65 years or above. The tool consists of 15 questions that included self-reported pain descriptions. The committee discussed that pain descriptors are thought to be different for men and women and also for Caucasians and non-Caucasians. This could mean that the tool may not work as well in these different populations. However, the committee were aware of a recent qualitative study that concluded that the Vfrac tool questionnaire did not have gender specific barriers and could be used for men.

The study did not include a younger population as it was thought that the tool would not be cost effective in a younger population where risk of vertebral fractures is lower. In addition,

the committee considered that postmenopausal women were more likely to get vertebral fractures as they are more likely to develop osteoporosis.

The committee discussed the importance of tools to identify vertebral fractures to reduce risk of future fractures. It is believed that approximately only a quarter of vertebral fractures are identified. Currently, vertebral fractures are often left undiagnosed and there would be a benefit for increased identification which would lead to appropriate treatment and a reduction in fractures. The committee discussed the fact that it would be a valuable tool in enabling access to anabolic treatments that depend on having had a previous fracture including vertebral fractures.

The committee agreed not to make recommendations at this time due to the limited evidence base of a single study. The committee were aware of an ongoing feasibility study and planned cluster RCT to compare the use of Vfrac in GP surgeries. The committee agreed to make a research recommendation on the clinical and cost effectiveness of Vfrac to identify people with vertebral fractures to match and support the existing planned research.

The committee had noted in the protocol that there are no known validated tools in men or women aged 65 or under and planned to make a research recommendation. However, the committee agreed to prioritise research to fully evaluate Vfrac in the population it was developed for before evaluating in this lower risk population.

1.3.7. Cost effectiveness and resource use

One UK economic evaluation was identified during the review, which compared Vfrac to standard care in women aged 65+ years with self-reported back pain in the previous four months from primary care. Sensitivity and specificity of Vfrac were taken from the cohort study identified in the clinical review and defined in the modelling as:

- True positive (with an osteoporotic vertebral fracture (OVF) and referred for radiograph): 9.1%
- False negative (with OVF but not referred for radiograph): 3.4%
- False positive (without OVF but referred for radiograph): 25%
- True negative (without OVF and not referred for radiograph): 62.5%.

Due to an absence of comparative data for standard care, an online survey was conducted to elicit this from a committee of seven clinicians and 12 patients. Based on the survey responses, it was assumed that under standard care all patients would have a GP consultation, resulting in:

- A true positive rate of 2.5%,
- A false negative rate of 10%,
- A false positive rate of 17%
- A true negative rate of 68.5%.

Overall in the analysis Vfrac lead to a greater number of referrals for radiography (both accurate and inaccurate) than standard care and a higher number of vertebral fractures identified.

All patients diagnosed with an OVF were assumed to initiate treatment with alendronate. Those not diagnosed with an OVF were assumed to not initiate pharmacological treatment. Consequently, those who truly had an OVF but were not diagnosed (false negatives) were considered to face a higher risk of subsequent fractures over the model's time horizon compared with those correctly identified and treated.

Patients without an OVF who were nevertheless referred for radiography (false positives) were assumed to incur the additional cost of the radiograph. After imaging, they were expected to be correctly identified as not requiring treatment.

A decision tree was used for the within-study analysis, with decision nodes applied at the points of referral for radiograph, with a positive diagnosis of OVF leading to initiation of

treatment. After this, lifetime costs and QALYs were extrapolated using a previously published discrete event simulation model for osteoporosis. Overall, the study was graded as partially applicable with potentially serious limitations.

Probabilistic results were presented, which showed that Vfrac was cost effective versus standard care at a threshold of £20,000 per QALY gained (ICER: £16,545 per QALY), though the probability that Vfrac was cost effective was 49.4%, indicating high uncertainty. No scenario analyses were conducted.

The committee raised concerns about the assumptions made to inform standard care. Some committee members felt that the percentage of patients referred for radiograph was too high, whilst others felt it was too low. There was a consensus that better data were needed to inform this parameter since it is a key component of cost effectiveness and resource use. The committee noted that some people with OVF would be eligible for anabolic treatments in current practice instead of alendronate, which the analysis did not account for. Anabolic treatments are more expensive but also more effective than alendronate. They therefore believed that the analysis likely underestimated the true cost-effectiveness of treatment. Since the analysis relies on the sensitivity and specificity of Vfrac, the limitations in this evidence—highlighted during the clinical review—are also important to consider when interpreting the results.

No additional costs are incorporated related to using Vfrac in the analysis. The committee noted that it comprises 15 questions based on self-reported information and a physical examination. They agreed that, in practice, patients would present to their GP with symptoms suggestive of vertebral fracture, allowing them to use the tool. The authors indicate that Vfrac is available online via UK primary care IT systems and takes about 5 minutes to complete. The committee therefore agreed that it was reasonable to assume it could be used within the GP consultation without additional NHS resource.

An expected value of perfect information (EVPI) analysis indicated that the cost of obtaining perfect information for decision-making purposes was £526 per person and between £229-£458 million at a population level, suggesting a high value for future research. However, the EVPI analysis does not account for the uncertainty surrounding the definition of standard care, which was a key concern raised by the committee. Therefore, any future research should aim to address this issue alongside other identified uncertainties.

Overall, the committee concluded that a recommendation for Vfrac could not be made until further economic analysis is undertaken, supported by additional clinical evidence and more robust data on current practice.

1.3.8. Other factors the committee took into account

The committee noted that access to Vfrac could be a barrier as, although the tool is completed by a healthcare professional, there is an option of self-completion of the questionnaire element. There could also be language barriers to complete the tool, although it has been translated into Urdu so it is possible this could be done for other languages.

Risk factors for vertebral fractures include increasing age, steroid use, and heavy alcohol intake (especially in men).

1.3.9. Recommendations supported by this evidence

These evidence reviews support the research recommendation on the clinical and cost-effectiveness of Vfrac (vertebral fracture clinical decision tool) to identify people with a vertebral fracture. No recommendations were made from these evidence reviews.

1.4. References

1.4.1. Effectiveness and economic

Khera TK, Hunt LP, Davis S et al 2022. A clinical tool to identify older women with back pain at high risk of osteoporotic vertebral fractures (Vfrac): a population-based cohort study with exploratory economic evaluation. Age Ageing. 1;51(3):afac031.

1.4.2. Other

Davis S, Simpson E, Hamilton J et al 2020. Denosumab, raloxifene, romosozumab and teriparatide to prevent osteoporotic fragility fractures: a systematic review and economic evaluation. Health Technol Assess. 24: 1–314.

Appendices

Appendix A Review protocols

A.1 Diagnostic accuracy of Vfrac

A.1.1 Review protocol for the diagnostic accuracy of Vfrac for those who should have imaging to identify vertebral fractures?

Field	Content
Review title	Diagnostic accuracy of the Vfrac (vertebral fracture risk assessment tool)
Review question	What is the diagnostic accuracy of the Vfrac (vertebral fracture clinical decision tool) for determining who needs imaging to identify people with a suspected vertebral fracture?
Objective	The review aims to find out what is the diagnostic accuracy of Vfrac to determine those who should get imaging to confirm vertebral fractures.
Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos Searches will be restricted by: • English language studies • Human studies Other searches:

	• Reference searching • Citation searching • Inclusion lists of systematic reviews The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
Condition or domain being studied	Osteoporosis or people at risk of vertebral fractures. Vertebral fractures are a common type of fragility fractures, yet they are often not suspected so a significant proportion go undiagnosed. Vertebral fractures are a strong predictor of future fracture risk and are associated with significant morbidity, even when they do not present clinically and are associated with increased mortality.
Population	Inclusion: • Older adults (65 years and older) who are at risk of fragility fracture and have had back pain in the last 4 months. Pre-menopausal and post-menopausal women under 65 and men of all ages are populations of interest too. There are no known validated tools in these groups so we will not be doing an evidence search but will make a research recommendation. Exclusion: • People under 65 years of age.
Test	• The Vfrac vertebral fracture risk assessment tool
Reference standard	• Vertebral fracture found by standard imaging procedures (X-ray, CT, and MRI)

Types of study to be included	Diagnostic: cross sectional studies will be included. If cross-sectional studies are not found diagnostic cohort studies will be included.
Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available. Case-control studies.
Context	All settings.
Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical: Accuracy of estimation of vertebral fracture: • Sensitivity/specificity • Likelihood ratio • Positive predictive value/negative predictive value • Area under the curve (AUC)
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI R5 and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary.

	Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data, and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Diagnostic test accuracy studies: QUADAS-2
Strategy for data synthesis	EndNote will be used for reference management, sifting, citations, and bibliographies. All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions

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• a sample of the risk of bias assessments

Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.</td></tr>
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• Expertise of the operator/interpreter of results (specialist versus non-specialist)</td></tr>
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	Formal screening of search results against eligibility criteria	☑	☑
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
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	Muksitur Rahman, NICE Sarah Glover, NICE
Funding sources/sponsor	Development of this systematic review is being funded by NICE.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/GID-NG10216
Other registration details	NA
Reference/URL for published protocol	NA
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	NA

Details of existing review of same topic by same authors	NA	
Current review status	☐	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published, and being updated
	☐	Discontinued
Additional information	NA	
Details of final publication	www.nice.org.uk	

1

A.2 Clinical and cost effectiveness of Vfrac

A.2.1 Review protocol for the clinical and cost effectiveness of Vfrac for predicting vertebral fractures

Field	Content
Review title	Vfrac (vertebral fracture clinical decision tool) for identifying people with vertebral fractures?
Review question	What is the clinical and cost effectiveness of Vfrac (vertebral fracture clinical decision tool) to identify people with a suspected vertebral fracture?
Objective	This is a review of intervention studies to evaluate the outcomes of the Vfrac (vertebral fracture clinical decision tool) for identifying who needs imaging for a suspected vertebral fracture.
Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos Searches will be restricted by: • English language studies • Human studies Other searches: • Reference searching • Citation searching • Inclusion lists of systematic reviews

	The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
Condition	Osteoporosis or people at risk of vertebral fractures. Vertebral fractures are a common type of fragility fractures yet they are often not suspected and so few come to clinical attention. Vertebral fractures are a strong predictor of future fracture risk and are associated with significant morbidity, even when they do not present clinically and are associated with increased mortality.
Population	Inclusion: • Older adults (65 years and older) who have had back pain in the past 4 months. • Pre-menopausal and post-menopausal women and men of all ages are populations of interest too. There are no known validated tools in this group so we will not be doing an evidence search but will make a research recommendation Exclusion: people under 65 years of age. Strata: • post-menopausal women • men
Risk assessment tool	• Vfrac Followed by imaging and then appropriate treatment. Treatments: • Alendronate • Ibandronate • Risedronate

	• Abaloparatide • Denosumab • Raloxifene • Romosozumab • Teriparatide • Strontium ranelate • HRT (Newer forms)
Comparator	• Usual care/no Vfrac Followed by imaging and then appropriate treatment. Treatments: • Alendronate • Ibandronate • Risedronate • Abaloparatide • Denosumab • Raloxifene • Romosozumab • Teriparatide • Strontium ranelate • HRT (Newer forms)
Types of study to be included	Diagnostic randomised controlled trials (RCTs). Published NMAs and IPDs will be considered for inclusion. Systematic reviews of randomised controlled trials: For a systematic review (SR) to be included it must be conducted in line with the methodological processes described in the NICE manual. If sufficient details are provided, reviewers will either include the SR fully or use it as the basis for further analyses where possible. If sufficient details are not provided to include a relevant SR, the review will only be used for citation searching.

	Exclusion: • Non-randomised studies.
Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded.
Context	All settings where NHS-funded care or social care is provided or commissioned.

Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical:
	• Vertebral fracture
	• Generic health-related quality of life (continuous outcomes will be prioritised [validated measures]). The hierarchy for extracting will be as follows, if measures higher on hierarchy are reported others will not be:
	  ○ EQ-5D
	  ○ SF-6D
	  ○ SF-36
	  ○ SF-12
	  ○ Other utility measures (AQOL, HUI, 15D, QWB)
	• Health-related quality of life measure for vertebral fractures (QUALEFFO-41)
	• Change in management.

Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI R5 and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary.

	Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data, and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For Intervention reviews • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0)
Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random effects If sufficient data is available, meta-regression or NMA-meta-regression will be conducted. GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency, and imprecision) will be appraised for each outcome. Publication bias will be considered with the guideline committee, and if suspected will be tested for when there are more than 5 studies for that outcome.

	The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/			
Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: • Expertise of the operator/interpreter of results (specialist versus non-specialist)			
Type and method of review	☒	Intervention		
	☐	Diagnostic		
	☐	Prognostic		
	☐	Qualitative		
	☐	Epidemiologic		
	☐	Service Delivery		
	☐	Other (please specify)		
Language	English			
Country	England			
Anticipated or actual start date	NA			
Anticipated completion date	November 2025			
Stage of review at time of this submission	Review stage	Started	Completed	
	Preliminary searches	X	X	

	Piloting of the study selection process	X	X
	Formal screening of search results against eligibility criteria	X	X
	Data extraction	X	X
	Risk of bias (quality) assessment	X	X
	Data analysis	X	X
Named contact	5a. Named contact Guideline Development Team NGC 5b Named contact e-mail osteoporosis@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE)		
Review team members	From NICE: Carlos Sharpin, NICE Clare Jones, NICE Annette Chalker, NICE		

	Kate Lovibond, NICE Claire Sloan, NICE Muksitur Rahman, NICE Sarah Glover, NICE
Funding sources/sponsor	Development of this systematic review is being funded by NICE.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/GID-NG10216
Other registration details	NA
Reference/URL for published protocol	NA
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts

	• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
Keywords	NA	
Details of existing review of same topic by same authors	NA	
Current review status	☐	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published, and being updated
	☐	Discontinued
Additional information	NA	
Details of final publication	www.nice.org.uk	

1

A.2.2 Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions in the guideline update.
Search criteria	• Populations, interventions, and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A global health economic study search will be undertaken for the guideline update using population-specific terms and a health economic study filter – see Appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2009 (including those included in the previous guideline), abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published 2009 onwards that were included in the previous guideline will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual. Inclusion and exclusion criteria • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed, and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded, then a health economic evidence table will not be completed, and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable,' with 'Potentially serious limitations' or both then there is discretion over whether it should be included. Where there is discretion The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be

included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies:

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2009 or later (including any such studies included in the previous guideline) but that depend on unit costs and resource data entirely or predominantly from before 2009 will be rated as ‘Not applicable’.
- Studies published before 2009 (including any such studies included in the previous guideline) will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B Literature search strategies

- The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual. For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

- Q4.1a What is the diagnostic accuracy of the Vfrac (vertebral fracture clinical decision tool) for determining who needs imaging to identify people with a suspected vertebral fracture?

- Q4.1b What is the clinical and cost effectiveness of Vfrac (vertebral fracture clinical decision tool) to identify people with a suspected vertebral fracture?

Table 8: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 10 April 2024	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 10 April 2024	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
The Cochrane Library (Wiley)	Cochrane Reviews to 2024 Issue 4 of 12 CENTRAL to 2024 Issue 4 of 12	Exclusions (clinical trials, conference abstracts)
Epistemonikos (The Epistemonikos Foundation)	Inception to 10 April 2024	Systematic review studies Exclusions (Cochrane reviews) English language

Medline (Ovid) search terms

1	Vfrac*.tw,kf.
2	(vertebr* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
3	(vertebr* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
4	(vertebr* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
5	(vertebr* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
6	(vertebr* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
7	(vertebr* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
8	(vertebr* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
9	(vertebr* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
10	(vertebr* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
11	(vertebr* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
12	(vertebr* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
13	(vertebr* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
14	(vertebr* adj4 fracture* adj4 checklist*).tw,kf.
15	(spin* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
16	(spin* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
17	(spin* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
18	(spin* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
19	(spin* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
20	(spin* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
21	(spin* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
22	(spin* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
23	(spin* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
24	(spin* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
25	(spin* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
26	(spin* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
27	(spin* adj4 fracture* adj4 checklist*).tw,kf.
28	(back adj4 pain adj4 screen* adj4 aid*).tw,kf.
29	(back adj4 pain adj4 screen* adj4 tool*).tw,kf.
30	(back adj4 pain adj4 screen* adj4 questionnaire*).tw,kf.
31	(back adj4 pain adj4 decision* adj4 aid*).tw,kf.
32	(back adj4 pain adj4 decision* adj4 tool*).tw,kf.
33	(back adj4 pain adj4 decision* adj4 questionnaire*).tw,kf.
34	(back adj4 pain adj4 assessment* adj4 aid*).tw,kf.
35	(back adj4 pain adj4 assessment* adj4 tool*).tw,kf.

36	(back adj4 pain adj4 assessment* adj4 questionnaire*).tw,kf.
37	(back adj4 pain adj4 clinical* adj4 aid*).tw,kf.
38	(back adj4 pain adj4 clinical* adj4 tool*).tw,kf.
39	(back adj4 pain adj4 clinical* adj4 questionnaire*).tw,kf.
40	(back adj4 pain adj4 checklist*).tw,kf.
41	(ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671).tw,kf.
42	or/1-41
43	animals/ not humans/
44	42 not 43
45	limit 44 to english language

Embase (Ovid) search terms

1	Vfrac*.tw,kf.
2	(vertebr* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
3	(vertebr* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
4	(vertebr* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
5	(vertebr* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
6	(vertebr* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
7	(vertebr* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
8	(vertebr* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
9	(vertebr* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
10	(vertebr* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
11	(vertebr* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
12	(vertebr* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
13	(vertebr* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
14	(vertebr* adj4 fracture* adj4 checklist*).tw,kf.
15	(spin* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
16	(spin* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
17	(spin* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
18	(spin* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
19	(spin* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
20	(spin* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
21	(spin* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
22	(spin* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
23	(spin* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
24	(spin* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.

25	(spin* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
26	(spin* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
27	(spin* adj4 fracture* adj4 checklist*).tw,kf.
28	(back adj4 pain adj4 screen* adj4 aid*).tw,kf.
29	(back adj4 pain adj4 screen* adj4 tool*).tw,kf.
30	(back adj4 pain adj4 screen* adj4 questionnaire*).tw,kf.
31	(back adj4 pain adj4 decision* adj4 aid*).tw,kf.
32	(back adj4 pain adj4 decision* adj4 tool*).tw,kf.
33	(back adj4 pain adj4 decision* adj4 questionnaire*).tw,kf.
34	(back adj4 pain adj4 assessment* adj4 aid*).tw,kf.
35	(back adj4 pain adj4 assessment* adj4 tool*).tw,kf.
36	(back adj4 pain adj4 assessment* adj4 questionnaire*).tw,kf.
37	(back adj4 pain adj4 clinical* adj4 aid*).tw,kf.
38	(back adj4 pain adj4 clinical* adj4 tool*).tw,kf.
39	(back adj4 pain adj4 clinical* adj4 questionnaire*).tw,kf.
40	(back adj4 pain adj4 checklist*).tw,kf.
41	(ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671).tw,kf,cn.
42	or/1-41
43	nonhuman/ not human/
44	42 not 43
45	limit 44 to english language
46	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
47	45 not 46

Cochrane Library (Wiley) search terms

#1	(Vfrac*):ti,ab,kw
#2	((vertebr* near/4 fracture* near/4 screen* near/4 aid*)):ti,ab,kw
#3	((vertebr* near/4 fracture* near/4 screen* near/4 tool*)):ti,ab,kw
#4	((vertebr* near/4 fracture* near/4 screen* near/4 questionnaire*)):ti,ab,kw
#5	((vertebr* near/4 fracture* near/4 decision* near/4 aid*)):ti,ab,kw
#6	((vertebr* near/4 fracture* near/4 decision* near/4 tool*)):ti,ab,kw
#7	((vertebr* near/4 fracture* near/4 decision* near/4 questionnaire*)):ti,ab,kw
#8	((vertebr* near/4 fracture* near/4 assessment* near/4 aid*)):ti,ab,kw
#9	((vertebr* near/4 fracture* near/4 assessment* near/4 tool*)):ti,ab,kw
#10	((vertebr* near/4 fracture* near/4 assessment* near/4 questionnaire*)):ti,ab,kw

#11	((vertebr* near/4 fracture* near/4 clinical* near/4 aid*)):ti,ab,kw
#12	((vertebr* near/4 fracture* near/4 clinical* near/4 tool*)):ti,ab,kw
#13	((vertebr* near/4 fracture* near/4 clinical* near/4 questionnaire*)):ti,ab,kw
#14	((vertebr* near/4 fracture* near/4 checklist*)):ti,ab,kw
#15	((spin* near/4 fracture* near/4 screen* near/4 aid*)):ti,ab,kw
#16	((spin* near/4 fracture* near/4 screen* near/4 tool*)):ti,ab,kw
#17	((spin* near/4 fracture* near/4 screen* near/4 questionnaire*)):ti,ab,kw
#18	((spin* near/4 fracture* near/4 decision* near/4 aid*)):ti,ab,kw
#19	((spin* near/4 fracture* near/4 decision* near/4 tool*)):ti,ab,kw
#20	((spin* near/4 fracture* near/4 decision* near/4 questionnaire*)):ti,ab,kw
#21	((spin* near/4 fracture* near/4 assessment* near/4 aid*)):ti,ab,kw
#22	((spin* near/4 fracture* near/4 assessment* near/4 tool*)):ti,ab,kw
#23	((spin* near/4 fracture* near/4 assessment* near/4 questionnaire*)):ti,ab,kw
#24	((spin* near/4 fracture* near/4 clinical* near/4 aid*)):ti,ab,kw
#25	((spin* near/4 fracture* near/4 clinical* near/4 tool*)):ti,ab,kw
#26	((spin* near/4 fracture* near/4 clinical* near/4 questionnaire*)):ti,ab,kw
#27	((spin* near/4 fracture* near/4 checklist*)):ti,ab,kw
#28	((back near/4 pain near/4 screen* near/4 aid*)):ti,ab,kw
#29	((back near/4 pain near/4 screen* near/4 tool*)):ti,ab,kw
#30	((back near/4 pain near/4 screen* near/4 questionnaire*)):ti,ab,kw
#31	((back near/4 pain near/4 decision* near/4 aid*)):ti,ab,kw
#32	((back near/4 pain near/4 decision* near/4 tool*)):ti,ab,kw
#33	((back near/4 pain near/4 decision* near/4 questionnaire*)):ti,ab,kw
#34	((back near/4 pain near/4 assessment* near/4 aid*)):ti,ab,kw
#35	((back near/4 pain near/4 assessment* near/4 tool*)):ti,ab,kw
#36	((back near/4 pain near/4 assessment* near/4 questionnaire*)):ti,ab,kw
#37	((back near/4 pain near/4 clinical* near/4 aid*)):ti,ab,kw
#38	((back near/4 pain near/4 clinical* near/4 tool*)):ti,ab,kw
#39	((back near/4 pain near/4 clinical* near/4 questionnaire*)):ti,ab,kw
#40	((back near/4 pain near/4 checklist*)):ti,ab,kw
#41	((ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671)):ti,ab,kw
#42	{or #1-#41}
#43	((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or

	ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp)):an
#44	#42 not #43
#45	conference:pt
#46	#44 not #45

Epistemonikos search terms

Search 1

1	(title:(Vfrac*) OR abstract:(Vfrac*)) OR (title:((vertebr* AND fracture* AND screen* AND aid*)) OR abstract:((vertebr* AND fracture* AND screen* AND aid*))) OR (title:((vertebr* AND fracture* AND screen* AND tool*)) OR abstract:((vertebr* AND fracture* AND screen* AND tool*))) OR (title:((vertebr* AND fracture* AND screen* AND questionnaire*)) OR abstract:((vertebr* AND fracture* AND screen* AND questionnaire*))) OR (title:((vertebr* AND fracture* AND decision* AND aid*)) OR abstract:((vertebr* AND fracture* AND decision* AND aid*))) OR (title:((vertebr* AND fracture* AND decision* AND tool*)) OR abstract:((vertebr* AND fracture* AND decision* AND tool*))) OR (title:((vertebr* AND fracture* AND decision* AND questionnaire*)) OR abstract:((vertebr* AND fracture* AND decision* AND questionnaire*))) OR (title:((vertebr* AND fracture* AND assessment* AND aid*)) OR abstract:((vertebr* AND fracture* AND assessment* AND aid*))) OR (title:((vertebr* AND fracture* AND assessment* AND tool*)) OR abstract:((vertebr* AND fracture* AND assessment* AND tool*))) OR (title:((vertebr* AND fracture* AND assessment* AND questionnaire*)) OR abstract:((vertebr* AND fracture* AND assessment* AND questionnaire*))) OR (title:((vertebr* AND fracture* AND clinical* AND aid*)) OR abstract:((vertebr* AND fracture* AND clinical* AND aid*))) OR (title:((vertebr* AND fracture* AND clinical* AND tool*)) OR abstract:((vertebr* AND fracture* AND clinical* AND tool*))) OR (title:((vertebr* AND fracture* AND clinical* AND questionnaire*)) OR abstract:((vertebr* AND fracture* AND clinical* AND questionnaire*))) OR (title:((vertebr* AND fracture* AND checklist*)) OR abstract:((vertebr* AND fracture* AND checklist*)))

Search 2

1	(title:((spin* AND fracture* AND screen* AND aid*)) OR abstract:((spin* AND fracture* AND screen* AND aid*))) OR (title:((spin* AND fracture* AND screen* AND tool*)) OR abstract:((spin* AND fracture* AND screen* AND tool*))) OR (title:((spin* AND fracture* AND screen* AND questionnaire*)) OR abstract:((spin* AND fracture* AND screen* AND questionnaire*))) OR (title:((spin* AND fracture* AND decision* AND aid*)) OR abstract:((spin* AND fracture* AND decision* AND aid*))) OR (title:((spin* AND fracture* AND decision* AND tool*)) OR abstract:((spin* AND fracture* AND decision* AND tool*))) OR (title:((spin* AND fracture* AND decision* AND questionnaire*)) OR abstract:((spin* AND fracture* AND decision* AND questionnaire*))) OR (title:((spin* AND fracture* AND assessment* AND aid*)) OR abstract:((spin* AND fracture* AND assessment* AND aid*))) OR (title:((spin* AND fracture* AND assessment* AND tool*)) OR abstract:((spin* AND fracture* AND assessment* AND tool*))) OR (title:((spin* AND fracture* AND assessment* AND questionnaire*)) OR abstract:((spin* AND fracture* AND assessment* AND questionnaire*))) OR (title:((spin* AND fracture* AND clinical* AND aid*)) OR abstract:((spin* AND fracture* AND clinical* AND aid*))) OR (title:((spin* AND fracture* AND clinical* AND tool*)) OR abstract:((spin* AND fracture* AND clinical* AND tool*))) OR (title:((spin* AND fracture* AND clinical* AND questionnaire*)) OR abstract:((spin* AND fracture* AND clinical* AND questionnaire*))) OR (title:((spin* AND fracture* AND checklist*)) OR abstract:((spin* AND fracture* AND checklist*)))

1
2
3 Search 3

1	(title:((back AND pain AND screen* AND aid*)) OR abstract:((back AND pain AND screen* AND aid*))) OR (title:((back AND pain AND screen* AND tool*)) OR abstract:((back AND pain AND screen* AND tool*))) OR (title:((back AND pain AND screen* AND questionnaire*)) OR abstract:((back AND pain AND screen* AND questionnaire*))) OR (title:((back AND pain AND decision* AND aid*)) OR abstract:((back AND pain AND decision* AND aid*))) OR (title:((back AND pain AND decision* AND tool*)) OR abstract:((back AND pain AND decision* AND tool*))) OR (title:((back AND pain AND decision* AND questionnaire*)) OR abstract:((back AND pain AND decision* AND questionnaire*))) OR (title:((back AND pain AND assessment* AND aid*)) OR abstract:((back AND pain AND assessment* AND aid*))) OR (title:((back AND pain AND assessment* AND tool*)) OR abstract:((back AND pain AND assessment* AND tool*))) OR (title:((back AND pain AND assessment* AND questionnaire*)) OR abstract:((back AND pain AND assessment* AND questionnaire*))) OR (title:((back AND pain AND clinical* AND aid*)) OR abstract:((back AND pain AND clinical* AND aid*))) OR (title:((back AND pain AND clinical* AND tool*)) OR abstract:((back AND pain AND clinical* AND tool*))) OR (title:((back AND pain AND clinical* AND questionnaire*)) OR abstract:((back AND pain AND clinical* AND questionnaire*))) OR (title:((back AND pain AND checklist*)) OR abstract:((back AND pain AND checklist*))) OR (title:((ISRCTN18000119 OR ISRCTN12150779 OR ISRCTN42028479 OR ISRCTN16550671)) OR abstract:((ISRCTN18000119 OR ISRCTN12150779 OR ISRCTN42028479 OR ISRCTN16550671)))

B.1.2 Health Economics literature search strategy

Health economic evidence was identified by conducting searches using terms for a population at risk of fragility fracture or for vertebral fracture assessment. The following databases were searched: NHS Economic Evaluation Database (NHS EED - this ceased to be updated after 31st March 2015), Health Technology Assessment database (HTA - this ceased to be updated from 31st March 2018) and The International Network of Agencies for Health Technology Assessment (INAHTA). Searches for recent evidence were run on Medline and Embase from 2014 onwards for health economics.

Table 9: Database parameters, filters and limits applied for population at risk of fragility fracture

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 August 2025	Health economics studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	Health Economics 1 January 2014 – 22 August 2025	Health economics studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception - 22 August 2025	English language

Medline (Ovid) search terms

1	exp Osteoporosis/
2	(osteopor* or osteo-por* or osteop?eni* or osteo-p?eni*).tw,kf.
3	((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 bone* adj4 (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit*)).tw.

4	((abnormal* or secondary or early or prematur*) adj4 bone* adj4 (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)).tw.
5	((low* or reduc* or decreas* or los*) adj4 bone* adj4 (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)).tw.
6	((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 BMD).tw.
7	((low* or los* or reduc* or decreas* or abnormal* or secondary) adj4 BMD).tw.
8	(bone* adj4 (deteriorat* or weak* or fragil* or decalc* or brittle* or atroph*)).tw.
9	((trabecula* or cancellous) adj4 (loss* or thin* or reduc* or decreas* or deteriorat* or low* or abnormal*)).tw.
10	((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 skeletal adj4 (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit* or decalc* or atroph*)).tw.
11	((abnormal* or secondary or early or prematur*) adj4 skeletal* adj4 (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit* or atroph*)).tw.
12	((low* or reduc* or decreas* or los*) adj4 skeletal adj4 (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)).tw.
13	Bone Diseases, Metabolic/
14	Osteoporotic Fractures/
15	(fragil* adj4 (fracture or fractures)).tw.
16	((low-impact* or low-energy or low-trauma* or insufficien*) adj4 fracture*).tw.
17	((risk* or frequen* or inciden* or suscept* or suspect* or predict* or prevent* or stop*) adj4 fracture*).tw.
18	((recurrent or recurring or repeat* or history or chronic or previous or prior or habitual) adj4 fracture*).tw.
19	refracture*.tw.
21	or/1-19
22	Economics/
23	Value of Life/
24	exp "Costs and Cost Analysis"/
25	exp Economics, Hospital/
26	exp Economics, Medical/
27	Economics, Nursing/
28	Economics, Pharmaceutical/
29	exp "Fees and Charges"/
30	exp Budgets/
31	budget*.ti,ab.

32	cost*.ti.
33	(economic* or pharmaco?economic*).ti.
34	(price* or pricing*).ti,ab.
35	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36	(financ* or fee or fees).ti,ab.
37	(value adj2 (money or monetary)).ti,ab.
38	or/22-37
39	21 and 38
40	limit 39 to ed=20140101-20250822

1

2 Embase (Ovid) search terms

1	exp osteoporosis/
2	exp Osteopenia/
3	(osteopor* or osteo-por* or osteop?eni* or osteo-p?eni*).tw,kf.
4	((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 bone* adj4 (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit*)).tw.
5	((abnormal* or secondary or early or prematur*) adj4 bone* adj4 (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)).tw.
6	((low* or reduc* or decreas* or los*) adj4 bone* adj4 (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)).tw.
7	((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 BMD).tw.
8	((low* or los* or reduc* or decreas* or abnormal* or secondary) adj4 BMD).tw.
9	(bone* adj4 (deteriorat* or weak* or fragil* or decalc* or brittle* or atroph*)).tw.
10	((trabecula* or cancellous) adj4 (loss* or thin* or reduc* or decreas* or deteriorat* or low* or abnormal*)).tw.
11	((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 skeletal* adj4 (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit* or decalc* or atroph*)).tw.
12	((abnormal* or secondary or early or prematur*) adj4 skeletal* adj4 (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit* or atroph*)).tw.

13	((low* or reduc* or decreas* or los*) adj4 skeletal* adj4 (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)).tw.
14	metabolic bone disease/ or exp bone demineralization/
15	fragility fracture/
16	(fragil* adj4 (fracture or fractures)).tw.
17	((low-impact* or low-energy or low-trauma* or insufficien*) adj4 fracture*).tw.
18	((risk* or frequen* or inciden* or suscept* or suspect* or predict* or prevent* or stop*) adj4 fracture*).tw.
19	((recurrent or recurring or repeat* or history or chronic or previous or prior or habitual) adj4 fracture*).tw.
20	refracture*.tw.
21	or/1-20
22	health economics/
23	exp economic evaluation/
24	exp health care cost/
25	exp fee/
26	budget/
27	funding/
28	budget*.ti,ab.
29	cost*.ti.
30	(economic* or pharmaco?economic*).ti.
31	(price* or pricing*).ti,ab.
32	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
33	(financ* or fee or fees).ti,ab.
34	(value adj2 (money or monetary)).ti,ab.
35	or/22-34
36	21 and 35
37	Limit 36 to dd=20140101-20250822
38	Limit 36 to dc=20140101-20250822
39	37 or 38

NHS EED and HTA (CRD) search terms

1	MeSH DESCRIPTOR osteoporosis EXPLODE ALL TREES
2	(((osteopor* or osteo-por* or osteopeni* or osteopaeni* or osteo-peni* or osteopaeni*)))

3	(((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 bone* adj4 (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit*)))
4	(((abnormal* or secondary or early or prematur*) adj4 bone* adj4 (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))
5	(((low* or reduc* or decreas* or los*) adj4 bone* adj4 (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))
6	(((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 BMD))
7	(((low* or los* or reduc* or decreas* or abnormal* or secondary) adj4 BMD))
8	((bone* adj4 (deteriorat* or weak* or fragil* or decalc* or brittle* or atroph*)))
9	(((trabecula* or cancellous) adj4 (loss* or thin* or reduc* or decreas* or deteriorat* or low* or abnormal*)))
10	((((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) adj4 skeletal adj4 (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit* or decalc* or atroph*))))
11	((((abnormal* or secondary or early or prematur*) adj4 skeletal* adj4 (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit* or atroph*))))
12	((((low* or reduc* or decreas* or los*) adj4 skeletal adj4 (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*))))
13	MeSH DESCRIPTOR Bone Diseases, Metabolic
14	MeSH DESCRIPTOR osteoporotic fractures
15	((fragil* adj4 (fracture or fractures)))
16	(((low-impact* or low-energy or low-trauma* or insufficien*) adj4 fracture*))
17	(((risk* or frequen* or inciden* or suscept* or suspect* or predict* or prevent* or stop*) adj4 fracture*))
18	(((recurrent or recurring or repeat* or history or chronic or previous or prior or habitual) adj4 fracture*))
19	(refracture*)
20	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19

1

2 INAHTA search terms

1	("Osteoporosis"[mhe])
2	(((osteopor* or osteopeni* or osteopaeni*))[Title] OR ((osteopor* or osteopeni* or osteopaeni*))[abs])
3	(((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) AND bone* AND (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit*)))[Title] OR (((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) AND bone* AND (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit*)))[abs]
4	(((abnormal* or secondary or early or prematur*) AND bone* AND (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))[Title] OR (((abnormal* or secondary or early or prematur*) AND bone* AND (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))[abs]
5	(((low* or reduc* or decreas* or los*) AND bone* AND (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*))) OR (((low* or reduc* or decreas* or los*) AND bone* AND (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))
6	(((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) AND BMD))[Title] OR (((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) AND BMD))[abs]
7	((low* or los* or reduc* or decreas* or abnormal* or secondary) AND BMD))[Title] OR (((low* or los* or reduc* or decreas* or abnormal* or secondary) AND BMD))[abs]
8	((bone* AND (deteriorat* or weak* or fragil* or decalc* or brittle* or atroph*)))[Title] OR ((bone* AND (deteriorat* or weak* or fragil* or decalc* or brittle* or atroph*)))[abs]
9	(((trabecula* or cancellous) AND (loss* or thin* or reduc* or decreas* or deteriorat* or low* or abnormal*)))[Title] OR (((trabecula* or cancellous) AND (loss* or thin* or reduc* or decreas* or deteriorat* or low* or abnormal*)))[abs]
10	(((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) AND skeletal AND (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit* or decalc* or atroph*)))[Title] OR (((age-relat* or agerelat* or perimenopaus* or peri-menopaus* or postmenopaus* or post-menopaus* or menopaus* or pathologic*) AND skeletal AND (los* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or demineral* or strength* or quality or quantit* or decalc* or atroph*)))[abs]

11	(((abnormal* or secondary or early or prematur*) AND skeletal* AND (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit* or atroph*)))[Title] OR (((abnormal* or secondary or early or prematur*) AND skeletal* AND (los* or reduc* or mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit* or atroph*)))[abs]
12	(((low* or reduc* or decreas* or los*) AND skeletal AND (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))[Title] OR (((low* or reduc* or decreas* or los*) AND skeletal AND (mass or architectur* or microarchitectur* or micro-architectur* or dens* or mineral* or content or strength* or quality or quantit*)))[abs]
13	"Bone Diseases, Metabolic"[mh]
14	"Osteoporotic Fractures"[mh]
15	(fragil* AND (fracture or fractures))
16	((low-impact* or low-energy or low-trauma* or insufficien*) AND fracture*)
17	((risk* or frequen* or inciden* or suscept* or suspect* or predict* or prevent* or stop*) AND fracture*)
18	((recurrent or recurring or repeat* or history or chronic or previous or prior or habitual) AND fracture*)
19	refracture*
20	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19

Table 10: Database parameters, filters and limits applied for vertebral fracture assessment

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1946 – 22 August 2025	Health economics studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	Health Economics 1974 – 22 August 2025	Health economics studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language

Database	Dates searched	Search filters and limits applied
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception - 22 August 2025	English language

Medline (Ovid) search terms

1	exp Densitometry/
2	(densitometr* or BMD-test* or BMD-tool* or densimetr*).tw.
3	(bone adj4 mineral adj4 dens* adj4 test*).tw.
4	(bone adj4 mineral adj4 dens* adj4 tool*).tw.
5	(absorptiometr* adj4 (dpx* or dual-energ* or dual-photon* or photon*)).tw.
6	(DXA* or DXA).tw.
7	or/1-6
8	Spinal Fractures/
9	((spin* or vertebr* or neck or cervical or lumbar or sacral or thoracic or coccy* or cord or backbone* or back) adj4 (fracture* or compress*)).tw.
10	(compress* adj4 fracture*).tw.
11	(VCF or VFA* or IVA* or LVA* or DVA* or MXA*).tw.
12	((instant or lateral or densitometric or morphometric or dual-energ*) adj4 (vertebr* adj4 assess*)).tw.
13	(physician* adj4 viewer*).tw.
14	or/8-13
15	7 and 14
16	Vfrac*.tw,kf.
17	(vertebr* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
18	(vertebr* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
19	(vertebr* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
20	(vertebr* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
21	(vertebr* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
22	(vertebr* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
23	(vertebr* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.

24	(vertebr* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
25	(vertebr* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
26	(vertebr* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
27	(vertebr* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
28	(vertebr* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
29	(vertebr* adj4 fracture* adj4 checklist*).tw,kf.
30	(spin* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
31	(spin* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
32	(spin* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
33	(spin* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
34	(spin* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
35	(spin* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
36	(spin* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
37	(spin* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
38	(spin* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
39	(spin* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
40	(spin* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
41	(spin* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
42	(spin* adj4 fracture* adj4 checklist*).tw,kf.
43	(back adj4 pain adj4 screen* adj4 aid*).tw,kf.
44	(back adj4 pain adj4 screen* adj4 tool*).tw,kf.
45	(back adj4 pain adj4 screen* adj4 questionnaire*).tw,kf.
46	(back adj4 pain adj4 decision* adj4 aid*).tw,kf.
47	(back adj4 pain adj4 decision* adj4 tool*).tw,kf.
48	(back adj4 pain adj4 decision* adj4 questionnaire*).tw,kf.
49	(back adj4 pain adj4 assessment* adj4 aid*).tw,kf.
50	(back adj4 pain adj4 assessment* adj4 tool*).tw,kf.
51	(back adj4 pain adj4 assessment* adj4 questionnaire*).tw,kf.
52	(back adj4 pain adj4 clinical* adj4 aid*).tw,kf.
53	(back adj4 pain adj4 clinical* adj4 tool*).tw,kf.
54	(back adj4 pain adj4 clinical* adj4 questionnaire*).tw,kf.
55	(back adj4 pain adj4 checklist*).tw,kf.
56	(ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671).tw,kf.
57	or/16-56
58	15 or 57
59	Economics/

60	Value of life/
61	exp "Costs and Cost Analysis"/
62	exp Economics, Hospital/
63	exp Economics, Medical/
64	Economics, Nursing/
65	Economics, Pharmaceutical/
66	exp "Fees and Charges"/
67	exp Budgets/
68	budget*.ti,ab.
69	cost*.ti.
70	(economic* or pharmaco?economic*).ti.
71	(price* or pricing*).ti,ab.
72	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
73	(financ* or fee or fees).ti,ab.
74	(value adj2 (money or monetary)).ti,ab.
75	or/59-74
76	58 and 75
77	animals/ not humans/
78	76 not 77
79	limit 78 to english language
80	limit 79 to (letter or historical article or comment or editorial or news or case reports)
81	79 not 80

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2 Embase (Ovid) search terms

1	Bone densitometry/ or dual energy X ray absorptiometry/
2	(densitometr* or BMD-test* or BMD-tool* or densimetr*).tw.
3	(bone adj4 mineral adj4 dens* adj4 test*).tw.
4	(bone adj4 mineral adj4 dens* adj4 tool*).tw.
5	(absorptiometr* adj4 (dpx* or dual-energ* or dual-photon* or photon*)).tw.
6	(DXA* or DXA).tw.
7	or/1-6
8	exp Spine Fracture/
9	((spin* or vertebr* or neck or cervical or lumbar or sacral or thoracic or coccy* or cord or backbone* or back) adj4 (fracture* or compress*)).tw.
10	(compress* adj4 fracture*).tw.
11	(VCF or VFA* or IVA* or LVA* or DVA* or MXA*).tw.

12	((instant or lateral or densitometric or morphometric or dual-energ*) adj4 (vertebr* adj4 assess*)).tw.
13	(physician* adj4 viewer*).tw.
14	or/8-13
15	7 and 14
16	Vfrac*.tw,kf.
17	(vertebr* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
18	(vertebr* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
19	(vertebr* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
20	(vertebr* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
21	(vertebr* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
22	(vertebr* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
23	(vertebr* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
24	(vertebr* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
25	(vertebr* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
26	(vertebr* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
27	(vertebr* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
28	(vertebr* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
29	(vertebr* adj4 fracture* adj4 checklist*).tw,kf.
30	(spin* adj4 fracture* adj4 screen* adj4 aid*).tw,kf.
31	(spin* adj4 fracture* adj4 screen* adj4 tool*).tw,kf.
32	(spin* adj4 fracture* adj4 screen* adj4 questionnaire*).tw,kf.
33	(spin* adj4 fracture* adj4 decision* adj4 aid*).tw,kf.
34	(spin* adj4 fracture* adj4 decision* adj4 tool*).tw,kf.
35	(spin* adj4 fracture* adj4 decision* adj4 questionnaire*).tw,kf.
36	(spin* adj4 fracture* adj4 assessment* adj4 aid*).tw,kf.
37	(spin* adj4 fracture* adj4 assessment* adj4 tool*).tw,kf.
38	(spin* adj4 fracture* adj4 assessment* adj4 questionnaire*).tw,kf.
39	(spin* adj4 fracture* adj4 clinical* adj4 aid*).tw,kf.
40	(spin* adj4 fracture* adj4 clinical* adj4 tool*).tw,kf.
41	(spin* adj4 fracture* adj4 clinical* adj4 questionnaire*).tw,kf.
42	(spin* adj4 fracture* adj4 checklist*).tw,kf.
43	(back adj4 pain adj4 screen* adj4 aid*).tw,kf.
44	(back adj4 pain adj4 screen* adj4 tool*).tw,kf.
45	(back adj4 pain adj4 screen* adj4 questionnaire*).tw,kf.
46	(back adj4 pain adj4 decision* adj4 aid*).tw,kf.
47	(back adj4 pain adj4 decision* adj4 tool*).tw,kf.

48	(back adj4 pain adj4 decision* adj4 questionnaire*).tw,kf.
49	(back adj4 pain adj4 assessment* adj4 aid*).tw,kf.
50	(back adj4 pain adj4 assessment* adj4 tool*).tw,kf.
51	(back adj4 pain adj4 assessment* adj4 questionnaire*).tw,kf.
52	(back adj4 pain adj4 clinical* adj4 aid*).tw,kf.
53	(back adj4 pain adj4 clinical* adj4 tool*).tw,kf.
54	(back adj4 pain adj4 clinical* adj4 questionnaire*).tw,kf.
55	(back adj4 pain adj4 checklist*).tw,kf.
56	(ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671).tw,kf.
57	or/16-56
58	15 or 57
59	health economics/
60	exp economic evaluation/
61	exp health care cost/
62	exp fee/
63	budget/
64	funding/
65	budget*.ti,ab.
66	cost*.ti.
67	(economic* or pharmaco?economic*).ti.
68	(price* or pricing*).ti,ab.
69	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
70	(financ* or fee or fees).ti,ab.
71	(value adj2 (money or monetary)).ti,ab.
72	or/59-71
73	58 and 72
74	nonhuman/ not human/
75	73 not 74
76	limit 75 to english language
77	clinical trial.pt.
78	76 not 77
79	(letter or editorial).pt.
80	78 not 79
81	(conference abstract* or conference review or conference paper or conference proceeding).db,pt,su.
82	80 not 81

NHS EED and HTA (CRD) search terms

1	MeSH DESCRIPTOR densitometry EXPLODE ALL TREES
2	((densitometr* or BMD-test* or BMD-tool* or densimetr*))
3	((bone adj4 mineral adj4 dens* adj4 test*))
4	((bone adj4 mineral adj4 dens* adj4 tool*))
5	((absorptiometr* adj4 (dpx* or dual-energ* or dual-photon* or photon*)))
6	((DXA* or DXA))
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
8	MeSH DESCRIPTOR Spinal Fractures
9	(((spin* or vertebr* or neck or cervical or lumbar or sacral or thoracic or coccy* or cord or backbone* or back) adj4 (fracture* or compress*)))
10	((compress* adj4 fracture*))
11	((VCF or VFA* or IVA* or LVA* or DVA* or MXA*))
12	(((instant or lateral or densitometric or morphometric or dual-energ*) adj4 (vertebr* adj4 assess*)))
13	((physician* adj4 viewer*))
14	#8 OR #9 OR #10 OR #11 OR #12 OR #13
15	#7 AND #14
16	(Vfrac*)
17	((vertebr* adj4 fracture* adj4 screen* adj4 aid*))
18	((vertebr* adj4 fracture* adj4 screen* adj4 tool*))
19	((vertebr* adj4 fracture* adj4 screen* adj4 questionnaire*))
20	((vertebr* adj4 fracture* adj4 decision* adj4 aid*))
21	((vertebr* adj4 fracture* adj4 decision* adj4 tool*))
22	((vertebr* adj4 fracture* adj4 decision* adj4 questionnaire*))
23	((vertebr* adj4 fracture* adj4 assessment* adj4 aid*))
24	((vertebr* adj4 fracture* adj4 assessment* adj4 tool*))
25	((vertebr* adj4 fracture* adj4 assessment* adj4 questionnaire*))
26	((vertebr* adj4 fracture* adj4 clinical* adj4 aid*))
27	((vertebr* adj4 fracture* adj4 clinical* adj4 tool*))
28	((vertebr* adj4 fracture* adj4 clinical* adj4 questionnaire*))
29	((vertebr* adj4 fracture* adj4 checklist*))
30	((spin* adj4 fracture* adj4 screen* adj4 aid*))
31	((spin* adj4 fracture* adj4 screen* adj4 tool*))
32	((spin* adj4 fracture* adj4 screen* adj4 questionnaire*))
33	((spin* adj4 fracture* adj4 decision* adj4 aid*))
34	((vertebr* adj4 fracture* adj4 assessment* adj4 tool*))

35	((spin* adj4 fracture* adj4 decision* adj4 questionnaire*))
36	((spin* adj4 fracture* adj4 assessment* adj4 aid*))
37	((spin* adj4 fracture* adj4 assessment* adj4 tool*))
38	((spin* adj4 fracture* adj4 assessment* adj4 questionnaire*))
39	((spin* adj4 fracture* adj4 clinical* adj4 aid*))
40	((spin* adj4 fracture* adj4 clinical* adj4 tool*))
41	((spin* adj4 fracture* adj4 clinical* adj4 questionnaire*))
42	((spin* adj4 fracture* adj4 checklist*))
43	((back adj4 pain adj4 screen* adj4 aid*))
44	((back adj4 pain adj4 screen* adj4 tool*))
45	((back adj4 pain adj4 screen* adj4 questionnaire*))
46	((back adj4 pain adj4 decision* adj4 aid*))
47	((back adj4 pain adj4 decision* adj4 tool*))
48	((back adj4 pain adj4 decision* adj4 questionnaire*))
49	((back adj4 pain adj4 assessment* adj4 aid*))
50	((back adj4 pain adj4 assessment* adj4 tool*))
51	((back adj4 pain adj4 assessment* adj4 questionnaire*))
52	((back adj4 pain adj4 clinical* adj4 aid*))
53	((back adj4 pain adj4 clinical* adj4 tool*))
54	((back adj4 pain adj4 clinical* adj4 questionnaire*))
55	((back adj4 pain adj4 checklist*))
56	((ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671))
57	#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56
58	#15 OR #57

INAHTA search terms

1	"Densitometry"[mhe]
2	((densitometr* or BMD-test* or BMD-tool* or densimetr*))
3	((bone and mineral and dens* and test*))
4	((bone and mineral and dens* and tool*))
5	((absorptiometr* and (dpx* or dual-energ* or dual-photon* or photon*)))
6	((DXA* or DXA))
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6

8	"Spinal Fractures"[mh]
9	((spin* or vertebr* or neck or cervical or lumbar or sacral or thoracic or coccy* or cord or backbone* or back) and (fracture* or compress*))
10	(compress* and fracture*)
11	(VCF or VFA* or IVA* or LVA* or DVA* or MXA*)
12	((instant or lateral or densitometric or morphometric or dual-energ*) and (vertebr* and assess*))
13	(physician* and viewer*)
14	#8 OR #9 OR #10 OR #11 OR #12 OR #13
15	#7 AND #14
16	Vfrac*
17	(vertebr* and fracture* and screen* and aid*)
18	(vertebr* and fracture* and screen* and tool*)
19	(vertebr* and fracture* and screen* and questionnaire*)
20	(vertebr* and fracture* and decision* and aid*)
21	(vertebr* and fracture* and decision* and tool*)
22	(vertebr* and fracture* and decision* and questionnaire*)
23	(vertebr* and fracture* and assessment* and aid*)
24	(vertebr* and fracture* and assessment* and tool*)
25	(vertebr* and fracture* and assessment* and questionnaire*)
26	(vertebr* and fracture* and clinical* and aid*)
27	(vertebr* and fracture* and clinical* and tool*)
28	(vertebr* and fracture* and clinical* and questionnaire*)
29	(vertebr* and fracture* and checklist*)
30	(spin* and fracture* and screen* and aid*)
31	(spin* and fracture* and screen* and tool*)
32	(spin* and fracture* and screen* and questionnaire*)
33	(spin* and fracture* and decision* and aid*)
34	(spin* and fracture* and decision* and tool*)
35	(spin* and fracture* and decision* and questionnaire*)
36	(spin* and fracture* and assessment* and aid*)
37	(spin* and fracture* and assessment* and tool*)
38	(spin* and fracture* and assessment* and questionnaire*)
39	(spin* and fracture* and clinical* and aid*)
40	(spin* and fracture* and clinical* and tool*)
41	(spin* and fracture* and clinical* and questionnaire*)
42	(spin* and fracture* and checklist*)

43	(back and pain and screen* and aid*)
44	(back and pain and screen* and tool*)
45	(back and pain and screen* and questionnaire*)
46	(back and pain and decision* and aid*)
47	(back and pain and decision* and tool*)
48	(back and pain and decision* and questionnaire*)
49	(back and pain and assessment* and aid*)
50	(back and pain and assessment* and tool*)
51	(back and pain and assessment* and questionnaire*)
52	(back and pain and clinical* and aid*)
53	(back and pain and clinical* and tool*)
54	(back and pain and clinical* and questionnaire*)
55	(back and pain and checklist*)
56	(ISRCTN18000119 or ISRCTN12150779 or ISRCTN42028479 or ISRCTN16550671)
57	#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56
58	#15 OR #57

1

Appendix C Diagnostic evidence study selection

Figure 1: Flow chart of clinical study selection for review of diagnostic accuracy of Vfrac

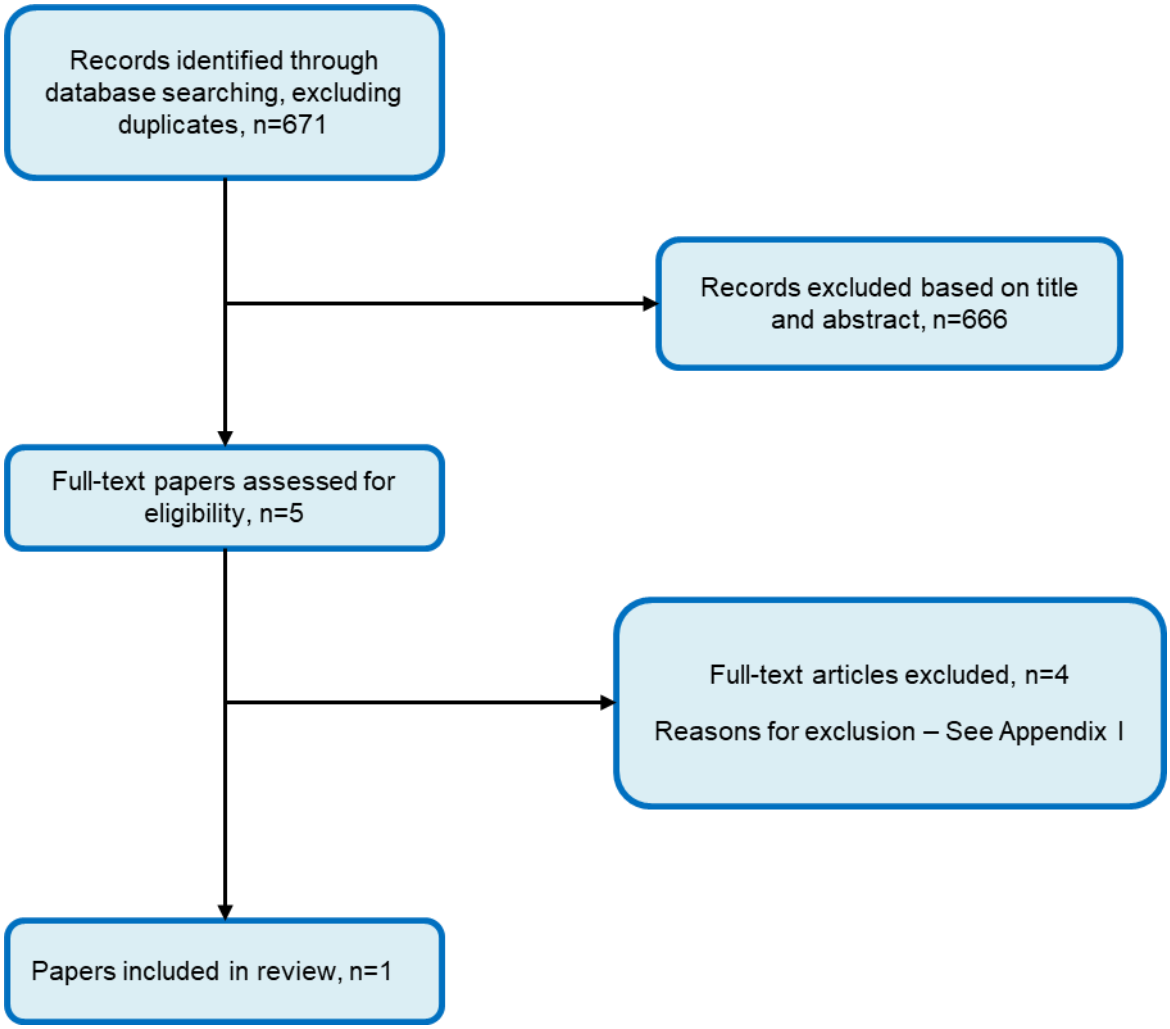
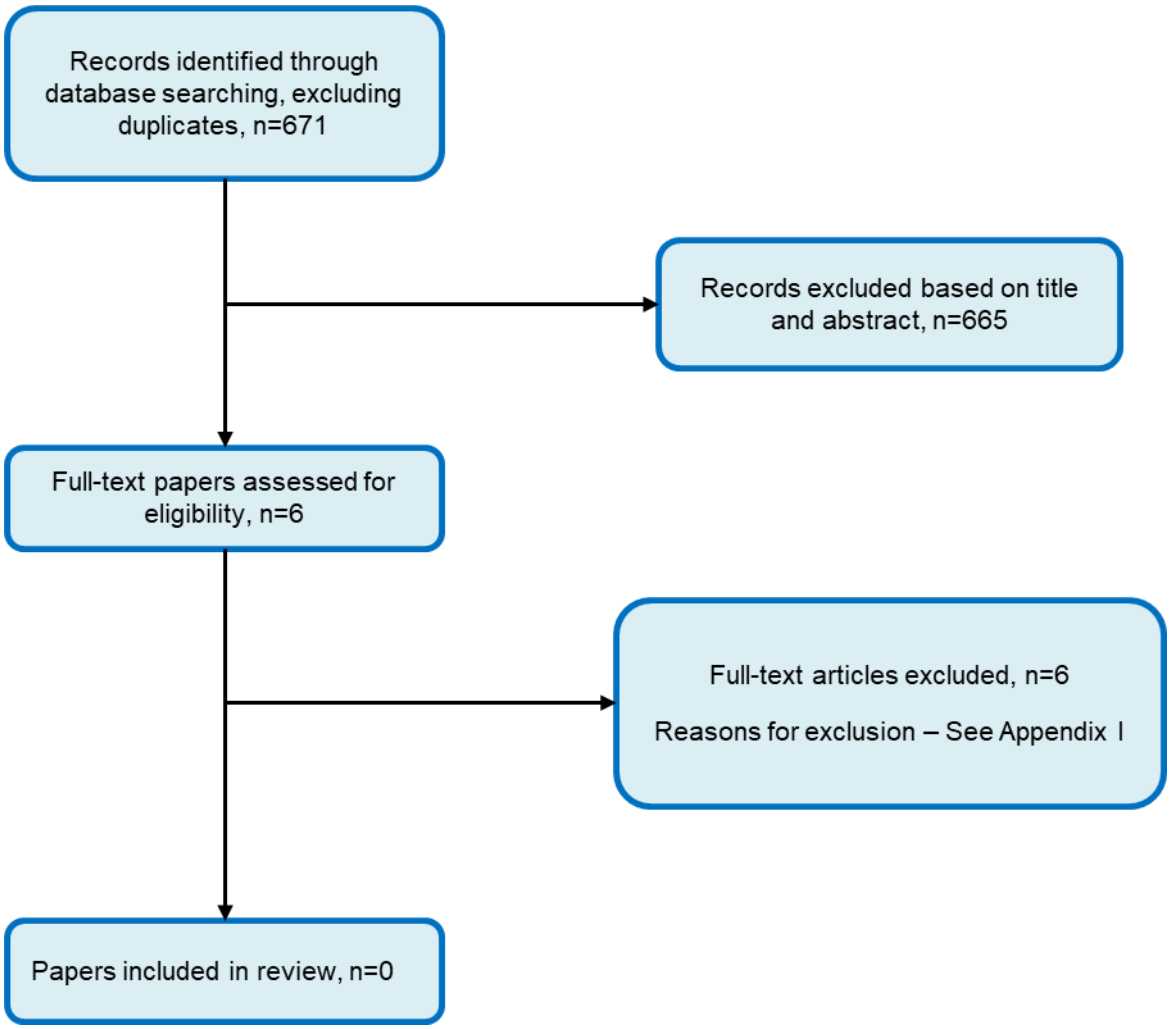


Figure 2: Flow chart of clinical study selection for review of diagnostic clinical and cost effectiveness of Vfrac



Appendix D Diagnostic evidence

D.1 Khera, 2022

Bibliographic Reference	Khera, Tarnjit K; Hunt, Linda P; Davis, Sarah; Gooberman-Hill, Rachael; Thom, Howard; Xu, Yixin; Paskins, Zoe; Peters, Tim J; Tobias, Jon H; Clark, Emma M; A clinical tool to identify older women with back pain at high risk of osteoporotic vertebral fractures (Vfrac): a population-based cohort study with exploratory economic evaluation.; Age and ageing; 2022; vol. 51 (no. 3)

Study details

Secondary publication of another included study- see primary study for details	N/A
Other publications associated with this study included in review	N/A
Trial name / registration number	NR/ ISRCTN registry SRCTN16550671
Study type	Prospective cohort study Derivation and internal validation study with bootstrapping
Study location	United Kingdom (Stoke-on-Trent and Bristol)
Study setting	General practices
Study dates	Not specified
Sources of funding	Funded by unrestricted Clinical Studies grant from Versus Arthritis (grant no 21507)
Recruitment / selection of participants	General practices from a range of deprivation scores as assessed by the Index of Multiple Deprivation were recruited from Stoke-on-Trent and Bristol. Women aged 65 years or older with a self-reported episode of back pain in the previous 4 months were recruited.
Inclusion criteria	Women aged 65 years or older with a self-reported episode of back pain in the previous 4 months

Exclusion criteria	Excluding fractures of the hands, feet, and head. Excluding high trauma.
Population subgroups	N/A
Index test	Vfrac is a web-based online tool, with source code that can be adapted to a mobile website or an app. Vfrac is targeted at those presenting with back pain. Vfrac is a clinical tool consisting of 15 questions which can be performed by a practice nurse. The output is a recommendation, or not, for spinal radiographs.
Reference standard	Radiographs used to confirm an osteoporotic vertebral fracture (OVF). Radiographs were assessed for the presence or absence of OVF using the Algorithm-based qualitative method. Radiographs were categorised by those with no fracture or with fracture. OVFs were further categorised into mild, moderate, or severe fractures based on their 'worst' fracture using the Genant semi-quantitative method.
Indirectness	None
Additional comments	Predictor variables: age, weight, wall to tragus, reported height loss, pain described as sharp, pain described as like a toothache, agreement with ‘If I’m working in the kitchen like chopping vegetables or washing my back pain gets worse and worse to reach a peak—then I have to sit down immediately,' pain in thoracic area of Margolis diagram, pain in low back/buttock area of Margolis diagram, pain increased by walking, pain affected by sitting on straight-backed chairs, pain affected by sitting on soft chairs, pain increased by reclining, fracture after age 50 (excluding hands, feet, head, and excluding high trauma), steroids for more than 3 months.

Characteristics

Study-level characteristics

Characteristic	**Study (N = 1337)**
Mean age (SD) Mean (SD)	73.9 (5.6)
Comorbidities Sample size	n = NR ; % = NR
Inflammatory arthritis without OVF Sample size	n = 179 ; % = 12.6
Inflammatory arthritis with OVF Sample size	n = 22 ; % = 12.8
Depression without OVF Sample size	n = 157 ; % = 13.3

Characteristic	Study (N = 1337)
Depression with OVF Sample size	n = 44 ; % = 10.7
Memory problems without OVF Sample size	n = 167 ; % = 12.4
Memory problems with OVF Sample size	n = 34 ; % = 13.8
Anxiety without OVF Sample size	n = 139 ; % = 13.4
Anxiety with OVF Sample size	n = 62 ; % = 11.2
Diabetes (type 1 or 2) without OVF Sample size	n = 185 ; % = 13
Diabetes (type 1 or 2) with OVF Sample size	n = 16 ; % = 9.7
COPD without OVF Sample size	n = 187 ; % = 12.6
COPD with OVF Sample size	n = 14 ; % = 12.8
Heart disease without OVF Sample size	n = 177 ; % = 12.4
Heart disease with OVF Sample size	n = 24 ; % = 14.1

Outcomes

Study timepoints

- 3 month (3 months)

Area under the curve

Outcome	Vfrac, 3-month, N = 1337
Area under the curve Area under the curve (95%CI)- full model including all predictors Custom value	NA
Area under the curve - Full model including all predictors Custom value	0.802 (0.764 to 0.840)
Area under the curve - Full model excluding self-reported back pain descriptors Custom value	0.802 (0.764 to 0.840)

Area under the curve - Polarity - Higher values are better

Sensitivity and specificity

Outcome	Vfrac, 3-month, N = 1337
Sensitivity Custom value	NA
Sensitivity - Full model including all predictors Custom value	0.72 (0.65 to 0.79)
Sensitivity - Full model excluding self-reported back pain descriptors Custom value	0.66 (0.58 to 0.73)
Specificity Custom value	NA
Specificity - Full model including all predictors Custom value	0.73 (95%CI 0.70 to 0.75)
Specificity - Full model excluding self-reported back pain descriptors Custom value	0.73 (95%CI 0.70 to 0.76)

Sensitivity - Polarity - Higher values are better
Specificity - Polarity - Higher values are better
Sensitivity and specificity are reported at a cut-point of the linear predictor of -2.0.

Predictive values

Outcome	Vfrac, 3-month, N = 1337
Negative predictive value Custom value	NA
Full model including all predictors Custom value	0.95
Full model excluding self-reported back pain descriptors Custom value	0.928
Positive predictive value Custom value	NA
Positive predictive value - Full model including all predictors Custom value	0.27
Positive predictive value - Full model excluding self-reported back pain descriptors Custom value	0.29

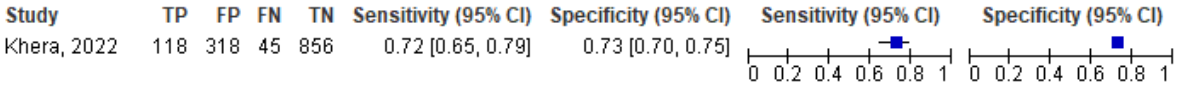
Negative predictive value - Polarity - Higher values are better

Positive predictive value - Polarity - Higher values are better

Appendix E Forest plots

E.1 Diagnostic test accuracy review

Figure 3: Sensitivity and specificity of Vfrac for determining suspected vertebral fractures



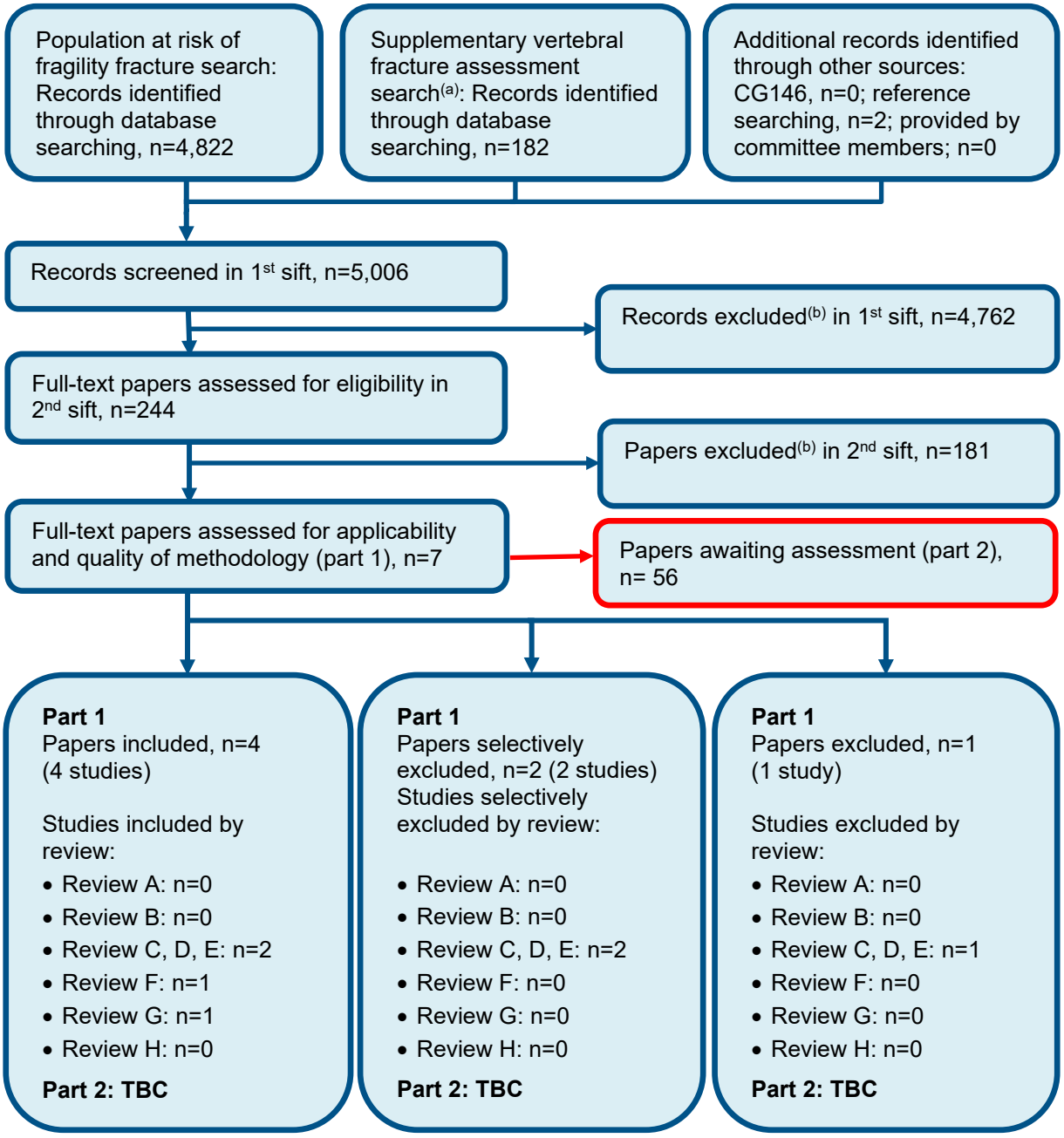
Note: sensitivity and specificity are reported using a cut-point of -2.0 for the linear predictor.

E.2 Diagnostic clinical and cost effectiveness review

None

Appendix F Economic evidence study selection

Note that this guideline is being consulted on it two parts, but the health economic review search covered the full guideline. Only studies related to part 1 are included below. Studies that may be relevant to part 2 are noted but are not finalised.



TBC= to be checked. These review questions will form the second instalment of this guideline update.

(a) Supplementary search for review questions F and G. Search methods in Appendix B of relevant evidence reports.
(b) Non-relevant population, intervention, comparison, design or setting; non-English language.

Appendix G Economic evidence tables

Study	Khera 2022			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis (health outcome: QALYs) **Study design:** Probabilistic decision analytic model. **Approach to analysis:** A diagnostic decision tree captures the number of individuals referred for radiography (both correctly and incorrectly) as well as those with OVF who are correctly diagnosed and treated, and those with OVF who remain undiagnosed and untreated. A previously published DES model (Davis 2020) was used to estimate lifetime costs and QALYs for people with OVF who are	**Population:** Women aged 65+ years from primary care with self-reported back pain in the previous 4 months **Population settings:** Start age: 76 years. Male: 0% **Intervention 1:** Standard care (defined via an online survey of seven clinicians and 12 patients). It was assumed all patients had a GP consultation, the outcomes of which were: • with OVF and referred for radiograph (2.5%), • with OVF but not referred for radiograph (10%) • without OVF but referred for radiograph (19%)	**Total costs (mean per patient):** Intervention 1: £315.67 Intervention 2: £322.95 Incremental (2−1): £7.28 (95% CI: -£58.59, £73.04; p=NR) **Currency & cost year:** UK pounds. Cost year not stated, however the DES model used 2018 as the cost year for estimating lifetime costs for treated and untreated OVF cases. **Cost components incorporated:** Cost of radiograph to diagnose OVF, treatment costs (alendronate), fracture costs, residential care following hip fracture.	**QALYs (mean per patient):** Intervention 1: 0.63 Intervention 2: 0.63 Incremental (2−1): 0.00044 (95% CI: -0.13, 0.13; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £16,545 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost effective versus Intervention 1 (£20K threshold): 49.4% Net benefit at £20k per QALY gained: 1.47 (95% CI: -2.587, 2.456) **Analysis of uncertainty:** No one-way or scenario analysis were reported. An EVPI analysis indicated a per person value of £526 and a population value between £229-£458 million.

diagnosed and receive treatment, and those with OVF who remain undiagnosed and therefore untreated. Long term costs and QALYs for people without OVF were excluded, as these will be identical in both groups. Clinical events captured by the model included subsequent fractures, all-cause mortality, and fracture-related mortality following hip or vertebral fracture. **Perspective:** UK NHS **Time horizon:** lifetime **Discounting:** Costs: 3.5%; Outcomes: 3.5%	• Without OVF and not referred for radiograph (68.5%) **Intervention 2:** Vfrac: Based on the cohort study, the following proportions were assumed: • with OVF and referred for radiograph (9.1%), • with OVF but not referred for radiograph (3.4%) • without OVF but referred for radiograph (25%) • Without OVF and not referred for radiograph (62.5%) **Treatment** All patients diagnosed with an OVF were assumed to initiate treatment with alendronate.			
Data sources				
Health outcomes: Diagnostic decision tree: prevalence of OVF and sensitivity and specificity of Vfrac were taken from the cohort study reported in the same paper (Khera 2022). Standard care inputs were based on expert opinion. Lifetime cost and QALY for people with OVF, treated and untreated: A published osteoporosis economic evaluation (Davis 2020) was used to estimate costs and QALYs with and without treatment. The population				

characteristics used to simulate a population in the model were set to match the distribution in the 118 study participants with a positive Vfrac score and a confirmed OVF (Khera 2022). The clinical effectiveness of alendronate in the model was based on a systematic review and network meta-analysis (Davis 2020). **Quality-of-life weights:** EQ-5D-3L values were derived using the UK tariff, except for one adverse effect, which used the US tariff. **Cost sources:** The cost of a radiograph (£72) was reported as a standard NHS cost, although no reference or cost year was specified. The published DES model used to estimate long term costs with and without treatment used 2018 costs from standard national cost references and published values inflated.

Comments

Source of funding: Funded using an unrestricted grant from Versus Arthritis. **Limitations:** The cost year for the radiograph was not reported. The published model used to estimate long-term costs applied a 2018 cost year, and no updates were stated – therefore, these values may not reflect the current NHS cost context. Resource-use estimates for the standard care arm were derived from a clinician- and patient-led committee. Population characteristics informing the DES model for treated and untreated OVF were taken from the 118 patients in the associated cohort study with a positive Vfrac score and confirmed OVF; comparison with the 2011 UK Census indicated under-representation of non-white groups. No one-way or scenario analyses were conducted. **Other:** n/a

Overall applicability:[a] Partially applicable **Overall quality:**[b] Potentially serious limitations

Abbreviations: 95% CI= 95% credible interval; AE= adverse event; CUA= cost–utility analysis; DES= discrete event simulation; EQ-5D-3L= Euroqol 5 dimensions 3 levels; EVPI= expected value of perfect information; GP= general practitioner; ICER= incremental cost-effectiveness ratio; NR= not reported; OVF= osteoporotic vertebral fracture; pa= probabilistic analysis; QALYs= quality-adjusted life years; QoL= quality of life.

(a) Directly applicable / Partially applicable / Not applicable

(b) Minor limitations / Potentially serious limitations / Very serious limitations

Appendix H Health economic model

This review question was not prioritised for original modelling.

Appendix I Excluded studies

I.1 Clinical studies

Table 11: Studies excluded from the diagnostic test accuracy of Vfrac review

Study	Exclusion Reason
Aubry-Rozier, B, Fabreguet, I, Iglesias, K et al. (2017) Impact of level of expertise versus the statistical tool on vertebral fracture assessment (VFA) readings in cohort studies. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 28(2): 523-527	- Study does not contain an intervention relevant to this review protocol
Han, Christopher S, Hancock, Mark J, Downie, Aron et al. (2023) Red flags to screen for vertebral fracture in people presenting with low back pain. The Cochrane database of systematic reviews 8: cd014461	- Study does not contain an intervention relevant to this review protocol
Khera, T K, Burston, A, Davis, S et al. (2019) An observational cohort study to produce and evaluate an improved tool to screen older women with back pain for osteoporotic vertebral fractures (Vfrac): study protocol. Archives of osteoporosis 14(1): 11	- Study protocol
Middleton, Edward T; Gardiner, Eric D; Steel, Susan A (2009) Which women should be selected for vertebral fracture assessment? Comparing different methods of targeting VFA. Calcified tissue international 85(3): 203-10	- Study does not contain an intervention relevant to this review protocol

Table 12: Studies excluded from the clinical and cost effectiveness of Vfrac review

Study	Exclusion Reason
Khalid, Tanzeela Y, Peters, Tim J, Pocock, Lucy V et al. (2024) An online clinical decision tool to screen for vertebral fragility fractures (Vfrac) in older women presenting with back pain in general practice: protocol for a feasibility study in preparation for a future cluster randomised controlled trial. Archives of osteoporosis 19(1): 12	-Study protocol.
Lems, W F, Paccou, J, Zhang, J et al. (2021) Vertebral fracture: epidemiology, impact and use of DXA vertebral fracture assessment in	- Review article but not a systematic review

Study	Exclusion Reason
fracture liaison services. Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA 32(3): 399-411	
Miller, S, Caragea, M, Carson, D et al. (2023) The Effectiveness of Intradiscal Corticosteroid Injection for the Treatment of Chronic Discovertebral Low Back Pain: A Systematic Review. Pain medicine (Malden, Mass.)	- Study does not contain an intervention relevant to this review protocol
Rajan, R., Paul, J., Kapoor, N. et al. (2020) Postmenopausal osteoporosis-An Indian perspective. Current Medical Issues 18(2): 98-104	- Review article but not a systematic review
Vogt, T M, Ross, P D, Palermo, L et al. (2000) Vertebral fracture prevalence among women screened for the Fracture Intervention Trial and a simple clinical tool to screen for undiagnosed vertebral fractures. Fracture Intervention Trial Research Group. Mayo Clinic proceedings 75(9): 888-96	- Study does not contain an intervention relevant to this review protocol
Yang, J; Mao, Y; Nieves, JW (2020) Identification of prevalent vertebral fractures using Vertebral Fracture Assessment (VFA) in asymptomatic postmenopausal women: A systematic review and meta-analysis. Bone 136: 115358	- Study does not contain an intervention relevant to this review protocol

I.2 Health Economic studies

If any published health economic studies relevant to this question met the inclusion criteria (relevant population, comparators, economic study design, published 2009 or later and not from non-OECD country or USA) but were excluded following appraisal of applicability and methodological quality they are listed below with reasons. See the health economic protocol for more details.

None.

Appendix J Recommendation for research

What is the clinical and cost-effectiveness of Vfrac (vertebral fracture clinical decision tool) to identify people with a vertebral fracture?

J.1 Why this is important

A clinical tool to identify people at high risk of vertebral fractures would be beneficial as many remain undetected. Back pain is common and can be due to many underlying causes, including vertebral fracture (VF). It is not considered clinically appropriate to obtain medical imaging in all patients presenting with back pain as in many cases this does not alter management and use of modalities such as x-ray or CT pose a risk associated with exposure to ionising radiation. Vfrac was developed because it is not easy to identify clinically which people have back pain due to a VF. The identification of vertebral fractures and subsequent treatment would reduce people's risk of future fractures and associated morbidity and mortality

J.1.1 Rationale for the recommendation for research

Importance to 'patients' or the population	The identification of vertebral fractures and subsequent treatment would reduce people's risk of future fractures and associated morbidity and mortality.
Relevance to NICE guidance	High: the research is essential to inform future updates of key recommendations in the guidance.
Relevance to the NHS	The aim would be to identify people in primary care at risk of vertebral fracture who may need treatment to reduce the risk of fractures.
National priorities	High Consistent with 10-year plan to move management into the community and focus on prevention.
Current evidence base	Diagnostic accuracy: One diagnostic accuracy study was identified that developed a decision tool (Vfrac) to identify people with back pain at high risk of osteoporotic vertebral fractures. Diagnostic randomised controlled trials: No studies were identified that compared use of Vfrac to usual care. Cost effectiveness: One cost-effectiveness model was identified that utilised data from the diagnostic accuracy study combined with other inputs. This found that Vfrac followed by imaging and treatment as deemed clinically appropriate may be cost-effective compared to current practice but with high uncertainty. The study found there was high value in further research to reduce uncertainty. Additional uncertainty was also highlighted by the committee in the inputs used for the current practice comparator group.
Equality considerations	Different deprivation levels of areas should be considered when randomisation done to ensure balanced across groups. Vertebral fractures less common in men but should be balanced across groups.

J.1.2 Modified PICO table

Population	Adults (65 years and older) who have had back pain in the last 4 months
Intervention	The vertebral fracture risk assessment tool (Vfrac)

	Followed by appropriate imaging and treatment
Comparator	Usual care / No Vfrac Followed by appropriate imaging and treatment in line with usual care
Outcome	- Vertebral fracture at baseline - Subsequent vertebral and non-vertebral fractures - Health-related quality of life measure (including quality of life for vertebral fractures (QUALEFFO-41) - Change in management - Resource use
Study design	Cluster randomised controlled trial (by GP surgeries)
Timeframe	Completed prior to future updates of the osteoporosis guideline to inform future recommendations
Additional information	None

1