UK National Screening Committee

Screening for Adolescent Idiopathic Scoliosis

External review against programme appraisal criteria for the UK National Screening Committee (UK NSC)

Version: 3

Bazian Ltd.

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The UK NSC advises Ministers and the NHS in all four UK countries about all aspects of screening policy. Its policies are reviewed on a 3 yearly cycle. Current policies can be found in the policy database at http://www.screening.nhs.uk/policies and the policy review process is described in detail at http://www.screening.nhs.uk/policyreview

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Abbreviations List

AAOS	American Academy of Orthopaedic Surgeons
AAP	American Academy of Pediatrics
AIS	Adolescent idiopathic scoliosis
ARR	Absolute risk reduction
ATR	Angle of trunk rotation
BRAIST	Bracing in Adolescent Idiopathic Scoliosis Trial
CI	Confidence interval
FBT	Forward Bend Test
FPs	False positives
FPR	False positive rate
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ITT	Intention to treat
LR	Likelihood ratio
NNT	Number needed to treat
NPV	Negative predictive value
OR	Odds ratio
POSNA	Pediatric Orthopaedic Society of North America
PPV	Positive predictive value
RCT	Randomised controlled trial
SD	Standard deviation
SOSORT	Scientific Society on Scoliosis Orthopaedic and Rehabilitation Treatment
SRS	Scoliosis Research Society
SRSITF	Scoliosis Research Society International Task Force
TLSO	Thoracolubosacral orthosis
TPs	True positive

Plain English Summary

The Condition

Adolescent idiopathic scoliosis (AIS) is a curve of the spine that can develop during puberty. Someone who has a spine that curves more than 10^{o} is said to have scoliosis. Around 2 to 3% of people are believed to have scoliosis. In some people these curves can improve without any treatment. There are many factors that influence whether the level of scoliosis improves, stays the same or becomes more severe.

The Treatment

Treatment decisions are usually based upon the severity of scoliosis and other factors such as the person's age and stage of development. Less extreme treatments for mild scoliosis involve exercise therapy. Bracing is the most accepted form of treatment to correct moderate scoliosis. Surgery may be used to correct more severe scoliosis.

Screening and Previous/ Current UK NSC Recommendations

Screening has been suggested as a way to identify children with scoliosis and hopefully give early treatment to prevent the condition becoming worse. The screening test would involve using the Adam Forward Bend Test (FBT) with scoliometer measurement of angle of trunk rotation (ATR). The most recent review in 2012 recommended against screening due to many uncertainties. This review searched for evidence since 2012. It focussed on the areas in the 2012 review that required further evidence or were unmet.

Findings

The review found:

- there is an agreed screening test to detect AIS but there is no single agreed cut-off. It is also not clear what the best age to screen is and whether additional follow-up screening testing (Moiré topography) will be used.
- the accuracy of the test for predicting AIS that is likely to become more severe and need treatment is poor. This would lead to follow-up testing using X-rays that may cause harm to people who would not need any treatment.
- there is no agreed single angle that would indicate specific AIS treatment. Decisions on treatment are likely to be more complicated and depend on lots of different factors. This is likely to affect how accurate the screening test is to identify those people who need treatment.
- it is not clear whether there is any added benefit from giving treatments for AIS following detection at screen compared with after clinical detection.

Recommendation

The evidence suggests that the recommendation not to screen for Adolescent idiopathic scoliosis should be retained.

Executive Summary

The Condition

Adolescent idiopathic scoliosis (AIS) is a three dimensional curvature of the spine that presents during puberty and is of uncertain cause. The degree of curvature is the marker for scoliosis and is measured by the angle of the deformity on X-ray, called the Cobb angle. An angle over 10^{o} is widely accepted as the diagnostic threshold of clinically significant scoliosis.

Population prevalence of AIS using this diagnostic definition of 10^{o} is estimated to be around 2 to 3%, though may vary globally, and prevalence of more severe curves is lower. Adolescent idiopathic scoliosis can improve, remain stable or progress over adolescence. The natural history is influenced by the degree of curvature and type of curvature, age and skeletal maturity, and for females, menarchal status.

The Adam Forward Bend Test (FBT) with scoliometer measurement of angle of trunk rotation (ATR) is accepted as a simple, quick, reliable and low cost testing method. Cases can then be referred for radiological confirmation of diagnosis. However, universal screening for AIS using this method has long been debated.

The Treatment

Treatment decisions are usually based upon the severity of scoliosis and other patient characteristics such as stage of skeletal maturity. Conservative treatment for mild scoliosis usually involves exercise therapy, with bracing being the most commonly accepted form of treatment to correct moderate scoliosis. Surgery is often used to correct more severe scoliosis.

Screening

Screening has been suggested as a way to allow early detection of children with scoliosis and so hopefully allow early treatment to prevent more severe progression of the condition. The screening test would be likely to involve using the Adam Forward Bend Test (FBT) with scoliometer measurement of angle of trunk rotation (ATR). Cases would then be referred for radiological confirmation of diagnosis (that is to confirm that the angle of scoliosis is severe enough to warrant further observation or treatment).

Previous/ Current UK NSC Recommendations

The current UK NSC recommendation on screening for Adolescent Idiopathic Scoliosis is from 2012. This recommended against screening due to a number of uncertainties. Bazian Ltd were commissioned to undertake this rapid review, which considers whether the volume and direction of the evidence produced since the 2012 external review indicates that the previous recommendation should be reconsidered. Five main criteria will be considered, with particular focus given to areas the 2012 review identified as uncertain, or supported by insufficient evidence.

Findings

The review found that:

- consensus recommendations have established FBT with scoliometer as the screen test to use. The recommendations suggest an angle of 5-7^{o} should indicate referral for radiography. However, there is no single agreed cut-off. There also remain further uncertainties regarding the additional use of Moiré topography and the optimal age to screen.

- the PPV of the screening test for identifying scoliosis likely to progress and scoliosis requiring treatment is very low. This would lead to unnecessary use of resources and X-ray exposure for the follow-up of many mild cases that would not require treatment despite meeting diagnostic criteria.

- there are no guidelines from national or professional bodies that give recommendations on absolute Cobb angles indicating specific AIS treatment approaches. Decisions on treatment are likely to depend on various factors including patient age, skeletal maturity and further assessment of risk.

- there are still many uncertainties around treatment. Evidence on the benefit of bracing is only in clinically detected and not screen-detected populations. There is no statistically significant evidence that bracing prevented more severe progression or the need for surgery. The adherence to bracing and more conservative treatment like exercise therapy is unclear. It is also unclear whether conservative treatments and more radical treatment like surgery following screen detection offer any more benefit than after clinical detection.

Recommendation

The evidence suggests that the recommendation not to screen for Adolescent idiopathic scoliosis should be retained.

Introduction

Adolescent Idiopathic Scoliosis

Adolescent idiopathic scoliosis (AIS) is a three dimensional curvature of the spine that presents during puberty and is of uncertain cause. The degree of curvature is the marker for scoliosis and is measured by the angle of the deformity on X-ray, called the Cobb angle. An angle over 10^{o} is widely accepted as the diagnostic threshold of clinically significant scoliosis.[1, 2]

Adolescent idiopathic scoliosis is associated with an increased likelihood of poorer health-related quality of life and back pain.[3-6] However, the degree of curvature and the impact on quality of life may vary between individuals. Population prevalence of AIS using this diagnostic definition of 10^{o} is estimated to be around 2 to 3%, though may vary globally, and prevalence of more severe curves is lower.[7] Adolescent idiopathic scoliosis can improve, remain stable or progress over adolescence. The natural history is influenced by the degree of curvature and type of curvature, age and skeletal maturity, and for females, menarchal status.

The Adam Forward Bend Test (FBT) with scoliometer measurement of angle of trunk rotation (ATR) is accepted as a simple, quick, reliable and low cost testing method.[8] Cases can then be referred for radiological confirmation of diagnosis. However, universal screening for AIS using this method has long been debated. There are various issues, including the low population prevalence of AIS and low positive predictive value (PPV) of the screening test leading to unnecessary diagnostic follow-up of unaffected children, which includes exposure to radiation through X-ray. Also only a low proportion of AIS cases may progress or gain any benefit from early treatment. It is reported that between 25 and 75% of cases detected through screening may remain unchanged over time, while between 3 and 12% may improve.[9] Of all people with AIS (not just screen-detected), only 8 to 9% are reported to receive treatment with a brace, and 0.1% require surgery.[1]

In 2004 the United States Preventive Services Task Force (USPSTF) recommended against the routine screening of asymptomatic adolescents for AIS. This led to the discontinuation of many national screening programmes. Meanwhile the American Academy of Orthopaedic Surgeons (AAOS), the Scoliosis Research Society (SRS), the Pediatric Orthopaedic Society of North America (POSNA), and the American Academy of Pediatrics (AAP) do not currently support any formal recommendation for screening in light of insufficient evidence.[1]

An SRS International Task Force (SRSITF) was set up in 2010 with the purpose of exploring AIS screening from a multinational perspective. The SRSITF subsequently published a consensus information statement in 2013 on the value of AIS screening based on the available scientific literature.[1]

Basis for current recommendation

The most recent UKNSC external review of adolescent idiopathic scoliosis conducted in 2012[10] was an update review, following on from a full review in 2006 that was undertaken in light of the USPSTF recommending against AIS screening in 2004. The update review concluded that "Owing to the remaining uncertainties surrounding the test and treatment the updated evidence does not suggest that changing the current policy would be appropriate."

Several key uncertainties were highlighted by the 2012 evidence review:

- Though screening tests are safe and simple, the positive predictive value is low leading to unnecessary follow-up and X-ray exposure
- Though there is some evidence to suggest that screening programmes identify more people with minor curves than would present outside of screening, there is no high level evidence to suggest that treatment of minor curvatures will prevent progression
- There is low quality evidence for the effectiveness of treatments for scoliosis, and no agreed evidence based recommendations for when treatment is indicated

Following the 2012 review, the National Screening Committee concluded that systematic population screening of children or adolescents for AIS was not recommended.

Current update review

The current review was prepared by Bazian Ltd., and then adapted in discussion with the UK National Screening Committee. The review considers whether the volume and direction of the evidence produced since the 2012 external review warrants a change to the current recommendation not to screen for AIS. Five main criteria will be considered, with particular focus given to areas the 2012 review identified as uncertain, or supported by insufficient evidence. The main criteria and key questions reviewed are:

Table 1. Key questions for current AIS update review

Criterion	Key Questions (KQ)	# KQ Studies Included
6. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.	1) Is there an agreed cut-off value for the AIS screening test?	1
5. There should be a simple, safe, precise and validated screening test.	2) How accurate is the test? Does the test(s) cut-off effectively distinguish between cases whose scoliosis would progress and need future treatment (i.e. bracing and surgery) and those that would not require future treatment?	2
11. There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.	3) Are there agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered, particularly what conservative treatment is indicated and for whom it is indicated?	1
10. There should be an effective treatment or	4) Is there evidence of treatment benefit following screening?	

intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.	a) Is there evidence that early treatment (following screen) of mild curvature with conservative options offers more benefit than clinically detected cases in terms of preventing progression to more severe scoliosis and the need for bracing?	0
	b) Is there high quality evidence that early treatment (following screen) of moderate curvature with bracing prevents progression to more severe scoliosis and the need for surgery?	3
	c) Is there evidence that early surgical treatment (following screen) leads to greater benefits than surgery following clinical detection?	0
14. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public.	What is the evidence regarding the acceptability of treatment to patients, as assessed by treatment adherence rate?	5

A systematic literature search of studies published between August 2011 and March 2015 yielded 1244 references addressing AIS. Of these, 435 were assessed as being potentially relevant to the key questions outlined in Table 1. These studies were further filtered at title and abstract level, and 61 were selected for appraisal at full text. Each section below provides additional information on the evidence selection process for the given criterion.

Appraisal against UK NSC Criteria

These criteria are available online at http://www.screening.nhs.uk/criteria.

6. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.

Description of the previous UK NSC evidence review conclusion

The previous UK NSC review concluded that there was no clear consensus or evidence-based recommendations on a suitable cut-off level for screening tests which could be used as a threshold for referral for radiography follow-up.

Current UK NSC key question

The current review addressed whether this has subsequently changed and whether there was now guidance or consensus statements on an agreed cut-off level for AIS screening tests.

Results

A single piece of consensus guidance on AIS screening was identified by the search. This was the 2013 information statement by the SRSITF.[1]

The consensus document was developed through a process of: establishing a framework for assessment of studies on the effectiveness of AIS screening; identifying specific screening questions needing to be addressed; and contextualising the knowledge through expert consultation.[11] The group carried out a systematic review to identify studies evaluating AIS screening published up to July 2010.[11] A separate and specific MEDLINE search was subsequently performed to identify studies of bracing treatment published up to 2012.[1] Individual study quality was assessed using the Downs and Black 28-item tool. The GRADE system was then used to assess the overall body of evidence related to each outcome in forming consensus statements or recommendations.

The SRSITF consensus statements related to AIS screening methods and cut-offs are:[1]

- The scoliometer is currently the best tool available for scoliosis screening
- There is moderate evidence to recommend referral with scoliometer values between 5^{o} and 7^{o} or greater
- The addition of Moiré topography may improve sensitivity
- Females should be screened twice, at age 10 and 12, and boys once, at age 13 or 14
- Suspected cases of scoliosis will be referred for diagnostic evaluation and confirmed, or ruled out, with a clinically significant scoliosis (>10^{o} of Cobb angle)

Consensus recommendations on a suitable cut-off for screening have therefore been made. However, the SRSITF acknowledge the limitations of their qualitative review and that the body of knowledge is based on observational studies only, which are subject to many sources of bias.[11] With the exception of studies specifically on bracing, the evidence reviewed by the SRSITF on AIS screening (search date July 2010) predates that of the last external UK NSC review (search date August 2011).[10] The previous UK NSC review had noted that lack of consensus about age of screening, screening method and cut-off used, and the variability across published studies.

Though the SRSITF have now formed consensus recommendations following expert review of this evidence, there is still lack of a conclusive recommendation on cut-off. The FBT with scoliometer measurement of ATR is recommended as the most reliable and validated test, but the suggested cut-off interval is between 5^{o} and 7^{o} rather than a single threshold.

There is also lack of clarity about the use of Moiré topography. The SRSITF report the evidence that Moiré topography in combination with scoliometer may improve sensitivity as "controversial".[1] There is also no recommendation on the difference in contour lines on topography that would indicate referral.

The SRSITF also state that the recommended screening age needs further clarification. The literature on this is said to be "difficult to interpret" but there was agreement that screening should be performed two years before onset of menstruation in girls. Age at menarche varies between individuals, which would make it difficult in the context of universal screening to select an age that would be two years before onset in all girls.[1]

When considering the positive predictive value (PPV) of the screen test, there is consensus that the standard diagnostic definition of AIS should be used; that is curves of >10^{o}. However, the SRSITF document the debate among experts over the clinical significance of diagnosis, when many cases <20^{o} do not normally need follow-up and treatment.[1]

Summary: Criterion 6 partially met

Consensus statements have been published that recommend the FBT with scoliometer as the screen test to use, with 5-7^{o} as the measurement interval that indicates radiography follow-up. However, there is no single established cut-off value, and there remain other uncertainties related to the additional use of Moiré topography and the optimal screening age.

5. There should be a simple, safe, precise and validated screening test.

Description of the previous UK NSC evidence review conclusion

The 2011 UK NSC review concluded that there was uncertainty about the accuracy of screening tests for AIS. Previous studies demonstrated variable test performance, but overall the PPV for identifying clinically significant AIS requiring treatment was low. The high false positive rate (FPR) would lead to the risks of unnecessary follow-up and treatment. There was also uncertainty over the timing of screening and the number and frequency of screening tests during adolescence.

Current UKNSC key question

The ideal AIS screening programme would facilitate early detection of people with AIS that is likely to progress, and so enable early treatment that would give maximal benefit, meanwhile minimising the unnecessary identification of non-progressive cases. The current review therefore focuses on the question of whether the screening test effectively distinguishes between people with AIS who would progress and need future treatment (e.g. bracing and surgery) from those who would not require treatment.

Description of the evidence

Overall 16 studies were identified as potentially relevant during title and abstract sifting and were further assessed at full text. We aimed to prioritise studies where i) the screening method and cut-off were in-line with current SRSITF consensus recommendations; and ii) information on test performance, either for overall AIS diagnosis or for distinguishing between cases likely to progress and unlikely to progress was provided.

No randomised or non-randomised controlled trials evaluating AIS screening programmes were identified. Two cohorts were identified where the screen test was consistent with current SRSITF recommendations and that provided information on test performance. Both of these studies were included in the final analysis. Fong (2015)[12] was an evaluation of the national screening programme in Hong Kong where screening has been performed since 1995 (Appendix 1). Adobor (2011)[8] reported the results of a regional programme conducted in Norway, where

national screening has been discontinued (Appendix 2). A summary of the screen test and performance data for these two studies is given in Table 2.

No other studies of any design were identified that contained information of relevance to the question. One additional screening study was excluded as screening was performed by Moiré topography alone without FBT, and there is no recommendation for its isolated use by the SRSITF. Other excluded studies included those evaluating methods for diagnosis of AIS and assignment of Cobb angle and Risser sign (indicating stage of skeletal maturity). Several studies compared inter- and intra-rater reliability of assigning these values, or compared manual measurement of Cobb angle with new digital procedures (e.g. smartphone applications). Studies evaluating other new diagnostic systems were also excluded (e.g. 3D X-rays, DEXA scan [dual energy X-ray absorptiometry] or new topography scanners).

Results

Table 2. Screen test performance in two screening cohorts

Study	Screen test	Referral rate, TPs, FPs and FNs	Test performance	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Fong (2015)[12] Nationwide screening programme n=306,144 (78% of those eligible for screening) 5 consecutive screened years with 10 year follow-up	FBT ATR = > 5° <15° → Topography ≥2 lines difference; or clinical deformity → Refer for X-ray (ATR ≥15° direct referral) Screen age: ≥10 years, screened 2-yearly to 19 years	**Referred**: 12,536 (4.1% of screened) **TPs (angle ≥10°)**: 10,160 (81.0% of referred) FPs: 2376 (19.0%) **FNs (not referred and clinically diagnosed with angle ≥10°)**: 671 (0.23% of non-referred)	Overall diagnosis: Angle ≥10°[(a)]	93.8 (93.3 to 94.3)	99.2 (99.2 to 99.2)	81.0 (80.3 to 81.7)	99.8 (99.8 to 99.8)
			Test performance for greater severity at time of diagnosis				
			Angle ≥20°[(b)]	91.0 (90.2 to 91.7)	97.5 (97.4 to 97.5)	39.8 (38.9 to 40.6)	99.8 (99.8 to 99.8)
			Angle ≥40°[(c)]	77.6 (74.5 to 80.6)	96.1 (96.0 to 96.2)	4.6 (4.2 to 5.0)	99.9 (99.9 to 100)
			"Given Treatment" [(d)]	83.3 (81.1 to 85.3)	96.2 (96.2 to 96.3)	8.4 (7.9 to 8.9)	99.9 (99.9 to 99.9)

(a) Overall test performance data based on total 10,160 TPs screen detected with AIS diagnosis (angle ≥10°) and 671 FNs later clinically diagnosed by 19 years; 2376 FPs and 292,875 TNs

(b) Based on 4985 TPs with angle ≥20° at screen detection and 495 FNs later clinically detected by 19 years with angle ≥20°; 7551 FPs (with angle <20°) and 293051 TNs (with angle <20°)

(c) Based on 573 TPs with angle ≥40° at screen detection and 165 FNs later clinically detected by 19 years with angle ≥40°; 11963 FPs (with angle <40°) and 293381 TNs (with angle <40°)

(d) Performance data of screen test for those given any form of treatment for AIS – no further clarification on types of treatment or indication given in publication.

Study	Screen test	Referral rate, TPs, FPs and FNs	Test performance	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Adobor (2011)[8] Regional study programme in South Norway (nationwide screen discontinued) n=4000 (33.3% of those eligible to participate) (follow-up duration unclear)	FBT ATR ≥7° → Refer for X-ray Screen age: 12	Referred: 60 (1.5% of screened) TPs (angle ≥10°): 22 (36.7% of referred) FPs: 38 (63.3%) FNs: Unknown (performance based on assumed population prevalence 0.8%)	Overall diagnosis: Angle ≥10° (Test performance by greater severity and treatment need is not given.)	69	99	37	99

The key question is whether the screen test would effectively distinguish between cases that would progress and require treatment, from less severe cases that would not require treatment. The main outcome examined by both studies was overall AIS diagnosis as indicated by Cobb angle ≥10°. The PPV of the screen test for overall diagnosis was 81% in the nationwide screening cohort by Fong (2015),[12] though much lower at 37% in Adobor (2011).[8] The high FPR would lead to unnecessary use of resources and X-ray exposure for children without AIS. However, even for those meeting a clinical diagnosis, the PPV for those with angle ≥10° is not a good indicator for those at risk of progression or who would need treatment.

Alongside overall diagnosis, Fong (2015)[12] also separately assessed test performance for diagnosis of more severe Cobb angle categories that may infer greater risk of progression and indicate specific management approach: ≥20° and ≥40°. Though there are no fixed definitions for severity grading from mild to severe and the management indicated for these (see Criterion 11), many of those with a diagnosis of 10-19° would receive observation only. Half of those diagnosed were in this category. The PPV for those with Cobb angle ≥20° (who may be eligible for bracing) was only 40%. The PPV for more severe Cobb angles ≥40° (who may require surgery) was even lower at 5%. To clarify, these PPV calculations are based on defining as true positives only those screen-positives with an angle severity ≥20° or ≥40°, respectively. False positives were thus extended to include not only those who did not have AIS (angle <10°), but also those with lesser severity of AIS, angle <20° or <40°, respectively. As such the lower PPV of the screen test for angles of greater severity may be as expected. If the primary aim of the screen test was not to detect all those meeting diagnostic criteria for AIS, but only to detect those with greater severity who may require treatment, then the currently recommended screen cut-offs may not be suitable for this.

Fong (2015)[12] also calculated the PPV of the screen test for those who went onto receive treatment, which was only 8%. The study provides no further information on treatment, with several unknown factors. This includes: the severity by Cobb angle of those treated, what type of treatment was given (e.g. whether "treatment" would include conservative measures such as exercise), and whether treatment was given at initial diagnosis or upon progression during later follow-up. Only the overall proportion of the screened cohort who received AIS treatment is given (0.4%). This figure would include both TPs and FNs who were treated after later clinical diagnosis.

The Adobor (2011)[8] cohort provides lower quality evidence of screen test performance. Accuracy measures are not given by severity or treatment need, but the results again suggest the limited reliability for identifying progressive cases that require treatment. Over-three quarters of those diagnosed had Cobb angle 10-20°, none of whom received treatment or progressed during follow-up to maturity. Only 5/22 detected cases had Cobb angle >20° and none were treated with bracing as they were too skeletally mature at the time of detection.

While the cohort findings suggest the screening test may have reasonable performance for identifying those who meet diagnostic criteria for AIS (angle ≥10°), it is poor at distinguishing those at risk of progression who would benefit from treatment from those who require observation only. This would therefore increase resource use and lead to unnecessary X-ray exposure and follow-up of children with AIS that is not clinically significant and would not have progressed.

In Fong (2015)[12] sensitivity was 93.8% for overall diagnosis. False negatives at screening who were later clinically diagnosed included a higher proportion with Cobb angle ≥20° compared to true positives detected through screening. This difference in the distribution of severities among true positives compared with false negatives clinically diagnosed by 19 years is the cause of the lower sensitivity of the screen test for angle ≥20° (91.0%) and ≥40° (77.6%). This may suggest that clinical diagnosis primarily identifies cases when they are at a more advanced stage. However, index of suspicion for AIS may be different in screen-negatives compared with a general non-screened population. Also clinical diagnosis in the absence of screening may predominantly identify cases that actually require treatment, while minimising unnecessary diagnosis of mild, non-progressive cases that wouldn't need treatment.

The two cohorts were not directly comparable on either the timing of the screen test(s), or the cut-off used, again highlighting the lack of clarity on these aspects. The two cohorts had screening tests that fell within the broad consensus recommendations of SRSITF[1]: Fong (2015)[12] used an FBT threshold of >5° with further confirmation by Moiré topography to indicate referral; Adobor (2011)[8]used an FBT threshold of >7° alone. However, the studies identified were insufficient to determine the optimal test threshold to use, or whether this is influenced depending on second tier screen with topography, is uncertain.

The screening age is also likely to influence test performance, particularly for treatment. Cases need to be identified when still skeletally immature in order to gain benefit from treatment to prevent progression. SRSITF[1] recommend screening girls twice at ages 10 and 12, and boys once at 13 or 14. The two cohorts did not use these precise ages. The Hong Kong screening programme covered more comprehensive screening of both boys and girls every two years between the age 10 and 19. The Norwegian programme screened both boys and girls once only at 12 years. As the Norway cohort suggests, the detected cases were already too skeletally mature at this time to be treated.

Overall it is not known what timing for screening or what FBT cut-off would be optimal for a UK programme, or whether this would be combined with topography. Even if an identical screening programme to that of either the Hong Kong or Norway cohorts were used, the PPV and NPV may not be applicable if the population prevalence of AIS differs in the UK.

Summary: Criterion 5 not met

The review does not clarify uncertainties about test performance raised by the previous UK NSC review. Two screening cohorts were identified. The studies suggest that screening is sensitive for detecting overall diagnoses of AIS (Cobb angle ≥10°). However, the screening test is poor for distinguishing between AIS of greater severity or those who need treatment from milder cases who would need observation only. In the larger population-based study, the PPV was 40% for those with Cobb angle ≥20° (who may be eligible for bracing) and only 5% for Cobb angles ≥40° (who may require surgery). The PPV for identifying those who required any treatment (either initially or during follow up) was only 8%. This would lead to unnecessary use of resources and X-ray exposure for milder cases who may not have been clinically diagnosed without screening.

The applicability of these study results to the UK is unknown, and questions remain over the optimal age and frequency of screening, test cut-off and combination of tests to use.

11. There should be agreed evidence based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.

Description of the previous UK NSC evidence review conclusion

The previous UK NSC review found that no treatment guidelines for scoliosis of any aetiology had been published by national or professional bodies. The review concluded that there were uncertainties about the effectiveness of treatments for scoliosis which would need to be resolved before an evidence-based policy for treatment could be made.

Current UKNSC key question

The current review aimed to see whether evidence-based policies have since been published covering which individuals should be offered treatment and the appropriate treatment to be offered. In particular what form of conservative treatment is indicated and for whom.

Results

The updated literature search identified no treatment guidelines for AIS published by national or professional bodies.

The SRSITF[1] consensus document states that "there is strong evidence to support the value of bracing for the treatment of AIS", and that scientific literature supports the short and long term efficacy of full-time brace wear to prevent progression. However, they give no consensus recommendation on the criteria that indicate bracing.

One 2012 evidence-based review by the Scientific Society on Scoliosis Orthopaedic and Rehabilitation Treatment (SOSORT) was identified.[9] This was an update review on the conservative treatment of idiopathic scoliois (regardless of age), which followed on from a previous 2006 consensus document produced by the SOSORT committee after a conference.[7] The updated review was informed by a systematic literature review of bracing and other conservative options conducted in February 2011.

This review discusses the evidence for the effectiveness of conservative treatment programmes and their requirements.

SOSORT give recommendations that:[9]

- Bracing is not recommended for curves below 15 ± 5^{o} (unless otherwise justified by specialist opinion)
- Bracing is recommended for curves above 20 ± 5^{o}, where patients are still growing, and demonstrate progression of deformity or elevated risk of worsening (unless otherwise justified by specialist opinion)

However, there are no other specific recommendations on patient criteria or indications for other conservative treatments (either alone or alongside bracing) such as specific physiotherapy exercise programmes or manual therapy, or for observation alone. The previous SOSORT document had suggested observation or different conservative treatment plans depending on Cobb angle, risk of progression and signs of skeletal maturity.[7]

The review also discusses the general consensus on diagnostic thresholds:[9]

- The diagnosis is made at angle over 10^{o}
- Over 30^{o} the risk of progression increases, as well as the risk of health problems and reduction of quality of life
- Over 50^{o} it is almost certain that scoliosis is going to progress in adulthood and cause health problems and reduction of quality of life
- A threshold for surgery of 45-50^{o} is generally recognised
- There is a continuum from one stage to the other and 5^{o} is considered as a measurement of error

As such, though there are very general agreed thresholds, there is no single fixed Cobb angle to indicate management approach and decisions are likely to be on an individual basis taking into account nature of the curve and stage of skeletal maturity.

Summary: Criterion 11 partially met

No guidelines on the range of treatments for AIS from national or professional bodies were identified. One evidence-based update review of conservative treatment of scoliosis was identified. There is agreement on the general curve thresholds that indicate different risk of scoliosis progression and when bracing or surgery may be considered. However, there is no absolute threshold indicating a particular treatment approach, or when observation only or other conservative treatment is appropriate. This is likely to depend on various factors including skeletal maturity. This makes it difficult in the context of a screening programme to identify a specific Cobb angle cut-off that would distinguish between those needing treatment and those not.

10. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.

Description of the previous UK NSC evidence review conclusion

The previous UK NSC review concluded that there is low level of evidence for the effectiveness of conservative treatments for AIS. There were no RCTs or controlled trials comparing the effectiveness of conservative treatments such as bracing or exercise with observation, and as such no evidence that conservative treatment prevented progression compared with no treatment. Additionally no studies were identified which had assessed whether screen-detected cases fare better than clinically detected cases following treatment with conservative treatments. There were also no high quality studies assessing surgery. Overall there was uncertainty surrounding treatments for AIS and whether treatment following screening improved outcomes.

Current UKNSC key question

The current review aimed to assess whether this evidence situation has changed, and whether there is any evidence of additional treatment benefit following screening.

The aim was to see whether there is high quality evidence that early treatment following screening of:

- a) “mild” curvature with conservative options offers benefit compared with clinical detection in terms of preventing progression and need for bracing
- b) “moderate” curvature with bracing offers benefit compared with clinical detection in terms of preventing progression and need for surgery
- c) more “severe” cases with early surgery offers benefit compared with surgery after clinical detection

Description of the evidence

Overall, 17 studies were identified as potentially relevant during title and abstract sifting and further assessed at full text.

In selection of evidence we aimed to prioritise RCTs or non-randomised controlled studies that had compared treatment following screen detection with treatment following clinical detection. Only one such study was identified (Adobor [2012][13], Appendix 3). This was a before-after study comparing treatment of cases clinically detected in Norway after discontinuation of the AIS screening programme (2003-2011) with treatment of cases diagnosed when the screening programme was in place (1976-1988).

The next priority was to identify RCTs or non-randomised controlled studies of clinically detected cases where the compared study groups could have relevance to screen detection. This primarily included studies examining the effect on progression of:

- treatment compared with no treatment/observation (where it could be inferred that screen detection may facilitate treatment of cases who would otherwise have remained untreated until clinical detection)
- early compared with delayed treatment, or treatment given at a younger compared with older age (where it could be inferred that screening may facilitate treatment earlier /at a younger age than through clinical detection)

Two studies were identified and included in this evidence review. Weinstein (2013, Appendix 4)[14] was a multicentre RCT comparing the effect of bracing vs. observation on curve progression. Wiemann (2014, Appendix 5)[15] was a smaller non-randomised controlled trial examining the effect of early bracing for mild curves vs. observation on curve progression.

No randomised or non-randomised controlled studies were identified that compared treatment started at different ages. One prospective cohort of girls treated with bracing was identified, which examined the factors associated with progression or non-progression at follow-up. The main focus of the analysis was on the association with baseline bone mineral density, but it also examined the influence of age at start of treatment (Sun [2013][16]). As this study provides limited direct evidence for this question it was not prioritised for in-depth discussion, but is summarised in Table 5.

The identified evidence was primarily of relevance to key question 4b) of whether bracing following screen detection may offer benefit compared with clinical detection in terms of preventing progression and need for surgery.

There were no studies of relevance to key question 4a) comparing early non-bracing conservative treatment options (e.g. exercise programmes) with no/later conservative treatment, or 4c) early surgery with no/later surgery. One study was identified comparing the

risk of complications with AIS surgery at a younger (0-5 and 5-10) and older age (above 10 years) Given screening would only start above the age of 10 years, this study was not relevant and was excluded.

We excluded studies at full text or abstract level that did not include comparison to a control group (e.g. treated vs. untreated), or that did not perform narrative or statistical analysis of the effect of age at starting treatment, or the effect of treatment delay, upon curve progression. On this basis we excluded prospective cohorts that reported outcomes for a particular treatment (e.g. a group all receiving bracing) where none of these comparative effects was examined.

We excluded controlled studies evaluating different treatment approaches for AIS, but with no relevance to screening issues. For example, studies comparing two different types of exercise programme, two different types of brace, or two different surgical approaches, instrumentation or fusion methods. We excluded at abstract level a large number of controlled studies and cohorts looking at perioperative management issues; for example, use of neuromonitoring, strategies to minimise blood loss, infection or other complications, or pain management strategies. We also excluded studies where only a conference abstract was available without full study publication.

Results

Treatment after screen vs. clinical detection

Adobor (2012, Appendix 3)[13] was the only identified study that compared treatment after screening with treatment after clinical detection.

It reported the characteristics of 752 adolescents with AIS clinically detected in Norway during 2003-2011 after discontinuation of screening. These adolescents in the post-screening era were generally clinically diagnosed at quite advanced stage, age and skeletal maturity (measured by Risser's sign). Mean age at clinical diagnosis was 14.6 years, mean Cobb angle 37.8^{o}, and 60% were Risser sign 3 or over. Three-quarters of girls were post-menarche at diagnosis. Treatment summary is shown in Table 3.

Table 3: Characteristics of those receiving different management in the post-screening era, Norway[13]

Management up to 6 months after referral	*Patients % (n)*	*Age mean/range*	*Curve size mean/SD*	*Risser sign median (range)*
Discharge	27 (204)	16.2±2.0	25.4±8.1	5 (0 to 5)
Observation	26 (192)	15.0±2.0	32.4±9.8	4 (0 to 5)
Bracing	21 (161)	12.8±1.9	36.0±8.7	0 (0 to 4)
Surgery	26 (195)	14.4±1.7	58.3±10.9	3 (0 to 5)

Comparison was made to treatment during the era when national screening was in place (1976-1988). During the screening era bracing was more common, with an average of 41 individuals braced per year and 19 surgically treated. In the post-screening era the ratio had reversed: an average 20 individuals were braced per year to 32 surgically treated.

The findings may suggest that in the absence of screening cases are diagnosed at a later and more progressed stage, leading to a higher proportion requiring surgery. However, this conclusion should be made cautiously for a number of reasons:

i) The study does not provide comparative characteristics for those diagnosed during the screening era, and so it is not possible to say they were detected at an earlier stage and younger age with skeletal immaturity.

ii) The before-after study design of two separate treatment eras raises the possibility that the difference may be due to factors other than screening, for example different healthcare resources and management protocols. Additionally, as data is only given on the average numbers treated per year, rather than the proportion of cases, the numbers during and after screening may not be directly comparable due to changes in diagnostic methods and criteria, or even population size.

iii) Though 1976-1988 represents the screening era, it is not possible to say whether all of these cases were actually screen- rather than clinically-detected.

iv) Follow-up in the 2003-2011 post-screening era was limited to six months only. It is not clear what treatment may have been given over a longer period for those clinically detected. For example, whether those receiving initial observation may have later progressed and required treatment, or what proportion of those receiving bracing would have still progressed and needed surgery.

Importantly the study does not inform the key question of effect of treatment on progression. Though bracing appeared the more common treatment modality during screening and surgery during clinical detection, this does not directly inform whether bracing after screen-detection is superior to bracing after clinical-detection for preventing progression or need for surgery.

The study also does not inform on the use or effectiveness of any other conservative treatment options given after screening or clinical detection. It similarly doesn't address surgery outcomes and inform whether surgery after screening gives greater benefit over surgery after clinical detection.

Treatment after clinical detection: bracing vs. observation

In the absence of further studies examining treatment after screen- compared with after clinical-detection, the next evidence considered were controlled studies in clinically detected populations that provide indirect evidence on the possible effect of early treatment after screening.

Two studies were identified that examined the effect of bracing on curve progression compared with observation only. These studies were both in adolescents of mean age 12 who are therefore representative of those who may be detected by a screening programme. The BRAIST RCT and preference cohort by Weinstein (2013, Appendix 4)[14] included individuals who would normally be eligible for bracing, being skeletally immature and with Cobb angle 20-40^{o}. Wiemann (2014, Appendix 5)[15] was a non-randomised controlled study evaluating night-time bracing for skeletally immature girls with milder curves of 15-25^{o}, who may be on the border of current treatment thresholds for bracing.

Table 4: Bracing vs. observation in clinically detected populations

Study	Population	Intervention	Comparator	Outcomes
Weinstein (2013)[14] BRAIST RCT and preference cohort Multicentre, North America	n=242* clinically detected, previously untreated Cobb angle 20-40° Mean age 12 years, skeletally immature (Risser 0, 1 or 2) n=116 in randomised group, n=126 in preference cohort * Early termination due to superiority of bracing: 383 initially recruited; 119 had not reached one of study endpoints by this time; 22 other withdrawals due to other reason	Rigid TLSO brace worn ≥18 hours per day Average follow-up 24.2 months (early termination) 146/242 as-treated included in primary analysis 51/116 as-randomised included in ITT analysis	Observation, no treatment Average follow-up 21.3 months (early termination) 96/242 as-treated included in primary analysis 65/116 as-randomised included in ITT analysis	Treatment success: skeletal maturity without progression ≥50° Bracing increased chance of success in both analyses: • Primary: 72% braced vs. 48% observed, OR 1.93, 95% CI 1.08 to 3.46 • ITT: 75% braced vs. 42% observed, OR 4.11, 95% CI 1.85 to 9.16 • NNT to prevent one case of progression to surgery: 3.0, 95% CI 2.0 to 6.2
Wiemann (2014)[15] Non-randomised controlled trial 2 clinics, US	n=46 girls clinically detected, previously untreated Cobb angle 15-25° Mean age 12 years, skeletally immature (Risser 0), premenarchal	Night-time-only bending brace to skeletal maturity (≥2 years) Analysed: 21/23 allocated	Observation, no treatment to skeletal maturity(≥2 years) Analysed: 16/23 allocated	Skeletal maturity without progression >5° • 29% braced vs. 0% observed (p=0.023) Progression >5° but <10° • 19% braced vs. 50% observed (no p) Progression >10° • 52% braced vs. 50% observed (no p) Needing surgery: • 19% braced vs. 12% observed (p=0.472)

Table 5: Non-prioritised studies evaluating treatment

Sun (2013)[16] Cohort of girls aged 10-15 years, skeletal immaturity and Cobb angle 20-40^{o} (n=68) Primarily assessing influence of bone mineral density on bracing outcome	Treatment: Bracing with follow-up 3-6 monthly until weaning or progression (>6^{o} or curve >45^{o})	Relevant analysis: Age at initiation of bracing not significantly associated with progression: non-progressed (13.1 yrs) vs. progressed (12.8yrs) (p=0.383)

The two studies both concluded that bracing is effective at preventing progression compared with observation when used for the treatment of skeletally immature individuals with AIS.

The BRAIST trial by Weinstein (2013)[14] included a preference cohort who chose their own treatment, as well as a randomised cohort, and people in both cohorts were free to switch their treatment on request during the study. However, strengths of the study were that the primary as-treated analysis was adjusted for propensity score to reduce bias from non-random assignment, and that superiority of bracing was similarly demonstrated in intention to treat (ITT) analysis. Assessors were also blinded to treatment assignment.

As requested by the data and safety monitoring board, the study was terminated early at prespecified interim analysis at around two years of follow-up due to the superiority of bracing. At this time 242 had reached the study endpoint of either treatment failure (progression ≥50^{o}) or success (skeletal maturity without this progression). The 242 participants were representative of 63% recruited. Further outcomes were not reported for the remaining participants who had not reached these endpoints at this time, and they would likely have received further treatment as appropriate. Whether progression could have occurred in the bracing group in later years after skeletal maturity had been achieved is unclear.

Overall the study provides evidence that when used to treat skeletally immature adolescents with Cobb angle 20-40^{o}, bracing is more effective than observation at preventing progression to a surgical range by the time of skeletal maturity.

However, a key limitation is applicability to screening as these were likely to be clinically detected cases (no mention is made of detection through screening programmes). As these cases were likely to have been identified without screening, it is not known whether screening would enhance detection of other cases similarly eligible for bracing who would not otherwise have been detected clinically. It is unknown whether screening would have led to such individuals being detected at an earlier stage or younger age and greater skeletal immaturity (e.g. age 10 years), and so whether earlier treatment could have given greater benefit.

Wiemann (2014)[15] specifically evaluated giving early treatment with night-time bracing to premenarchal girls with curve 15-25^{o} who may fall below thresholds for bracing in clinical practice (though this is difficult to say with certainty in the absence of guideline recommendations giving set eligibility criteria). The study demonstrated that almost a third of the bracing group did not have over 5^{o} progression by skeletal maturity compared with such progression in 100% of the observation only group. However, bracing was not associated with reduction in those with more severe progression, or requiring surgery. Methodologically it is limited by the non-randomised design, small sample size and incomplete follow-up (analysis of 80%).

Like the BRAIST study, the main limitation is again applicability to screening as these were clinically detected cases. It is not known whether screening could lead to greater detection of cases with "mild" AIS at a stage of skeletal immaturity and so allow treatment to prevent progression to greater severity.

Overall studies are needed that evaluate curve progression following treatment after screen-detection, with treatment after clinical detection. This includes comparing outcomes for people with different curve severities treated with conservative treatment such as exercise programmes, bracing, or requiring surgery.

Summary: Criterion 10 not met

No controlled studies have compared treatment after screen detection with treatment after clinical detection. One before-after study demonstrated a higher rate of surgery relative to bracing currently compared with the era when national screening was in progress. However, there are significant methodological limitations to this study design, and it does not demonstrate that screening allowed earlier conservative treatment or prevented progression.

There is evidence that bracing is better than observation at preventing curve progression by the time of skeletal maturity in skeletally immature adolescents with Cobb angle 20-40^{o} (who would meet current criteria for bracing). There is also some lower quality evidence that early night-time bracing for skeletally immature girls who are around the treatment threshold (15-25^{o}) may prevent progression >5^{o}. However, there was no evidence for a significant effect on more severe progression or need for surgery. Importantly, both of these studies were in clinically detected cases and do not inform whether bracing after screening is associated with better outcomes than bracing after clinical detection.

No relevant evidence was identified relating to the questions of whether other conservative treatments for "mild" AIS (e.g. exercise programmes) prevent progression after screening compared to after clinical detection, or whether outcomes are better for people with "severe" AIS receiving surgery after screen detection compared with after clinical detection.

14. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public.

Current UK NSC key question

The previous UK NSC evidence review did not find relevant evidence assessing the acceptability of screening to health professionals and the public. This review aimed to specifically look at the evidence regarding acceptability of treatment to patients, as assessed by treatment adherence rates.

Description of the evidence

Twenty studies were considered to have potential relevance to this question during title and abstract sifting and were assessed at full text. We aimed to identify studies of any design that assessed adherence to any conservative treatment approach or acceptance of surgery.

We identified five prospective studies that examined adherence rates and looked at how this was associated with treatment outcomes and curve progression or correction, one of which was the BRAIST study by Weinstein (2013) (Appendix 4).[14] All studies examined compliance with bracing as prescribed, one of the studies examined bracing in combination with an exercise programme. These five studies were included in this evidence review and are summarised in Table 6. The populations in at least some of these studies may have included people detected following screening, but none of the studies specifically describe whether any proportion of their included population were receiving treatment after screen detection.

We excluded studies assessing adherence rates that had a sample size of less than 20.

No studies were identified that assessed compliance with non-bracing conservative programmes alone (e.g. exercise recommendations), or that looked at acceptance or uptake of surgery.

While the five included studies assessing adherence also examined how this was associated with treatment outcomes, we excluded studies that analysed the statistical association between compliance and outcomes but did not give adherence rates or report how compliance was defined.

The focus of the question was upon acceptance as indicated by adherence to treatment, rather than to identify factors associated with compliance or ways it might be improved. We therefore excluded studies looking at the association between AIS treatment or its compliance and quality of life, stress or mental health effects. We also excluded studies examining ways to try and improve compliance; for example, bracing started as an inpatient vs. an outpatient, or validating use of heat sensors.

Results

Table 6: Prospective cohorts evaluating adherence to treatment in AIS

Study	Population	Treatment	Compliance/Adherence
Weinstein (2013)[14] (Appendix 4) Multicentre, North America RCT and preference cohort, North America	n=116 (those with wear data available) Cobb angle 20-40°, age 10-15 years, skeletal immaturity (Risser <3)	Rigid TLSO (Boston brace in 68%) Prescribed wear: ≥18 hours per day	Assessment: objective, temperature sensor in brace • Mean wear during first 6 months: 12.1 hours (+/-6.5, range 0 to 23)
Brox (2012)[17] (Appendix 6) Single centre, Norway (1976-1988)	n=495 Cobb angle >20° with >5° progression after 4 months, skeletal immaturity (Risser <3)	Rigid TLSO (Boston brace) Prescribed wear: 23 hours daily	Assessment: subjective, direct physician questioning Non-compliance: wear <20 hours daily or aborted bracing Compliant: 79% (389/495) Non-compliant: 21% (106/495) • 54 (10.9%) wear < 20 hours • 52 (10.5%) aborted bracing (not further defined)
Sanders (2014)[18] (Appendix 7) Single centre, US (1998-2000)	n=100 Cobb angle 25-45°, skeletally immature (Risser 0, 1 or 2), age ≥10 years	Rigid TLSO (Boston brace) Prescribed wear: 16 or 23 hours daily (physician choice)	Assessment: objective, temperature sensor in brace Non-compliance: wear <2 hours per day Two measures high compliance: ≥10 or ≥14 hours per day Compliant (≥2 hours): 73% • ≥10 hours: 31% • ≥14 hours: 13% Non-compliant: 27%
Chan (2014)[19] (Appendix 8) Single centre, Hong Kong (study years not reported)	n=55 females (76.4% follow-up, n=42) Cobb angle 25-40°, skeletally immature (Risser 0, 1 or 2), age ≥10 years	Rigid TLSO (Hong Kong brace) Prescribed wear: not reported	Assessment: subjective, self-reported on log sheet Compliance: • 0-8 hours: 9.5% (4/42) • 9-16 hours: 16.7% (7/42) • 17-23 hours: 73.8% (31/42) (Wear objectively verified for 2-4 months by force sensor in 33%: significant correlation to subjective measure)

Study	Population	Treatment	Compliance/Adherence
Rivett (2014)[20] (Appendix 9) Single centre, South Africa (study years not reported)	n=47 females Cobb angle 20-50°, age 12-16 years	Rigid Rigo System Cheneau brace Prescribed wear: 23 hours daily PLUS: Home exercise programme Prescribed: (20-25 minute exercises, 4-5 days a week)	Assessment: subjective, self-reported in patient diaries Non-compliance: <20 hours daily and exercise <3 times per week Compliant: 55.3% • Mean hours brace: 21.5 • Mean exercise session: 3.92 Non-compliant: 44.7% • Mean hours brace: 12.19 • Mean exercise session: 1.71

The five prospective studies report adherence with prescribed treatment and its association with progression. With the exception of the BRAIST trial by Weinstein (2013),[14] the remaining four studies were from single treatment centres. It is possible that all or a proportion of the people in some of these studies had been diagnosed following detection through a screening programme. For example, the Brox (2012)[17] cohort covers the years 1976-1988 when nationwide screening was in place in Norway. Similarly Hong Kong is a country that still has an existing AIS screening programme so the Chan (2014)[19] study may have included a screen-detected population. However, none of the studies report whether the participants were detected clinically or following screen detection. Therefore it is not known whether the results could be generalised to adherence with bracing prescribed specifically following screen detection.

The included studies varied considerably in their definitions of compliance and included populations, meaning their results are not directly comparable.

Weinstein (2013)[14] and Sanders (2014)[18] used an objective measure of readings from a heat sensor worn in the brace, and so these studies may give the most reliable indication of compliance. Weinstein (2013)[14] found that in the first six months of prescription, the brace was worn for a mean 12.1 hours per day of the prescribed 18 hours or over. Sanders (2014)[18] found that around a quarter of patients were non-compliant as defined by brace wear for less than two hours a day compared with the prescribed 16 or 23 hours. Only a third wore the brace for at least 10 hours a day, and only just over 1 in 10 wore for at least 14 hours a day. These studies may not be representative of all people prescribed bracing, as they had measures from only 116 and 100 people, respectively, but both suggest that adherence to bracing as prescribed may be quite low.

The remaining studies relied on subjective measures of compliance. Brox (2012)[17] defined non-compliance as less than 20 hours wear per day of the prescribed 23 hours, which was reported for just under a quarter (21%) of the cohort. In the two smaller studies, Chan (2014)[19] similarly found just over a quarter were non-compliant as defined by wear of less than 17 hours daily. Rivett (2014)[20], which assessed bracing in combination with exercise, found just under a half (45%) were non-compliant as defined by less than 20 hours daily wear and exercise less than three times weekly.

These subjective measures of assessing compliance may be less reliable. In the era when the Brox (2012)[17] study was conducted there was, as the study authors acknowledge, no valid method of assessing compliance. It was therefore assessed through direct physician questioning which may be inaccurate and possibly give an over-estimation of compliance. Chan (2014)[19] and Rivett (2014)[20] assessed compliance by self-report on diaries or log sheets, and though this may be more reliable than direct physician questioning, it still may be subject to inaccurate reporting.

Even with objective measures as used by Weinstein (2013)[14] and Sanders (2014)[18], compliance may be influenced by the person's knowledge that their wear was being monitored. Such studies may not be representative of clinical practice where brace wear is not monitored, or assessed infrequently or not at all.

Previous studies have identified that compliance with bracing is associated with reduced risk of curve progression, and these studies generally supported this. Overall 4 of the 5 studies found associations between bracing compliance and treatment success (see Appendices 4 and 6-9 for full results). This supports the established notion that adherence to treatment is important for it to be effective.

The studies have not examined the reasons for non-compliance with treatment, but various factors may influence this. This may include curve severity, pattern and flexibility; type of brace and prescribed wear hours; and personal characteristics of the individual such as age, gender, culture and activity patterns. Therefore this makes it difficult to give an overall accurate estimate of the likelihood of compliance with bracing following screen detection and diagnosis.

Though one of the five studies examined bracing in combination with an exercise programme, the compliance data was for the combined treatment. We did not identify studies specifically examining adherence to exercise programmes or other conservative management approaches following diagnosis. This may be particularly relevant for the large number of screen-detected cases with milder AIS who would fall below the threshold for bracing and for whom other conservative treatments may form the mainstay of management.

We also did not identify any studies informing uptake following recommendation for surgery.

Summary: Criterion 14 not met

Five prospective studies examined acceptance as measured by adherence to bracing as prescribed for AIS. It is unclear what proportion of people in these studies may have been diagnosed following a screening programme. The studies varied in their population, assessments of, and definitions of compliance. The two studies assessing compliance through the objective measure of a heat sensor in the brace suggested that adherence to the prescribed bracing hours may be quite low. Compliance may further be influenced by many factors including nature of the curve, characteristics of the individual and whether wear was being followed up and support given where needed. Overall this makes it difficult to conclude on the likely adherence to bracing prescribed following screen detection.

No studies were identified examining adherence to other conservative treatments (e.g. exercise programmes alone), or assessing uptake following recommendation for surgery.

Conclusions

Implications for policy

This review assesses screening for adolescent idiopathic scoliosis (AIS) against select UK National Screening Committee (UK NSC) criteria for appraising the viability, effectiveness and appropriateness of a screening programme. The topic was last assessed in 2012 which was an update review, following on from a full review in 2006 that was undertaken in light of the USPSTF recommendation against AIS screening in 2004. The update review concluded that "Owing to the remaining uncertainties surrounding the test and treatment the updated evidence does not suggest that changing the current policy would be appropriate."

The 2012 review identified several key uncertainties including the low PPV of the screening test, and high detection rate of minor curves with no evidence that treatment of these curves prevents progression. There were also no agreed evidence-based recommendations for when treatment is indicated. The UK NSC subsequently decided not to recommend screening for AIS.

This review assessed key questions to determine if evidence published since the last review resolves any of the identified uncertainties. The identified body of evidence does not suggest that overturning the previous UK NSC recommendation not to screen for AIS in the UK. A summary of key findings for the five assessed criteria is provided below:

- **An agreed cut-off value for the screening test –** Consensus recommendations have established FBT with scoliometer as the screen test to use and an angle of 5-7^{o} being the interval that indicates referral for radiography. However, there is no single agreed cut-off, and there remain further uncertainties regarding the additional use of Moiré topography and the optimal age to screen.
- **A precise and validated screening test –** Two prospective cohorts demonstrate that screening has high sensitivity for detecting overall diagnoses of AIS (Cobb angle ≥10^{o}). However, the PPV of the screening test for identifying more severe cases likely to progress and those that require treatment is very low. This low PPV would be associated with unnecessary use of resources and X-ray exposure for the follow-up of many mild cases who would not require treatment despite meeting diagnostic criteria. The cohorts also differed in screen test used (single or combination), cut-off value, and timing of screening. Additionally, the studies have uncertain applicability to the UK.
- **Agreed evidence-based policies about treatment –** There are no treatment guidelines from national or professional bodies that give recommendations on AIS treatment. One evidence-based update review of conservative treatment gives general agreement on the curve thresholds that indicate different risk of progression and when bracing or surgery may be considered. However, there are no absolute Cobb angles indicating a specific treatment approach, and decisions are likely to depend on various factors including patient age, skeletal maturity and assessment of risk. This creates further difficulties in the context of a screening programme in selecting an FBT cut-off indicating treatment need.
- **Evidence that early treatment following screening leads to better outcomes than late treatment following clinical detection –** Bracing has been demonstrated to be effective for people who meet criteria for bracing. One multicentre RCT and preference cohort demonstrated that skeletally immature adolescents with Cobb angle 20-40^{o} were more

likely to reach skeletal maturity without progression ≥50^{o} with bracing than with observation only. Whether those receiving bracing could still have progressed in subsequent years after maturity is unknown. Another smaller comparative study demonstrated that night-time bracing for skeletally immature girls around the treatment threshold (15-25^{o}) may prevent progression >5^{o}. However, there was no evidence for a significant effect on preventing more severe progression or need for surgery. Importantly, these studies were in clinically detected populations. No controlled studies have compared bracing after screen detection with bracing after clinical detection. Additionally, no controlled studies have informed whether other conservative approaches (e.g. exercise programmes) or surgery give greater benefit after screen detection than after clinical detection.

- **Evidence that the treatment is acceptable as assessed by adherence rates –** Five prospective studies examined adherence to bracing as prescribed, but varied in their population, sample size, assessments and definitions, of compliance. Two studies assessing compliance objectively suggest that adherence to prescribed bracing of at least 16 or 18 hours a day may be quite low. It is unclear what proportion of people in these studies may have been screen-detected. Compliance with bracing has been shown to increase the likelihood of treatment success. However, various factors may influence compliance including characteristics of the curve, the individual and whether wear was being followed up and support given. Overall this makes it difficult to conclude on the likely adherence to bracing prescribed following screen detection. There were also no studies examining adherence to other conservative treatments, or assessing uptake following recommendation for surgery.

Implications for research

Additional high quality studies in the following areas would help to resolve uncertainties regarding AIS screening in the UK:

- Further controlled studies looking at the performance of different ATR cut-offs on FBT, when used alone or in combination with Moiré topography, and how this is influenced by the timing of the screen test in boys and girls. Ideally such studies would look at UK adolescent populations.
- Further research into whether there is a test threshold with one-step or two-step screening that could reliably identify curves that would progress and require treatment, while minimising over-detection of mild AIS that would not require any treatment.
- Controlled studies comparing curve outcomes in screen detected compared with clinically detected populations. Such studies would ideally need to compare outcomes for adolescents with different curve severity receiving treatment with conservative treatments (e.g. exercise programmes), bracing or surgery after diagnosis following screening compared with clinical detection.
- Further good quality studies evaluating adherence to bracing, other conservative treatments, and uptake of surgery when recommended after diagnosis following screen detection.

Methodology

The draft update report was prepared by Bazian Ltd., and then adapted in discussion with the National Screening Committee. Each criterion was summarised as 'met', 'partially met' or 'not met' by considering the results of the included studies in light of the volume, quality and consistency of the body of evidence. Several factors were assessed to determine the quality of the identified evidence, including study design and methodology, risk of bias, directness and applicability of the evidence. Factors that were determined to be pertinent to the quality of the body of evidence identified for each criterion are outlined in the results section as well as the comment section of the Appendix tables.

For Criterion 5, quality assessment focused on four main domains: patient selection, the index test, the reference standard, and flow and timing of index test and reference standard. Each domain was assessed for risk of bias, and the first three domains were assessed for applicability to a potential UK screening programme population. Details of these assessments can be found in the comment section of the Appendix tables.

Search strategy

BACKGROUND: The literature search was based on the search strategy used for the 2011 NSC review of this topic. It retrieved citations on screening for adolescent idiopathic scoliosis published since the search for the previous review, which was carried out in August 2011.

SOURCES SEARCHED: EMBASE, PubMed and the Cochrane Library (Wiley).

A simple search was also carried out for relevant guidance, using: NICE Evidence, National Guidelines Clearinghouse and the Guidelines Information Network.

DATES OF SEARCH: August 2011 to 16 March 2015

SEARCH STRATEGY: EMBASE.com

1 'scoliosis'/exp OR scoliosis

2 'child'/exp OR child

3 child*

4 'adolescent'/exp OR adolescent

5 'adolescence'/exp OR adolescence

6 adolescen*

7 2 OR 3 OR 4 OR 5 OR 6

8 'screening'/exp OR screening

9 test OR tests OR testing

10 detect*

11 8 OR 9 OR 10

12 'predictive value of tests'/exp OR 'predictive value of tests'

13 'sensitivity and specificity'/exp OR 'sensitivity and specificity'

14 sensitiv* OR specific*

15 false NEXT/1 positiv*

16 false NEXT/1 negativ*

17 'forward bend test'

18 'forward bending test'

19 'cobb angle'/exp OR 'cobb angle'

20 'angle of trunk rotation'

21 'moire topography'/exp OR 'moire topography'

22 'questionnaires'/exp

23 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22

24 11 AND 23

25 'spinal fusion'/exp OR 'spinal fusion'

26 'braces'/exp

27 brace*

28 'casts and noninvasive traction devices'/exp

29 cast*

30 25 OR 26 OR 27 OR 28 OR 29

31 'quality of life'/de OR 'quality of life'

32 'treatment outcome'/de

33 'disease progression'/de

34 31 OR 32 OR 33

35 30 AND 34

36 24 OR 35

37 1 AND 7 AND 36

38 1 AND 7 AND 36 AND ([conference abstract]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [short survey]/lim)

39 37 NOT 38 AND [english]/lim AND [2006-2015]/py

This was then limited by year (2011 to March 2015) and to articles in English.

RESULTS: The above strategy retrieved 946 citations from EMBASE.com. A similar search was conducted in PubMed and the Cochrane Library (Wiley).

Database	Number of references
EMBASE	946
PubMed	454

Cochrane Library	140
Total	1537

There was some duplication of references between different database searches. After de-duplication, the titles and abstracts of these citations were scanned for relevance to idiopathic scoliosis in adolescents. 435 citations were deemed to be relevant.

Appendices

Appendix number	1
Relevant criteria	5
Publication details	Fong DYT, Cheung KMC, Wong YW, et al. A population-based cohort study of 394,401 children followed for 10 years exhibits sustained effectiveness of scoliosis screening. Spine Journal. 2015.[12]
Study details	Population-based cohort study Hong Kong Setting: nationwide community screening programme (screened in regional clinics)
Study objectives	To assess the sustainability of scoliosis screening in the community in the longer term by following children through their academic years until age 19 years.
Inclusions	Five annual cohorts of students in the fifth grade (or that have reached aged 10 years) during the academic years 1995/1996 to 1999/2000. Students were followed for at least 10 years to 19 years of age through the Department of Health and medical records, including screening history and diagnoses.
Exclusions	None reported.
Population	Five annual cohorts, total n=394,401 Screening participants, n=306,144 (78%) Chose non-participation in screening, n=88,131 (excluding 126 [0.1%] not participating due to diagnosis before screening)
Intervention/test	Two tier screening: • Forward bend test (FBT) with scoliometer measurement of angle of trunk rotation (ATR)

	• Cut-off: 5 > ATR <15^{o} - further screened by moiré topography. Difference ≥2 lines, or clinical signs of deformity – referred for X-ray diagnosis (ATR ≥15^{o} directly referred for X-ray) Screening every 2 years up to 19 years.
Comparator	Not applicable

Results/outcomes	**Screened n=306,114**
	Referred for X-ray following screening:
	• 12,536 (4.1% of screened)
	  ○ NB. text reports 9,726 (3.2%, 95% CI 3.1 to 3.2%) referred following screen tests and 12,536 (4.1%, 95% CI 4.0 to 4.2%) following clinical suspicion; presumed the latter figure is inclusive
	• X-rays performed for 11,194
	  ○ AIS detected by 19 years (TPs): 10,160 (81.0% of referred)
	  ▪ Cobb angle 10-19^{o}: 5175 (41.3% of referred, 50.9% of diagnosed)
	  ▪ Cobb angle 20-39^{o}: 4412 (35.2% of referred, 43.4% of diagnosed)
	  ▪ Cobb angle ≥40^{o}: 573 (4.6% of referred, 5.6% of diagnosed)
	  ▪ No AIS detected by 19 years: 1034 (8.2% of referred)
	• No X-ray performed for 1342 (considered non-AIS)
	• Overall FPs: 2376 (19.0% of referred - 1034 negative X-ray; 1342 no X-ray performed)
	Not-referred following screening:
	• 293,546 (95.9%)
	• X-rays performed by 19 years for 722
	  ○ No AIS detected by 19 years: 51
	  ○ AIS clinically detected by 19 years (FNs): 671 (0.23% of non-referred)

- Cobb angle 10-19°: 176 (26.2%)
- Cobb angle 20-39°: 330 (49.2%)
- Cobb angle ≥40°: 165 (24.6%)

Non-participants in screening n=88,131

- No AIS detected by 19 years: 87,616
- AIS detected by 19 years: 515 (0.58% of non-participants)
  - Cobb angle 10-19°: 101
  - Cobb angle 20-39°: 277
  - Cobb angle ≥40°: 137

Prevalence of AIS in screened group (306,114):

- Overall diagnosis – Cobb angle ≥10°: 3.5% (95% CI 3.5 to 3.6) (TPs + FNs: 10,831/306,144)
- Cobb angle ≥20°: 1.8% (95% CI 1.7 to 1.8) (5480/306,144)
- Cobb angle ≥40°: 0.2% (95% CI 0.2 to 0.3) (738/306,144)
- Treatment: 0.4% (no further information given). Unclear:
  - type of treatment given
  - whether given initially upon diagnosis or following progression at follow-up
  - the proportion of those treated who were screen-detected or not referred but later clinically diagnosed

Accuracy of screening

	Sensitivity	Specificity	PPV	NPV
	% (95% CI)			
Angle ≥10°	93.8 (93.3 to 94.3)	99.2 (99.2 to 99.2)	81.0 (80.3 to 81.7)	99.8 (99.8 to 99.8)
Angle ≥20°	91.0 (90.2 to 91.7)	97.5 (97.4 to 97.5)	39.8 (38.9 to 40.6)	99.8 (99.8 to 99.8)
Angle ≥40°	77.6 (74.5 to 80.6)	96.1 (96.0 to 96.2)	4.6 (4.2 to 5.0)	99.9 (99.9 to 100)
Given treatment	83.3 (81.1 to 85.3)	96.2 (96.2 to 96.3)	8.4 (7.9 to 8.9)	99.9 (99.9 to 99.9)

- Sensitivity: proportion of AIS subjects in whom AIS was detected by screen
- Specificity: proportion of non-AIS subjects who were screen negative
- PPV: proportion of referred subjects who developed AIS by 19
- NPV: proportion non-referred subjects who didn't develop AIS by 19

	(The above presents data for the full dataset. Focus of the study discussion is on the fluctuation in prevalence and accuracy measures across the five annual cohorts – data not further reported here.)

Comments

Screening criteria – age 10 years then 2-yearly for both sexes - does not match consensus. Similarly the screen positive criteria is within the recommended range but it may not be directly applicable to what would be used in UK.

Specific data for those ≥20^{o} or 40^{o} can infer those with moderate to severe curves who would be at risk of progression and so require treatment. However, only the proportion treated is given; no information is given on the modality of treatment, which severity groups these people were, or whether they were among the screen-detected or non-screen detected.

Unknown whether those with AIS diagnosis in the mild 10-19^{o} category would progress or have required any treatment.

Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	Y	Low	Five consecutive annual cohorts participating in national community screening programme.
Case-control design avoided?	Y	Low	Not a case control study.
Inappropriate exclusions avoided?	Y	Low	National screening programme. No apparent exclusions.
Domain II: Index Test			
Index test results interpreted without knowledge of reference standard results?	Y	Low	Prospective cohort, screening staff not aware of diagnosis.
Threshold pre-specified?	Y	Low	Cut-off for referral specified
Domain II: Reference standard			
Reference standard likely to correctly classify condition?	Y	Low	Accepted diagnostic threshold for AIS diagnosis of Cobb angle ≥10^{o}

Reference standard results interpreted without knowledge of index test results?	Unclear	Unclear	Blinding of diagnostic X-rays to screen results not reported.
Domain IV: Test strategy flow and timing			
Appropriate interval between index test and reference standard?	Y	Low	No apparent delay between screen and diagnostic X-ray; progression not expected between the two points.
Did all participants receive same reference standard?	Y	Low	Screen positive 5^{o} > ATR <15^{o} on FBT plus ≥ 2 lines difference on moiré topography, or clinical signs of deformity. ATR ≥15^{o} directly referred without topography.
All patients included in analysis?	Y	Low	All eligible for screening in the 5 consecutive years accounted for.
Applicability			
Applicable to UK screening population of interest?	Unclear	Unclear	Prevalence of AIS in Hong Kong may differ from UK which could affect PPV and NPV. Recommendations on timing of screening test and selected test thresholds are by consensus only with no fixed values. Those used in this study are broadly within the range of consensus recommendations but it is not known whether they would be applicable to the UK population.
Applicable to UK screening test of interest?	Unclear	Unclear	As above, 2 yearly screening from 10 years of age for boys and girls and the screen positive thresholds selected may not be applicable in the UK.
Target condition measured by reference test applicable to UK screening condition of interest?	N	High	AIS diagnosis is accepted to be Cobb angle ≥10^{o}, and the screen test aims to identify these cases. However, this does not effectively distinguish between cases that will progress and require treatment from those that would not progress.

Appendix number	2
Relevant criteria	5
Publication details	Adobor RD, Rimeslatten S, Steen H, et al. School screening and point prevalence of adolescent idiopathic scoliosis in 4000 Norwegian children aged 12 years. Scoliosis. 2011;6:23.[8]

Study details	Prospective cohort study Norway Setting: screening in conjunction with routine school health examination and vaccination programme in Health Region South of Norway (nationwide school screening discontinued)
Study objectives	To evaluate the point prevalence, and the effectiveness of school screening of AIS in a Norwegian population of 12000 children aged 12 years.
Inclusions	Eligibility: 12,000 children aged 12 years living in Health Region South
Exclusions	None reported
Population	4000 children included out of an eligible population of 12,000. The health authorities in Norway were not willing to support the study with a recommendation due to discontinuation of nationwide screening, and many professionals were not willing to participate in a non-recommended programme.
Intervention/test	Screening test: • Combined visual inspection and FBT with scoliometer measurement of ATR • Cut-off: ATR ≥7^{o} – referred for X-ray diagnosis
Comparator	Not applicable

Results/outcomes	**Estimated point prevalence of AIS in general population**
	Prevalence of AIS (Cobb Angle ≥10^{o}) estimated from two previous epidemiological studies as 0.8%.
	Referrals following screening
	• Referred: 60/4000 (1.5% of screened)
	• AIS confirmed (Cobb Angle ≥10^{o}): 22/60 (36.7% TPs)
	  ○ 16/39 girls (41.0%)
	  ○ 6/21 boys (28.6%)
	• AIS not detected: 38/60 (63.3% FPs):
	  ○ 23/39 girls (59.0%)
	  ○ 15/21 boys (71.4%)

Point prevalence AIS in sample (based on TPs only; no follow-up for FNs)

- Overall diagnosis **(**Cobb Angle ≥10^{o}): 0.55% (22/4000)
- AIS 10-20^{o}: 0.43% (17/4000) (28.3% of those referred, 17/60)
    - Observed to maturity – none progressed >25^{o}
- AIS >20^{o}: 0.13% (5/4000) (8.3% of those referred, 5/60)
    - None braced (all Risser 4 and/or >1 year post-menarche therefore not eligible)
    - 4/5 did not progress >5^{o} during long-term follow-up (time not specified)
    - 1/5 progressed from 37-45^{o} and had surgery

Accuracy of screening for AIS diagnosis ≥10^{o}

Sensitivity	Specificity	PPV	NPV	LR+	LR-
69% (22/32)	99% (3962/4000)	37% (22/60)	99% (3968/3962)	69 (0.69/0.01)	0.31 (0.31/0.99)

Data based on estimated population point prevalence 0.8% and observed 0.55%

- Sensitivity: proportion of AIS subjects in whom AIS was detected by screen
- Specificity: proportion of non-AIS subjects who were screen negative
- PPV: proportion of referred subjects who were diagnosed with AIS
- NPV: proportion non-referred subjects who didn't have AIS

Comments

Screening at 12 years for both sexes does not match consensus and may not be directly applicable to what would be used in UK. The selected cut-off though within the recommended range may also not be as used in the UK.

Accuracy data based on estimated point prevalence – the true prevalence of AIS in the study population was unknown. Prevalence was assumed equal for males and females and may differ. May also differ in other countries.

Included study population representative of only one third those eligible.

Accuracy data only for overall AIS diagnosis ≥10^{o}, rather than specifically for different severities who would have differing risk of progression and treatment needs. The majority detected by screening were in the mild category, only received observation only and did not progress during follow-up.

Those detected with moderate-mild severity were not eligible for bracing as considered too mature, so earlier screening may be needed.

Healthcare resources and X-ray exposure to consider with high FPR and low number eligible for treatment.

Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Domain I: Patient selection			
Consecutive or random sample of population enrolled?	N	High	National screening discontinued. Sample representative of only one third of those eligible because lack of willingness to participate.
Case-control design avoided?	Y	Low	Not a case control study.
Inappropriate exclusions avoided?	Unclear	Unclear	No study exclusions intended. However, difficult to know whether the characteristics and AIS prevalence of the two-thirds not participating may have differed.
Domain II: Index Test			
Index test results interpreted without knowledge of reference standard results?	Y	Low	Prospective cohort, screening staff not aware of diagnosis.
Threshold pre-specified?	Y	Low	Cut-off for referral specified.
Domain II: Reference standard			
Reference standard likely to correctly classify condition?	Y	Low	Accepted diagnostic threshold for AIS diagnosis of Cobb angle ≥10^{o}
Reference standard results interpreted without knowledge of index test results?	Unclear	Unclear	Blinding of diagnostic X-rays to screen results not reported.
Domain IV: Test strategy flow and timing			
Appropriate interval between index test and reference standard?	Y	Low	No apparent delay between screen and diagnostic X-ray; progression not expected between the two points.
Did all participants receive same reference standard?	Y	Low	Screen positive ATR ≥7^{o}on FBT.
All patients included in	N	High	Results only given for the screen positives. No apparent follow-up of screen negatives.

analysis?			Accuracy estimates calculated from expected population prevalence in previous epidemiological studies which may be inaccurate.
Applicability			
Applicable to UK screening population of interest?	Unclear	Unclear	Prevalence of AIS in Norway may differ from UK which could affect PPV and NPV. Recommendations on timing of screening test and selected test thresholds are by consensus only with no fixed values. Those used in this study are broadly within the range of consensus recommendations but it is not known whether they would be applicable to the UK population.
Applicable to UK screening test of interest?	Unclear	Unclear	As above, one-off screening at 12 years of age for boys and girls and the screen positive thresholds selected may not be applicable in the UK.
Target condition measured by reference test applicable to UK screening condition of interest?	N	High	AIS diagnosis is accepted to be Cobb angle $\geq 10^{o}$, and the screen test aims to identify these cases. However, this does not effectively distinguish between cases that will progress and require treatment from those that would not progress.

Appendix number	3
Relevant criteria	10
Publication details	Adobor RD, Riise RB, Sorensen R, et al. Scoliosis detection, patient characteristics, referral patterns and treatment in the absence of a screening program in Norway. Scoliosis. 2012;7(1):18.[13]
Study details	Before-after evaluation of screening programme (prospective post-screening cohort, with retrospective analysis of screening cohort) Norway, scoliosis clinic
Study objectives	To describe the detection, patient characteristics, referral patterns and treatment of idiopathic scoliosis at a scoliosis clinic during the period 2003–2011, when there was no screening and to compare treatment modalities to the period 1976–1988 when screening was performed.
Inclusions	All new patients with late juvenile (≥7 years) or adolescent idiopathic scoliosis

<table>
<tr><td></td><td>referred to the specialist scoliosis clinic at Oslo University Hospital during 2003-2011.

Retrospective analysis of the comparable patient group treated with bracing or surgery during 1976–1988.</td></tr>
<tr><td>Exclusions</td><td>Infantile and early-onset juvenile idiopathic, neuromuscular, congenitalor syndromic scoliosis.</td></tr>
<tr><td>Population</td><td><u>Post-screening cohort</u>

n=752 (644, 86% female)

Mean age at diagnosis: 14.6 +/- 2.1 years (range 7–20). Mean age for girls 14.5 and boys 15.5 years (both +/- 2.1).

Detection: 71% by family members/friends (31% had positive family history), 27% by healthcare providers, 2% by non-healthcare providers.

Cobb angle at diagnosis:
• 10 to 24.9°:16%
• 25 to 34.9°: 31%
• 35 to 39.9°: 15%
• 40 to 44.9°: 12%
• >45°: 27%
Mean major curve at diagnosis 37.8 +/-14.5° (range 10.95°). Mean for girls 37.8+/-14.1° and boys 37.5+/-16.8°.
In those measured with scoliometer: mean ATR 8.4° thoracic and 7.9° lumbar.

Risser sign (skeletal maturity): 60% ≥ Risser 3
• 0: 24%
• 1: 5%
• 2: 10%
• 3: 9%
• 4: 34%
• 5: 18%
Post-menarche at diagnosis in females: 78%, 36% ≥ 2 years earlier.

<u>Screening cohort</u>
No characteristics reported.</td></tr>
<tr><td>Intervention/test</td><td>Not applicable</td></tr>
<tr><td>Comparator</td><td>Not applicable</td></tr>
<tr><td>Results/outcomes</td><td><u>Post-screening cohort</u>

Treatment recommendations up to 6 month follow-up:

<table><tr><td></td><td>Patients</td><td>Age</td><td>Curve size</td><td>Risser sign</td></tr></table></td></tr>
</table>

		% (n)	mean/range	mean/SD	median (range)
	Bracing	21 (161)	12.8±1.9	36.0±8.7	0(0 to 4)
	Surgery	26 (195)	14.4±1.7	58.3±10.9	3(0 to 5)
	Observation	26 (192)	15.0±2.0	32.4±9.8	4(0 to 5)
	Discharge	27 (204)	16.2±2.0	25.4±8.1	5(0 to 5)
	<u>Screening cohort 1976-1988</u> Bracing: average 41 treated per year Surgery: average 20 treated per year (total numbers diagnosed during screening not given) <u>Comparison of treatment modalities during screening and post-screening</u> Screening: 41 braced to 19 surgically treated Post-screening: 20 braced to 32 surgically treated Overall proportion braced during screening was higher than post-screening: • 68% vs. 38% • Mean difference 30% (95% CI 10 to 47) • OR bracing during screening 3.5 95%, CI 1.6 to 7.5 (p=0.002)				
Comments	Demonstrates higher ratio of bracing:surgery during screening and reverse after screening, but doesn't inform whether bracing after screen-detection is superior for preventing progression or need for surgery compared to bracing or other conservative treatment after clinical-detection. No characteristics given for screen-detected cohort, so not possible to say they're detected at an earlier stage and skeletal maturity. Before-after study design of separate treatment eras, rather than screened and non-screened cases from the same era. Difference may be due to factors other than screening, e.g. different protocols. Only raw data on numbers treated per year, may very due to changes in population size or diagnostic methods. Don't know whether those in the screening era were all screen-detected.				

Appendix number	4
Relevant criteria	10, 14
Publication details	Weinstein SL, Dolan LA, Wright JG, et al. Effects of bracing in adolescents with idiopathic scoliosis. N Engl J Med. 2013;369(16):1512-21.[14] Further methods: Weinstein SL, Dolan LA, Wright JG, et al. Design of the bracing in adolescent idiopathic scoliosis trial (BrAIST). Spine. 2013;38(21):1832-41.[21]
Study details	Bracing in Adolescent Idiopathic Scoliosis Trial (BRAIST) RCT and preference cohort. Setting: 25 sites in North America, recruitment March 2007 to January 2010.
Study objectives	To determine the effectiveness of bracing, as compared with observation, in preventing progression of the curve to ≥50^{o} (a common indication for surgery).
Inclusions	Previously untreated individuals presenting to scoliosis clinics with high-risk AIS who met current indications for bracing: age 10-15 years, skeletal immaturity (Risser sign 0, 1 or 2), and Cobb angle for the largest curve of 20-40^{o}.
Exclusions	None other than not meeting above criteria.

Population	383 consented to participate out of 1086 eligible: 155 in randomised cohort, 228 in preference cohort (chose treatment)
	
	Assessments every 6 months, first interim analysis Sept 2012, second Jan 2013.
	
	Trial terminated early due to superiority of bracing: 242/383 were included in primary analysis, excluding withdrawals before treatment and 119 who didn't reach either primary outcome when study was terminated
	
	242 included in primary analysis:
	
	• 116 (48%) in randomised group (mean age 12.7, 87% female)
	  ○ 51 bracing (49 received bracing, 2 observation)
	  ○ 65 observation (57 observation, 8 bracing)
	• 126 (52%) in preference cohort (mean age 12.6, 95% female)
	  ○ 88 chose bracing (87 received bracing, 1 observation)
	  ○ 38 chose observation (36 observation, 2 bracing)
	
	Primary analysis included randomised and preference as-treated (rather than

	randomised or chosen): • bracing 146 • observation 96 ITT analysis included only the randomised group according to allocated treatment.
Intervention	Rigid thoracolumbosacral brace (TLSO, 68% Boston) advised to be worn ≥18 hours per day. Wear time was logged by temperature sensor, though in analysis all patients considered treated, regardless of compliance. Average follow-up 24.2 months
Comparator	Observation, no treatment Average follow-up 21.3 months
Results/outcomes	<u>Criterion 10</u> Primary outcome (whichever was met): • treatment failure: curve progression to ≥50^{o} • treatment success: skeletal maturity (Risser 4 in girls, 5 in boys) without this progression Treatment success bracing vs. observation: • Primary analysis: 72% (105/146) braced vs. 48% (46/96) observed: OR 1.93, 95% CI 1.08 to 3.46 • ITT analysis: 75% (38/51) braced vs. 42% (27/65) observed: OR 4.11, 95% CI 1.85 to 9.16 • NNT to prevent one case of curve progression needing surgery: 3.0, 95% CI 2.0 to 6.2 • Relative risk reduction with bracing 56%, 95% CI 26 to 82. Secondary outcome: Pediatric Quality of Life Inventory (PedsQL) mean scores: • Primary analysis: 82.0 bracing vs. 81.9 observation (p=0.97) • ITT analysis: 79.1 bracing vs. 81.2 observation (p=0.45) No significant difference in adverse events (p=0.32) including back pain (p=0.29). One serious adverse event in one person receiving bracing: hospitalisation for anxiety and depression.

	Criterion 14 • Assessed for 116 from both RCT and preference cohorts • Patient wear during the first 6 months: mean 12.1 hours (SD +/-6.5, range 0 to 23) • Quartile of duration of brace wear was positively associated with the rate of success (P<0.001) • Lowest quartile of wear (mean 0 to 6hrs daily) treatment success rate 41% • Highest quartile of wear (≥12.9 hrs daily) treatment success rate 90-93%
Comments	Study strengths and limitations: Blinded assessment of outcomes should reduce bias. Decision to include the preference cohort due to low enrolment rate and assess as-treated. However, primary analysis was adjusted for propensity score to reduce bias from non-random assignment. ITT analysis for the randomised group gave similar results. Brace-dose response may be confounded by patient characteristics such as curve type and flexibility. Applicability to review question: Indirect evidence to the question of whether bracing after screen detection prevent progression. Non-screened population, all clinically diagnosed, of children age 10-15 years with "moderate" curves who all meet bracing treatment criteria. Bracing is demonstrated to prevent progression, though it is not known whether: screening would have improved detection rates; whether patient characteristics would have been different when diagnosed (e.g. earlier stage); whether treatment success with bracing would have been superior after screening compared to clinical detection.

Appendix number	5
Relevant criteria	10
Publication details	Wiemann JM, Shah SA, Price CT. Nighttime bracing versus observation for early adolescent idiopathic scoliosis. Journal of Pediatric Orthopaedics. 2014;34(6):603-6.[15]
Study details	Prospective controlled cohort 2 orthopaedic clinics, US. Assigned to intervention or control groups depending on clinic of presentation

Study objectives	To determine whether night-time bracing using a Charleston bending brace is effective in preventing progression of smaller curves (15 to 25^{o}) in skeletally immature, premenarchal females relative to current standard of care (observation for curves <25^{o}).
Inclusions	Previously untreated premenarchal girls with AIS, Risser sign 0 with Cobb angle of primary curve 15-25^{o}
Exclusions	None other than not meeting above criteria.
Population	n=46 total, 23 allocated to each group. 37 analysed, 21 in the treatment and 16 in the control group (9 exclusions due to failure to complete follow-up). Mean age: 11.9 years intervention, 12.0 years control (p=0.697) Average curve 19^{o} both groups, no significant differences for any characteristics.
Intervention	Night-time-only (Charleston) bending brace worn to skeletal maturity. Addition of daytime brace if progression to Cobb angle ≥25^{o} or > 5^{o} Surgical consideration if progression to > 50^{o}.
Comparator	Observation, no treatment. Fulltime bracing commenced if progression to Cobb angle ≥25^{o} or > 5^{o} and then continued to skeletal maturity. Surgical consideration if progression to > 50^{o}.
Results/outcomes	Follow-up to skeletal maturity or minimum 2 years, analysis regardless of compliance. Bracing: • 29% (6/21) no progression >5^{o} by skeletal maturity (p=0.023 vs. control) • 19% (4/21) progressed >5^{o} but <10^{o} • 52% (11/21) progressed >10 • Surgery: 19% (4/21) (p=0.472 vs. control) Observation: • 100% (16/16) with progression • 50% (8/16) progressed >5^{o} but <10^{o} • 50% (8/16) progressed >10^{o} • Surgery: 12% (2/16)
Comments	Small sample size with only 80% follow-up; may be underpowered. Non-randomised controlled trial, though no significant differences in

	characteristics between groups. Applicability to review question: Indirect evidence to the question of whether bracing after screen detection prevent progression. Non-screened population, all clinically diagnosed. Children average 12 years with skeletal immaturity and curves that would normally fall below threshold for bracing. Shows night-bracing may prevent progression though it is not known whether: screening would have improved detection rates; whether patient characteristics would have been different when diagnosed (e.g. earlier stage); whether treatment success with bracing would have been superior if commenced after screening compared to clinical detection.

Appendix number	6
Relevant criteria	14
Publication details	Brox JI, Lange JE, Gunderson RB, et al. Good brace compliance reduced curve progression and surgical rates in patients with idiopathic scoliosis. European Spine Journal. 2012;21(10):1957-63[17]
Study details	Prospective cohort Single hospital centre, Norway (1976 to 1988).
Study objectives	To examine the association between compliance of brace wear and curve compression, including surgical rate in people with idiopathic scoliosis treated with a Boston brace.
Population/Inclusions	495 patients with scoliosis treated with a Boston brace between 1976 and 1988. Bracing indication of major curve >20^{o} and >5^{o} progression after 4 months and skeletal immaturity (Risser sign <3).
Exclusions	Patients who started bracing >2 years after menarche, received bracing for <6 months, or with infantile, syndrome or congenital scoliosis.
Intervention	(Rigid) Boston brace with recommended wear 23 hours per day. Wear to skeletal maturity (>2 years after menarche or Risser 4 or 5), with 4 monthly follow-up. Follow-up after weaning 6, 12 and 24 months.
Comparator	Not applicable
Results/outcomes	<u>Primary outcomes</u> Compliance with brace wear assessed by a single surgeon and scored on

	standardised form with questions: • "Has the brace been used as prescribed? If not, do you use the brace at all?" • "For how many hours weekly or daily are you not using the brace?" Compliance >20 hours daily, non-compliance including "irregular users" (wearing <20 hours) and those who aborted treatment Other primary outcomes: • curve progression (≥6^{o} and inclusive of those needing surgery) • surgery (indication >45^{o} during bracing or weaning, >50^{o} in later follow-up) <u>Results</u> Compliant: 389/495 (79%) Non-compliant: 106/495 (21%) • 54 (10.9%) "irregular users" (wearing < 20 hours daily) • 52 (10.5%) aborted bracing (not further defined) Reasons for non-compliance: psychological (30), pain (24), skin problems (12), unknown (40). At weaning: • Curve progression: 76/389 compliers vs. 59/106 non-compliers (OR 5.2, 95% CI 3.3 to 8.2). • Surgery: 11/389 compliers vs. 22/106 non-compliers (OR 9.0, 95% CI 4.2 to 19.3) At long-term follow-up (mean/median 24 years, n=355) • Curve progression: 68/284 compliers vs. 46/71 non-compliers (OR 5.8, 95% CI 3.3 to 10.2) • Surgery: 10/284 compliers vs. 17/71 non-compliers (OR 8.6, 95% CI 3.7 to 19.9) • Proportion with curve progression: 24% compliant, 62% irregular users and 69% who aborted bracing • Proportion having surgery: 3.5% compliant, 26% irregular users and 22% who aborted bracing

	Significant differences at baseline and short-term follow-up between compliers and non-compliers: • Gender: compliers 6% male vs. non-compliers 13% male (p=0.017) • Age at weaning: 16 vs. 15.3 years (p<0.001) • Bone age at weaning: 15.4 vs. 14.7 (p<0.001) • Major curve at weaning: 26.4^{o} vs. 33.5^{o} (p<0.001) • Major curve at 1 year: 27.4^{o} vs. 33.7^{o} (p<0.001) • Major curve at weaning: 28.1^{o} vs. 33.2^{o} (p<0.001) Age at or curve angle at start or bracing not significantly associated with compliance. No significant differences in characteristics between those attending or not attending longer-term follow-up. Health-related quality of life was also assessed (not further reported here).
Comments	Large sample size and long duration of follow-up. Compliance assessment may be inaccurate. Researchers acknowledge a lack of a reliable method of assessing compliance when the study was started. Was assessed by direct questioning which may not give a reliable answer. Also unclear how many times compliance was questioned. May not be comparable to other studies in terms of brace used, prescribed wear time, definition of compliance, or characteristics of wearers.

Appendix number	7
Relevant criteria	14
Publication details	Sanders JO, Newton PO, Browne RH, et al. Bracing for idiopathic scoliosis: How many patients require treatment to prevent one surgery? Journal of Bone and Joint Surgery - American Volume. 2014;96(8):649-53.[18]
Study details	Prospective cohort Single hospital centre, US (1998-2000)
Study objectives	To determine NNT with bracing in order to prevent curve progression to a surgical range (≥50^{o}). Further follow-up of a 2010 publication reporting bracing, curve progression

	and patient compliance.
Population/Inclusions	100 patients with AIS, age ≥10 years, Cobb angle 25-45^{o}, skeletally immature (Risser 0, 1 or 2).
Exclusions	Patients receiving surgery without ≥6^{o} curve progression; previous treatment.
Intervention	(Rigid) Boston brace fitted with temperature logger to continuously sample temperature inside brace every 15mins. Prescribed bracing 16 or 23 hours per day according to physician preference.
Comparator	Not applicable.
Results/outcomes	<u>Outcomes</u> Progression to surgical range (≥50^{o}) measured against hours of brace wear. Non-compliance defined as <2 hours wear per day. High compliance: two definitions of ≥10 or ≥14 hours per day <u>Results</u> High compliance prevents surgery: • 28/100 patients (28%) had progression to surgical range (follow-up time not specified) • Compliance <2 hours per day: 27/100 (27%) of whom 12/27 (44.4%) required surgery o ARR for any brace wear compared with non-compliance: 16.4% (44.4 - 28.0) (95% CI 0 to 36.3%, non-significant [i.e. brace wear in general doesn't significantly prevent surgery]) • Compliance ≥10 hours per day: 31/100 (31%) of whom 2/31 (6.5%) required surgery o ARR 37.9% (44.4 - 6.5) (95% CI 15.9 to 56.8%, significant), NNT 3 (95% CI 2 to 7) people with compliance ≥10 hours to prevent one surgery • Compliance ≥14 hours per day: 13/100 (13%) of whom 0 required surgery o ARR 44.4% (44.4 - 0) (95% CI 16.1 to 62.7%, significant), NNT 3 (95% CI 2 to 7) people with compliance ≥14 hours to prevent one surgery
Comments	Objective monitoring of compliance with temperature sensor, all assessors blind to wear data. Unclear whether participants were aware of temperature

	sensor which may have influenced compliance. May not be comparable to other studies in terms of brace used, prescribed wear time, definition of compliance, or characteristics of wearers. In assessment of NNT with bracing to prevent surgery, non-compliant patients are used as the reference and considered to have the same outcomes as non-braced patients which may not be so.

Appendix number	8
Relevant criteria	14
Publication details	Chan SL, Cheung KMC, Luk KDK, et al. A correlation study between in-brace correction, compliance to spinal orthosis and health-related quality of life of patients with Adolescent Idiopathic Scoliosis. Scoliosis. 2014;9(1).[19]
Study details	Prospective cohort Single hospital centre, Hong Kong
Study objectives	To assess the link between effectiveness in terms of in-brace correction, brace compliance and health related quality of life.
Population/Inclusions	55 females with AIS, age ≥10 years, Cobb angle 25-40^{o}, skeletally immature (Risser 0, 1 or 2). Mean age 12.6 years, 22 (40%) pre-menarche.
Exclusions	None reported other than previous treatment.
Intervention	Rigid TLSO (Hong Kong) brace. Prescribed wear time not reported. Instructed how to fasten and tighten brace. Compliance measured subjectively by self-reported daily wear time on the Log Sheet for Wearing Orthosis. Verified objectively by a force sensor installed in the brace (for 2-4 months only).
Comparator	Not applicable.
Results/outcomes	Analysis covered 42/55 participants (76.4%): 6 voluntary withdrawals, 5 lost to follow-up, 2 seeking alternative therapy. Follow-up 4-6 monthly with 2 consecutive visits (exact follow-up time not reported). <u>Correlation between compliance and in-brace correction</u> Compliance:

	• 0-8 hours: 4/42 (9.5%) • 9-16 hours: 7/42 (16.7%) • 17-23 hours: 31/42 (73.8%) In logistic regression no significant difference was observed between the three groups for in-brace correction (<40% or ≥40% correction). Risk of brace correction <40% compared with 17-23 hours wear: • 0-8 hours: OR 1.19, 95% CI 0.08 to 17.71 (p=0.90) • 9-16 hours: OR 0.96, 95% CI 0.15 to 6.13 (p=0.96) <u>Correlation between subjective and objective measures of compliance</u> Analysed for 14 subjects (33.3%), recorded wear period 39 to 120 days. • Mean hours per day as logged by subjects: 10.7 (+/- 5.8) hours (range 0-21) • Mean hours per day as recorded by sensor: 10.7 (+/- 5.5) hours (range 2.3 to 19) Significant correlation between subjective and objective wear (p=0.000) Other outcomes examined (not further reported here) included correlations between: • compliance and quality of life • in-brace correction and quality of life • curve patterns and Cobb angle
Comments	Patient self-report of compliance, but verified objectively with sensor in one third showing significant correlation. However, this was only a temporary assessment for 2-4 months. Unclear whether participants were aware of temperature sensor which may have influenced compliance. Small initial sample size with <80% completion rate. Recruited participants and completers may not be representative. Female only. Comparison with visit 1 (pre-brace) and 2 consecutive visits, unclear follow-up time but participants don't appear to have been followed to skeletal maturity. Progression categorised into two groups, which may be non-comparative measures of treatment success or failure compared with other studies. May not be comparable to other studies in terms of brace used, prescribed

	wear time, definition of compliance, or characteristics of wearers.

Appendix number	9
Relevant criteria	14
Publication details	Rivett L, Stewart A, Potterton J. The effect of compliance to a Rigo System Cheneau brace and a specific exercise programme on idiopathic scoliosis curvature: A comparative study: SOSORT 2014 award winner. Scoliosis. 2014;9(1).[20]
Study details	Prospective cohort (pre-test/post-test comparison) Single physiotherapy practice, South Africa.
Study objectives	To determine the effect of compliance to the Rigo System Cheneau brace and a specific exercise programme on curvature, quality of life and psychological traits.
Population/Inclusions	47 females with AIS, age 12-16 years, Cobb angle 20-50°. Participants divided into two groups according to compliance at brace weaning.
Exclusions	Other types of scoliosis, Cobb angle >50°, previous treatment.
Intervention	(Rigid) Rigo System Cheneau brace with prescribed wear 23 hours per day, worn to skeletal maturity (Risser 5 and height static for 6 months). Home exercise programme (20-25 minute exercises, 4-5 days a week) Compliance self-reported in patient diaries.
Comparator	Not applicable.
Results/outcomes	<u>Compliance</u> Compliant group: brace wear 20-23 hours per day, and exercise ≥3 times per week: n=26 (55.3%) • Mean hours brace wear 21.5 (+/- 1.17) • Mean exercise session: 3.92 (+/-0.63) Non-compliant group: brace wear <20 hours per day, and exercise <3 times per week: n=21 (44.7%) • Mean hours brace wear 12.19 (+/- 7.05) • Mean exercise session: 1.71 (+/-1.06) <u>Progression</u>

	All Cobb angles at follow-up were significantly lower in the compliant group with the worst angle 25.38^{o} (+/-8.3) vs. 36.71^{o} (+/-9.3) in the non-compliant group (p=0.0001). Mean change in Cobb angles from baseline to study end, compliant vs. non-compliant: • All thoracic curves: improved by 8.96 (+/- 6.10) vs. worsen by 5.81 (+/- 6.87) (<0.0001) • All lumbar curves: improved by 7.11 (+/- 4.99) vs. worsen by 3.11 (+/- 4.98) (<0.0001) • Worst Cobb angle: improved by 10.19 (+/- 5.46) worsen by 5.52 (+/- 4.31) (<0.0001) Quality of life assessments were also made (not further reported here).
Comments	Patient self-report of compliance, which may be inaccurate. Small initial sample size. Results are only reported for 47 as a further 4 dropped out, who could have been considered non-compliers. Female only. May not be comparable to other studies in terms of brace used, prescribed wear time, definition of compliance, or characteristics of wearers.

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