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Structured Abstract

**Background:** Scoliosis is a lateral curvature of the spine of 10 degrees or more, often with a rotational component; adolescent idiopathic scoliosis (AIS) is the most common form of scoliosis in adolescence. Curves progress in approximately two-thirds of AIS patients before they reach skeletal maturity. Curves of greater than 40 degrees at the end of growth are likely to continue to progress after skeletal maturity, while curves of less than 30 degrees at skeletal maturity are unlikely to progress significantly during adulthood. Very large degrees of curvature may be associated with adverse long-term health outcomes.

**Purpose:** The USPSTF will use this evidence review to update its 2004 D recommendation on screening for adolescent idiopathic scoliosis.

**Data sources:** Cochrane Central Register of Controlled Trials, OVID Medline, ERIC (Eric.ed.gov), PubMed publisher-supplied, CINAHL, and relevant systematic reviews. We searched for articles published from January 1966 to October 31, 2015. We updated our search on October 20, 2016.

**Study selection:** Two reviewers independently reviewed 8,230 titles and abstracts and 1,088 articles against pre-specified inclusion criteria, resolving discrepancies through consensus. We included fair- or good-quality studies. For screening questions (Key Questions 1, 2, and 5) the population of interest was asymptomatic children aged 10 to 18 years, screened in primary care-referable settings using forward bend test (FBT) with or without a scoliometer, surface topography, or other methods. For treatment questions (KQ3 and KQ6) we included studies of children and adolescents aged 10 to 18 years diagnosed with AIS with a Cobb angle of 10 to 50 degrees at detection. For long-term outcomes (KQ4) we included randomized clinical trials (RCTs), controlled trials, or large observational studies of adult health outcomes in individuals diagnosed with AIS with a Cobb angle of ≥10 degrees.

**Data extraction and analysis:** We extracted key elements of included studies into standardized evidence tables. Evidence tables were tailored for each KQ and to specific study designs. We provided a narrative synthesis of results. Because of heterogeneity between studies, we did not conduct pooling or meta-analyses.

**Results:** We included seven studies (13 articles) on screening accuracy (KQ2), seven studies (nine articles) on the effectiveness of treatment (KQ3), one study (two articles) on the harms of treatment (KQ6), and two studies (five articles) on long-term outcomes (KQ4). No studies met our inclusion criteria on the effect of AIS screening on long-term health outcomes (KQ1) or on the harms of screening (KQ5).

**KQ1. Does screening for adolescent idiopathic scoliosis improve: a) health outcomes and b) the degree of abnormal spinal curvature in childhood or adulthood? No studies.**
KQ2. What is the accuracy of screening for adolescent idiopathic scoliosis?

Seven fair-quality screening programs (13 articles) including 447,243 adolescents met our inclusion criteria. Six of the seven programs were conducted in school settings, and there was heterogeneity in the screening tests used and in the training of the practitioners conducting screening. Three of the seven studies included some followup data on children who screened negative.

Screening accuracy increased with the number of screening tests used. Sensitivity and specificity were highest (93.8% and 99.2%), predictive value was highest (81.0%), and false positive rates were lowest (0.8%; 6.2% false negative) in a clinic-based screening program using FBT, scoliometer, and Moiré topography screening; accuracy was lower (71.1% sensitivity, 97.1% specificity, 2.9% false positive, 28.9% false negative) in a U.S.-based study of FBT with scoliometer. Sensitivity for single-modality screening in a school-based program screening children aged eight and older ranged from 84.4 percent with FBT alone to 100 percent with Moiré screening. False positive rates ranged from 0.8 percent to 21.5 percent; false negative rates ranged from zero percent for Moiré screening to 15.6 percent for FBT alone, with 28.9 percent for FBT plus or minus scoliometer. Predictive value estimates were 29.3 percent to 54.1 percent for FBT plus scoliometer, and ranged from 5.0 percent to 17.3 percent for a single screening modality to 81.0 percent for FBT with scoliometer and Moiré screening.

KQ3. Does treatment of adolescent idiopathic scoliosis that has a Cobb angle of less than 50 degrees at diagnosis improve: a) health outcomes and b) the degree of spinal curvature in childhood or adulthood?

We found seven studies (nine articles) on the effectiveness of treatment. Five studies (seven articles) of 651 adolescents examined effectiveness of bracing treatment. Three of these studies were of fair quality and two were of good quality. Two studies (two articles) of 184 adolescents examined effectiveness of exercise treatment. One of these studies was of good quality and one was of fair quality.

**Brace treatment.** Four of five prospective controlled studies found evidence for benefit of bracing treatment on curve progression compared to observed controls, measured either in favorable proportions of children with 5 to 6 degrees’ progression (three of five studies) or in curve progression to a degree considered bracing failure (one study). Quality of life outcomes associated with bracing were reported in one study and were similar between treatment arms.

**Exercise treatment.** In two studies (one good-quality RCT and one fair-quality controlled clinical trial) of tailored physiotherapeutic scoliosis-specific exercise, the intervention group experienced significant improvement compared to a generic exercise control group at 12-month followup. In the RCT, there was a favorable reduction in Cobb angle of 4.9 degrees in the intervention group compared to the control group’s unfavorable increase of 2.8 degrees (p<0.001). Quality of life measures were improved at 12 months in the intervention group compared to stable or slightly improving measures in the control group. By the end of the CCT’s 12-month treatment period, the intervention group had experienced a favorable decrease in
average magnitude of all curves of 0.67 degrees, compared to the control group’s unfavorable progression of 1.38 degrees (p<0.05).

**Surgical treatment.** No studies of surgical treatment in screening-relevant populations met our inclusion criteria.

*KQ4. What is the association between severity of spinal curvature in adolescence and health outcomes in adulthood?*

Two fair-quality studies (five articles) of 339 people with AIS followed up in adulthood met our inclusion criteria. In both studies adult outcomes were stratified by treatment received in adolescence. Quality of life as measured by the SRS-22 or the SF-36 were similar between observed and braced participants at adult followup, though braced participants felt their body appearance was more distorted than did untreated participants, and braced participants reported more negative treatment experiences than those treated surgically. No significant adult outcome differences were found between braced and surgically treated participants on the Oswestry Disability Index, general well-being, or self-esteem and social activity. Pulmonary outcomes and childbearing and pregnancy outcomes were similar in braced and surgically treated participants.

*KQ5. What are the harms of screening for adolescent idiopathic scoliosis?* No studies.

*KQ6. What are the harms of treatment of adolescent idiopathic scoliosis that has a Cobb angle of less than 50 degrees at diagnosis?*

Harms of bracing were reported in one good-quality study (two articles) of 242 adolescents. Skin problems on the trunk (under the brace) and non-back body pains were more frequently reported in braced participants than in observed controls. Anxiety and depression rates were low and similar between groups. One of the 146 braced participants reported anxiety and depression requiring hospitalization.

**Limitations:** Direct evidence for a benefit of AIS screening into adulthood is lacking. Screening programs vary with regard to setting, persons administering the screening test, and screening modalities used, and have very limited followup of screen-negative children. Data on surgery in screen-detected children whose curves have progressed is lacking. Long-term followup studies rarely report data on curve in adolescence and its association with adult health outcomes. We found no evidence on possible harms of screening (e.g., radiation exposure, overtreatment, and/or psychosocial consequences associated with diagnosis of clinically insignificant scoliosis), and very limited data on harms of treatment.

**Conclusions:** We found no direct evidence for a benefit of AIS screening in adolescence on adult health outcomes. AIS can be identified with screening with varying accuracy. There is little evidence addressing harms of screening. A growing body of evidence suggests that brace treatment can interrupt or slow scoliosis progression, and two studies suggest that curves of smaller magnitude may respond similarly to physiotherapeutic scoliosis-specific exercise treatment. There is very limited direct evidence on the association between curve magnitude at
skeletal maturity and adult health outcomes for people with mild-to-moderate scoliosis curves at diagnosis.
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Chapter 1. Introduction

Condition Definition

Scoliosis is characterized by anatomic structural alteration, a lateral curvature of the spine in the coronal plan that is usually accompanied by rotation. The direction (right or left) is defined by the curve’s convexity. The location is defined by the vertebra that is most deviated and rotated from midline, called the apical vertebra. By convention, scoliosis is defined as a curvature of at least 10 degrees (as measured by the Cobb angle); curves with Cobb angles of less than 10 degrees are referred to as “spinal asymmetry.”

Idiopathic scoliosis is a diagnosis of exclusion for cases with no definite etiology and is categorized based on age of presentation.

- Infantile: presents between zero and three years of age
- Juvenile: presents between four and nine years of age
- Adolescent: presents at 10 years of age or older

Adolescent idiopathic scoliosis (AIS) is the most common form of idiopathic scoliosis, and accounts for 80 percent to 85 percent of cases of idiopathic scoliosis. The clinical course associated with infantile and juvenile idiopathic scoliosis appears to be different than that seen in AIS; therefore, these conditions generally are considered as separate entities.

Non-idiopathic scoliosis is scoliosis that is attributable to or associated with other underlying conditions. This is usually categorized by cause, e.g., neuromuscular scoliosis (secondary to nervous system or peripheral neuromuscular dysfunction; typically seen in persons with underlying neurologic and/or musculoskeletal conditions such as cerebral palsy) and congenital scoliosis (resulting from anatomic abnormalities of the vertebra that lead to progressive spinal deformity as a child grows). The clinical course of non-idiopathic scoliosis varies by etiology, and is also quite often different than that seen in individuals with AIS.

Prevalence and Burden

Commonly cited estimates of prevalence of AIS vary, but usually are around one percent to three percent (both U.S. and non-U.S. studies) for AIS with a Cobb angle ≥10 degrees in children aged 10 to 16 years. Prevalence estimates for curves of greater severity are somewhat lower: a retrospective cohort study conducted to characterize school-based screening for scoliosis conducted in the United States found a cumulative incidence of 1.8 percent (95% confidence interval [CI], 1.2 to 2.3) for curves of more than 10 degrees, 1.0 percent (95% CI, 0.6 to 1.5) for curves of at least 20 degrees, and 0.4 percent (95% CI, 0.1 to 0.6) for curves of 40 degrees or more. Prevalence also varies by gender. Based on school screening studies conducted internationally, the prevalence of AIS in children aged 10 to 18 ranges from 0.15 percent to 0.66 percent in boys.
and 0.24 percent\(^8\) to 3.1 percent in girls.\(^9\) However, the discrepancy between genders is greatly affected by increased degree of curvature: males and females have a similar prevalence of scoliosis with Cobb angles of 10 degrees, but females are ten times more likely than males to have progression of their Cobb angle to 30 degrees or more.\(^{10}\)

The prevalence of AIS and the female-to-male ratio, by degree of Cobb angle severity, is approximately as follows:

- Cobb angle \(\geq 10^\circ\): Prevalence of 2-3% in adolescents; female-to-male ratio 1.4-2.4 to 1
- Cobb angle \(\geq 20^\circ\): Prevalence of 0.3-0.5% in adolescents; female-to-male ratio 5.4 to 1
- Cobb angle \(\geq 30^\circ\): Prevalence of 0.1-0.3% in adolescents; female-to-male ratio 10 to 1
- Cobb angle \(\geq 40^\circ\): Prevalence of 0.1% in adolescents; female-to-male ratio not available\(^6\)

### Etiology and Natural History

The etiology of AIS is, by definition, unknown, although there is some evidence suggesting a possible genetic contribution.\(^{11}\) Studies show a higher concordance in incidence and degree of AIS in monozygotic twins,\(^{12}\) and an increased prevalence of AIS in siblings, children, and some close relatives of those with AIS.\(^4,\)\(^{13}\) The inheritance pattern of familial AIS is not clear,\(^{14,\)\(^{15}\) although some research suggests that expression of familial AIS may be linked to the X chromosome (with dominant inheritance),\(^{16}\) and genetic loci for AIS also have been mapped to certain chromosomes.\(^{17-20}\) Other possible etiologies for AIS include abnormalities of the growth and structure of vertebral bodies and discs, abnormal spinal mechanics with secondary spinal instability, body asymmetry, neurologic dysfunction, abnormal ribcage anatomy, abnormal platelet microstructure, and melatonin secretion (as it relates to growth). None of these conditions has been found to be universally associated with development of AIS, suggesting that this most likely is a multifactorial condition.\(^{21}\)

AIS curves typically progress most rapidly during the adolescent growth spurt before skeletal maturity. Skeletal maturity is associated with decreased growth rate and a decrease in the likelihood of progression of the scoliosis curve. Clinically, skeletal maturity is most often assessed in AIS patients by their Risser sign (the stage of ossification of the iliac apophysis as seen on X-ray; this is measured on a scale of one to five, with five indicating the full ossification seen in developmentally mature adolescents and adults); however, other measures of developmental maturity (e.g., age at menarche in girls) are used as well.\(^{22}\)

Curves progress in approximately two-thirds of skeletally immature patients before they reach skeletal maturity (defined in most studies as a Risser sign of 4 or greater in females, or 5 in males); however, only one-third of individuals with scoliosis will experience more than a 10 degree increase in curve magnitude, and less than 10 percent will have an increase of 30 degrees or more.\(^{23}\) The likelihood of progression varies depending upon gender, curve magnitude, curve location, and maturity or remaining growth potential.\(^{24}\) One study followed 123 skeletally immature adolescents with AIS (mean age 14 years, Cobb angles <50°) without treatment until skeletal maturity.\(^{23}\) In this study, the average curve measured 33 degrees (range 10° to 49°) at the time of diagnosis and 49 degrees (range 12° to 97°) at skeletal maturity. Curves remained
unchanged (progressed by $<5^\circ$) in 32 percent of patients, progressed by $\geq 5$ degrees in 68 percent, progressed by greater than 10 degrees in 34 percent, progressed by greater than 20 degrees in 18 percent, and progressed by greater than 30 degrees in eight percent.

Older studies, such as those involving a cohort of 444 patients in Iowa, also have examined curve progression in untreated patients. These studies show curves can continue to progress after skeletal maturity in untreated patients, especially in those with curves measuring greater than 40 degrees at the end of growth. Curves greater than 50 degrees are thought to progress one degree per year after skeletal maturity, while curves less than 30 degrees at skeletal maturity have a low likelihood of significant progression during adulthood. However, the likelihood of continued curve progression in any individual is affected by other factors such as curve location and direction, apical vertical rotation, and trunk imbalance.

The extent to which AIS is associated with other adverse health outcomes is not well understood. Most individuals with AIS curves of mild severity do not appear to have clinical symptoms during adolescence, although recent research suggests a higher likelihood of back pain at age 18 for individuals with curves of 6–10 degrees at age 15 when compared to persons without spinal curvature, as well as an increased likelihood of missed school and avoidance of activities at age 18 in adolescents with slightly larger curves. Older studies with long-term followup of untreated cohorts suggest that back pain and cardiopulmonary compromise, with associated disability, are common. However, many of these studies included subjects with non-idiopathic scoliosis and/or scoliosis with onset before adolescence, newer studies composed exclusively of individuals with AIS suggest a more benign natural history.

Adults with AIS may be at higher likelihood of having back pain and possibly degenerative disc changes than unaffected adults. Reports are mixed with regard to whether this significantly affects functioning. Some studies suggest the presence and severity of back pain are greater in adults with AIS than in the general population, and cause a significant impact on function. However, other studies did not find excessive disability in adults with AIS despite increased prevalence of back pain, or found the frequency of back pain to be similar in adults with AIS and in the general population. Back pain does not appear to be correlated with the severity of scoliotic curve, and studies have not shown that treatment of AIS impacts the likelihood of development of back pain.

Abnormal pulmonary function is strongly associated with thoracic curve size, but clinically significant cardiopulmonary problems are seen only with severe scoliosis. Adolescents with curves of greater than 50 degrees are at increased risk for shortness of breath in later adulthood, and those with curves greater than 70 degrees have diminished lung volumes, but pulmonary function appears to be most significantly affected in those with curves greater than 100 degrees.

The extent of the psychosocial impact of scoliosis during adolescence and adulthood is unclear. In addition to concerns about body image and deformity, individuals with AIS may have a poorer perception of their own health status and of their ability to interact socially compared to unaffected adults, although the presence and severity of psychological problems does not necessarily correlate with the severity of the scoliosis curve.
There is little data on mortality in untreated scoliosis. Observational data from a long-term (50-year) cohort study of individuals with untreated AIS does not suggest an increase in mortality compared with the general population. However, the loss-to-followup in this cohort was substantial (roughly 40 percent of individuals could not be located).

**Risk Factors**

Scoliosis of non-idiopathic etiology (i.e., neuromuscular or congenital scoliosis) often is associated with other clinical findings and/or symptoms that should prompt evaluation of the spine. As noted above, however, AIS most often is asymptomatic during adolescence, and is not typically associated with clinical findings other than body asymmetry (which itself may be subtle with mild degrees of spinal curvature and/or trunk rotation).

Gender is not predictive of development of AIS, although the risk of curve progression is ten times higher in females than in males, and females therefore are more likely to require treatment for AIS. As noted previously, evidence exists of a possible genetic contribution to AIS development, with studies showing increased prevalence of AIS in siblings and children of affected individuals and in monozygotic (as compared to dizygotic) twins; see section on “Etiology and Natural History” for details and references. Skeletal immaturity, and by association younger age, is associated with greater risk for curve progression, as is the magnitude-of-curvature at the time of detection of scoliosis.

**Screening**

The need for and benefit derived from universal population screening to identify adolescents with mild or moderate idiopathic scoliosis (i.e., scoliotic curves of <40° to 50°) has been a subject of debate and disagreement in the medical community for several decades. Curves of this degree are often asymptomatic in adolescence with the exception of cosmetic deformity, the majority of such curves will not progress significantly during adolescence, and the likelihood of continued progression in adulthood is low in curves that are less than 30 degrees at skeletal maturity. However, the ability to identify which cases of AIS are likely to worsen significantly during adolescence is limited. Therefore, the rationale behind screening for milder degrees of scoliosis is that if early, effective treatment can be instituted for people with AIS, then curve progression can be slowed or halted before skeletal maturity, which theoretically could improve long-term outcomes.

Most AIS screening methods are low-cost and non-invasive; however, because they measure trunk rotation or trunk asymmetry rather than actual spinal curvature, and because inter-examiner error precludes reliable correlation of screening results with a specific degree of spinal curvature, a confirmatory X-ray is needed to quantify severity of AIS.

**Forward Bend Test**

Most school-based scoliosis screening programs use the forward bend test (FBT), commonly
attributed to Adams, with or without a scoliometer. For the FBT, a child bends forward at the waist until the spine is parallel to the horizontal plane. The examiner then checks the child’s back for rib humps or other spinal asymmetries.

**Scoliometer**

A scoliometer is a handheld, non-invasive device used to measure the angle of trunk rotation (ATR). The examiner places the instrument on the child’s spine during the FBT, and reads the angle represented on the scoliometer. The Scoliosis Research Society (SRS) recommends an ATR of 5–7 degrees as a threshold for referral for X-ray.

**Humpometer**

Although less common, a humpometer also may be used in conjunction with the FBT. A humpometer is a series of movable strips placed along a child’s back perpendicular to the spine. The examiner locks the strips into place, and then transfers the resulting contour lines to graph paper. By adding the size of rib humps and depressions, the examiner can obtain a measure of back deformity. A back deformity of 5 millimeters or more may indicate a positive screening result.

**Plumb Line Test**

The plumb line test allows examiners to check for spinal deformities while the child is standing upright. For this test, an examiner holds a plumb line at the child’s C7 vertebra (in the neck) and allows the line to hang below the child’s hips. The examiner then measures the extent to which the plumb line deviates from the center of the child’s spine.

**Moiré Surface Topography**

During Moiré screening, the child stands inside a specialized device that projects contour lines, called Moiré fringes, onto the child’s back; a photograph is then taken of the projection. An examiner counts the number of asymmetric contour lines. Students with two or more asymmetric Moiré fringes often are referred for radiography.

**Treatment**

The goal of AIS treatment is to slow or halt the progression of the scoliotic curve during the adolescent growth period. Options for treatment include observation, bracing, surgery, or non-surgical intervention such as physiotherapy. Exercise therapy is recommended for mild scoliosis in some countries but has not been routine in the United States. The choice of therapy depends primarily on the degree of curvature and potential for further growth (both of which determine the risk for progression). Because most cases of AIS will not have symptoms other than spinal curvature during adolescence, the typical approach to treatment for AIS is informed by an
individual’s Cobb angle and developmental maturity: higher Cobb angles and lower levels of maturity generally are felt to warrant more aggressive intervention.\textsuperscript{55}

There are no guidelines for management of AIS published by professional societies in the United States.\textsuperscript{43} International organizations have published such guidelines,\textsuperscript{55} and current practice in the United States is relatively uniform with regard to basic elements of management. However, there is some variability among primary care providers with regard to imaging and referral for treatment.\textsuperscript{56} Individuals with Cobb angles of less than 20 degrees (or an ATR of <7º) usually are observed without treatment; this often is done by the primary care provider, with referral to a specialist being made in the event of continued curve progression. Those who recommend exercise treatment often direct it at mild scoliosis of this magnitude. According to some guidelines for management of adolescents with substantial growth remaining (Risser sign 0 to 2),\textsuperscript{49} those with Cobb angles of 20–29 degrees are braced if they exhibit curve progression (i.e., increase in Cobb angle ≥5º over 3–6 months), those with Cobb angles of 30–40 degrees usually should be braced, those with Cobb angles of 40–50 degrees may be managed with bracing or surgery, and those with Cobb angles greater than 50 degrees usually require surgical intervention. Some research suggests a correlation between severity-of-curve and the risk and complexity of surgical treatment.\textsuperscript{57}

### Brace Treatment

There are several types of braces used for treatment of AIS. Braces fall into three general categories: full-time rigid bracing, nighttime rigid bracing, and soft bracing. Brace selection is based on curve location and characteristics, and on the anticipated tolerance of the patient.\textsuperscript{58} Most rigid braces are prescribed for use 20 to 24 hours per day.\textsuperscript{22, 55, 59} Thoracolumbosacral rigid braces, such as the Boston brace, are the most frequently used in North America.\textsuperscript{60} Nighttime braces are worn 8 to 12 hours while sleeping; they are used for certain types of curves.\textsuperscript{55, 61} Soft braces are adjustable, flexible, and noninvasive compared to other braces.\textsuperscript{58, 62} The most widely used brace in the United States until the 1970s was the Milwaukee brace; this still may be used for very high thoracic curves, but most AIS now is managed with braces that do not rise to the neck, and which therefore are more cosmetically acceptable.\textsuperscript{58, 60, 63, 64}

Brace treatment is not intended to correct curvature but rather to slow or halt curve progression; bracing therefore primarily is indicated for skeletally immature patients (Risser sign 0 to 2) at high likelihood of rapid curve progression. Skeletal immaturity traditionally has been defined as Risser sign 0 to 2; newer measures of skeletal maturity such as digital skeletal age increasingly are being used as these correlate better with acceleration of curve progression.\textsuperscript{65} Treatment generally is continued until skeletal maturity (Risser 4 in girls, Risser 5 in boys). Skeletally mature patients with Cobb angles of less than 30–40 degrees are thought to be at low risk for continued progression, and typically are not monitored in adulthood.

### Surgical Treatment

Surgical intervention generally is considered in individuals with curves that have progressed past the point where brace treatment is thought to be effective (i.e., over 40–50º, depending on
developmental maturity and type of curve). Harrington rod instrumentation was the standard surgical method used for scoliosis from the 1960s to the 1990s. This procedure involved placing one or more steel rods along the spine and using hooks to attach rods to the top and bottom of the scoliotic curve. After surgery, patients were immobilized in a full body cast for 2–6 months, and then braced for up to 6 months. Since the 1990s, the use of Harrington instrumentation has been superseded by newer surgical methods that use three-dimensional correction.

Segmental instrumentation, first introduced in the 1980s, allows for three-dimensional correction through the application of different forces along the spinal curve. The procedures involve attaching one or more rods to each level of the spine using sublaminar wires (for Luque instrumentation), hooks (for Cotrel-Dubousset instrumentation), or (now more commonly used) pedicle screws inserted into vertebral bones at either side of the spinal canal. Pedicle screws provide stronger biomechanical fixation than earlier instrumentations, and patients treated with pedicle screws do not need to undergo a long immobilization period following surgery. Patients typically can perform daily activities and return to school within 2–4 weeks post-surgery, and resume participation in sports and other activities within 3–6 months.

Current Clinical Practice in the United States

Several specialty groups have published recommendations or information statements in support of screening, but none are based on a systematic review of evidence.

Routine screening for AIS has been recommended as long ago as the 1980s by the American Academy of Orthopedic Surgeons (AAOS), the American Academy of Pediatrics (AAP), and the Scoliosis Research Society (SRS), and either was required by law or established voluntarily in more than half of U.S. states at that time. However, contemporaneous recommendations from other countries either recommended against screening or acknowledged the poor evidence base in support of it.

The U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to recommend for or against routine screening in 1993, and recommended against screening in 2004 (see section on Previous USPSTF Recommendations for details). However, routine screening for AIS continues to be endorsed by the AAOS, AAP, and SRS, and the International Society on Scoliosis Orthopedic and Rehabilitation Treatment (SOSORT).

Previous USPSTF Recommendation

In 2004, the USPSTF recommended against the routine screening of asymptomatic adolescents for AIS (D recommendation), based on the results of a brief evidence update. This constituted a change from their previous 1993 C recommendation (equivalent to an I statement under current methodology), in which they found insufficient evidence to recommend for or against routine screening.
The USPSTF did not find good evidence that screening asymptomatic adolescents detects idiopathic scoliosis at an earlier stage than detection without screening. The accuracy of the most common screening test—the FBT with or without a scoliometer—in identifying adolescents with idiopathic scoliosis is variable, and there is evidence of poor followup of adolescents with idiopathic scoliosis who are identified in community screening programs.

The USPSTF found fair evidence that treatment of idiopathic scoliosis during adolescence leads to health benefits (decreased pain and disability) in only a small proportion of people. Most cases detected through screening will not progress to a clinically significant form of scoliosis. Scoliosis needing aggressive treatment, such as surgery, is likely to be detected without screening.

The USPSTF found fair evidence that treatment of adolescents with idiopathic scoliosis detected through screening leads to moderate harms, including unnecessary brace wear and unnecessary referral for specialty care. As a result, the USPSTF concluded that the harms of screening adolescents for idiopathic scoliosis exceed the potential benefits.
Chapter 2. Methods

Scope and Purpose

The USPSTF will use this evidence review to update the 2004 recommendation regarding effectiveness of screening for AIS. This review addresses the benefits and harms associated with screening and treatment of screen-detected cases of AIS.

Analytic Framework and Key Questions

We developed an analytic framework with five Key Questions (KQs) based on the previous review and a scan of the research conducted since the previous review (Figure 1). The analytic framework and KQs are more comprehensive than the previous evidence review, which had two questions designed to identify new evidence about whether (1) screening asymptomatic adolescents leads to improved health outcomes, and (2) the rate at which minor scoliosis progresses to a clinically significant form that causes health problems later in life.87

Key Questions

1. Does screening for adolescent idiopathic scoliosis improve: a) health outcomes and b) the degree of abnormal spinal curvature in childhood or adulthood?
2. What is the accuracy of screening for adolescent idiopathic scoliosis?
3. Does treatment of adolescent idiopathic scoliosis that has a Cobb angle of less than 50 degrees at diagnosis improve: a) health outcomes and b) the degree of spinal curvature in childhood or adulthood?
4. What is the association between severity of spinal curvature in adolescence and health outcomes in adulthood?
5. What are the harms of screening for adolescent idiopathic scoliosis?
6. What are the harms of treatment of adolescent idiopathic scoliosis that has a Cobb angle of less than 50 degrees at diagnosis?

Data Sources and Searches

We conducted an initial literature search for existing systematic reviews and guidelines on the topic of idiopathic scoliosis in adolescent and pediatric populations. The search was limited to English language articles published between 2004 and May 2015. We searched in the Canadian Agency for Drugs and Technologies in Health, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (Centre for Reviews and Dissemination), DynaMed, First Consult, Health Technology Assessment (Centre for Reviews and Dissemination), National Institute for Health and Clinical Excellence, Ovid MEDLINE and PubMed publisher-supplied. These studies helped clarify our KQs.
We worked with a research librarian to develop our search strategy for this evidence review. The search strategy was peer-reviewed by a second research librarian. We searched Cochrane Central Register of Controlled Trials, Ovid MEDLINE, ERIC (Eric.ed.gov), PubMed publisher-supplied, and the Cumulative Index to Nursing and Allied Health Literature. Results of the literature search were imported into EndNote and duplicates were removed. We searched for articles published from January 1966 to October 31, 2015. The search strategies for existing systematic reviews and our comprehensive evidence review are included in Appendix A. We supplemented our database searches by reviewing reference lists from recent and relevant systematic reviews. We also searched ClinicalTrials.gov and WHO International Clinical Trials Registry Platform (ICTRP), for relevant ongoing trials (Appendix B). We updated our search on October 20, 2016.

Study Selection

Two reviewers independently reviewed 8,230 titles and abstracts using an online platform (Abstrackr91) and 1,088 articles (Appendix A Figure 1) against specified inclusion criteria (Appendix A Table 1). We resolved discrepancies through consensus and consultation with a third investigator. We excluded articles that did not meet inclusion criteria or those we rated as poor quality. Appendix C lists all excluded trials.

For screening questions (KQ1, 2 and 5) the screening population of interest for all questions was asymptomatic children aged 10–18 years. We included screening studies in primary care-referable settings or school-based screening programs using FBT with or without a scoliometer, as well as surface topography (Moiré). No screening tests were excluded. For KQ1 through KQ4, we included randomized trials, controlled trials, and cohort studies; for KQ5 and KQ6 (harms) we also included case series and case-control studies. Studies of poor quality, case reports, qualitative studies, and cost-effectiveness studies were excluded. Screening accuracy studies had to include X-ray confirmation; we excluded screening studies in which screening was done by a single person or the screening practitioner was not well described. We excluded studies in which the referral criteria were not quantitatively described (e.g., referral to X-ray “at 5 degrees or higher trunk rotation on scoliometer” would be included, while referral to X-ray based “on any asymmetry in appearance” would be excluded). We also excluded studies in which the flow of participants was incompletely described, and studies in which less than 60 percent of those who screened positive received X-ray. For screening effectiveness (KQ1), we included studies that reported curve severity or any health outcomes, quality of life, pain or functional outcomes, and mortality. For screening accuracy (KQ2), we defined scoliosis as a Cobb angle greater than or equal to 10 degrees. For harms of screening (KQ5), we included studies that reported any direct harm of screening procedures persisting 6 months after screening.

For treatment questions (KQ3 and KQ6), we included studies of children and adolescents aged 10–18 years diagnosed with AIS with a Cobb angle of 10–50 degrees at detection. We excluded populations with infantile- or juvenile-onset scoliosis and scoliosis of other known etiology. Since children with curves above 45–50 degrees are likely to present clinically and therefore are not likely to be candidates for screening, we required included studies to contain some data on a screening population of children with curves between 10–50 degrees, which we operationalized as curve data reported before the curve has reached 50 degrees. We included studies with a
comparison of observation or usual care, and excluded comparative effectiveness studies and studies in which the comparison group was determined post-hoc or represented stratified results, such as compliant and non-compliant with brace wear. Studies of surgical and non-surgical treatments were eligible, but we excluded studies that exclusively evaluated out-of-date treatments (Harrington rod instrumentation, Milwaukee brace, and electrical surface stimulation) and studies in which treatment was conducted by a single practitioner (e.g., single surgeon, single therapist, single bracer). For treatment effectiveness (KQ3), we included studies that reported adult health outcomes pertaining to morbidity, quality of life, functional outcomes, or mortality. We included treatment harms (KQ6) persisting 6 months or more after treatment initiation. We considered pain and functional outcomes as health outcomes for KQ3 (e.g., quality of life, pain, morbidity).

For the natural history question (KQ4), we included randomized clinical trials (RCTs), controlled trials, cohort studies, and large registry-based observational studies of screen-detected children and adolescents aged 10–18 years who were diagnosed with AIS that has a Cobb angle ≥10 degrees. We included studies of any treatment type (including Harrington rod or Milwaukee brace). We excluded healthy controls from analysis.

For applicability to U.S. practice, we focused on studies that were conducted in countries deemed “very high” development according to the United Nations’ Human Development Index. We only included studies published in English. We excluded studies rated as poor quality, case reports, cross-sectional studies, and cost-effectiveness studies.

**Quality Assessment and Data Abstraction**

At least two reviewers critically appraised all articles that met the inclusion criteria based on the USPSTF’s design-specific quality criteria (Appendix A Table 2). We supplemented these criteria with the Newcastle Ottawa scales for cohort and case-control studies. We rated articles as good, fair, or poor quality. In general, a good-quality study met all criteria. A fair-quality study did not meet, or it was unclear if it met, at least one criterion but had no known important limitations that could invalidate its results. A poor-quality study had a single fatal flaw or multiple important limitations. The most common fatal flaws for screening studies included unclear referral criteria for the screening exam or unclear diagnostic threshold. We excluded poor-quality studies from this review. Disagreements about critical appraisal were resolved by consensus and, if needed, in consultation with a third independent reviewer.

One reviewer extracted key elements of included studies into standardized evidence tables in Microsoft Excel® (Microsoft Corporation, Redmond, Washington). A second reviewer checked the data for accuracy. Evidence tables were tailored to each KQ and to specific study designs. Tables generally included details on study design and quality, setting and population (e.g., country, inclusion criteria, age, sex, race/ethnicity, maturity of population), screening and treatment details, reference standard or comparator details (if applicable), length of followup, and outcomes (e.g., accuracy, effectiveness, harms).
Data Synthesis and Analysis

Because of the limited number of studies and the heterogeneity of outcomes assessed, interventions used, and presentation of results (such as categories of scoliosis curves), we provided a narrative synthesis of results and used summary tables to compare results across different studies. For KQ2 (accuracy), we calculated values from data provided where possible.

We used a standardized summary of evidence table to summarize the overall strength of evidence for each KQ. This table included the number and design of included studies, summary of findings by outcome, consistency or precision of results, reporting bias, summary of study quality, limitations of the body of evidence, and applicability of the findings.

Grading the Strength of the Body of Evidence

We graded the strength of the overall body of evidence for each KQ. We adapted the Evidence-based Practice Center approach,91 which is based on a system developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.92 Our method explicitly addresses four of the five Evidence-based Practice Center-required domains: consistency (similarity of effect direction and size), precision (degree of certainty around an estimate), reporting bias (potential for bias related to publication, selective outcome reporting, or selective analysis reporting), and study quality (i.e., study limitations). We did not address the fifth required domain—directness—as it is implied in the structure of the KQs (i.e., pertains to whether the evidence links the interventions directly to a health outcome).

Consistency was rated as reasonably consistent, inconsistent, or not applicable (e.g., single study). Precision was rated as reasonably precise, imprecise, or not applicable (e.g., no evidence). Reporting bias was rated as suspected, undetected, or not applicable (e.g., when there is insufficient evidence for a particular outcome). Study quality reflects the quality ratings of the individual trials and indicates the degree to which the included studies for a given outcome have a high likelihood of adequate protection against bias. The body of evidence limitations field highlights important restrictions in answering the overall KQ (e.g., lack of replication of interventions, nonreporting of outcomes important to patients).

We graded the overall strength of evidence as high, moderate, or low. “High” indicates high confidence that the evidence reflects the true effect and that further research is very unlikely to change our confidence in the estimate of effects. “Moderate” suggests moderate confidence that the evidence reflects the true effect and that further research may change our confidence in the estimate of effect and may change the estimate. “Low” indicates low confidence that the evidence reflects the true effect and that further research is likely to change our confidence in the estimate of effect and is likely to change the estimate. A grade of “insufficient” indicates that evidence is either unavailable or does not permit estimate of an effect. Two independent reviewers rated each KQ according to consistency, precision, reporting bias, and overall strength of evidence grade. We resolved discrepancies through consensus discussion involving more reviewers.
Expert Review and Public Comment

A draft research plan that included the analytic framework, KQs, and inclusion criteria was available for public comment in October 2015. We made only minor changes to our scope and review methods based on the comments received.

A draft version of this report was reviewed by invited content experts and federal partners listed in the acknowledgements. Comments received during this process were presented to the USPSTF during its deliberation of the evidence and, subsequently, addressed in this version of the report.

USPSTF Involvement

The authors worked with four USPSTF liaisons at key points throughout the review process to develop and refine the analytic framework and KQs and to resolve issues regarding the scope for the final evidence synthesis. This research was funded by the Agency for Healthcare Research and Quality (AHRQ) under a contract to support the work of the USPSTF. AHRQ staff provided oversight for the project, assisted in external review of the draft report, and reviewed the draft report.
Chapter 3. Results

Literature Search

We reviewed 8,230 unique abstracts and 1,088 full-text articles (Appendix A Figure 1). We included 26 unique articles. We included seven studies (13 articles) on screening accuracy (KQ2), seven studies (nine articles) on the effectiveness of treatment (KQ3), one study (two articles) on the harms of treatment (KQ6), and two studies (five articles) on long-term outcomes (KQ4). No studies met our inclusion criteria on the effect of AIS screening on long-term health outcomes (KQ1) or on the harms of screening (KQ5).

Of 179 full-text articles reviewed for eligibility for KQ2, seven fair-quality screening programs (13 articles) including 447,243 adolescents met our inclusion criteria. Articles were most commonly excluded for ineligible or inadequately described screening programs or for lack of relevant outcomes.

Of the 733 full-text articles reviewed for eligibility for KQ3, seven studies (nine articles) of 835 individuals with AIS met our inclusion criteria, including two studies of physiotherapeutic scoliosis-specific exercise treatment (one of fair quality and one of good quality) and five studies of bracing treatment (three of fair quality and two of good quality). No studies of surgery or other treatments met our inclusion criteria. Most common reasons for exclusion were ineligible study design and ineligible outcomes, most commonly for incomplete data to inform the question. Among the six studies excluded based on quality, the most common reasons for exclusion were inadequate information on the study population and imprecise selection of control groups.

Of the 263 full-text articles reviewed for KQ4, two fair-quality studies (five articles) of 339 individuals with AIS met our inclusion criteria. Most common reasons for exclusion were ineligible study design and ineligible outcomes, most commonly for lack of adult health outcomes reported.

Of the 733 full-text articles reviewed for eligibility for KQ6, one good-quality observational study (two articles) of 242 individuals with AIS met our inclusion criteria.

Results of Included Studies

KQ1. Does Screening for Adolescent Idiopathic Scoliosis Improve: a) Health Outcomes and b) the Degree of Abnormal Spinal Curvature in Childhood or Adulthood?

We found no RCTs or controlled clinical trials that evaluated the impact of screening for AIS on severity of curve or adult health outcomes compared to no screening.
KQ2. What Is the Accuracy of Screening for Adolescent Idiopathic Scoliosis?

Summary of Results

Seven fair-quality screening programs (13 articles) of 447,243 adolescents met our inclusion criteria. Three of the seven studies included some followup data on children who screened negative. Accuracy increased with the number of screening tests used. Sensitivity and specificity (93.8% and 99.2%) and predictive value (81.0%) were highest, and false positive rates were lowest (0.8%; 6.2% false negative) in a Hong Kong clinic-based screening program using FBT with scoliometer followed by intermediate Moiré screening in suspected cases, a screening approach that may have limited practical applicability in U.S. settings. A retrospective review of a U.S. school-based screening program that initially used FBT alone and added scoliometer partway through the study period found a sensitivity of 71.1 percent (95% CI, 54.1 to 84.6), a specificity of 97.1 percent (95% CI, 96.3 to 97.7) and a false negative rate of 28.9 percent (2.9% false positive rate). The lower sensitivity of the U.S. screening program may be due to the absence of Moiré screening and absence of scoliometer use for part of the program.93 Estimates of positive predictive value for FBT plus scoliometer ranged from 29.3 percent7 to 54.1 percent.94-96 Predictive values were lowest for single modalities, from 5.0 percent for rib hump measurement to 17.3 percent for FBT alone.52 Detected curves were 10–20 degrees at screening for 40.7 percent to 87.4 percent of true-positive children, and above 40 degrees for 0.8 percent to 22.2 percent of true-positive children.

Detailed Results

Description of Included Studies

Screening programs ranged from 2,242 children screened7 to 306,082 children screened54, 93, 97 (Table 1 and Table 2). The Hong Kong screening program was conducted in regional clinics; all other screening programs were conducted in school settings. Children screened ranged from age 8 to 16, though precise ages were inconsistently reported across studies, sometimes using grade levels or age ranges. One of the seven programs, which had the smallest study population, took place in the United States.

All studies used the FBT with some quantitative measurement of trunk rotation; six of seven studies used a scoliometer; one used a level plane and ruler.98-100 A screening program conducted in Samos Island, Greece, also screened children with Moiré topography and measurement with a humpometer; however, estimates were not provided for any combinations of screening modalities such as FBT plus scoliometer.52 The large screening program from Hong Kong also included an intermediate post-FBT Moiré topography screening for children with ATR between 5–15 degrees on scoliometer.54, 93, 97 Screenings were conducted by nurses, physical therapists, or school physicians; in two screening programs, both conducted in Greece, orthopedic surgeons conducted the screenings.52, 98-100 Referral criteria to X-ray testing varied from any trunk rotation52 to trunk rotation of 15 degrees or more54, 93, 97 many programs referred to X-ray on one of multiple criteria, including subjective judgment of the screener. All studies used either 10 degrees or greater than 10 degrees Cobb angle of the major curve as criteria for a diagnosis of
scoliosis.

Five of seven studies reported results of a single screening episode; eight, fifty-two, ninety-four to ninety-six, ninety-eight to one hundred and one two reported cumulative results of multiple years of repeated screening. Seventy, fifty-four, ninety-three, ninety-seven Three of the seven screening programs reported data on 311,086 children who had screened negative at initial screening using a case definition of greater than 10 degrees or ≥10 degrees Cobb angle fifty-two, fifty-four, ninety-three, ninety-seven (Table 1). In the U.S.-based study, a regional epidemiologic index was used to identify all cases of AIS in the region where the screening program had been conducted, thus enabling the detection of the eventual development of scoliosis in someone who had screened negative. In Hong Kong, data from the regional health department and two specialist hospitals were reviewed to identify scoliosis cases diagnosed until age nineteen. Fifty-four, ninety-three, ninety-seven It is worth noting that in both of these programs, significant time could have elapsed between screening and eventual detection of AIS. In Samos Island, Greece, a companion study of screening for lung disease allowed X-ray screening of all children regardless of their scoliosis screening results. Fifty-two Although incomplete data is provided on each screening modality explored, accuracy measures can be calculated from the numbers provided.

In the Ireland screening program, screen-negative children were re-screened after 1 to 4 years; however, data is only provided for cases ≥40 degrees Cobb angle. Ninety-four to ninety-six

Study Results: Screening Accuracy

Three of the seven screening programs reported data on 311,086 children who had screened negative at initial screening, allowing estimation of sensitivity, specificity, false positives, false negatives, and predictive value. The remaining four studies did not report followup data on screen-negative children; for these only positive predictive values are reported (Table 3).

Sensitivity/specificity. Sensitivity was 71.1 percent (95% CI, 54.1 to 84.6) and specificity was 97.1 percent (95% CI, 96.3 to 97.7) for FBT with scoliometer over multiple years of screening. For FBT with scoliometer plus intermediate Moiré screening before X-ray confirmation, sensitivity was 93.8 percent (95% CI, 93.3 to 94.3) and specificity was 99.2 percent (95% CI, 99.2 to 99.2). For FBT alone on one-time screening, sensitivity was 84.4 percent (95% CI, 67.2 to 94.7) and specificity was 95.2 percent (95% CI, 94.3 to 95.9). Estimates for other single modality, one-time screenings included rib hump measure (sensitivity 93.8% [95% CI, 79.2 to 99.2], specificity 78.5% [95% CI, 76.9 to 80.0]); scoliometer alone (sensitivity 90.6% [95% CI, 75.0 to 98.0], specificity 80.7% [95% CI, 79.1 to 82.1]); and Moiré topography (sensitivity 100% [95% CI, 84.2 to 100], specificity 85.4% [95% CI, 84.0 to 86.7]). The variation in reported sensitivity may be due to the heterogeneity of screening modalities used; one analysis of the cohort screened with FBT, scoliometer, and Moiré demonstrated that the sensitivity would drop substantially if Moiré screening was excluded from the program. Another analysis of this cohort also demonstrated that accuracy of screening (defined as sensitivity + positive predictive value) was directly related to the number of screening tests used in combination, being highest when three tests (ATR + Moiré + clinical signs) were employed, lower with various combinations of two tests, and lowest when a single test (ATR) was used alone.
**False-positive and false-negative rates.** The lowest false negative and false positive rates were for FBT with scoliometer followed by Moiré topography for suspected cases before X-ray confirmation (0.8% false positive, 6.2% false negative). A U.S.-based study of FBT with scoliometer found 2.9 percent false positives and 28.9 percent false negatives.\(^7\) FBT alone had 4.8 percent false positive (15.6% false negative) in one study. Other single-modalities were associated with the highest false positive rates: 19.3 percent (9.4% false negative) for scoliometer alone; 14.6 percent (0% false negative) for Moiré topography alone; and 21.5 percent (6.3% false negative) for rib hump measure alone.\(^52\)

**Predictive value.** Estimates of positive predictive value were available in all seven studies; predictive value estimates for FBT plus scoliometer ranged from 29.3 percent\(^7\) (95% CI, 20.3 to 39.8) to 54.1 percent (95% CI, 40.8 to 66.9).\(^94-96\) The highest predictive value was 81.0 percent (95% CI, 80.3 to 81.7) for FBT with scoliometer and Moiré screening;\(^54, 93, 97\) The lowest estimates were for single modalities, ranging from 5.0 percent (95% CI, 3.4 to 7.0) for rib hump measurement to 17.3 percent (95% CI, 11.7 to 24.2) for FBT alone.\(^52\)

**Study Results: Curve at Screen-Detection**

Two of seven studies provided data comparing the degree of curvature in children with screen-positive and false-negative screening results and eventual scoliosis diagnosis.\(^7, 54, 93, 97\) In the U.S.-based study, distributions of curve were similar for children detected through school-based screening compared to those who were detected clinically\(^7\) (Table 4). However, in the Hong Kong-based, multi-tiered screening program, curve distributions in screen-detected cases tended to be a lower degree of curvature (curves of 10–19 degrees comprised 50.9 percent of the screen-detected versus 26.2 percent of the false-negative population).\(^54, 93, 97\)

In the five studies with data on screen-detected cases only, the majority of cases detected were at Cobb angles of less than 20 degrees (Table 4), a level at which expectant management may be the most common treatment. All studies reported different categories of curvature. Four studies reported proportions of children with curves over 40 degrees at detection (a degree that may warrant surgical intervention), of 0.8 percent,\(^98-100\) 5.6 percent,\(^54, 93, 97\) 6.1 percent,\(^94-96\) and an especially high 22.2 percent in the U.S.-based study.\(^7\) This study also found the lowest reported sensitivity with use of either FBT alone or FBT plus scoliometer. Curves of milder magnitude would be less likely to be identified by less-sensitive screening regimens, especially FBT alone. Two studies reported proportion of screen-detected cases at 30 degrees (where bracing may be recommended); of 14.2 percent\(^8\) for 30 degrees or higher and 1.8 percent for 30 to 39 degrees.\(^98-100\)

**Limitations**

All studies were fair-quality observational studies with heterogeneity of screening modality, screeners, and screening procedures. The single U.S.-based study began with FBT alone and progressed to FBT with scoliometer during the study period, which may attenuate estimates of screening accuracy. In addition, the only study that prospectively conducted gold-standard X-ray on all children regardless of screening result screened children as young as age 8, which is outside the accepted definition of AIS (age 10–18).\(^52\) Further, the accuracy of combinations of
screening modalities, such as FBT plus scoliometer, are not reported and thus may not completely reflect current clinical practice. This heterogeneity precluded direct comparison across studies, and resulted in significant variation in reported screening sensitivity and in the percentage of individuals with higher degrees of curvature at diagnosis. The single study that had very high accuracy was clinic-based, conducted by physicians and nurses, and used a unique multi-tiered screening procedure, in which children with suspected AIS were screened with Moiré topography before referral to X-ray confirmation. Screening populations and disease-positive populations were generally not described in detail, and no subgroup analyses were reported, limiting assessment of population characteristics and their potential contributions to the heterogeneous accuracy estimates.

KQ3. Does Treatment of Adolescent Idiopathic Scoliosis That Has a Cobb Angle of Less Than 50 Degrees at Diagnosis Improve: a) Health Outcomes and b) the Degree of Spinal Curvature in Childhood or Adulthood?

Summary of Results

Five studies (seven articles) of bracing (n=651) and two studies (two articles) of exercise treatment (n=184) met our inclusion criteria. No studies of surgery met our criteria.

Of the bracing studies, four of five prospective controlled studies (including one RCT) provide evidence for benefit of bracing treatment on curve progression compared to observed controls, either in favorable proportions of children with 5–6 degrees progression (three of five studies) or in curve progression to a degree considered bracing failure (one study). Two included trials were terminated early because of evidence of benefit favoring bracing. Quality of life outcomes associated with bracing were reported in one study and were similar between treatment arms.

The two studies of exercise treatment (one RCT, one CCT) compared an intervention group treated with a tailored, physiotherapeutic scoliosis-specific exercise regimen to a generic exercise control group. Different exercise regimens were assessed in each study; both are based on active self-correction principles. In both studies, the intervention group experienced a favorable reduction in Cobb angle at 12-month followup (RCT) or at the end of the 12-month treatment period (CCT), compared to an unfavorable increase in Cobb angle in the control group. The RCT included measures of quality of life; all of these were notable for steadily improving values at 12 months in the intervention group, compared to stable or slightly improving measures in the control group.

Detailed Results

Description of Included Studies

Brace treatment. The five studies of bracing effectiveness included one fair-quality RCT, one fair- and one good-quality prospective clinical controlled trial, one good-quality prospective observational study, and one fair-quality retrospective observational study.
The one good-quality prospective clinical controlled trial began as an RCT but was later converted to a patient preference controlled trial. All studies included a comparison group that was not initially treated with bracing; however, the studies pre-specified a clinical threshold beyond which treatment (bracing or surgery) would be initiated. Sample sizes ranged from 37 to 242 participants (Table 5).

Bracing effectiveness studies were conducted at 38 clinical sites in five countries. One study (the Scoliosis Research Society’s multi-center bracing trial, or the SRS bracing cohort) included participants from Canada, Sweden, the United Kingdom, and the United States, one included participants from both Ireland and the United States, one from Canada and the United States, one from Canada only, and one exclusively from the United States. Participants were drawn from populations referred to specialty orthopedic centers in the four prospective studies. Participants in the retrospective study were drawn from two sources: braced adolescents were identified from an earlier treatment study of girls referred to a specialty orthopedic center in Boston, USA; the observation group was identified from a school scoliosis screening program in Dublin, Ireland (Table 6).

Average age at enrollment varied from 11.9–13.1 years in the four studies that reported this; the fifth study reported that participants were between ages 10 and 15 years. Three studies included female participants only, and over 90 percent of participants in another study were female as well. The remaining study reported that about 85 percent of those who completed the study were female. Race was reported in one included study; in that trial, 78 percent of subjects were white, nine percent were black, and 13 percent were another race or unknown. Three studies specify that enrollment was limited to persons who had not previously received treatment for scoliosis; the other two studies do not comment on any previous treatment.

All studies included adolescents with different types of scoliotic curves. One study included only subjects with single major curves, two studies included subjects with both single major and double major curves, and two studies provided no information on curve type. Of the 546 adolescents for which such data are available, 397 (73%) had a single major curve, with nearly all of these (377) being single thoracic or thoracolumbar major curves.

All studies provided data on the major curve. Four studies reported the severity of curve at treatment initiation; one reported severity of curve at diagnosis. Average curve severity varied from near 20 degrees to close to 30 degrees.

Overall, 85 percent of adolescents (554/649) in the five included studies were skeletally immature (Risser sign 0 to 2). History of menarche, another marker of maturity, at the time of enrollment was reported in three studies and ranged from zero percent (0/37) to 35 percent (19/55) to 50 percent (119/240). In the randomized trial, Risser sign 0, 1, or 2 was an inclusion criteria for study entry but the baseline distribution of the enrolled population was not reported.

Two studies examined the Boston brace (the most commonly used brace in the United States) as the brace of interest, one study predominately used the Boston brace (68%) along
with multiple types of rigid thoracolumbosacral orthoses,\textsuperscript{104, 105} one study used the Charleston bending brace,\textsuperscript{103} and one study used the Spine-Cor brace.\textsuperscript{102} People in the intervention group were advised to wear the brace 23 hours per day,\textsuperscript{96, 108} 20 hours per day,\textsuperscript{102} 18 hours per day,\textsuperscript{104, 105} at least 16 hours per day,\textsuperscript{106, 107} or only at nighttime.\textsuperscript{103} Most adolescents were braced until they reached skeletal maturity or until they had curve progression significant enough to warrant surgical intervention.

Three studies reported average duration of bracing treatment, which ranged from around 2 years\textsuperscript{102, 104, 105} to around 3 years.\textsuperscript{103} Three studies ended bracing and assessed outcomes at skeletal maturity,\textsuperscript{96, 103, 106, 107} and another study ended bracing and assessed outcomes at either skeletal maturity or treatment failure (Cobb angle progression to \(\geq 50^\circ\)).\textsuperscript{104, 105} One study ended bracing at skeletal maturity, and then assessed outcomes at 5 years post-randomization (at which point all patients were at least 2 years post-skeletal maturity).\textsuperscript{102}

**Exercise treatment.** Two studies of physiotherapeutic scoliosis-specific exercise met our inclusion criteria; one good-quality RCT\textsuperscript{109} and one fair-quality CCT\textsuperscript{110} (Table 7). Both studies were conducted in Italy, and used control groups whose participants were assigned a general exercise regimen (not designed to treat scoliosis).

The RCT included 110 adolescents with AIS who were randomized to receive either an active self-correction physical therapy program focused on scoliosis and tailored to each patient’s curve, or a general exercise program. Participants received one 60-minute session per week, with instructions for home exercise, from study enrollment to skeletal maturity. Outcomes were assessed at baseline, at the end of treatment, and at 12 months. The primary outcome of the study was spinal curve described with Cobb angle on X-ray. Secondary outcomes were measures of trunk rotation assessed via scoliometer, and health-related quality of life outcomes assessed by self-administered paper survey using the SRS-22 Italian version.

Inclusion criteria included AIS patients with Cobb angle 10 to 25 degrees of major curve, skeletally immature (Risser sign 0 or 1), and age greater than 10 years. People with non-idiopathic scoliosis or other serious illness, leg-length discrepancy greater than 1 centimeter, lower limb deformities, cardiac or respiratory dysfunction, previous spinal surgery, or cognitive impairment were excluded. To recruit the participants, the authors assessed 209 consecutively seen patients of a specialist rehabilitation clinic for eligibility. Of these, 110 were found eligible, 18 refused consent to participate and 81 were ineligible. Patients were blinded to the study hypothesis but were not blinded to their treatment assignment group. Physical therapists and physiatrists could not be blinded to treatment assignment, but the principal investigator and biostatistician were both blinded.

Analyses were conducted using intent-to-treat methods and included all participants lost to followup at both end of treatment and at 12-month followup. Complete followup data was available on 90.9 percent of the intervention group (50/55) and 87.3 percent of the control group (48/55). Treatment fidelity was assessed by a physical therapist at each session. Adherence to home advice was assessed by patient diary, but results were not reported. Program completion was 94.5 percent in the intervention group (52/55) and 92.7 percent in the control group (51/55).
The CCT included 74 participants (mean age 12 years, 70.3% female) who were assigned based on patient preference to either a physiotherapeutic scoliosis-specific exercise regimen (Scientific Exercises Approach to Scoliosis) or to a general exercise program. Intervention group participants received one 90-minute session at the Italian Scientific Spine Institute every 2–3 months, which included evaluation by a physiotherapist and instruction in an individually-adapted exercise protocol, plus twice-weekly 40-minute sessions at a rehabilitation facility near their home and instructions to perform one daily exercise at home. Control group participants performed various different exercise protocols at a local facility 2–3 times per week. The primary outcome measures included progression of Cobb angle and ATR; authors also reported on the number of participants in each group that required additional treatment with bracing. Outcomes were reported after 12 months of treatment.

Study enrollees included 74 consecutive new AIS patients who fit inclusion criteria seen at a specialty referral center for management of scoliosis. Included participants had AIS without previous treatment and were considered “at risk of bracing,” defined as either proven radiographic progression; Cobb angle >15 degrees or ATR >7 degrees with first signs of puberty, pre-menarchal status, and Risser value 0–1; or Cobb angle >20 degrees and Risser value of 2 or 3. Persons with secondary scoliosis, conditions known to be possible causes of scoliosis, neurological deficits, leg length discrepancy of >10 mm, Risser value >3, or previous treatment for scoliosis were excluded.

As noted above, participants were assigned to intervention or control groups based on personal preference. Treating physicians and physiotherapists were not blinded to the treatment of each subject but were unaware of the study being performed. Clinical evaluation occurred every 6 months; radiographic measurement was repeated after 12 months of treatment, when the study ended. The overall compliance rate was reported as 95%; no statistically significant difference was found between the two groups. Completion rates were 94% (33/35) in the intervention group and 92% (36/39) in the control group.

Study Results: Bracing Studies

Curve progression in adolescence. All three controlled studies\(^{103-107}\) and the one RCT\(^{102}\) showed evidence supporting the effectiveness of bracing in reducing curve progression. The one included retrospective study did not demonstrate an effect of bracing on curve progression\(^{96}\) (Table 8).

All bracing studies reported measures of scoliotic curve progression assessed by X-ray and reported as Cobb angle in degrees, although the specific criteria used to define meaningful progression varied. Measures included either the absolute increase in curvature,\(^{96, 102, 103, 106, 107}\) or curve progression to a threshold at which bracing treatment was felt to have failed, typically to 45–50 degrees Cobb angle, when surgery may be considered.\(^{96, 102-105}\) Only one study presented dose-response data on the association between daily hours of brace wear and curve progression.\(^{104, 105}\) The different endpoints reported provide information on different aspects of treatment effect but precluded pooling of results and direct comparison between studies. In addition, any possible effect associated with different braces, different curves, or different populations cannot adequately be assessed with the data available.
Association between bracing and curve progression of a defined number of degrees. The four studies that evaluated number of degrees of increase in curvature in braced versus observed populations reported mixed results. Three controlled prospective studies\textsuperscript{102, 103, 106, 107} suggested a benefit to bracing in slowing curve progression of 5 or 6 degrees; one prospective study\textsuperscript{103} and one retrospective study\textsuperscript{96} showed limited differences in progression of 10 degrees or more between braced and observed groups.

Three studies that evaluated relatively small amounts of curve progression (5 and 6 degrees) showed significantly less progression in the braced compared to control group.\textsuperscript{102, 103, 106, 107} In the randomized trial of SpineCor bracing, progression of 6 or more degrees over the 5-year study period occurred less frequently in the intervention group than the control group (34.4\% vs. 75\%; p=0.0008).\textsuperscript{102} In this trial, the control group was halted early (after the recruitment of 68 patients) because of evidence of benefit in the braced group. One study of nighttime-only bracing\textsuperscript{103} was performed exclusively in 37 pre-menarchal girls with a Risser sign of 0 (average age 12.0 years); results showed that after about three years of treatment, curve progression of 5 degrees or more was less likely in the braced group compared to control (15/21 intervention vs. 16/16 control; p=0.023). A study in which 240 subjects aged 10 to 15 were braced at least 16 hours per day and followed until skeletal maturity for up to four years\textsuperscript{106, 107} found that 17/111 braced subjects had a curve progression of 6 degrees or more compared with 58/129 control subjects (does not include 23/111 braced subjects and 9/129 control subjects who were lost to followup). A worst-case analysis—which assumed the 23 braced subjects who were lost to followup were treatment failures—found that brace treatment was successful at preventing curve progression of 6 degrees or more compared with the control group (p=0.0005).

Conversely, one study of full-time bracing (23 hours per day) did not show a significant difference in curve progression between braced and control subjects. The retrospective study followed 64 Risser 0 girls from brace initiation up to the point of weaning to part-time bracing,\textsuperscript{96} and it demonstrated progression of at least 10 degrees in 18.8\% of intervention subjects versus 28.1\% of observed subjects, and a mean change in Cobb angle of 1.6 (standard deviation [SD] 8.2) in intervention subjects compared to 4.9 (SD 10.2) in control subjects. However, neither of these differences is statistically significant, and it should be noted that this study is not adequately powered to address this question.

Association between bracing and curve progression past a “failure” threshold. Four studies evaluated the progression of curvature past an absolute threshold at which bracing treatment was considered failed.\textsuperscript{96, 102-105} The largest of these demonstrated a significant benefit associated with bracing; the randomized trial suggested lesser progression in the braced group but significance was not reported; two smaller studies found similar results between braced and control populations.

One international prospective clinical controlled trial (the Bracing in Adolescent Idiopathic Scoliosis Trial, or BrAIST) assessed the effectiveness of bracing 18 hours per day at preventing progression of Cobb angle past 50 degrees.\textsuperscript{104, 103} The study planned to follow participants through skeletal maturity. However, as with the SpineCor bracing trial, the BrAIST study was terminated early by the safety monitoring board due to a marked treatment benefit in favor of bracing. In the full as-treated analysis (which included both randomized and preference cohorts),
28 percent (41/146) of braced subjects had progression of Cobb angle past 50 degrees, compared to 52 percent (50/96) of untreated subjects. The odds ratio for the study’s definition of a successful outcome (skeletal maturity without progression past 50 degrees) was 1.93 (95% CI, 1.08 to 3.46), adjusted for propensity score quintile and duration of followup. Data from the intention-to-treat analysis (RCT cohort) likewise showed a statistically significant effect of bracing, with progression past 50 degrees in 25 percent of braced subjects and 58 percent of untreated subjects (the odds ratio for a successful outcome was 4.11; 95% CI, 1.85 to 9.16, unadjusted). The number needed to treat in order to prevent one case of curve progression past 50 degrees was 3.0 (95% CI, 2.0 to 6.2), and the reduction in relative risk with bracing was 56 percent (95% CI, 26 to 82).

In the randomized trial of SpineCor bracing, more participants progressed to a curve of 45 degrees or more (3/26 in the intervention versus 3/21 in the control group, significance not reported). 102 One prospective study of 37 Risser 0 girls examined the effect of nighttime-only bracing on prevention of progression of Cobb angle past 50 degrees. 103 Adolescents were followed for about three years; during that time, 19 percent (4/21) of braced subjects and 12 percent (2/16) control subjects had curves that progressed past 50 degrees, which was not statistically significant (p=0.472). A second retrospective study of 64 Risser 0 girls examined data on braced subjects from treatment initiation up to the point of weaning to part-time brace or progression-of-curve past 45 degrees; control subjects were drawn from a different cohort, and selected for matching age, Cobb angle, maturity, and length of followup. 96, 108 The study found that 3.1 percent (1/32) of braced subjects and 6.3 percent (2/32) of control subjects had progression of Cobb angle to 45 degrees or more (reported as not significant; no p value provided).

**Association between daily hours of brace wear and curve progression past a defined number of degrees.** The single included study that assessed the association between daily hours of brace wear and degrees of increase of curvature demonstrated a benefit associated with increased hours of brace wear. This study (BrAIST, discussed previously in this section) included 116 subjects for whom data on daily duration of brace use was available. Results demonstrated a significant inverse correlation between quartile of daily duration of brace wear (measured by heat sensors) and the likelihood of progression of curve to 50 degrees or more. Average brace wear of 0–6 hours per day was associated with a 59 percent likelihood of progression to 50 degrees or more, while brace wear of 12.9 or more hours per day was associated with a 7–10 percent likelihood of progression to 50 degrees or more (p<0.001).

**Curve progression in adulthood.** Cobb angle in adulthood was assessed in one included study, which suggested little progression in adulthood in either treated or observed individuals with curves of moderate magnitude. Seventy-seven of the original 106 girls that had been enrolled at two of the centers in the SRS bracing cohort were re-evaluated an average of 16 years after skeletal maturity (average age 32 years). 111, 112 Average Cobb angles at maturity in this cohort were similar in both observed and braced groups (30.6 degrees in observed participants, 27.7 degrees in braced participants; p=0.067). Between skeletal maturity and adult followup, average Cobb angle had increased by an average of 4.4 degrees (SD 4.1) in observed patients; and by an average of 6.4 degrees (SD 5.8) in braced patients. Only 7.5 percent (3/40) of observed individuals and 5.4 percent (2/37) of braced individuals had progression of the curve past 45
degrees at the time of followup (p>0.99).

**Other health outcomes.** One included study of bracing effectiveness collected data on quality-of-life and back pain.\(^{104, 105}\) Quality-of-life data was collected using the Pediatric Quality of Life Inventory (PedsQL). Data on specific questions were not provided; however, the authors stated that average PedsQL scores did not differ between intervention and control groups at baseline (braced subjects 83.8, observed subjects 83.3; p=0.80) or at the final followup assessment (braced subjects 82.0, observed subjects 81.9; p=0.97). There also was no significant difference in reported back pain between intervention and control groups at baseline (p=0.32) or at final followup (p=0.29) (Table 9 and Appendix D).

**Study Results: Exercise Treatment**

**Curve progression.** Both included studies reported outcomes that favored the active self-correction intervention group at statistically significant levels.

In the RCT,\(^{109}\) the intervention group experienced a mean improvement in Cobb angle of 4.9 degrees at 12-month followup, compared to the control group’s increase of 2.8 degrees (p<0.001). Similar trends were seen in ATR measured on scoliometer, with a mean improvement of 3.7 degrees in the intervention group compared with a 0.4 degree improvement in the control group (p<0.001) (Table 10). The control group had a higher rate of progressing 5 degrees or more at the end of treatment (8% vs 0%, no test of significance reported). Conversely, the intervention group saw a higher rate of improvement of 5 degrees or less at the end of treatment (62% vs 0%, no test of significance reported) (Table 11).

In the CCT,\(^{110}\) the average magnitude of all curves (reported as Cobb angle) for each individual decreased by 0.67 degrees at 12-month followup in the intervention group, and increased by 1.38 degrees in the control group (p<0.05) (Table 10). Changes in ATR and in the magnitude of the major curve alone also were reported; results showed a similar pattern, but were not statistically significant.

**Quality of life.** Quality of life outcomes reported in the RCT were measured with the SRS-22 Italian version. All measures suggested generally stable to slightly improving self-reported measures of pain, function, self-image, and mental health in the control group, compared to steadily improving assessment of each of these in the intervention group. All trends were statistically significant between groups (Table 10).

**Limitations**

For studies of brace treatment, heterogeneity in the type of braces and outcome measures used—especially of curve progression reported—limits our ability to make direct comparisons across studies and to accurately assess the magnitude of treatment effect. Only one study reported long-term followup data that described a limited subset of the study population. Information on quality of life and other health outcomes also was available in only one bracing study. As noted above, two included trials were terminated early because of evidence of benefit favoring bracing.
The evidence base for the other two categories of treatment for AIS (exercise and surgery) is hampered by a lack of evidence pertinent to a screening-relevant population (i.e., curves of <50 degrees at diagnosis). Only two studies of exercise treatment met our inclusion criteria. A large body of literature on surgical treatment of AIS exists, but studies that include any comparison group are sparse. We found none that include a comparison group of non-surgically treated individuals, not surprising given that surgery generally is reserved for more severe curves. However, we found no data on surgical outcomes in children with screen-detected AIS, and no data on the course of progression or treatments used pre-surgery.

KQ4. What Is the Association Between Severity of Spinal Curvature in Adolescence and Health Outcomes in Adulthood?

Summary of Results

Two fair-quality studies (five articles) of 339 people with AIS followed up in adulthood met our inclusion criteria. Both included studies were retrospective observational long-term followup analyses of individuals with AIS diagnosed during adolescence. One study evaluated a cohort of 77 adults who were either braced or observed during adolescence as part of a bracing study; the other included various subsets of a cohort of 283 persons with AIS who had been consecutively referred to a regional center for bracing or surgical treatment during adolescence, 262 of whom were assessed in adulthood. Followup occurred at least 11 years after skeletal maturity in the smaller cohort, and at least 20 years post-treatment in the larger cohort.

No included studies reported health outcomes data stratified by degree of curvature at skeletal maturity, and therefore no included studies directly address this question as worded. The included studies provide insight into adult health outcomes stratified by treatment regimen during adolescence. Both general and scoliosis-specific quality of life measures (SF-36 and SRS-22) were similar between observed and braced participants at adult followup in one study. Oswestry Disability Index scores, general well-being, self-esteem, social activity, pulmonary outcomes, and childbearing and pregnancy outcomes were similar in adulthood in people braced or surgically treated in adolescence.

Braced participants rated their body appearance as more distorted than did untreated participants. Braced individuals also recalled experiencing a negative effect on their life during the treatment period compared to those treated surgically.

Detailed Results

Description of Included Studies

Treatment in adolescence. Both included studies were conducted in Sweden. One study comprised 100 adults with AIS who originally had participated in the SRS bracing cohort as adolescents, and had been enrolled at one of the two Swedish centers in the study; 77 of these participants enrolled in the followup study. The other cohort consisted of 283 individuals with AIS (referred to here as the “Goteborg cohort”) who as adolescents had been consecutively referred to Sahlgrenska University Hospital in Goteborg, Sweden, for bracing or surgical
treatment between 1968 and 1977. The largest follow-up paper on this cohort enrolled 262 participants.

The average age of participants in the SRS bracing cohort was 32 years at the time of follow-up, and all were evaluated between 11–18 years after skeletal maturity (mean of 16 years). Participants in the Goteborg cohort were an average age of 39 years at followup and were at least 20 years post-treatment (average of 22–23 years) (Table 12). The SRS bracing cohort consisted of females only, and more than 90 percent of the Goteborg cohort were female. No other demographic data were reported (Table 13).

Degree of curvature at diagnosis and at skeletal maturity was similar in the braced and observation groups in the SRS followup study. Mean Cobb angle of the largest curve was similar in the two groups at baseline (30.5° in the braced group, 29.2° in the observation group) and at skeletal maturity (27.7° and 30.6°, respectively). Consistent with treatment recommendations for bracing and surgery, Cobb angle at diagnosis differed between braced and surgical groups in the Goteborg cohort (33.2° in the braced group, 61.8° in the surgery group) but was similar at the end of treatment (29.7° in the braced group, 33.1° in the surgery group; p<0.05) (Table 13). Type of curve at diagnosis was reported in one study: in the Goteborg cohort, 60 percent of braced participants and 76 percent of surgically treated participants had single thoracic or thoracolumbar curves.

Twenty-six adolescents in the SRS bracing cohort were treated with a Boston brace for 22–24 hours daily until skeletal maturity; none of these had curve progression that required surgical treatment in adolescence. Sixty-five adolescents in the observed cohort were untreated unless their major curve increased by ≥6 degrees before skeletal maturity; these participants were braced if the curve reached 30–40 degrees (13 participants, 11 of whom enrolled in the followup study) or treated surgically if the Cobb angle reached greater than 40 degrees (6 participants, none of whom enrolled in the followup study). All participants in the Goteborg cohort received either brace treatment for curves of 24–50 degrees until skeletal maturity. Curves greater than 50 degrees (and lumbar curves >60 degrees) were treated surgically with Harrington distraction and fusion, followed by postoperative bracing for 6–12 months.

**Followup in adulthood.** Long-term followup of 77 of the original 100 who had participated in the SRS bracing cohort was performed an average of 16 years after skeletal maturity, when participants were an average age of 32 years. Between skeletal maturity and adult followup, Cobb angles had increased by an average of 4.4 degrees (SD 4.1) in observed patients; and by an average of 6.4 degrees (SD 5.8) in braced patients. Quality-of-life assessments also were conducted using the SRS-22, SF-36, and Spinal Appearance Questionnaire (SAQ).

In the Goteborg cohort, adult outcomes were assessed in 262 of the 283 original study cohort at an average of 22–23 years after completion of treatment, when participants were an average age of 39 years. Average Cobb angle at adult followup was 37.6 degrees (SD 14.7) for braced participants and 36.5 degrees (SD 9.7) for surgically-treated participants (this study did not meet inclusion criteria for KQ3). Quality of life assessments were done at adult followup using SF-36, the Oswestry Disability Index, and the Psychological General Well-Being Index.
Pulmonary function was assessed in 251 participants from the Goteborg cohort. Total lung capacity (TLC), forced expiratory volume (FEV1), and vital capacity (VC) were measured in the 141 surgically treated and 110 brace-treated participants before the beginning of treatment, 1.4 years after surgery (for the subset of surgically treated participants), and at followup. In addition, pregnancy outcomes were assessed by self-report in 247 participants from the Goteborg cohort.

**Study Results: Quality-of-Life Outcomes**

No data were provided in either included study on the association between curve at skeletal maturity and adult quality-of-life outcomes. However, both included studies presented adult outcomes based on treatment received in adolescence. The SRS-22, SF-36, and Oswestry Disability Index are all widely validated measures used in research; several other measures are also reported.

**SRS-22.** The SRS-22 is a scoliosis-specific measure of quality of life and function for scoliosis patients; it contains 22 items that are categorized into pain, self-image, function, and mental health domains, scored from one (worst) to five (best); a total score also is calculated with or without satisfaction with management. One paper measured SRS-22 in adulthood, but did not provide measures of association with curvature at skeletal maturity. Adult scores on all SRS-22 domains were similar and not statistically significant between people braced and observed in adolescence (Table 14).

**SF-36.** The SF-36 is a global, not disease-specific, measure of health-related quality of life. It contains 36 items that are scored into eight domains of physical or mental health, scored from zero (worst) to 100 (best), calibrated to a population norm of 50. SF-36 questionnaire results were reported in both cohorts; both studies found no statistically significant differences between groups (braced vs. observed; or braced vs. surgically treated) on any domains (Table 15).

In the Goteborg cohort followup, the authors report no correlation between curve size after treatment and scores on the physical functioning, general health, and mental health subscales of the SF-36, but numeric data were not provided. There also was no difference between participants with curves of greater than 50 degrees at followup and those with curves of less than 50 degrees on the physical functioning, general health, and mental health subscales, or between brace-treated participants whose major curve had increased by greater than 20 degrees or less than 20 degrees since the end of treatment. ATR at followup also was found not to be correlated with the Mental Component Summary or Physical Component Summary scores on the SF-36.

**Oswestry Disability Index and back pain.** The Goteborg cohort study assessed the Oswestry Disability Index and sick leave due to back pain. There was no significant difference between brace-treated and surgically-treated participants on either measure (Table 16).

**Other quality-of-life assessments.** The Spinal Appearance Questionnaire (SAQ) was assessed in the SRS bracing cohort. The SAQ consists of a set of seven sketches representing visible aspects of spinal deformity, each showing five levels of spinal asymmetry. The patient selects their perception of their own appearance; scores are added and scored from seven (least distorted
appearance) to 35 (most distorted appearance). Subjectively perceived body asymmetry was correlated with major curve size for braced, observed, and all participants (p=0.0004), though whether the curve was at last followup or during treatment is not described. Participants who had been braced reported a more distorted appearance than those who had not been braced (average SAQ score of 15.0 for braced participants vs. 12.9 for observed participants; p=0.028) (Table 17).

The Psychological General Well-Being (PGWB) Index was assessed in the Goteborg cohort. No correlation was reported between curve size at the end of treatment and PGWB scores, though numeric data were not provided. There also was no difference in PGWB scores between participants with curves of greater than 50 degrees at the time of followup and those with curves of less than 50 degrees, or between brace-treated participants whose major curve had increased by greater than 20 degrees or less than 20 degrees since the end of treatment. ATR at followup was not correlated with PGWB scores.

A self-esteem and social activity questionnaire also was administered to this group. Results were not stratified based on ATR at the end of treatment; however, the authors report that there was no correlation between ATR at followup and how participants self-rated their appearance in a bathing suit or whether they had social limitations related to their appearance. The braced and surgically treated groups in this cohort did differ with regard to the recollection of their experience of the treatment period, with individuals in the braced group significantly more likely to recall that the treatment had a negative rather than positive effect on their life (p=0.0001) (Table 18).

Study Results: Pulmonary Outcomes

In surgically-treated participants there was a correlation between curve size and both percentage-predicted VC and FEV1 prior to surgery (p<0.001). However, at followup there was no correlation between curve size after treatment and VC or FEV1 (numeric data not provided) (Table 19).

Study Results: Childbearing and Pregnancy Outcomes

One paper analyzed pregnancy and childbirth outcomes in the 247 females in the Goteborg cohort. Results were not stratified based on degree of curve at skeletal maturity. There was no significant difference in Cobb angle at completion of treatment between women who had children and those who did not. There were no significant differences between braced or surgically treated women in marital status, number of children, birthweight, or pregnancy complications (Table 20).

Limitations

Only two studies met our criteria, both of fair quality. Most data were presented according to treatment received in adolescence, rather than stratified by curve magnitude at skeletal maturity; therefore, data that directly informs the KQ as worded (“what is the association between severity of spinal curvature in adolescence and health outcomes in adulthood?”) is lacking. Reporting

Screening for Adolescent Idiopathic Scoliosis
bias may be an issue since multiple measures were assessed in both studies, but this was difficult to assess. One of the included studies has data from several individuals that were treated with methods that have now been superseded (e.g., Harrington rod placement, Milwaukee brace); however, newer treatment methods are thought to have fewer adverse effects, so inclusion of these data may overestimate treatment harms.

**KQ5. What Are the Harms of Screening for Adolescent Idiopathic Scoliosis?**

No studies on harms of screening met our inclusion criteria. False positive rates ranged from 0.8 percent for clinic-based FBT with scoliometer and Moiré screening to 21.5 percent for hump assessment alone (reported in KQ2), though the harms associated with false positive screening are unclear. There are potential psychosocial harms associated with a false positive screening result, and radiation exposure to the chest during childhood also is a potential harm. Several studies have suggested that radiation exposure over the course of management and surveillance for scoliosis is associated with increased cancer risk in adulthood, but the impact of screening-only exposure was not reported in any studies.

**KQ6. What Are the Harms of Treatment of Adolescent Idiopathic Scoliosis That Has a Cobb Angle of Less Than 50 Degrees at Diagnosis?**

**Summary of Results**

Harms of bracing were reported in one good-quality study (two articles; n=242). These harms were relatively benign and limited to skin problems on the trunk (under the brace) and non-back body pains that were more frequently reported in braced participants than in controls (none of these events were deemed serious). One of the 146 braced participants reported a serious adverse event (anxiety and depression requiring hospitalization).

**Detailed Results**

*Description of Included Study*

The included study is a prospective clinical controlled trial of 242 subjects with AIS, 116 of whom were randomly assigned to bracing or observation, and 126 of whom were assigned based on patient preference. In total, 146 subjects were braced and 96 were assigned to the observation group. This study included subjects drawn from populations referred to specialty orthopedic centers at 25 sites in Canada and the United States. Average age of participants was 12.7 years. Ninety-one percent of subjects were female, 78 percent were white, nine percent were black, and 13 percent were another race or unknown. Enrollment was limited to persons who had not previously received treatment for scoliosis (Table 21).

Subjects with different types of scoliotic curves, as well as subjects with both single-major and multiple-major curves, were included in this study. Magnitude of the largest curve at initiation of
treatment (reported as Cobb angle) averaged 30.5 degrees (SD 5.8) in braced subjects. Skeletal maturity of subjects was assessed by Risser sign; 96 percent had a Risser sign of 0 to 2 at enrollment.

This multicenter study allowed participating centers to prescribe “the type of brace used in their normal clinical practice,” but specified that this must be a rigid thoracolumbosacral orthosis; 68 percent of subjects were treated with a Boston brace. Intervention group subjects were braced until skeletal maturity or until Cobb angle of the largest scoliotic curve surpassed 50 degrees. Subjects were observed for an average of 2 years (intervention group) or 1.8 years (control group); the study was stopped early by the data and safety monitoring board due to evidence of significant treatment effect in favor of bracing.

Study Results

Adverse events assessed as part of this trial included skin problems on the trunk (e.g., bruising, lacerations, ulcers, pressure sores, rash), abnormal breast development, anxiety, depression, and several other self-reported adverse events which can be broadly categorized as non-back body pain (e.g., leg pain or neck pain), neurologic symptoms (e.g., headache, numbness/tingling in limbs), and other isolated complaints (e.g., gastrointestinal symptoms, asthma exacerbation). Overall, 39 adverse events that were deemed “related” to the study (based on the judgment of the investigator or research coordinator) were reported in the 146 braced subjects, compared to six such events that were reported in the 96 control subjects (Appendix D).

Only one serious adverse event was reported during the study period (hospitalization for anxiety and depression in a braced subject). The most frequently reported non-serious adverse events were those involving the skin under the brace; there were 12 reports of such symptoms in the 146 braced subjects compared to zero reports in the 96 observed subjects. There were 12 reports of various types of body pain (other than back pain) from braced subjects, compared to two such reports in observed subjects. There was no significant difference between groups with regard to the frequency of reporting other non-serious adverse events.

Limitations

Although the included study was of good quality, the lack of additional studies for comparison precludes our ability to determine the true consistency and magnitude of the findings reported here. Among the four studies excluded based on quality, the most common reasons for a poor quality rating were excessive loss to followup, lack of an untreated control group with AIS, and poor comparability of baseline characteristics of compared groups.
Chapter 4. Discussion

Summary of Evidence

Screening

As was the case for both the 1993 and 2004 USPSTF reviews on this subject, we found no direct evidence for a benefit of universal AIS screening of adolescents on long-term health outcomes. No prospective randomized trials of screening have been conducted, and there are no well-conducted cohort studies that compare health outcomes in screened and unscreened groups.

We included data on the accuracy of screening from seven different programs, but the heterogeneity of screening modalities, screeners, and referral criteria makes it challenging to compare across studies. It is clearly possible to detect children with AIS through screening, although the sensitivity and positive predictive value of screening programs appears to vary depending on whether a single mode of screening or multiple modes are used, and on the threshold used to define a positive screening result. The FBT with scoliometer measurement—the screening modality recommended by organizations advocating screening—had estimated predictive values of 29 percent to 54 percent for detecting scoliosis curves of ≥10 degrees in the studies included in this review. One study found that sensitivity and predictive value estimates are higher when a measurement of ATR (e.g., scoliometer) is combined with intermediate Moiré topography assessment; however, Moiré screening is used infrequently in the United States and its feasibility as a population- or school-based screening modality may be limited where access to specialized equipment is unavailable.

A low threshold for a positive screening result may increase the likelihood of detecting children with severe AIS who could benefit from immediate intervention; an analysis of patients referred to the single scoliosis referral center in the western district of Sweden during the ten-year period in which a systematic screening program for AIS was introduced demonstrated declines in the most severe curves detected each year and in the number of individuals that required surgical treatment. However, it also may identify screen-positive individuals who will never require treatment. Luk and colleagues noted that although 2.5 percent of the adolescents in their survey population of over 150,000 fit the diagnostic criteria for scoliosis (curve of ≥10 degrees), only a little more than half of these individuals had curves of 20 degrees or more (approaching the threshold at which brace treatment often is instituted), and only 0.2 percent of adolescents had curves ≥40 degrees (approaching the threshold for surgical treatment). Using a higher cutoff point to designate a positive screening test (e.g., curves ≥20 degrees) would be a possible alternative approach; however, this may preclude the ability to identify and monitor or preemptively treat individuals with mild curves that may progress. As noted above, it is difficult to accurately predict which individuals with AIS will be most likely to have their curves progress during adolescence. There is a greater likelihood of curve progression associated with female gender, greater severity of curve, significant remaining growth potential, and certain curve types. However, gender is the only of these factors that can be known at the time of screening, and because the majority of females with AIS will not have significant progression of
curve, the predictive value of gender for risk stratification may be limited. Gender-based approaches to screening have been endorsed by several organizations, but no studies of gender-targeted screening approaches met our inclusion criteria. In the studies included in this review, females comprised between 68 percent and 82 percent of detected cases of scoliosis with curves of ≥10 degrees, which is consistent with previously-reported averages. There currently are insufficient data on the association of other physical findings or genetic markers with progression of disease to enable identification of high-risk and low-risk populations in whom targeted screening approaches may be beneficial. Finally, it must be emphasized that the value of screening for AIS—of any severity, and in any population—ultimately is dependent on whether potential interventions are effective.

No studies on harms of screening met our inclusion criteria. False positive rates ranged from 0.8 percent to 21.5 percent, but the harms associated with these rates are unclear. It is conceivable that there are psychosocial harms associated with screening, especially with a false positive result, and radiation exposure to the chest during childhood also may be associated with harms. Several studies have suggested that radiation exposure over the course of management and surveillance for scoliosis is associated with increased cancer risk in adulthood, but the impact of screening-only exposure was not reported in any studies.

**Treatment**

Several new treatment studies have been published since the previous evidence reviews for the USPSTF. The mode of treatment recommended by scoliosis treatment guidelines varies according to curve severity, with observation or conservative interventions (e.g., exercise) for curves less than 20 degrees, brace treatment for curves ≥20–30 degrees, and surgical treatment for curves ≥40–50 degrees. Remaining growth until skeletal maturity also informs treatment decisions, and algorithms for treatment decisions based on multiple categories of curve severity and skeletal maturity have been proposed. Bracing generally is not indicated for curves of less than 20 degrees based on data suggesting lower likelihood of curve progression during adolescence for curves of this severity.

Exercise therapy has long been advocated outside of the United States for cases of milder scoliosis (10° to 20° Cobb angle); however, good-quality evidence in support of this was lacking until very recently. We found one good-quality RCT that suggests the use of physiotherapeutic scoliosis-specific exercises in adolescents with curves of 10 to 25 degrees may prevent progression of the curve, and may even reverse the major curve in some cases. An earlier fair-quality study of exercise treatment in a similar population also suggests possible benefit, albeit of small magnitude. Both studies were performed exclusively in otherwise untreated individuals, and therefore the utility of exercise as an adjunct to other treatment is unknown. Nonetheless, the clinical importance of limiting progression of mild curves may be significant, as curves of less than 20–30 degrees at skeletal maturity are much less likely to continue to progress in adulthood than are curves of greater magnitude. No other studies of other exercise treatments for AIS met our inclusion criteria; however, a multicenter randomized trial of Schroth exercises for treatment of AIS is currently underway with estimated completion in 2017. If future good-quality studies of exercise therapy confirm the efficacy and relative safety of exercise treatment for milder AIS, this could have potential implications for the utility of population-based
screening for persons with mild scoliosis.

The 1993 USPSTF review found insufficient evidence to determine whether brace treatment limited the natural progression of scoliosis in a significant percentage of cases; this finding was not re-assessed as part of the limited 2004 evidence update. Our review includes five studies published since that time.\textsuperscript{96, 102-104, 106} Four of these are prospective controlled studies (including one RCT), all of which provide evidence for some benefit of bracing treatment, although they assess slightly different outcomes that precluded meta-analysis or pooling. The fifth study, a small retrospective study,\textsuperscript{96} showed nonsignificant differences between groups, but was not sufficiently powered. Three studies demonstrated that brace treatment until skeletal maturity was associated with a decreased likelihood of curve progression of more than 5–6 degrees.\textsuperscript{102, 103, 106} In most studies, progression of ≤5 degrees is considered equivalent to absence of progression; therefore, these results were thought to indicate that bracing could successfully arrest progression of the scoliosis curve, resulting in a curve of smaller magnitude at the end of growth that would be less likely to progress during adulthood. However, two small studies that included data on slightly larger degrees of progression did not show a significant difference between braced and control participants.\textsuperscript{96, 103} A prospective controlled trial\textsuperscript{104} showed a marked difference (odds ratio 1.9) between braced and control subjects with regard to preventing progression of curve past 50 degrees, at which point brace treatment generally is considered to have failed and surgical treatment is considered. This trial was ended early by the trial’s data safety and monitoring board because of strong evidence for benefit in the bracing arm. This trial also showed a dose-response relationship between hours-per-day of brace wear and decreased likelihood of curve progression, a finding that is reflected in other studies that demonstrate an inverse association between hours-per-day of brace wear and likelihood of curve progression or surgical intervention.\textsuperscript{129-131} Three other studies provided data on subjects that passed a threshold in this range; however, none were powered to detect a difference of the magnitude seen.

Harms of bracing were reported in only one study;\textsuperscript{104} these were relatively benign and limited to skin problems on the trunk (under the brace) and non-back body pains that were reported more frequently in braced participants than in controls (none of these events were deemed serious). One of the 146 braced participants reported a serious adverse event (anxiety and depression requiring hospitalization). Two other studies on long-term followup of individuals with AIS reported outcome findings that may suggest possible adverse consequences of brace treatment. One study administered the Spinal Appearance Questionnaire (SAQ) to a cohort of adults with AIS at least 11 years after skeletal maturity, and found that those who had been braced in adolescence felt their body appearance was more distorted than those who were not treated,\textsuperscript{112} despite equivalent curves in adulthood. A second study contacted a cohort of adults at least 20 years following treatment for AIS and asked about their impressions of their treatment period; a significantly higher percentage of brace-treated individuals experienced a negative effect on their life compared to those treated surgically, despite the fact that curve magnitude at followup was nearly identical in both groups and significantly higher in the surgical group prior to treatment.\textsuperscript{113}

No studies on effectiveness or harms of surgical treatment fit our inclusion criteria, largely because of our population of interest (adolescents with scoliosis of <50 degrees at diagnosis); this is consistent with other reviews.\textsuperscript{132} This situation is due in part to the fact that few studies of surgical treatment provided data on whether included subjects were initially identified through a
As with all major surgeries, spinal fusion for AIS involves short- and long-term risks. Estimates of blood loss during AIS surgery vary (averaging 1200mL to 2455mL, depending on the procedure). Pain following AIS surgery is fairly common, with 30 (16%) of 190 patients in a prospective cohort study reporting moderate to severe pain at 1 year post-operation. Other complications of AIS surgery include death, infection, pseudoarthrosis, and neurologic deficits (Table 22). About six to seven percent of patients experience complications from surgery for AIS, and very few patients (0.03%) die of those complications. Some of the more common complications are pulmonary (1% to 4% of patients) and implant-related complications (1.1% to 1.5%). Neurologic complications—such as nerve root damage and spinal cord injuries—occur in about 0.6 to 0.8 percent of AIS surgery patients, most of whom experience complete or partial recovery. As noted earlier, some research suggests that surgical treatment of individuals with high degree of curvature (Cobb angle greater than 70°) is more complex and associated with a higher likelihood of short-term risks (such as increased surgical duration, blood loss, and need for transfusion).

In summary, there is a developing body of evidence suggesting that the progression of mild and moderate AIS curves during adolescence can be interrupted or slowed with non-surgical intervention. Whether this is beneficial to individuals with AIS over the life course, however, depends on whether the curve at the end of growth is associated with improved outcomes in adulthood.

**Health Outcomes in Adulthood**

The 1993 USPSTF review discussed the limited information available on long-term health outcomes in persons with AIS, but the evidence base was limited to uncontrolled studies, not restricted to subjects with AIS, and arrived at a recommendation of insufficient evidence for long-term health outcomes.

For the current review, two studies on long-term health outcomes met our inclusion criteria. Both studies assessed adult outcomes (1 to 2 decades or more after skeletal maturity) in individuals with mild-to-moderate AIS who were treated or observed in adolescence. However, results were stratified by treatment group in adolescence rather than by magnitude-of-curve at skeletal maturity, which significantly limits the ability to draw conclusions about the utility of limiting curve progression with brace treatment or exercise treatment during adolescence. At followup, braced participants felt their body appearance was more distorted than did untreated
participants, and also recalled experiencing a negative effect on their life during the treatment period compared to those treated surgically. No other significant differences between observed, braced, and surgically treated groups were reported for various measures of quality of life, and no significant difference in certain pulmonary outcomes or childbearing and pregnancy outcomes were reported in adulthood for either the braced or surgically treated participants.

**Limitations of the Review**

Among the most important limitations of this review is its scope, which was intentionally limited to evaluation of individuals with mild-to-moderate AIS (major curve <50 degrees) at diagnosis. This was done to ensure that the evidence reviewed would be pertinent to the population that would be identified through universal clinic-based or school-based screening programs. The proportion of adolescents who have curves of a greater magnitude than this is small (the prevalence of AIS with a curve of greater than 40 degrees in the general population is <0.1%), and many of these individuals will be identified even in the absence of screening programs. In addition, their expected clinical course (continued curve progression throughout adolescence and adulthood) is quite different than those with curves of lesser severity. Conversely, for the majority of screen-positive individuals, AIS will be a benign condition; however, a proportion of those who cannot readily be identified at the outset will have a more progressive course. It was therefore felt to be most important to limit our focus to the evidence on this group, as those individuals with larger curves at presentation are likely to have a vastly different clinical course.

AIS is a challenging condition to treat and to study, in large part because many characteristics of the condition (e.g., age of onset, type of curve, severity of curve, likelihood of progression, rapidity of progression, likelihood of continued progression in adulthood, treatment response) vary greatly and are further modified by gender and developmental maturity—all of which makes the results of trials with heterogeneous study populations difficult to interpret. There is a large body of literature that informs our overall clinical understanding of treatment and long-term prognosis of AIS; however, much of this research is not designed to specifically address a screening population rather than those AIS cases that would be picked up clinically as the curve progressed.

The literature itself has several limitations. We found no published studies that met our inclusion criteria for several KQs in this review. There is no direct evidence for the impact of screening for AIS on long-term health outcomes, and no high-quality evidence on the harms associated with screening. The evidence base for treatment of AIS that was less than 50 degrees at diagnosis has improved since the last review, but still has significant deficits (e.g., we found relatively few prospective controlled trials of treatment during our literature search, and there is an absence of high-quality studies on surgical procedures that include a comparison group of non-surgically treated individuals with AIS). Unfortunately, these gaps in the literature may not be easy to fill; for example, the difficulty in recruitment that occurred in the multi-site BRAIST trial (which was converted from an RCT to a patient preference controlled trial) and in a Dutch RCT (which was not completed due to insufficient enrollment) demonstrate that families of children with AIS are often reluctant to allow treatment decisions to occur as a result of randomization. Studies of surgical treatment in individuals with mild-to-moderate AIS also may not be feasible, as
bracing is often recommended as a first-line treatment to avoid an invasive spinal surgery (although newer surgical techniques intended for treatment of moderate AIS curves have been developed).\textsuperscript{145} Perhaps most significant, the lack of long-term outcomes data stratified by degree of curve at skeletal maturity significantly impedes our ability to draw a strong conclusion about whether the ability to limit curve progression during adolescence is in fact an important endpoint.

**Future Research Needs**

A number of observational cohorts of individuals with AIS have been identified; however, the utility of data from these cohorts often is limited by lack of a control group (e.g., a prospectively-identified comparison group of unscreened or untreated individuals) or by lack of pertinent baseline information (e.g., degree of curvature at diagnosis and at skeletal maturity, developmental maturity at diagnosis, etc.) The body of evidence on population-based screening for AIS would therefore be most significantly strengthened by prospective identification of cohorts at the time of diagnosis (e.g., from areas with and without routine AIS screening) or treatment (e.g., treated and observed cohorts) for the purpose of long-term followup.

Also needed are screening studies with a prospective controlled study design, for comparison of screened and non-screened populations, different screening settings (e.g., school versus clinic), screening personnel (e.g., school staff vs. general health care personnel vs. medical specialist), and screening procedures (i.e., trunk rotation with or without other physical findings, such as shoulder asymmetry). Data on screening results should be reported in subgroups, including females and children with a family history of scoliosis. Prospective, systematic collection of data on the potential harms of screening—including psychosocial effects and radiation exposure estimates for screened (as opposed to treated) populations—also is needed.

The utility of screening ultimately is determined by whether any treatment prescribed to those individuals identified through screening programs is effective at improving long-term health outcomes. Therefore, the body of evidence in support of screening would be strengthened by good-quality studies of treatment, such as additional prospective controlled studies on exercise treatment and brace treatment (including prospectively identified untreated control groups), and studies on surgical treatment, including—if appropriate—true prospectively-identified control groups that receive non-surgical treatment. Although the evidence on effectiveness of bracing compared to observation has improved, additional studies to help determine whether individual characteristics may influence response to treatment would be beneficial (e.g., there is recent research to suggest that high or low BMI may impact response to bracing).\textsuperscript{146} Whenever possible, treatment studies should include assessments of physical and psychological adverse events, and have a provision for long-term followup. Studies on long-term outcomes should have stratification of outcome results by degree of curvature at diagnosis and at skeletal maturity, for the purpose of better understanding the long-term outcomes for identifiable subgroups of individuals with AIS.
Conclusion

We found no direct evidence for a benefit of universal AIS screening of adolescents on long-term health outcomes. There is evidence that demonstrates that AIS can be identified with the most commonly used screening test for AIS (FBT with scoliometer, followed by referral for diagnostic imaging), although estimates of predictive value and sensitivity are variable, and the majority of individuals identified through screening will never require treatment. Theoretical harms of universal screening have been proposed, but high-quality evidence is lacking. A growing body of evidence suggests that brace treatment can interrupt or slow progression of scoliosis curves before skeletal maturity; and limited evidence suggests that curves of smaller magnitude may respond similarly to physiotherapeutic scoliosis-specific exercise treatment. Surgical treatment remains the standard of care for curves that progress to greater than 40–50 degrees; however, there are no controlled studies of surgical versus non-surgical treatment in individuals with lower degrees of curvature at AIS detection, which would represent a likely screening population. Although long-term observational studies suggest that continued curve progression in adulthood is less likely if the magnitude of the curve at skeletal maturity is smaller, and that very high degrees of curvature may be associated with pathology in later adulthood, direct evidence on the association between magnitude of curve at skeletal maturity and adult quality of life outcomes is lacking.
References


Figure 1. Analytic Framework

Screening

Asymptomatic children and adolescents aged 10 to 18 years

2. Idiopathic scoliosis

5. Harms of screening

Treatment

3. Intermediate outcome
   Curve severity

6. Harms of treatment

4. Health outcomes
   Morbidity, mortality
   Quality of life
   Functioning
Table 1. Description of Included Screening Programs That Provide Data on Screen-Negative Children (KQ2)

<table>
<thead>
<tr>
<th>Screening program</th>
<th>Population</th>
<th>Screening test</th>
<th>Screening procedure</th>
<th>Referral criteria</th>
<th>Diagnostic test</th>
<th>Diagnostic criteria</th>
<th>Followup of screen negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester, MN USA School Fair</td>
<td>Screened n=2,242 Age: NR (US grades 5-9) % Female: NR Race: NR All children entering public/private schools K (1979-1981) or 1st grade (1980-1982) and screened ≥3 times</td>
<td>FBT alone (1984-85) FBT with scoliometer (1986-91) Annual screenings over multiple years 1984-91 Follow up to 1994</td>
<td>Public health nurse supervised by orthopedic surgeon during PE class Repeat screening at 2-4 weeks for ATR &gt;6° or obvious curve on FBT</td>
<td>&gt;6° ATR on scoliometer or obvious curve on FBT</td>
<td>X-ray Standing full-spine Dose NR Operator NR</td>
<td>Cobb angle &gt;10°</td>
<td>Rochester Epidemiology Project Diagnostic Index searched for all diagnoses of &quot;scoliosis&quot; or &quot;rule out scoliosis&quot;</td>
</tr>
<tr>
<td>Hong Kong Regional clinics Fair</td>
<td>Screened n=306,082* Age: NR (Hong Kong 5th grade or ≥10 years old) % Female: NR Race: NR 5th graders screened at least once before age 19</td>
<td>FBT with scoliometer, then Moiré (≥5° to &lt;15° ATR only) Screenings biennially or more frequently 1995-2000 Followup 10 years or to age 19</td>
<td>Physicians and registered nurses</td>
<td>≥15° ATR on scoliometer -or- ≥2 Moiré lines difference -or- significant clinical signs</td>
<td>X-ray Standing posteroanterior Read by orthopedists</td>
<td>Cobb angle ≥10°</td>
<td>Department of Health and two scoliosis specialist hospitals on all visits of 5th grade students during screening period</td>
</tr>
<tr>
<td>Greece (Samos island) School Fair</td>
<td>Screened n=2,700 Age range: 8-16 % Female: NR Race: NR Inclusion: School children ≥8 years old in local schools</td>
<td>Clinical exam, FBT, humpometer, scoliometer, and Moiré topography Single screening: 1987 Follow up 10 years</td>
<td>Teams of 2 orthopedic surgeons; medical, nursing and paramedical staff Students assessed for all screening methods by two independent evaluations</td>
<td>Positive FBT -or- Positive Moiré (NR) -or- Humpometer: &gt;5 mm -or- Scoliometer: ATR &gt;0°</td>
<td>X-ray Conventional standing anteroposterior (for scoliosis) or low-dose long chest X-ray (for lung disease) Operator: NR</td>
<td>Cobb angle ≥10°</td>
<td>All students received low-dose long chest X-ray</td>
</tr>
</tbody>
</table>

* Does not include 62 students diagnosed with non-idiopathic scoliosis by age 19.

Abbreviations: KQ = key question; NR = not reported; FBT = forward bend test; PE = physical education; ATR = angle of trunk rotation.
Table 2. Description of Screening Programs With No Information on Screen-Negative Children for Detection of Scoliosis of Greater Than 10 Degrees (KQ2)

<table>
<thead>
<tr>
<th>Screening program</th>
<th>Population</th>
<th>Screening test and followup</th>
<th>Screening procedure</th>
<th>Referral criteria</th>
<th>Diagnostic test</th>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ireland (Dublin)</td>
<td>Screened n=8,669*</td>
<td>FBT with scoliometer Single screening 1986-1987 Followup 1-4 years</td>
<td>School doctors (primary); PE teachers or school nurses (post-primary). Findings confirmed by medical staff and at hospital-based clinic.</td>
<td>Premenarche: thoracic hump 8° or loin hump 10° Postmenarche: thoracic hump 10° or loin hump 15°</td>
<td>X-ray Standing posteroanterior Operator: NR</td>
<td>Cobb angle &gt;10°</td>
</tr>
<tr>
<td>Singapore</td>
<td>Screened n=40,649†</td>
<td>FBT with scoliometer Single screening (1997) Followup: NR</td>
<td>Nurse during PE class Scoliometer findings confirmed by medical officer</td>
<td>ATR ≥5° on scoliometer</td>
<td>X-ray Standing posteroanterior Read by 2 orthopedic surgeons</td>
<td>Cobb angle ≥10°</td>
</tr>
<tr>
<td>Norway</td>
<td>Screened n=4,000</td>
<td>FBT with scoliometer Single screening (year NR) Followup: NR</td>
<td>Public health/community nurses and physical therapists</td>
<td>ATR &gt;7° on scoliometer</td>
<td>X-ray Standing, at local hospitals and mailed to university hospital</td>
<td>Cobb angle &gt;10°</td>
</tr>
<tr>
<td>Greece (northwestern and central)</td>
<td>Screened n=82,901</td>
<td>FBT with level plane and ruler Single screening 1993-1994 Followup: NR</td>
<td>Teams of orthopedic residents, medical students, and senior orthopedic surgeons Repeat screen same-day for suspected scoliosis &gt;5 mm difference at thoracic or thoracolumbar -or- significant clinical signs</td>
<td>X-ray Standing posteroanterior at local hospital Operator: NR</td>
<td>Cobb angle ≥10°</td>
<td></td>
</tr>
</tbody>
</table>

Note: Italicized values were not provided in the article(s) and were calculated.
* Does not include 17 who did not show up for a re-examination and were excluded.
† Excludes ages 6-7 (n=32,050).
‡ Article reports there was “a similar distribution of girls and boys.”

Abbreviations: KQ = key question; SD = standard deviation; NR = not reported; FBT = forward bend test; PE = physical education; ATR = angle of trunk rotation; mm = millimeters.
Table 3. Results on Accuracy of Scoliosis Screening (KQ2)

<table>
<thead>
<tr>
<th>Screening programs with followup of screen-negative children</th>
<th>Screening test</th>
<th>Number of screenings</th>
<th>N screened</th>
<th>PPV (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>False positive rate</th>
<th>False negative rate</th>
<th>Prevalence of AIS &gt;10° Cobb angle*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester, USA† Fair</td>
<td>FBT±S†</td>
<td>Annual over multiple years</td>
<td>2,242</td>
<td>29.3% (20.3-39.8)</td>
<td>71.1% (54.1-84.6)</td>
<td>97.1% (96.3-97.7)</td>
<td>2.9%†</td>
<td>28.9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Hong Kong‡,§,‖,¶ Fair</td>
<td>FBT+S±M‡</td>
<td>Biennial or more often</td>
<td>306,082§</td>
<td>81.0% (80.3-81.7)</td>
<td>93.8% (93.3-94.3)</td>
<td>99.2% (99.2-99.9)</td>
<td>0.8%‡</td>
<td>6.2%</td>
<td>3.5%¶</td>
</tr>
<tr>
<td>Greece (Samos Island)† Fair</td>
<td>FBT One-time</td>
<td>2,700</td>
<td></td>
<td>17.3% (11.7-24.2)</td>
<td>84.4% (67.2-94.7)</td>
<td>95.2% (94.3-95.9)</td>
<td>4.8%</td>
<td>15.6%</td>
<td>1.2%</td>
</tr>
<tr>
<td></td>
<td>S One-time</td>
<td>2,700</td>
<td></td>
<td>5.3% (3.6-7.6)</td>
<td>90.6% (75.9-98.0)</td>
<td>80.7% (79.1-82.1)</td>
<td>19.3%</td>
<td>9.4%</td>
<td>1.2%</td>
</tr>
<tr>
<td></td>
<td>M One-time</td>
<td>2,700</td>
<td></td>
<td>7.6% (5.3-10.6)</td>
<td>100.0% (84.2-100)</td>
<td>85.4% (84.0-86.7)</td>
<td>14.6%</td>
<td>0%</td>
<td>1.2%</td>
</tr>
<tr>
<td></td>
<td>H One-time</td>
<td>2,700</td>
<td></td>
<td>5.0% (3.4-7.0)</td>
<td>93.8% (79.2-99.2)</td>
<td>78.5% (76.9-80.0)</td>
<td>21.5%</td>
<td>6.3%</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Screening programs with no followup of screen-negative children</th>
<th>Screening test</th>
<th>Number of screenings</th>
<th>N screened</th>
<th>PPV (95% CI)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>False positive rate</th>
<th>False negative rate</th>
<th>Screening yield of AIS &gt;10° Cobb angle**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ireland§,¶,‖,‖,¶ Fair</td>
<td>FBT+S†</td>
<td>One-time</td>
<td>8,669††</td>
<td>54.1% (40.8-66.9)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0.4%</td>
</tr>
<tr>
<td>Singapore§ Fair</td>
<td>FBT+S†</td>
<td>One-time</td>
<td>40,649†‡</td>
<td>41.2% (37.4-45.1)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0.7%†‡</td>
</tr>
<tr>
<td>Norway‖,¶ Fair</td>
<td>FBT+S†</td>
<td>One-time</td>
<td>4,000</td>
<td>36.7% (24.6-50.1)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0.6%</td>
</tr>
<tr>
<td>Greece (NWC)§,¶,‖,¶,‖,¶,‖ Fair</td>
<td>FBT+PL§</td>
<td>One-time</td>
<td>82,901</td>
<td>34.3% (32.9-35.8)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

Note: Italicized values were not provided in the article(s) and were calculated
* Calculated as number of disease positives (true positives + false negatives) divided by the total number screened
† Rochester screening program used FBT only (1984-85) before FBT plus scoliometer (1986-91)
‡ Assumes lost to f/u are false positive
§ Does not include 62 students diagnosed with non-idiopathic scoliosis by age 19
** Calculated as number of true positives divided by the total number screened
†† Does not include 17 who did not show up for a re-examination and were excluded
‡‡ Excludes ages 6-7 (n=32,050)

Abbreviations: KQ = key question; AIS = adolescent idiopathic scoliosis; NWC = northwestern and central; FBT = forward bend test; S = scoliometer; M = Moiré topography; H = humpometer; PL = plane/level; NR = not reported; PPV = positive predictive value; CI = confidence interval
Table 4. Characteristics of Screen-Detected AIS and False-Negative Populations (KQ2)

<table>
<thead>
<tr>
<th>Screening programs with followup of screen-negative children</th>
<th>N</th>
<th>Test</th>
<th>True positive (n)</th>
<th>Curve description (Cobb angle) of screen-detected AIS</th>
<th>False negatives (n)</th>
<th>Curve description of AIS false negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester, USA Fair</td>
<td>2,242</td>
<td>FBT±S*</td>
<td>27</td>
<td>11°-19°: 40.7%  20°-39°: 37.0%  ≥40°: 22.2%</td>
<td>11</td>
<td>Cobb 11°-19°: 45.5%  Cobb ≥ 20°-39°: 36.4%  Cobb ≥ 40°: 18.2%</td>
</tr>
<tr>
<td>Hong Kong Fair</td>
<td>306,082†</td>
<td>FBT+S±M</td>
<td>10,160</td>
<td>10°-19°: 50.9%  20°-39°: 43.4%  ≥40°: 5.6%</td>
<td>671</td>
<td>Cobb 10°-19°: 26.2%  Cobb 20°-39°: 49.2%  Cobb ≥ 40°: 24.6%</td>
</tr>
<tr>
<td>Greece (Samos Island) Fair</td>
<td>2,700</td>
<td>FBT, S, M, H</td>
<td>27 (FBT), 29 (S), 32 (M), 30 (H)</td>
<td>10°-15°: 68.8%†  15°-20°: 21.9%‡  &gt;20°: 9.4%‡</td>
<td>5 (FBT), 3 (S), 0 (M), 2 (H)</td>
<td>NR</td>
</tr>
<tr>
<td>Screening programs with no followup of screen-negative children</td>
<td>N</td>
<td>Test</td>
<td>True positive (n)</td>
<td>Curve description (Cobb angle) of screen-detected AIS</td>
<td>False negatives (n)</td>
<td>Curve description of AIS false negatives</td>
</tr>
<tr>
<td>Ireland Fair</td>
<td>8,669§</td>
<td>FBT+S</td>
<td>33</td>
<td>10°-39°: 93.9%  ≥40°: 6.1%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Norway Fair</td>
<td>4,000</td>
<td>FBT+S</td>
<td>22</td>
<td>10°-20°: 77.3%  &gt;20°: 22.7%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Greece (NWC) Fair</td>
<td>82,901</td>
<td>FBT+PL</td>
<td>1,436</td>
<td>10°-19°: 87.4%  20°-29°: 10.0%  30°-39°: 1.8%  ≥40°: 0.8%</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Note: Italicized values were not provided in the article(s) and were calculated
* Rochester screening program used FBT only (1984-85) before FBT plus scoliometer (1986-91)
† Represents 306,144 screened minus 62 students diagnosed with non-idiopathic scoliosis by age 19
‡ Refers to Cobb angles for disease positive AIS (true positive plus false negatives)
§ Does not include 17 who did not show up for a re-examination and were excluded
** Excludes ages 6-7 (n=32,050)

Abbreviations: KQ = key question; AIS = adolescent idiopathic scoliosis; FBT = forward bend test; S = scoliometer; M = Moiré topography; H = humpometer; PL = plane/level; NR = not reported; NWC = northwestern and central
Table 6. Study Populations: Included Bracing Studies (KQ3)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Setting</th>
<th>N</th>
<th>Type of brace (IG)</th>
<th>Hours/day of brace wear</th>
<th>Comparison group (CG)</th>
<th>Study endpoint</th>
<th>Additional treatment</th>
<th>Mean duration of treatment (IG) or followup (CG), years</th>
<th>Outcomes reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coillard 2014*</td>
<td>RCT</td>
<td>One university hospital</td>
<td>68</td>
<td>Spine-Cor</td>
<td>20</td>
<td>Observation</td>
<td>IG: 5 years</td>
<td>CG: 5 years or progression of ≥6°. If progression, offered treatment but not removed from CG.</td>
<td>IG: 2.1 (range 1.5-3)</td>
<td>CG: NR</td>
</tr>
<tr>
<td>Wiemann 2014†</td>
<td>CCT</td>
<td>2 pediatric orthopedic specialty practices</td>
<td>37</td>
<td>Charleston bending</td>
<td>Nights only</td>
<td>Observation</td>
<td>IG &amp; CG: Skeletal maturity. Surgery offered in IG &amp; CG at discretion of treating surgeon if curves progressed to &gt;50°</td>
<td>IG: 3.3</td>
<td>CG: 2.8</td>
<td>Curve progression</td>
</tr>
<tr>
<td>BRAIST* ‡</td>
<td>CCT</td>
<td>25 hospital-and/or university-based centers</td>
<td>242†</td>
<td>Rigid TLSO (various)</td>
<td>18</td>
<td>Observation</td>
<td>IG &amp; CG: Skeletal maturity or Cobb angle ≥50°</td>
<td>IG: 2.0</td>
<td>CG: 1.8</td>
<td>Curve progression Quality of life Back pain</td>
</tr>
<tr>
<td>SRS Bracing Study§</td>
<td>Prospective observational 1985-1989</td>
<td>Eight centers</td>
<td>240</td>
<td>Boston§</td>
<td>&gt;16</td>
<td>Observation</td>
<td>IG &amp; CG: Skeletal maturity</td>
<td>NR</td>
<td>Curve progression</td>
<td></td>
</tr>
</tbody>
</table>

* Recruitment in Coillard 2014 and BRAIST were terminated early because of evidence of benefit favoring bracing
† 47.9% of population from RCT
‡ Study reports severity of major curve at inclusion, not treatment initiation
§ Bracing system also involves a coordinated exercise program

Abbreviations: KQ = key question; RCT = randomized clinical trial; CCT = controlled clinical trial; IG = braced group; CG = observation group; NR = not reported; TLSO = thoracolumbosacral orthotic; BRAIST = Bracing in Adolescent Idiopathic Scoliosis Trial; SRS = Scoliosis Research Society
Table 7. Study and Population Characteristics, Included RCT of Exercise for Treatment of Scoliosis (KQ3)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Intervention and control group activities</th>
<th>Population characteristics</th>
<th>Skeletal maturity at baseline</th>
<th>Curve type</th>
<th>Curve at baseline</th>
<th>Length of treatment, months: mean (SD)</th>
<th>Data collection points</th>
<th>Outcomes assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monticone 2014</td>
<td>110</td>
<td>IG: Active self-correction: exercises tailored to type of curve; task oriented exercises; education&lt;br&gt;CG: General balance and walking exercises, spinal mobilization; spinal stretching/strength&lt;br&gt;IG and CG: 60-minute outpatient sessions with physiotherapist once per week; advice to continue exercises 30 minutes twice a week at home</td>
<td>Age, mean (SD):&lt;br&gt;IG: 12.5 (1.1)&lt;br&gt;CG: 12.4 (1.1)&lt;br&gt;Female&lt;br&gt;IG: 70.9%&lt;br&gt;CG: 74.5%&lt;br&gt;Family history of scoliosis&lt;br&gt;IG: 61.8%&lt;br&gt;CG: 65.5%</td>
<td>Risser sign 0&lt;br&gt;IG: 45.5%&lt;br&gt;CG: 45.5%&lt;br&gt;Risser sign 1&lt;br&gt;IG: 54.5%&lt;br&gt;CG: 54.5%&lt;br&gt;Menarche yes&lt;br&gt;IG: 71.8%&lt;br&gt;CG: 70.7%</td>
<td>Thoracic&lt;br&gt;IG: 14.5%&lt;br&gt;CG: 14.5%&lt;br&gt;Lumbar&lt;br&gt;IG: 23.6%&lt;br&gt;CG: 25.5%&lt;br&gt;Thoraco-lumbar&lt;br&gt;IG: 38.2%&lt;br&gt;CG: 36.4%&lt;br&gt;S-shaped&lt;br&gt;IG: 23.6%&lt;br&gt;CG: 23.6%</td>
<td>IG: 42.8 (9.1)&lt;br&gt;CG: 42.4 (7.7)</td>
<td>Baseline: Feb 2007-Dec 2008 (recruitment)&lt;br&gt;Post-treatment: 12 months after end of treatment</td>
<td>Primary&lt;br&gt;Spinal curve ATR&lt;br&gt;Secondary&lt;br&gt;Pain&lt;br&gt;Function&lt;br&gt;Self-image&lt;br&gt;Mental health</td>
<td></td>
</tr>
<tr>
<td>Negrini 2008</td>
<td>74</td>
<td>IG: Active self-correction (SEAS), 1.5-hour tailored sessions every 2-3 months evaluated by PT; 40 minute session twice a week, and 5 minute exercise at home&lt;br&gt;CG: Different exercise protocol (PT preference) in group setting 45-90 minutes, 2-3 times per week, some repeat at home</td>
<td>Age, mean (SD):&lt;br&gt;IG: 12.7 (2.2)&lt;br&gt;CG: 12.1 (2.1)&lt;br&gt;Female&lt;br&gt;IG: 71.4%&lt;br&gt;CG: 69.2%&lt;br&gt;Menarche yes NR&lt;br&gt;Menarche yes NR</td>
<td>Risser sign 0-3&lt;br&gt;IG: 100%&lt;br&gt;CG: 100%&lt;br&gt;Menarche yes NR&lt;br&gt;Menarche yes NR</td>
<td>NR</td>
<td>NR</td>
<td>IG: 12 months</td>
<td>Baseline: 6 months&lt;br&gt;‡ Only ATR reported at 6 months</td>
<td>Primary&lt;br&gt;Cobb angle&lt;br&gt;Total:* 15 (6)&lt;br&gt;Secondary&lt;br&gt;Avoidance of bracing</td>
</tr>
</tbody>
</table>

* Not reported by treatment group<br>† Only ATR reported at 6 months

Abbreviations: RCT = randomized clinical trial; IG = intervention group; CG = control group; SD = standard deviation; ATR = angle of trunk rotation, SEAS = Scientific Exercises Approach to Scoliosis; PT = physical therapist
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Brace, duration of treatment (months)</th>
<th>Study endpoint</th>
<th>Major curve at beginning of treatment, mean Cobb angle (SD)</th>
<th>Major curve at end of treatment, mean Cobb angle (SD)</th>
<th>Curve progressed ≤5° during study period</th>
<th>Curve progressed &gt;5° during study period</th>
<th>Curve progressed &gt;10° during study period</th>
<th>Curve progressed to &gt;50° during study period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coillard 2014</td>
<td>68</td>
<td>IG: 32, CG: 36</td>
<td>Spine-Cor Mean 25 (range 18-36)</td>
<td>IG: 22° (4.9) CG: 20° (4.1)</td>
<td>NR</td>
<td>IG: 65.6% CG: 25.0% p=NR</td>
<td>IG: 34.4% CG: 75.0% p=0.0008</td>
<td>NR</td>
<td>IG: 11.5% CG: 14.3% p=NR</td>
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<tr>
<td>Canada</td>
<td></td>
<td></td>
<td>5 years (patients were ≥2 years post stopping treatment)</td>
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<tr>
<td>RCT</td>
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</tr>
<tr>
<td>USA, Fair</td>
<td>37</td>
<td>IG: 21, CG: 16</td>
<td>Charleston bending Mean (SD) IG: 39 (15) CG: 34 (10)</td>
<td>IG: 19° (3.6) CG: 19° (2.6)</td>
<td>NR</td>
<td>IG: 28.6% CG: 0% p=0.023</td>
<td>IG: 71.4% CG: 100.0% p=NR</td>
<td>IG: 52.4% CG: 50.0% NS (p=0.472)</td>
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<tr>
<td>ummer, Good</td>
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<td>25°-35° (range)</td>
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<tr>
<td>Weinstein 2013</td>
<td>242</td>
<td>IG: 146, CG: 96</td>
<td>Rigid TLSO (various) Mean IG: 24.2 CG: 21.3</td>
<td>IG: 30.5° (5.8) CG: 30.3° (6.5)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>IG: 28% CG: 52% p=NR</td>
<td></td>
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<tr>
<td>BRAIST</td>
<td></td>
<td></td>
<td>Skeletal maturity</td>
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<tr>
<td>Nachemson 1995</td>
<td>240</td>
<td>IG: 111, CG: 129</td>
<td>Boston NR</td>
<td>25°-35° (range)</td>
<td>IG: 26.2 (5.8) CG: 29.8 (6.5)</td>
<td><strong>Progressed ≤6° IG: 64.0% CG: 48.1% p=NR</strong></td>
<td><strong>Progressed ≥6° IG: 36.0% CG: 51.9% p=NR</strong></td>
<td>NR</td>
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<tr>
<td>Sweden, USA, UK, Canada</td>
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<td>Good</td>
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<tr>
<td>Prospective observational</td>
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<td></td>
</tr>
<tr>
<td>Goldberg 1993</td>
<td>64</td>
<td>IG: 32, CG: 32</td>
<td>Boston NR</td>
<td>IG: 22.2 (4.5) CG: 20.6 (5.0)</td>
<td>NR</td>
<td><strong>Progressed ≤5° IG: 81.3% CG: 56.3%</strong></td>
<td><strong>Progressed 0° IG: 12.5% CG: 12.5%</strong></td>
<td><strong>Progressed &lt;0° IG: 40.6% CG: 25.0%</strong> p=NR</td>
<td>IG: 18.8% CG: 28.1% NS (p=NR)</td>
</tr>
<tr>
<td>USA, Ireland</td>
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<tr>
<td>Fair</td>
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<tr>
<td>Retrospective observational</td>
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</tbody>
</table>

* Recruitment in Coillard 2014 and BRAIST were terminated early because of evidence of benefit favoring bracing.
Table 8. Bracing Effectiveness Studies: Results of Included Studies (KQ3)

† Reported only for those who completed study (n=47)
‡ 47.9% of population from RCT
§ Bracing system also involves a coordinated exercise program
** Assumes those who were lost to followup (n=23 for intervention group; n=9 for control group) were treatment failures (progressed ≥6°)

Abbreviations: KQ = key question; SD = standard deviation; IG = braced group; CG = observation group; TLSO = thoracolumbosacral orthotic; NR = not reported; BRAIST = Bracing in Adolescent Idiopathic Scoliosis Trial; SRS = Scoliosis Research Society
Table 9. Bracing Effectiveness Studies: Other Outcomes (KQ3)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Quality of life assessment*</th>
<th>Mean score at baseline (SD)**</th>
<th>Mean score at final followup (SD)**</th>
<th>Back pain assessment</th>
<th>Back pain prevalence at baseline**</th>
<th>Back pain prevalence at final followup**</th>
<th>Back pain reported during study</th>
<th>Total reports† ††</th>
<th>Reports related to bracing or scoliosis‡‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAIST 104, 105</td>
<td>242†</td>
<td>Pediatric Quality of Life Inventory§</td>
<td>IG: 83.8 (14.1) p=0.80</td>
<td>IG: 82.0 (17.0) p=0.97</td>
<td>Self-report at 6 month intervals during study visit</td>
<td>IG: 38% p=0.32</td>
<td>IG: NR p=0.29</td>
<td></td>
<td>IG: 33</td>
<td>CG: 30</td>
</tr>
<tr>
<td>Weinstein 2013 USA, Canada Good</td>
<td>IG: 146</td>
<td>CG: 96</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>IG: 32</td>
<td>CG: 22</td>
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<tr>
<td>CCT</td>
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</tbody>
</table>

Note: No other bracing effectiveness study reported quality of life measures. No significant differences between groups.

* Recruitment in BRAIST was terminated early because of evidence of benefit favoring bracing
† 47.9% of population from RCT
‡ Child Health questionnaire, Self-image questionnaire for young adults, and Spinal Appearance questionnaire were also administered; however, results were not reported.
§ Scores range from 0 to 100; higher scores indicate higher quality of life
** All results are from as-treated analysis; authors report that results of intention-to-treat analysis were also not significant
†† Back pain events were all considered “not serious”, number of events not number of participants
‡‡ Events were considered related based on the judgement of the investigator

Abbreviations: KQ = key question; SD = standard deviation; BRAIST = Bracing in Adolescent Idiopathic Scoliosis Trial; IG = Braced; CG = observation; NR = not reported
Table 10. Results of RCT of Active Self-Correction vs Generic Exercise for Treatment of Scoliosis (KQ3)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Age; mean (SD)</th>
<th>Length of treatment in months, mean (SD)</th>
<th>Outcome</th>
<th>Baseline; mean (SD)</th>
<th>End of treatment; mean (SD)</th>
<th>12 month followup; mean (SD)</th>
<th>Change from baseline to 12-month followup; mean (SE)*</th>
<th>p-value (group effect)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monticone</td>
<td>110</td>
<td>IG: 12.5 (1.1)</td>
<td>IG: 42.8 (9.1)</td>
<td>Cobb angle</td>
<td>IG: 19.3 (3.9)</td>
<td>IG: 14.0 (2.4)</td>
<td>IG: 14.3 (2.3)</td>
<td>IG: -4.9 (0.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2014 Italy</td>
<td>110</td>
<td>CG: 12.4 (1.1)</td>
<td>CG: 42.4 (7.7)</td>
<td></td>
<td>CG: 19.2 (2.5)</td>
<td>CG: 20.9 (2.2)</td>
<td>CG: 22.0 (1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good RCT</td>
<td></td>
<td></td>
<td></td>
<td>ATR</td>
<td>IG: 7.1 (1.4)</td>
<td>IG: 3.6 (1.1)</td>
<td>IG: 3.3 (1.1)</td>
<td>IG: -3.7 (0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>CG: 6.9 (1.3)</td>
<td>CG: 6.6 (1.2)</td>
<td>CG: 6.5 (1.1)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Function†</td>
<td>IG: 3.8 (0.5)</td>
<td>IG: 4.7 (0.2)</td>
<td>IG: 4.8 (0.2)</td>
<td>IG: 1.0 (0.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>CG: 3.9 (0.5)</td>
<td>CG: 4.0 (0.4)</td>
<td>CG: 3.9 (0.4)</td>
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<td></td>
<td>Pain†</td>
<td>IG: 3.8 (0.4)</td>
<td>IG: 4.6 (0.3)</td>
<td>IG: 4.7 (0.2)</td>
<td>IG: 0.89 (0.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
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<td></td>
<td>CG: 3.9 (0.5)</td>
<td>CG: 4.3 (0.3)</td>
<td>CG: 4.2 (0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negirini</td>
<td>74</td>
<td>IG: 12.7 (2.2)</td>
<td>IG: 3.9 (0.6)</td>
<td>Self-image†</td>
<td>IG: 3.6 (0.6)</td>
<td>IG: 3.7 (0.5)</td>
<td>IG: 3.6 (0.4)</td>
<td>IG: 1.0 (0.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2008 Italy</td>
<td>74</td>
<td>CG: 12.1 (2.1)</td>
<td>CG: 3.9 (0.6)</td>
<td></td>
<td>CG: 3.4 (0.6)</td>
<td>CG: 4.4 (0.3)</td>
<td>CG: 3.6 (0.4)</td>
<td></td>
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</tr>
<tr>
<td>Fair RCT</td>
<td></td>
<td></td>
<td></td>
<td>Mental health†</td>
<td>IG: 3.8 (0.6)</td>
<td>IG: 4.5 (0.3)</td>
<td>IG: 4.7 (0.2)</td>
<td>IG: 0.95 (0.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>CG: 3.9 (0.6)</td>
<td>CG: 3.9 (0.5)</td>
<td>CG: 3.8 (0.4)</td>
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<td></td>
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<td></td>
<td>Change in Cobb angle of max curve</td>
<td>NR</td>
<td>IG: -0.33</td>
<td>NA</td>
<td>NA</td>
<td>NR, NS</td>
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<tr>
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<td></td>
<td>Change of Cobb angle of all curves</td>
<td>NR</td>
<td>IG: -0.67</td>
<td>NA</td>
<td>NA</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Change in Cobb angle of max curve</td>
<td>NR</td>
<td>IG: -0.33</td>
<td>NA</td>
<td>NA</td>
<td>NR, NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Change of Cobb angle of all curves</td>
<td>NR</td>
<td>IG: +0.12</td>
<td>NA</td>
<td>NA</td>
<td>NR, NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Change in ATR of all curves</td>
<td>NR</td>
<td>IG: +0.12</td>
<td>NA</td>
<td>NA</td>
<td>NR, NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Change in ATR of max curve</td>
<td>NR</td>
<td>IG: +0.52</td>
<td>NA</td>
<td>NA</td>
<td>NR, NS</td>
</tr>
</tbody>
</table>
| * For SRS-22 domains, minimal clinically important differences (MCID) reported for populations with adult spinal deformity and AIS were 0.4-0.6 (function); 0.6-0.8 (pain); 0.5-0.8 (self-image); and 0.4 (mental health).147, 148
† SRS-22 (Italian): scores range from one (worst) to five (best)

Abbreviations: KQ = key question; RCT = randomized clinical trial; IG = intervention group; CG = control group; SD = standard deviation; SE = standard error; ATR = angle of trunk rotation; NR = not reported; NS = not significant
Table 11. Results of RCT of Exercise for Treatment of Scoliosis: Progression 5 Degrees at End of Treatment (KQ3)

<table>
<thead>
<tr>
<th>Study</th>
<th>End of treatment N (%)</th>
<th>End of treatment N (%)</th>
<th>End of treatment N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Progressing (Cobb angle change ≥5°)</td>
<td>Stable (Cobb angle change of -5° to 5°)</td>
<td>Improved (Cobb angle change ≤-5°)</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monticone 2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>Good</td>
<td>RCT</td>
<td></td>
</tr>
<tr>
<td>Total (n=103)</td>
<td>IG: 0 (0%)*</td>
<td>IG: 20 (38%)</td>
<td>IG: 32 (62%)*</td>
</tr>
<tr>
<td></td>
<td>CG: 4(8%)*</td>
<td>CG: 47 (92%)</td>
<td>CG: 0 (0%)*</td>
</tr>
<tr>
<td>Age &lt;13 at admission</td>
<td>IG: 3 (9.7%)</td>
<td>IG: 6 (19.3%)</td>
<td>IG: 22 (71.0%)</td>
</tr>
<tr>
<td>(n=63)</td>
<td>CG: 10 (31.2%)</td>
<td>CG: 19 (59.4%)</td>
<td>CG: 3 (9.4%)</td>
</tr>
<tr>
<td>Age ≥13 at admission</td>
<td>IG: 1 (4.8%)</td>
<td>IG: 6 (28.5%)</td>
<td>IG: 14 (66.7%)</td>
</tr>
<tr>
<td>(n=40)</td>
<td>CG: 10 (52.6%)</td>
<td>CG: 9 (47.4%)</td>
<td>CG: 0 (0%)</td>
</tr>
<tr>
<td>Negrini 2008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>Fair</td>
<td>RCT</td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>Cobb angle:</td>
<td>Cobb angle:</td>
<td>Cobb angle:</td>
</tr>
<tr>
<td></td>
<td>IG: 11.8%</td>
<td>IG: 64.7%</td>
<td>IG: 23.5%</td>
</tr>
<tr>
<td></td>
<td>CG: 13.9%</td>
<td>CG: 75.0%</td>
<td>CG: 11.1%</td>
</tr>
<tr>
<td>ATR:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IG: 15.1%</td>
<td>IG: 75.8%</td>
<td>ATR:</td>
</tr>
<tr>
<td></td>
<td>CG: 27.8%</td>
<td>CG: 69.4%</td>
<td>IG: 9.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CG: 2.8%</td>
</tr>
</tbody>
</table>

*Data comes from Monticone 2014 response to letter to editor

Abbreviations: KQ = key question; RCT = randomized clinical trial; IG = intervention group; CG = control group; SD = standard deviation; ATR = angle of trunk rotation; NR = not reported
### Table 12. Characteristics of Studies on Health Outcomes in Adulthood (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Study design</th>
<th>Country, Setting, Years of treatment and followup</th>
<th>Mean age at start of treatment (SD), years</th>
<th>Mean age at followup (SD), years</th>
<th>Lost to followup from adolescence</th>
<th>Length of followup after skeletal maturity (years) Mean (SD), range</th>
<th>Adult outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2010,111 2012112 SRS bracing cohort</td>
<td>n=77</td>
<td>Observational</td>
<td>Sweden</td>
<td>OBS: 14.0 (0.9) BT: 13.4 (1.2) (p=0.0077)</td>
<td>OBS: 32.2 (1.2) BT: 32.4 (1.8) (p=0.54)</td>
<td>n=100 in adolescence; 77% assessed in adulthood</td>
<td>OBS 16.0 (1.2); 13.3-18.4 BT 16.0 (1.6); 11.4-18.6 (p=0.91)</td>
<td>SRS-22 SF-36 Spinal Appearance Questionnaire (SAQ)</td>
</tr>
<tr>
<td>n=100 in adolescence; 77% assessed in adulthood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Danielsson 2001a,113 2001b114 Pehrsson 2001115 Goteborg cohort</td>
<td>n=262</td>
<td>Observational</td>
<td>Sweden</td>
<td>BT: 14.4 (1.4) ST: 15.0 (1.8) (p=0.012)</td>
<td>BT: 39.3 (2.2) ST: 39.7 (2.5) (p=0.31)</td>
<td>n=283 assessed in adolescence; 93% assessed in adulthood</td>
<td>BT: 22.3 (1.9); 19.4-28.3 ST: 23.3 (1.6); 20.3-26.6 (p=0.0001)</td>
<td>SF-36 PGWB ODI Childbearing and pregnancy outcomes (n=247) Pulmonary outcomes (n=251)</td>
</tr>
<tr>
<td>2001b114</td>
<td>ST: 146 BT: 116</td>
<td>Long term followup of AIS cohort treated in adolescence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001115</td>
<td></td>
<td>University Hospital Treatment: 1968-1977 Followup: ≥20 years post-treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbreviations: KQ = key question; AIS = adolescent idiopathic scoliosis; SD = standard deviation; SRS = Scoliosis Research Society; OBS = observation group; BT = brace-treated group; ST = surgically treated group; SRS-22 = Scoliosis Research Society 22-item questionnaire; SF-36 = 36-Item Short Form Survey; PGWB = Psychological General Well-Being Index; ODI = Oswestry Disability Index</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 13. Population Characteristics of Studies on Health Outcomes in Adulthood (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>% Female</th>
<th>AIS treatment received in adolescence</th>
<th>Cobb angle at inclusion (pretreatment) Mean (SD); range</th>
<th>Cobb angle at skeletal maturity/end of treatment Mean (SD); range</th>
<th>Cobb angle at followup (in adulthood) Mean (SD); range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2010,111</td>
<td>n=77</td>
<td>OBS:100%</td>
<td>OBS: Observation only BT: Boston brace (22-24 hr/day until skeletal maturity)*</td>
<td>OBS: 29.2 (3.0); 23-35 BT: 30.5 (3.2); 25-38 (p=0.11)</td>
<td>OBS: 30.6 (4.9); 21-42 BT: 27.7 (6.8); 14-42 (p=0.067)</td>
<td>OBS: 35.0 (6.5); 21-48 BT: 34.1 (7.7); 19-48 (p=0.75)</td>
</tr>
<tr>
<td>2012,112</td>
<td></td>
<td>BT: 100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SRS bracing cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair Sweden</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pehrsson 2001115</td>
<td>n=262</td>
<td>BT: 95.7%</td>
<td>BT:\† Boston or Milwaukee brace 22-24 hr/day until skeletal maturity ST:\‡ Surgical treatment with Harrington distraction and fusion, followed by bracing for 6-12 months</td>
<td>ST: 61.8 (13.2); 38-122 BT: 33.2 (9.6); 12-60 (p=0.0001)</td>
<td>ST: 33.1 (9.4); 12-65 BT: 29.7 (11.2); 0-58 (p&lt;0.05)§</td>
<td>ST: 36.5 (9.7); 14-66 BT: 37.6 (14.7); 5-71 (p=0.48)</td>
</tr>
<tr>
<td>Goteborg cohort</td>
<td></td>
<td>ST: 93.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair Sweden</td>
<td></td>
<td>BT: 116</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 26 participants braced at time of enrollment, 11 braced after progression >6 degrees with significant growth remaining.
† Participants with curves 24-50 degrees (thoracic, thoracolumbar or double primary curves) or <60 degrees (lumbar curves)
‡ Participants with curves >50 degrees (thoracic, thoracolumbar or double primary curves) or >60 degrees (lumbar curves)
§ Reported in Danielsson 2001 paper38 with n=248 (ST=139; BT=109)

Abbreviations: KQ = key question; AIS = adolescent idiopathic scoliosis; SD = standard deviation; OBS = observation group; BT = brace-treated group; ST = surgically treated group; SRS = Scoliosis Research Society
Table 14. SRS-22 Scores* in Adulthood (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Cobb angle at skeletal maturity/ end of treatment Mean (SD); range</th>
<th>Function Mean (SD); range</th>
<th>Pain Mean (SD); range</th>
<th>Self-image/appearance Mean (SD); range</th>
<th>Mental health Mean (SD); range</th>
<th>Total score† Mean (SD); range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2010, 2012</td>
<td>n=77</td>
<td>OBS: 30.6 (4.9); 21-42</td>
<td>OBS: 4.5 (0.5); 2.8-5.0</td>
<td>OBS: 3.9 (0.8); 1.2-5.0</td>
<td>OBS: 4.1 (0.7); 2.0-5.0</td>
<td>OBS: 4.2 (0.5); 2.7-5.0</td>
<td>OBS: 3.5 (0.7); 2.0-5.0</td>
</tr>
<tr>
<td>SRS bracing cohort</td>
<td>OBS: 40</td>
<td>BT: 27.7 (6.8); 14-42 (p=0.067)</td>
<td>BT: 4.5 (0.5); 3.0-5.0</td>
<td>BT: 4.4 (0.6); 3.2-5.0</td>
<td>BT: 3.9 (0.7); 2.4-5.0</td>
<td>BT: 4.2 (0.4); 3.0-5.0</td>
<td>BT: 3.7 (0.7); 2.4-5.0</td>
</tr>
<tr>
<td>Fair Sweden</td>
<td>BT: 37</td>
<td></td>
<td>(p=0.60)</td>
<td>(p=0.94)</td>
<td>(p=0.98)</td>
<td>(p=0.93)</td>
<td>(p=0.74)</td>
</tr>
</tbody>
</table>

*Possible scores: one (worst) to five (best)
†Total score excluding “satisfaction with management”

Abbreviations: KQ = key question; SRS = Scoliosis Research Society; SD = standard deviation; OBS = observation group; BT = brace-treated group; SRS-22 = Scoliosis Research Society 22-item questionnaire
Table 15. SF-36 Scores* in Adulthood (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Physical functioning Mean (95% CI)</th>
<th>Role physical Mean (95% CI)</th>
<th>Bodily pain Mean (95% CI)</th>
<th>General health Mean (95% CI)</th>
<th>Vitality Mean (95% CI)</th>
<th>Social functioning Mean (95% CI)</th>
<th>Role emotional Mean (95% CI)</th>
<th>Mental health Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2010, 2012</td>
<td>111</td>
<td>OBS: 94.5 (91.9-97.1)</td>
<td>OBS: 93.1 (87.3-98.9)</td>
<td>OBS: 75.0 (67.4-82.5)</td>
<td>OBS: 83.7 (74.6-90.2)</td>
<td>OBS: 69.9 (63.3-76.1)</td>
<td>OBS: 91.9 (86.3-97.5)</td>
<td>OBS: 90.0 (81.3-97.0)</td>
<td>OBS: 83.5 (78.9-88.1)</td>
</tr>
<tr>
<td>SRS bracing cohort</td>
<td></td>
<td>BT: 94.9 (92.1-97.1)</td>
<td>BT: 91.9 (84.8-97.7)</td>
<td>BT: 68.1 (60.2-74.5)</td>
<td>BT: 79.8 (75.1-83.6)</td>
<td>BT: 68.2 (61.6-73.7)</td>
<td>BT: 89.5 (83.3-94.6)</td>
<td>BT: 86.5 (76.5-94.6)</td>
<td>BT: 81.2 (76.2-85.4)</td>
</tr>
<tr>
<td>Fair Sweden</td>
<td></td>
<td>p=0.80</td>
<td>p=0.94</td>
<td>p=0.19</td>
<td>p=0.15</td>
<td>p=0.78</td>
<td>p=0.34</td>
<td>p=0.79</td>
<td>p=0.51</td>
</tr>
<tr>
<td>Danielsson 2001a</td>
<td>262</td>
<td>ST: 85.8 (83.1-88.5)</td>
<td>ST: 86.8 (81.9-91.7)</td>
<td>ST: 70.8 (66.5-75.1)</td>
<td>ST: 75.1 (71.8-78.4)</td>
<td>ST: 68.4 (65.1-71.7)</td>
<td>ST: 90.7 (87.8-93.6)</td>
<td>ST: 88.1 (83.6-92.6)</td>
<td>ST: 81.0 (78.5-83.5)</td>
</tr>
<tr>
<td>Goteborg cohort</td>
<td></td>
<td>BT: 88.2 (85.5-90.9)</td>
<td>BT: 82.8 (76.7-88.9)</td>
<td>BT: 71.5 (66.6-76.4)</td>
<td>BT: 77.6 (74.3-80.9)</td>
<td>BT: 63.1 (59.2-67.0)</td>
<td>BT: 90.0 (86.7-93.3)</td>
<td>BT: 89.1 (84.6-93.4)</td>
<td>BT: 80.8 (77.7-83.9)</td>
</tr>
<tr>
<td>Fair Sweden</td>
<td></td>
<td>p=0.22</td>
<td>p=NR</td>
<td>p=0.73</td>
<td>p=0.49</td>
<td>p=NR</td>
<td>p=NR</td>
<td>p=NR</td>
<td>p=NR</td>
</tr>
</tbody>
</table>

*Possible scores 0 (worst) to 100 (best), scaled to population norm = 50

Abbreviations: KQ = key question; SRS = Scoliosis Research Society; OBS = observation group; CI = confidence interval; BT = brace-treated group; ST = surgically treated group; SF-36 = 36-Item Short Form Survey; NR = not reported
Table 16. Oswestry Disability Index Scores in Adulthood (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Cobb angle at end of treatment Mean (SD); range</th>
<th>ODI score* Mean (SD); range</th>
<th>Sick leave ever due to back problems n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2001a†</td>
<td>n=262</td>
<td>ST: 33.1 (9.4); 12-65</td>
<td>ST: 8.3 (10); 0-50</td>
<td>ST: 63 (43.2%)</td>
</tr>
<tr>
<td>Goteborg cohort Fair Sweden</td>
<td></td>
<td>BT: 29.7 (11.2); 0-58</td>
<td>BT: 7.6 (9.0); 0-36</td>
<td>BT: 44 (37.9%)</td>
</tr>
</tbody>
</table>

* Possible scores 0 (best) to 100 (worst)
† Reported in Danielsson 2001 paper with n=248 (ST=139; BT=109)

Abbreviations: KQ = key question; ODI = Oswestry Disability Index; SD = standard deviation; BT = brace-treated group; ST = surgically treated group
Table 17. Spinal Appearance Questionnaire (SAQ) Results (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Cobb angle at skeletal maturity/end of treatment Mean (SD); range</th>
<th>Spinal Appearance Questionnaire (SAQ)*† Mean (SD); range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2012†‡</td>
<td>n=77</td>
<td>OBS: 30.6 (4.9); 21-42 BT: 27.7 (6.8); 14-42 (p=0.067)</td>
<td>OVERALL: 13.9 (4.6); 7-29 OBS: 12.9 (4.4); 7-25 BT: 15.0 (4.6); 7-29 (p=0.028)</td>
</tr>
<tr>
<td>SRS bracing cohort Fair Sweden</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: no baseline reported for SAQ
* SAQ measures patient perceptions of spinal deformity and is scored on a scale from seven (least distorted) to 35 (most distorted)
† SAQ scores were correlated with major curve size for all participants, with Spearman rank correlation $r_s = 0.40$ (p=0.0004)

Abbreviations: KQ = key question; SD = standard deviation; OBS = observation group; BT = brace-treated group; SRS = Scoliosis Research Society
### Table 18. Experience of the Treatment Period (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Study</th>
<th>N</th>
<th>Cobb angle at skeletal maturity Mean (SD); range</th>
<th>Cobb angle at followup Mean (SD); range</th>
<th>How did you experience the treatment period?*</th>
<th>N (%)</th>
<th>How did the treatment affect you during the treatment time?*</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Danielsson 2001</td>
<td>262</td>
<td>Study: 33.1 (9.4); 12-65</td>
<td>Study: 36.5 (9.7); 14-66</td>
<td>Major positive</td>
<td>106 (50.0%)</td>
<td>Very often depressed or sad (p = 0.41)</td>
<td>115 (50.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Goteborg cohort</td>
<td>146</td>
<td>Study: 29.7 (11.2); 0-58</td>
<td>Study: 37.6 (14.7); 5-71</td>
<td>Minor positive</td>
<td>106 (49.5%)</td>
<td>- ST: 37 (25.3%)</td>
<td>115 (50.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fair</td>
<td>116</td>
<td>(p&lt;0.05)†</td>
<td>(p=0.48)</td>
<td>- BT: 37 (5.1%)</td>
<td>- BT: 6 (5.1%)</td>
<td>115 (50.5%)</td>
<td>- BT: 35 (30.2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sweden</td>
<td></td>
<td></td>
<td></td>
<td>Not affected</td>
<td>106 (49.5%)</td>
<td>More noticeable and helped (p = 0.0027)</td>
<td>115 (50.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- ST: 18 (12.3%)</td>
<td>- ST: 106 (72.6%)</td>
<td>- BT: 63 (54.3%)</td>
<td>- BT: 52 (44.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- BT: 17 (14.6%)</td>
<td>- BT: 96 (65.7%)</td>
<td>- BT: 63 (54.3%)</td>
<td>- BT: 52 (44.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Minor negative</td>
<td>106 (49.5%)</td>
<td>People were sympathetic (p = 0.0007)</td>
<td>115 (50.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- ST: 37 (25.3%)</td>
<td>- ST: 96 (65.7%)</td>
<td>- BT: 52 (44.8%)</td>
<td>- BT: 52 (44.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- BT: 43 (37.1%)</td>
<td>- BT: 52 (44.8%)</td>
<td>- BT: 52 (44.8%)</td>
<td>- BT: 52 (44.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Major negative</td>
<td>106 (49.5%)</td>
<td>Often teased (p = 0.027)</td>
<td>115 (50.5%)</td>
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<td></td>
<td>- ST: 21 (14.4%)</td>
<td>- ST: 18 (12.3%)</td>
<td>- ST: 15 (10.3%)</td>
<td>- ST: 15 (10.3%)</td>
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<td></td>
<td>- BT: 32 (27.6%)</td>
<td>- BT: 17 (14.6%)</td>
<td>- BT: 11 (9.5%)</td>
<td>- BT: 11 (9.5%)</td>
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<td></td>
<td></td>
<td>(p&lt;0.0001)</td>
<td></td>
<td>Kept to myself (n = 0.64)</td>
<td>115 (50.5%)</td>
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<td>- ST: 31 (21.2%)</td>
<td>- ST: 31 (21.2%)</td>
<td>- ST: 31 (21.2%)</td>
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<td>- BT: 21 (18.1%)</td>
<td>- BT: 21 (18.1%)</td>
<td>- BT: 21 (18.1%)</td>
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<td></td>
<td></td>
<td>Stopped spare time activities (p= 0.60)</td>
<td>115 (50.5%)</td>
<td>- ST: 52 (35.6%)</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>- BT: 37 (31.9%)</td>
<td>- BT: 52 (35.6%)</td>
<td>- BT: 52 (35.6%)</td>
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<td></td>
<td></td>
<td>Conflicts at home (p = 0.99)</td>
<td>115 (50.5%)</td>
<td>- ST: 6 (4.1%)</td>
</tr>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>- BT: 5 (4.3%)</td>
<td>- BT: 5 (4.3%)</td>
<td>- BT: 5 (4.3%)</td>
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<td></td>
<td></td>
<td>Treatment ruined my teenage period (p = 0.57)</td>
<td>115 (50.5%)</td>
<td>- ST: 34 (23.3%)</td>
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<td></td>
<td></td>
<td>- BT: 31 (26.7%)</td>
<td>- BT: 34 (23.3%)</td>
<td>- BT: 31 (26.7%)</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Treatment did not bother me much (p = 0.61)</td>
<td>115 (50.5%)</td>
<td>- ST: 53 (36.3%)</td>
</tr>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td>- BT: 46 (39.6%)</td>
<td>- BT: 53 (36.3%)</td>
<td>- BT: 46 (39.6%)</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>Limited contact with opposite sex (p = 0.99)</td>
<td>115 (50.5%)</td>
<td>- ST: 62 (42.5%)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>- BT: 50 (43.1%)</td>
<td>- BT: 62 (42.5%)</td>
<td>- BT: 50 (43.1%)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Treatment made me independent/mature sooner (p = 0.80)</td>
<td>115 (50.5%)</td>
<td>- ST: 73 (50.0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- BT: 45 (38.8%)</td>
<td>- BT: 73 (50.0%)</td>
<td>- BT: 45 (38.8%)</td>
</tr>
</tbody>
</table>

Note: ST had shorter treatment period (1.4 years) than BT (2.7 years)

* Questions are from a scoliosis treatment-specific questionnaire developed by the authors prior to the development of the Scoliosis Research Society’s 22-item questionnaire (SRS-22). Healthy controls did not answer the questionnaire

† Reported in Danielsson 2001 paper with N=248 (ST=139; BT=109)

Abbreviations: KQ = key question; SD = standard deviation; ST = surgically treated group; BT = brace-treated group
Table 19. Pulmonary Outcomes in Adulthood (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Cobb angle at end of treatment Mean (SD); range</th>
<th>Smoking status in adulthood (from British MRC)‡†</th>
<th>Lung function at mean 25-year followup‡ mean (SD), range</th>
<th>Self-reported pulmonary symptoms (from British MRC)‡‡</th>
<th>Self-reported disease outcomes§§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danielsson 2001a</td>
<td>n=251</td>
<td>ST: 33.1 (9.4); 12-65</td>
<td>Never smokers; n (%)</td>
<td>Total lung capacity (TLC)§</td>
<td>Dyspnoea score &gt; 3‡‡</td>
<td>Pulmonary disease</td>
</tr>
<tr>
<td>Pehrsson 2001†</td>
<td>ST: 141 BT: 110</td>
<td>BT: 29.7 (11.2); 0-58 (p&lt;0.05)*</td>
<td>ST: NR (55%); BT: NR (56%)</td>
<td>ST: 5.0 (0.9); 3.2-9.4</td>
<td>ST: 3 (% NR)</td>
<td>ST: 8</td>
</tr>
<tr>
<td>Goteborg cohort</td>
<td></td>
<td></td>
<td>Mean (SD) pack-years (current smokers and ex-smokers only)</td>
<td>BT: 5.1 (0.9); 3.3-7.4</td>
<td>BT: 1 (% NR)</td>
<td>BT: 6</td>
</tr>
<tr>
<td>Fair</td>
<td></td>
<td></td>
<td>ST: 11.6 (7.3); BT: 8.3 (5.6)</td>
<td>Vital capacity (VC)**</td>
<td></td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td></td>
<td></td>
<td>ST: 84 (13), 47-123</td>
<td></td>
<td>ST: 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BT: 89 (13), 56-127</td>
<td></td>
<td>BT: 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FEV1††</td>
<td></td>
<td>Neoplasms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ST: 84 (14), 52-122</td>
<td></td>
<td>ST: 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BT: 91 (16), 32-135</td>
<td></td>
<td>BT: 4</td>
</tr>
</tbody>
</table>

* Reported in Danielsson 2001 paper with n=248 (ST=139; BT=109)
† Values reported as available (unable to determine whether all participants completed questionnaire)
‡ P values not reported for differences between ST and BT
§ Values reported for n=246 (ST=138; BT=108)
** VC % predicted mean values are corrected for age and for loss of height due to scoliosis
†† FEV1 % predicted mean values corrected for age and for loss of height due to scoliosis
‡‡ Dyspnoea was graded on a scale of one to 5, where three = breathlessness when walking with someone else of similar age on level ground
††† Values reported for n=262 (ST=146; BT=116). Article reports that the frequency of pulmonary disease, coronary heart disease, and neoplasms was not significantly different between the patient groups (BT and ST) and the healthy controls

Abbreviations: KQ = key question; SD = standard deviation; BT = brace-treated group; ST = surgically treated group; NR = not reported; MRC = Medical Research Council; FEV1 = forced expiratory volume at one second
Table 20. Childbearing and Pregnancy Outcomes in Adults With AIS (KQ4)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Cobb angle at end of treatment</th>
<th>Number of children per person</th>
<th>Mean age at first delivery</th>
<th>Birthweight, grams</th>
<th>Pregnancy complications: first delivery†</th>
<th>Pregnancy complications: all births‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD); range</td>
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<td></td>
<td>Mean (SD); range</td>
<td>N (%)</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>ST: 33.1 (9.4); 12-65</td>
<td>ST: 1.8 (1.1)</td>
<td>ST: 26.6</td>
<td>ST: 3,488 (600);</td>
<td>Number of deliveries†</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BT: 29.7 (11.2); 0-58</td>
<td>BT: 1.9 (1.1)</td>
<td>BT: 28</td>
<td>1,470-4,890</td>
<td>- ST: 111</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>p&lt;0.05)*</td>
<td></td>
<td>(p=NR)</td>
<td>BT: 3,573 (522); 1,880-5,120</td>
<td>- BT: 96</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>(p=NR)</td>
<td>Low back pain during pregnancy‡</td>
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<td></td>
<td></td>
<td></td>
<td>- ST: 39 (35.1%)</td>
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</tr>
<tr>
<td>Danielsson 2001b††</td>
<td>n=247</td>
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<td></td>
<td></td>
<td></td>
<td>- BT: 41 (43.1%)</td>
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<tr>
<td></td>
<td>ST: 136</td>
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<td></td>
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<td></td>
<td>Low back pain during pregnancy‡</td>
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<td></td>
<td>BT: 111</td>
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<td></td>
<td></td>
<td></td>
<td>- ST: 39 (35.1%)</td>
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<td>- BT: 41 (43.1%)</td>
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<td></td>
<td></td>
<td>Vacuum extraction‡</td>
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<td></td>
<td>- ST: 18 (16.2%)</td>
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<td>- BT: 8 (8.4%)</td>
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<td></td>
<td></td>
<td></td>
<td>(p=0.14)</td>
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<td></td>
<td>Caesarean sections‡</td>
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<td>- ST: 21 (18.9%)</td>
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<td>- BT: 13 (13.7%)</td>
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<td></td>
<td>Number of deliveries‡</td>
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<td>- ST: 243</td>
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<td>- BT: 207</td>
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<td></td>
<td>Low back pain during pregnancy‡</td>
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<td>- ST: 88 (36.2%)</td>
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<td>- BT: 96 (46.4%)</td>
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<td></td>
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<td></td>
<td>Vacuum extraction‡</td>
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<td></td>
<td>- ST: 26 (10.7%)</td>
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<td></td>
<td></td>
<td>- BT: 10 (4.8%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Caesarean sections‡</td>
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<td></td>
<td>- ST: 37 (15.2%)</td>
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<td></td>
<td></td>
<td>- BT: 25 (12.1%)</td>
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</tr>
</tbody>
</table>

* Reported in Danielsson 2001 paper†† with n=248 (ST=139; BT=109)
†† Values reported for women who had ≥1 children (ST=111; BT=95)
‡‡ P values not reported

Abbreviations: KQ = key question; AIS = adolescent idiopathic scoliosis; SD = standard deviation; BT = brace-treated group; ST = surgically treated group; NR = not reported
### Table 21. Harms of Bracing: Included Study and Harms Reported (KQ6)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Intervention</th>
<th>Study population</th>
<th>How adverse events assessed</th>
<th>Adverse (psychological) % (Number of/ total participants)</th>
<th>Adverse (physical) % (Number of/ total participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAIST</td>
<td>Prospective</td>
<td>IG: Rigid TLSO (18 hours/day)</td>
<td>Female %: IG: 92%</td>
<td>Adverse events and quality-of-life scores were monitored at each followup assessment (every 6 months) and reported to the data and safety monitoring board.</td>
<td>Anxiety/depression requiring hospitalization: IG: 0.7% (1/146) CG: 0% (0/96)</td>
<td>Skin problems on trunk (bruising, laceration, ulcers, pressure sores, rash): IG: 8.2% (12/146) CG: 0% (0/96)</td>
</tr>
<tr>
<td>Weinstein 2013</td>
<td>CCT 2007-2013</td>
<td>CG: Observation</td>
<td>CG: 90 %</td>
<td></td>
<td>Anxiety, depression: IG: 2.1% (3/146) CG: 1.0% (1/96)</td>
<td>Abnormal breast development: IG: 0% (0/146) CG: 1.0% (1/96)</td>
</tr>
<tr>
<td>USA, Canada</td>
<td>Good</td>
<td>Mean length of treatment/ followup (years): IG: 2.0 (NR) CG: 1.8 (NR)</td>
<td>Age, mean IG: 12.7</td>
<td></td>
<td></td>
<td>Body pain (other than back pain):* IG: 8.2% (12/146) CG: 2.1% (2/96)</td>
</tr>
<tr>
<td>Good</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neurologic symptoms:* IG: 4.8% (7/146) CG: 2.1% (2/96)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>GI &amp; respiratory:* IG: 1.4% (2/146) CG: 0% (0/96)</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>Self-reported psychological:* IG: 1.4% (2/146) CG: 0% (0/96)</td>
</tr>
</tbody>
</table>

Note: study also included for KQ3

* Values and percentages were calculated based on data provided in Appendix of Weinstein 2013

Abbreviations: KQ = key question; BRAIST = Bracing in Adolescent Idiopathic Scoliosis Trial; CCT = controlled clinical trial; TLSO = thoracolumbosacral orthosis (various types); IG = intervention group; CG = control group; GI = gastrointestinal
Table 22. Estimated Complication Rates From Surgery for AIS

<table>
<thead>
<tr>
<th>Type of surgery or instrumentation</th>
<th>Estimated rate in AIS patients</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harrington rod</td>
<td>6.5%</td>
<td>Systematic review (5 studies; n=849)(^{150})</td>
</tr>
<tr>
<td>Cotrel-Dubousset</td>
<td>4.3%</td>
<td>Systematic review (6 studies; n=271)(^{74})</td>
</tr>
<tr>
<td>Pedicle screws</td>
<td>1.0%</td>
<td>Systematic review (12 studies; n=1045)(^{72})</td>
</tr>
<tr>
<td>Pseudoarthrosis (failed spinal fusion)</td>
<td>3.6%</td>
<td>Systematic review (10 studies; n=1484)(^{150})</td>
</tr>
<tr>
<td>Harrington rod</td>
<td>1.7%</td>
<td>Systematic review (6 studies; n=177)(^{74})</td>
</tr>
<tr>
<td>Cotrel-Dubousset</td>
<td>0.5%</td>
<td>Systematic review (5 studies; n=192)(^{72})</td>
</tr>
<tr>
<td>Pedicle screws</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurologic complications</td>
<td>0%</td>
<td>Systematic review (5 studies; n=577)(^{74})</td>
</tr>
<tr>
<td>Harrington rod</td>
<td>0.7%</td>
<td>Systematic review (7 studies; n=305)(^{74})</td>
</tr>
<tr>
<td>Cotrel-Dubousset</td>
<td>0.06%</td>
<td>Systematic review (21 studies; n=1666)(^{72})</td>
</tr>
<tr>
<td>Pedicle screws</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implant failure or removal</td>
<td>15.8%</td>
<td>Systematic review (8 studies; n=1278)(^{136})</td>
</tr>
<tr>
<td>Harrington rod</td>
<td>5%</td>
<td>Prospective cohort (n=100)(^{136})</td>
</tr>
<tr>
<td>Cotrel-Dubousset</td>
<td>7.1%</td>
<td>Systematic review (1 study; n=14)(^{150})</td>
</tr>
<tr>
<td>Pedicle screws</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-operation</td>
<td>11.9%</td>
<td>Systematic review (8 studies; n=1251)(^{136})</td>
</tr>
<tr>
<td>Harrington rod</td>
<td>1%</td>
<td>Prospective cohort (n=100)(^{136})</td>
</tr>
<tr>
<td>Cotrel-Dubousset</td>
<td>10.83%</td>
<td>Systematic review (16 studies; n=1436)(^{72})</td>
</tr>
<tr>
<td>Pedicle screws</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AIS = adolescent idiopathic scoliosis
<table>
<thead>
<tr>
<th>Key Question</th>
<th>No. of studies (k), no. of observations (n)</th>
<th>Study Designs</th>
<th>Summary of Findings by Outcome</th>
<th>Consistency/ Precision</th>
<th>Reporting Bias</th>
<th>Overall Quality</th>
<th>Body of Evidence Limitations</th>
<th>EPC Assessment of Strength of Evidence</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ1</td>
<td>No studies</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>KQ2</td>
<td>K=7, n=447,243</td>
<td>Observational studies of screening programs (6/7 school-based)</td>
<td>FBT ± S (4 studies): Sensitivity (1 study): 71.1% Specificity (1 study): 97.1% PPV (4 studies): 29.3%-54.1% FBT+S+M (1 study) Sensitivity: 93.8% Specificity: 99.2% PPV: 81.0%</td>
<td>Inconsistent</td>
<td>Undetected</td>
<td>7 Fair</td>
<td>Limited/ad hoc to no followup of screen-negative children; heterogeneity of screening modality and screening procedures; limited description of screening populations and subgroups</td>
<td>Low</td>
<td>Moiré topography and surgeon-conducted screening may not be feasible in US school-based screening programs</td>
</tr>
<tr>
<td>KQ3 bracing</td>
<td>K=3 n=347</td>
<td>RCT/CCT</td>
<td>K=2 n=304 observational</td>
<td>Curve progression: Four prospective studies (one RCT), suggest a benefit to bracing Dose-response: Evidence for dose-response relationship between hours of brace wear and curve progression in one study Quality of life: similar at baseline and followup in IG and CG</td>
<td>Reasonably consistent</td>
<td>Undetected</td>
<td>3 Fair</td>
<td>Higher quality studies show benefit of bracing; smaller studies not powered to look at curve outcomes found nonsignificant results. Very limited data on QOL associated with bracing.</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
Table 23. Summary of Evidence

<table>
<thead>
<tr>
<th>Key Question</th>
<th>No. of studies (k), no. of observations (n) Study Designs</th>
<th>Summary of Findings by Outcome</th>
<th>Consistency/ Precision</th>
<th>Reporting Bias</th>
<th>Overall Quality</th>
<th>Body of Evidence Limitations</th>
<th>EPC Assessment of Strength of Evidence</th>
<th>Applicability</th>
</tr>
</thead>
</table>
| KQ3 exercise | K=2  
n=184  
RCT/CCT                                           | Curve progression: In one good-quality RCT, the intervention group had a favorable reduction in Cobb angle of 4.9 degrees compared to an unfavorable 2.8 degree progression in the control group.  
A smaller, fair-quality CCT published earlier found similar results.  
Quality of life: Improved pain, function, self-image, and mental health; lack of improvement in control group | Reasonably consistent  
Imprecise | Undetected | 1 Good  
1 Fair | Only two included studies; blinding of treatment allocation not possible | Low | Likely applicable to U.S. setting given access to trained physiotherapist |
| KQ3 surgery  | No studies                                          | NA                             | NA                     | NA             | NA             | NA                          | NA                                   | NA            |
| KQ4          | K=2  
n=339                                           | No direct evidence on association between curve at skeletal maturity and adult outcomes. However, quality of life, pulmonary, and pregnancy outcomes were similar for adults who had received observation, bracing, and surgery in adolescence. | Reasonably consistent  
Imprecise | Undetected | 2 Fair | Small body of evidence, studies not designed to answer current KQ | Low | Limited; some obsolete treatments were included |
| KQ5          | No studies                                          | NA                             | NA                     | NA             | NA             | NA                          | NA                                   | NA            |
### Table 23. Summary of Evidence

<table>
<thead>
<tr>
<th>Key Question</th>
<th>No. of studies (k), no. of observations (n)</th>
<th>Study Designs</th>
<th>Summary of Findings by Outcome</th>
<th>Consistency/Precision</th>
<th>Reporting Bias</th>
<th>Overall Quality</th>
<th>Body of Evidence Limitations</th>
<th>EPC Assessment of Strength of Evidence</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ6 bracing</td>
<td>K=1 n=242 CCT</td>
<td></td>
<td>1/146 anxiety/depression requiring hospitalization in braced group vs 0/96 in control group; 3/146 anxiety/depression in IG vs 1/96 in CG</td>
<td>NA (1 study)</td>
<td>Undetected</td>
<td>1 Good</td>
<td>One study</td>
<td>Low</td>
<td>Likely applicable in U.S. primary care setting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Skin problems on trunk more likely in braced group (12/146) than controls (0/96); higher rate of non-back pain in braced vs controls (12/146 vs 2/96).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Similar rates of abnormal breast development, neurologic symptoms, and GI or respiratory symptoms in braced vs controls.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KQ6 surgery</td>
<td>No studies</td>
<td></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>KQ6 exercise</td>
<td>No studies</td>
<td></td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: KQ = key question; NA = not applicable; IG = intervention group; CG = control group; RCT = randomized clinical trial; CCT = controlled clinical trial; PPV = positive predictive value; ATR = angle of trunk rotation; GI = gastrointestinal; FBT = forward bend test; S = scoliometer; M = Moiré topography
Appendix A. Detailed Methods

Search Strategy

Cochrane Database of Systematic Reviews (Issue 5 of 12, May 2015)
#1 (scoliosis or scolioses):ti,ab,kw
#2 (idiopathic or ideopathic):ti,ab,kw
#3 (caus* or etiolog* or aetiolog*):ti,ab,kw near/3 (unknow* or undetermin* or undiscover*):ti,ab,kw
#4 #2 or #3
#5 (child* or teen or teens or teenage* or adolescen* or youth or youths or "young people" or pediatric* or paediatric* or toddler* or school* or girl* or boy*):ti,ab,kw
#6 #1 and #4 and #5 Publication Year from 2004 to 2015, in Cochrane Reviews (Reviews and Protocols)

Database of Abstracts of Reviews of Effects via Centre for Reviews and Dissemination

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<thead>
<tr>
<th>Line</th>
<th>Search</th>
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<tbody>
<tr>
<td>1</td>
<td>(scoliosis or scolioses) IN DARE FROM 2004 TO 2015</td>
</tr>
<tr>
<td>2</td>
<td>(child* or teen or teens or teenage* or adolescen* or youth or youths or &quot;young people&quot; or pediatric* or paediatric* or toddler* or school* or girl* or boy*) IN DARE FROM 2004 TO 2015</td>
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<tr>
<td>3</td>
<td>#1 AND #2</td>
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Health Technology Assessment via Centre for Reviews and Dissemination

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<tbody>
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OVID MEDLINE

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>, Ovid MEDLINE(R) Daily Update <May 11, 2015>
Search Strategy:

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</tr>
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<td>(scoliosis or scolioses).ti.</td>
</tr>
<tr>
<td>3</td>
<td>1 or 2</td>
</tr>
<tr>
<td>4</td>
<td>idiopathic.ti,ab.</td>
</tr>
<tr>
<td>5</td>
<td>ideopathic.ti,ab.</td>
</tr>
<tr>
<td>6</td>
<td>((caus* or etiolog* or aetiolog*) adj3 (unknow* or undetermin* or undiscover*)).ti,ab.</td>
</tr>
<tr>
<td>7</td>
<td>4 or 5 or 6</td>
</tr>
<tr>
<td>8</td>
<td>Child/</td>
</tr>
<tr>
<td>9</td>
<td>Child, Preschool/</td>
</tr>
<tr>
<td>10</td>
<td>Adolescent/</td>
</tr>
<tr>
<td>11</td>
<td>(child* or teen or teens or teenage* or adolescen* or youth or youths or young people or young adult* or pediatric* or paediatric* or toddler* or school* or girl* or boy*).ti.</td>
</tr>
<tr>
<td>12</td>
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<td>14</td>
<td>8 or 9 or 10 or 11 or 13</td>
</tr>
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<td>15</td>
<td>3 and 7 and 14</td>
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<td>18</td>
<td>remove duplicates from 17</td>
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Appendix A. Detailed Methods

**PubMed** [publisher-supplied references only]

<table>
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<th>Search</th>
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<td>Search #6 AND systematic[sh] AND publisher[sh] AND English[language]</td>
</tr>
<tr>
<td>#6</td>
<td>Search #1 AND #4 AND #5</td>
</tr>
<tr>
<td>#4</td>
<td>Search #2 OR #3</td>
</tr>
<tr>
<td>#2</td>
<td>Search idiopathic[tiab] OR ideopathic[tiab]</td>
</tr>
<tr>
<td>#1</td>
<td>Search scoliosis[tiab] OR scolioses[tiab]</td>
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</tbody>
</table>

**Adolescent Idiopathic Scoliosis**

<table>
<thead>
<tr>
<th>Sources Searched</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochrane Central Register of Clinical Trials</td>
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<tr>
<td>OVID Medline</td>
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<tr>
<td>ERIC (Eric.ed.gov)</td>
</tr>
<tr>
<td>PUBMED, publisher-supplied</td>
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<tr>
<td>CINAHL</td>
</tr>
</tbody>
</table>

Key:
/ = MeSH subject heading
* = truncation
ab = word in abstract
adj# = adjacent within x number of words
ae = adverse effects
co= complications
in= injuries
po= poisoning
re= radiation effects
mo= mortality
hw = subject heading word
tw= text word
kw= keyword
N# = adjacent within x number of words
Cochrane Central Register of Controlled Trials
Issue 9 of 12, September 2016
#1 (scolio*):ti,ab,kw
#2 (child* or teen or teens or teenage* or adolescen* or youth* or "young people" or "young adult" or "young adults" or pediatric* or paediatric* or toddler* or school* or girl* or boy*):ti,ab,kw
#3 #1 and #2 Publication Year from 1966 to 2016, in Trials

Ovid MEDLINE(R) Epub Ahead of Print <October 12, 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <October 07, 2016>, Ovid MEDLINE(R) <1946 to October Week 1 2016>, Ovid MEDLINE(R) Daily Update <October 03, 2016>

KQ1 & KQ2
What is the evidence that screening for adolescent idiopathic scoliosis improves a) health outcomes and b) degree of curve in childhood?
What is the accuracy of screening for adolescent idiopathic scoliosis?
Appendix A. Detailed Methods

28 Photogrammetry/
29 photogram*.ti,ab.
30 Radiostereometric Analysis/
31 (stereoradio* or radiostereo* or stereophoto* or photostereo* or stereoscop*).ti,ab.
32 Image Interpretation, Computer-Assisted/
33 Radiographic Image Interpretation, Computer-Assisted/
34 Radiographic Image Enhancement/
35 Tomography, X-Ray Computed/
36 (formetric* or biplanar* or digital slot* or auscan*).ti,ab.
37 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or
25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials
as topic/ or meta-analysis as topic/
39 (clinical trial or controlled clinical trial or meta analysis or randomized controlled trial).pt.
40 Random*.ti,ab.
41 control groups/ or double-blind method/ or single-blind method/
42 clinical trial*.ti,ab.
43 controlled trial*.ti,ab.
44 meta analy*.ti,ab.
45 cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or
retrospective studies/
46 cohort.ti,ab.
47 longitudinal.ti,ab.
48 (follow up or followup).ti,ab.
49 Registries/
50 (registri* or register*).ti,ab.
51 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
52 3 and 8 and 37 and 51
53 remove duplicates from 52
54 limit 53 to english language
55 Animals/ not (Humans/ and Animals/)
56 54 not 55

Ovid MEDLINE(R) Epub Ahead of Print <October 12, 2016>, Ovid MEDLINE(R) In-
Process & Other Non-Indexed Citations <October 07, 2016>, Ovid MEDLINE(R) <1946 to
October Week 1 2016>, Ovid MEDLINE(R) Daily Update <October 03, 2016>

KQ3
What are the harms of screening for adolescent idiopathic scoliosis?

1 Scoliosis/
2 scolio*.ti,ab.
3 1 or 2
4 Child/
5 Child, Preschool/
6 Adolescent/
Appendix A. Detailed Methods

7 (child* or teen or teens or teenage* or adolescen* or youth or youths or young people or young adult* or pediatric* or paediatric* or toddler* or school* or girl* or boy*).ti,ab.
8 4 or 5 or 6 or 7
9 Mass Screening/
10 screen*.ti,ab.
11 detect*.ti,ab.
12 forward bend*.ti,ab.
13 surface topograph*.ti,ab.
14 plumb line*.ti,ab.
15 ((spine or spinal or back) adj3 contour).ti,ab.
16 scoliomet*.ti,ab.
17 inclinomet*.ti,ab.
18 cobb angle*.ti,ab.
19 Moire Topography/
20 moire.ti,ab.
21 X-Rays/
22 (x ray* or xray*).ti,ab.
23 Radiography/
24 radiograph*.ti,ab.
25 Imaging, Three-Dimensional/
26 (three dimension* or 3d or 3 dimension*).ti,ab.
27 Image Processing, Computer-Assisted/
28 Photogrammetry/
29 photogram*.ti,ab.
30 Radiostereometric Analysis/
31 (stereoradio* or radiostereo* or stereophoto* or photostereo* or stereoscop*).ti,ab.
32 Image Interpretation, Computer-Assisted/
33 Radiographic Image Interpretation, Computer-Assisted/
34 Radiographic Image Enhancement/
35 Tomography, X-Ray Computed/
36 (formetric* or biplanar* or digital slot* or auscan*).ti,ab.
37 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or
25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38 Mortality/
39 Morbidity/
40 Death/
41 "Drug-Related Side Effects and Adverse Reactions"/
42 safety.ti,ab.
43 harm*.ti,ab.
44 mortal*.ti,ab.
45 toxic*.ti,ab.
46 complicat*.ti,ab.
47 (death or deaths).ti,ab.
48 (adverse adj2 (interaction* or response* or effect* or event* or reaction* or
outcome*)).ti,ab.
49 adverse effects.fs.
Appendix A. Detailed Methods

50 toxicity.fs.
51 mortality.fs.
52 complications.fs.
53 label*.ti,ab.
54 Radiation Injuries/
55 radiatior.ti,ab.
56 psycho*.ti,ab.
57 (social* or socio* or societ* or cultur*).ti,ab.
58 Self Concept/
59 Self Efficacy/
60 (self adj3 (aware* or percept* or perceiv* or imag* or doubt* or concept* or critic*)).ti,ab.
61 Body Image/
62 (body adj3 imag*).ti,ab.
63 (isolat* or lonely or loneliness).ti,ab.
64 Bullying/
65 Aggression/
66 (bully* or bullie* or aggressiv* or aggression* or teas* or harass*).ti,ab.
67 "Conflict (Psychology)/"
68 conflict*.ti,ab.
69 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68
70 3 and 8 and 37 and 69
71 remove duplicates from 70
72 limit 71 to english language
73 Animals/ not (Humans/ and Animals/)
74 72 not 73

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Process & Other Non-Indexed Citations <October 07, 2016>, Ovid MEDLINE(R) <1946 to
October Week 1 2016>, Ovid MEDLINE(R) Daily Update <October 03, 2016>

KQ4
What is the evidence that treatment of people with screening-relevant adolescent idiopathic
scoliosis improves a) health outcomes and b) degree of curve in childhood or adulthood?

1 Scoliosis/
2 scolio*.ti,ab.
3 1 or 2
4 Child/
5 Child, Preschool/
6 Adolescent/
7 (child* or teen or teens or teenage* or adolescen* or youth or youths or young people or young adult* or pediatric* or paediatric* or toddler* or school* or girl* or boy*).ti,ab.
8 4 or 5 or 6 or 7
9 clinical trials as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/ or meta-analysis as topic/
Appendix A. Detailed Methods

10 (clinical trial or controlled clinical trial or meta analysis or randomized controlled trial).pt.
11 Random*.ti,ab.
12 control groups/ or double-blind method/ or single-blind method/
13 clinical trial*.ti,ab.
14 controlled trial*.ti,ab.
15 meta analy*.ti,ab.
16 cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/
17 cohort.ti,ab.
18 longitudinal.ti,ab.
19 (follow up or followup).ti,ab.
20 Registries/
21 (registr* or register*).ti,ab.
22 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 Watchful Waiting/
24 observ*.ti,ab.
25 Braces/
26 (brace or braces or bracing or braced).ti,ab.
27 Surgical Procedures, Operative/
28 surg*.ti,ab.
29 operat*.ti,ab.
30 realign*.ti,ab.
31 Spinal Fusion/
32 (spondylodesis or spondylodeses or spondylosyndesis or spondylosyndeses).ti,ab.
33 (fusion* adj3 (spine or spinal)).ti,ab.
34 (instrument* adj3 (spine or spinal)).ti,ab.
35 harrington*.ti,ab.
36 Bone Screws/
37 Pedicle Screws/
38 screw*.ti,ab.
39 Bone Wires/
40 (wire or wires or wiring or wired).ti,ab.
41 Bone Nails/
42 nail*.ti,ab.
43 Bone Plates/
44 (plate* or plating).ti,ab.
45 Suture Anchors/
46 Internal Fixators/
47 sublaminar.ti,ab.
48 kirschner.ti,ab.
49 hook*.ti,ab.
50 Casts, Surgical/
51 cast*.ti,ab.
52 Splints/
53 splint*.ti,ab.
54 External Fixators/
Appendix A. Detailed Methods

55 Immobilization/
56 (immobil* or stabil*).ti,ab.
57 Restraint, Physical/
58 Orthopedics/
59 Orthopedic Procedures/
60 Manipulation, Orthopedic/
61 Orthopedic Fixation Devices/
62 (orthoped* or orthopaed*).ti,ab.
63 Orthotic Devices/
64 orthotic*.ti,ab.
65 Electric Stimulation Therapy/
66 (electric* adj3 stimulat*).ti,ab.
67 electrotherap*.ti,ab.
68 Spinal Cord Stimulation/
69 Exercise/
70 Exercise Movement Techniques/
71 Dance Therapy/
72 Exercise Therapy/
73 Motion Therapy, Continuous Passive/
74 Muscle Stretching Exercises/
75 Plyometric Exercise/
76 Resistance Training/
77 Movement/
78 (exercis* or movement* or motion*).ti,ab.
79 Locomotion/
80 Walking/
81 Running/
82 Jogging/
83 (run* or walk* or jog*).ti,ab.
84 Musculoskeletal Manipulations/
85 ((muscu* or muscle) adj3 manip*).ti,ab.
86 Kinesiology, Applied/
87 Manipulation, Chiropractic/
88 Manipulation, Osteopathic/
89 Manipulation, Spinal/
90 Therapy, Soft Tissue/
91 Acupressure/
92 Massage/
93 Acupuncture Therapy/
94 Electroacupuncture/
95 (kinesiolog* or kinesiotherap* or chiropract* or osteopath* or acupres* or massag* or electroacupunctur* or acupunctur*).ti,ab.
96 Rehabilitation/
97 rehabilit*.ti,ab.
98 Early Ambulation/
99 Physical Therapy Modalities/
Appendix A. Detailed Methods

100 physical therap*.ti,ab.
101 physiotherap*.ti,ab.
102 Balneology/
103 Hydrotherapy/
104 (balneo* or hydrotherap*).ti,ab.
105 (water adj3 therap*).ti,ab.
106 Swimming/
107 swim*.ti,ab.
108 (tape or tapes or taped or taping).ti,ab.
109 or/23-108
110 3 and 8 and 22 and 109
111 Scoliosis/dt [Drug Therapy]
112 Scoliosis/pc [Prevention & Control]
113 Scoliosis/rt [Radiotherapy]
114 Scoliosis/rh [Rehabilitation]
115 Scoliosis/su [Surgery]
116 Scoliosis/th [Therapy]
117 or/111-116
118 8 and 22 and 117
119 110 or 118
120 remove duplicates from 119
121 limit 120 to english language
122 Animals/ not (Humans/ and Animals/)
123 121 not 122

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KQ5
What are the harms of treatment for persons with screening-relevant adolescent idiopathic scoliosis?

1 Scoliosis/
2 scolio*.ti,ab.
3 1 or 2
4 Child/
5 Child, Preschool/
6 Adolescent/
7 (child* or teen or teens or teenage* or adolescen* or youth or youths or young people or young adult* or pediatric* or paediatric* or toddler* or school* or girl* or boy*).ti,ab.
8 4 or 5 or 6 or 7
9 Watchful Waiting/
10 observ*.ti,ab.
11 Braces/
12 (brace or braces or bracing or braced).ti,ab.
Appendix A. Detailed Methods

13 Surgical Procedures, Operative/
14 surg*.ti,ab.
15 operat*.ti,ab.
16 realign*.ti,ab.
17 Spinal Fusion/
18 (spondylodesis or spondylodeses or spondylosyndesis or spondylosyndeses).ti,ab.
19 (fusion* adj3 (spine or spinal)).ti,ab.
20 (instrument* adj3 (spine or spinal)).ti,ab.
21 harrington*.ti,ab.
22 Bone Screws/
23 Pedicle Screws/
24 screw*.ti,ab.
25 Bone Wires/
26 (wire or wires or wiring or wired).ti,ab.
27 Bone Nails/
28 nail*.ti,ab.
29 Bone Plates/
30 (plate* or plating).ti,ab.
31 Suture Anchors/
32 Internal Fixators/
33 sublaminar.ti,ab.
34 kirschner.ti,ab.
35 hook*.ti,ab.
36 Casts, Surgical/
37 cast*.ti,ab.
38 Splints/
39 splint*.ti,ab.
40 External Fixators/
41 Immobilization/
42 (immobil* or stabil*).ti,ab.
43 Restraint, Physical/
44 Orthopedics/
45 Orthopedic Procedures/
46 Manipulation, Orthopedic/
47 Orthopedic Fixation Devices/
48 (orthoped* or orthopaed*).ti,ab.
49 Orthotic Devices/
50 orthotic*.ti,ab.
51 Electric Stimulation Therapy/
52 (electric* adj3 stimulat*).ti,ab.
53 electrotherap*.ti,ab.
54 Spinal Cord Stimulation/
55 Exercise/
56 Exercise Movement Techniques/
57 Dance Therapy/
58 Exercise Therapy/
Appendix A. Detailed Methods

59 Motion Therapy, Continuous Passive/
60 Muscle Stretching Exercises/
61 Plyometric Exercise/
62 Resistance Training/
63 Movement/
64 (exercis* or movement* or motion*).ti,ab.
65 Locomotion/
66 Walking/
67 Running/
68 Jogging/
69 (run* or walk* or jog*).ti,ab.
70 Musculoskeletal Manipulations/
71 ((muscu* or muscle) adj3 manip*).ti,ab.
72 Kinesiology, Applied/
73 Manipulation, Chiropractic/
74 Manipulation, Osteopathic/
75 Manipulation, Spinal/
76 Therapy, Soft Tissue/
77 Acupressure/
78 Massage/
79 Acupuncture Therapy/
80 Electroacupuncture/
81 (kinesiolog* or kinesiotherap* or chiropract* or osteopath* or acupres* or massag* or electroacupunctur* or acupunctur*).ti,ab.
82 Rehabilitation/
83 rehabilit*ti,ab.
84 Early Ambulation/
85 Physical Therapy Modalities/
86 physical therap*ti,ab.
87 physiotherap*ti,ab.
88 Balneology/
89 Hydrotherapy/
90 (balneo* or hydrotherap*).ti,ab.
91 (water adj3 therap*).ti,ab.
92 Swimming/
93 swim*ti,ab.
94 (tape or tapes or taped or taping).ti,ab.
95 or/9-94
96 3 and 8 and 95
97 Scoliosis/dt [Drug Therapy]
98 Scoliosis/pc [Prevention & Control]
99 Scoliosis/rt [Radiotherapy]
100 Scoliosis/rh [Rehabilitation]
101 Scoliosis/su [Surgery]
102 Scoliosis/th [Therapy]
103 or/97-102
Appendix A. Detailed Methods

104  103 and 8
105  96 or 104
106  Mortality/
107  Morbidity/
108  Death/
109  "Drug-Related Side Effects and Adverse Reactions"/
110  safety.ti,ab.
111  harm*.ti,ab.
112  mortal*.ti,ab.
113  toxic*.ti,ab.
114  complication*.ti,ab.
115  (death or deaths).ti,ab.
116  (adverse adj2 (interaction* or response* or effect* or event* or reaction* or outcome*)).ti,ab.
117  adverse effects.fs.
118  toxicity.fs.
119  mortality.fs.
120  complications.fs.
121  Pain/
122  Acute Pain/
123  Back Pain/
124  Failed Back Surgery Syndrome/
125  Low Back Pain/
126  pain*.ti,ab.
127  backache*.ti,ab.
128  back ache*.ti,ab.
129  Intraoperative Complications/
130  Blood Loss, Surgical/
131  Postoperative Hemorrhage/
132  (blood* or bleed* or hemorrhag*or haemorrhag*).ti,ab.
133  Intraoperative Awareness/
134  Malignant Hyperthermia/
135  Postoperative Complications/
136  "delayed emergence from anesthesia"/
137  Pain, Postoperative/
138  "Postoperative Nausea and Vomiting"/
139  (nause* or vomit* or emetic or emesis).ti,ab.
140  shock, surgical/
141  shock.ti,ab.
142  Surgical Wound Dehiscence/
143  Surgical Wound Infection/
144  infect*.ti,ab.
145  Vasoplegia/
146  "Recovery of Function"/
147  ((decrease* or diminish* or reduce* or minim* or compromis* or lack* or lower* or improper* or incomplet* or damag* or limit*) adj3 function*).ti,ab.
Appendix A. Detailed Methods

148 mobility limitation/
149 psycho*.ti,ab.
150 or/106-149
151 105 and 150
152 remove duplicates from 151
153 limit 152 to english language
154 Animals/ not (Humans/ and Animals/)
155 153 not 154

Ovid MEDLINE(R) Epub Ahead of Print <October 12, 2016>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <October 07, 2016>, Ovid MEDLINE(R) <1946 to October Week 1 2016>, Ovid MEDLINE(R) Daily Update <October 03, 2016>

KQ6
What is the association between cobb angle in adolescence and health outcomes in adulthood?

1 Scoliosis/
2 scolio*.ti,ab.
3 1 or 2
4 Child/
5 Child, Preschool/
6 Adolescent/
7 (child* or teen or teens or teenage* or adolescen* or youth or youths or young people or young adult* or pediatric* or paediatric* or toddler* or school* or girl* or boy*).ti,ab.
8 4 or 5 or 6 or 7
9 cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/
10 cohort.ti,ab.
11 longitudinal.ti,ab.
12 (follow up or followup).ti,ab.
13 Registries/
14 (registr* or register*).ti,ab.
15 (evolv* or evolu*).ti,ab.
16 natural histor*.ti,ab.
17 (curv* adj3 (progress* or develop*)).ti,ab.
18 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19 3 and 8 and 18
20 remove duplicates from 19
21 limit 20 to english language
22 Animals/ not (Humans/ and Animals/)
23 21 not 22

ERIC http://eric.ed.gov/
Scoliosis OR scolioses OR scoliotic OR scoliosies OR scoliosi
### PubMed Publisher-Supplied

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<td>S108</td>
<td>(decrease* OR diminish* OR reduc* OR minim* OR compromis* OR lack* OR lower* OR improper* OR incomplet* OR damag* OR limit*) N3 (function* OR mobil*)</td>
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<td>S107</td>
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<td>S106</td>
<td>AB infect*</td>
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<tr>
<td>S105</td>
<td>TI infect*</td>
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<td>S104</td>
<td>(MH &quot;Surgical Wound Infection&quot;)</td>
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<td>S103</td>
<td>(MH &quot;Surgical Wound Dehiscence&quot;)</td>
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<td>AB shock</td>
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<tr>
<td>S101</td>
<td>TI shock</td>
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<tr>
<td>S100</td>
<td>(MH &quot;Shock, Surgical&quot;)</td>
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<tr>
<td>S99</td>
<td>AB (nause* or vomit* or emetic or emesis)</td>
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<td>S98</td>
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<td>S95</td>
<td>(MH &quot;Chronic Pain&quot;)</td>
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### Appendix A. Detailed Methods

| S94  | (MH "Postoperative Pain") |
| S93  | (MH "Postoperative Complications") |
| S92  | (MH "Malignant Hyperthermia") |
| S91  | (MH "Intraoperative Awareness") |
| S90  | AB (blood* or bleed* or hemorrhag*or haemorrhag*) |
| S89  | TI (blood* or bleed* or hemorrhag*or haemorrhag*) |
| S88  | (MH "Postoperative Hemorrhage") |
| S87  | (MH "Blood Loss, Surgical") |
| S86  | (MH "Intraoperative Complications") |
| S85  | AB (pain* OR backache* OR "back ache**") |
| S84  | TI (pain* OR backache* OR "back ache**") |
| S83  | (MH "Failed Back Surgery Syndrome") |
| S82  | (MH "Low Back Pain") |
| S81  | (MH "Back Pain") |
| S80  | (MH "Pain") |
| S79  | (TI conflict*) OR (AB conflict*) |
| S78  | (MH "Conflict (Psychology)") |
| S77  | AB (bully* or bullie* or aggressiv* or aggression* or teas* or harass* or abus*) |
| S76  | TI (bully* or bullie* or aggressiv* or aggression* or teas* or harass* or abus*) |
| S75  | (MH "Verbal Abuse") |
| S74  | (MH "Student Abuse") |
| S73  | (MH "Aggression") |
| S72  | (MH "Bullying") |
| S71  | AB (isolat* OR lonely OR loneliness) |
| S70  | TI (isolat* OR lonely OR loneliness) |
| S69  | AB (disfigur*) |
| S68  | TI (disfigur*) |
| S67  | AB (body N3 imag*) |
| S66  | TI (body N3 imag*) |
| S65  | (MH "Disfigurement") |
| S64  | (MH "Personal Appearance") |
| S63  | (MH "Body Image") |
## Appendix A. Detailed Methods

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<th>S30</th>
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<tr>
<td>S29</td>
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<td>S28</td>
<td>AB (morbid* OR mortal* OR death*)</td>
</tr>
<tr>
<td>S27</td>
<td>TI (morbid* OR mortal* OR death*)</td>
</tr>
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<td>S26</td>
<td>(MH &quot;Death&quot;)</td>
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<td>S25</td>
<td>(MH &quot;Child Mortality&quot;)</td>
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<td>S24</td>
<td>(MH &quot;Mortality&quot;)</td>
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<td>S21</td>
<td>S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20</td>
</tr>
<tr>
<td>S20</td>
<td>TI (&quot;comparison group*&quot; or &quot;control group*&quot;) OR AB (&quot;comparison group*&quot; or &quot;control group*&quot;)</td>
</tr>
<tr>
<td>S19</td>
<td>TI (&quot;controlled before and after&quot;) OR AB (&quot;controlled before and after&quot;)</td>
</tr>
<tr>
<td>S18</td>
<td>TI &quot;controlled before after&quot; OR AB &quot;controlled before after&quot;</td>
</tr>
<tr>
<td>S17</td>
<td>(TX cohort OR TI longitudinal OR AB longitudinal TI &quot;follow up&quot; OR AB &quot;follow up&quot; OR TI followup OR AB followup OR TI registr* OR AB regist* TI register* OR AB regist* OR TI evolv* OR AB evolv* OR TI evolu* OR AB evolu* OR TI &quot;natural histor*&quot; OR AB &quot;natural histor*&quot;)</td>
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<tr>
<td>S16</td>
<td>(MH &quot;Clinical Trial Registry&quot;)</td>
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| S15 | (MH "Prospective Studies") OR (MH "Concurrent Prospective Studies") OR (MH "Noncurrent Prospective Studies") OR (MH "Correlational Studies") OR (MH “Retrospective Panel Studies”)

| S14 | (MH "Meta Analysis") OR (MH "Control Group") OR (MH "Single-Blind Studies") OR (MH "Double-Blind Studies") OR (MH "Triple-Blind Studies") OR (MH "Randomized Controlled Trials") OR (MH "Clinical Trials") OR (MH "Random Assignment") OR (AB clinical n1 trial*) OR (AB controlled n1 trial*) OR (TI clinical n1 trial*) OR (TI controlled n1 trial*) OR (PT Clinical trial) OR (PT randomized controlled trial) |
| S13 | S11 OR S12 |
| S12 | (MH "Scoliosis, Idiopathic, Adolescent") |
| S11 | (S4 AND S10) |
| S10 | S5 OR S6 OR S7 OR S8 OR S9 |
| S9  | AB (child* OR teen OR teens OR teenage* OR adolescen* OR youth OR youths OR "young people" OR "young adult*" OR pediatric* OR paediatric* OR toddler* OR school* OR girl* OR boy*) |
| S8  | TI (child* OR teen OR teens OR adolescen* OR youth OR youths OR "young people" OR "young adult*" OR pediatric* OR paediatric* OR toddler* OR school* OR girl* OR boy*) |
| S7  | (MH "Child, Preschool") |
| S6  | (MH "Child") |
| S5  | (MH "Adolescence") |
| S4  | (S1 OR S2 OR S3) |
## Appendix A. Detailed Methods

<table>
<thead>
<tr>
<th>S3</th>
<th>AB (scolio*)</th>
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<tr>
<td>S2</td>
<td>TI (scolio*)</td>
</tr>
<tr>
<td>S1</td>
<td>(MH &quot;Scoliosis&quot;)</td>
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</table>
Appendix A Figure 1. Literature Flow Diagram

Number of citations identified through literature database searches: 10515

Number of citations identified through other sources (e.g., reference lists, peer reviewers): 45

Number of citations screened after duplicates removed: 8230

Number of citations excluded at title/abstract stage: 7142

Number of full-text articles assessed for eligibility: 1088

Screening full-text article: 172
Treatment full-text article: 726
Natural history full-text article: 256

Article reviewed for KQ1: 179
Article reviewed for KQ2: 179
Article reviewed for KQ5: 179
Article reviewed for KQ3: 733
Article reviewed for KQ6: 733
Article reviewed for KQ4: 263

Articles excluded for KQ1: Relevance: 0 Setting: 12 Population: 10 Quality: 0 Design: 34 Outcomes: 88 Language: 28 Intervention: 0 Screening: 7 Overlapping population: 0 Irretrievable: 0

Articles excluded for KQ2: Relevance: 0 Setting: 13 Population: 11 Quality: 0 Design: 34 Outcomes: 34 Language: 18 Intervention: 0 Screening: 56 Overlapping population: 0 Irretrieval: 0

Articles excluded for KQ5: Relevance: 26 Setting: 13 Population: 10 Quality: 0 Design: 32 Outcomes: 87 Language: 10 Intervention: 0 Screening: 9 Overlapping population: 0 Irretrieval: 0


Articles included for KQ1: 0 (0 studies)
Articles included for KQ2: 13 (7 studies)
Articles included for KQ5: 0 (0 studies)
Articles included for KQ3: 9 (7 studies)
Articles included for KQ6: 2 (1 study)
Articles included for KQ4: 5 (2 studies)
## Appendix A Table 1. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Include</th>
<th>Exclude</th>
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</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td><strong>Population</strong></td>
</tr>
</tbody>
</table>
| KQs 1, 2, 5: Asymptomatic children and adolescents ages 10 to 18 years | Persons with scoliosis of:  
- Neuromuscular etiology (e.g., cerebral palsy, myelomeningocele, muscular dystrophy, spinal muscular atrophy, spina bifida, spinal cord injuries)  
- Congenital etiology (e.g., hemivertebrae, failure of segmentation)  
- Mesenchymal/syndromic etiology (e.g., Marfan syndrome, mucopolysaccharidosis, osteogenesis imperfecta, inflammatory diseases, postoperative)  
- Early-onset idiopathic etiology (infantile [ages 0 to 3 years] or juvenile [ages 4 to 9 years]) |
| KQs 3, 6: Screen-detected* children and adolescents age 10 to 18 years diagnosed with adolescent idiopathic scoliosis that has a Cobb angle of 10° to 50° | |
| KQ 4: Screen-detected children and adolescents ages 10 to 18 years who are diagnosed with adolescent idiopathic scoliosis that has a Cobb angle of ≥10° | |
| **Settings** | **Settings** |
| • Primary care or generalizable to primary care  
• School-based screening programs  
• Countries categorized “High” on the Human Development Index (United Nations Development Programme)¹ | Specialty care (e.g., surgical clinics and clinics for conditions known to be associated with scoliosis) and other settings with a symptomatic population |
| **Screening tests** | **Screening tests** |
| KQs 1, 2, 5: Forward bend test (with or without scoliometer/inclinometer), surface topography, or other methods (e.g., back-contour device), followed by X-ray for confirmation | KQs 1, 2, 5: X-ray alone; studies where screening is completed by a single practitioner or where screening practitioner is not described; where referral criteria is not quantitatively described; or where the flow of participants through screening program incompletely described |
| **Treatments** | **Treatments** |
| KQs 3, 6:  
- Surgery  
- Nonoperative treatment, including but not limited to: bracing, physical/exercise therapy | KQs 3, 6:  
- Study treatments conducted by a single practitioner (surgeon, therapist, or bracer)  
- Population treated with exclusively Harrington rod instrumentation, Milwaukee brace (unless long-term followup study), or electrical surface stimulation |
| **Comparison** | **Comparison** |
| KQs 1, 2, 5: Usual care  
KQs 3, 6: Observation, usual care | KQs 3, 6:  
- Comparative effectiveness studies  
- Studies with a comparison group that was determined post-hoc (e.g., compliant vs. noncompliant) |
| **Outcomes** | **Outcomes** |
| Intermediate outcome in childhood or adulthood: Severity of spinal curvature  
**Health outcomes** in childhood or adulthood six months or more after surgery or treatment initiation:  
- Morbidity (e.g., pulmonary) | KQ4: People without AIS (healthy controls)  
| **Studies that do not report adult health outcomes**  
**Studies that report only spinal curve in adulthood with no adult health outcomes** |
## Appendix A Table 1. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Include</th>
<th>Exclude</th>
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<tbody>
<tr>
<td>symptoms, hypertension, lumbar radiculopathy, mortality)</td>
<td>Function, pain (these are considered outcomes, not harms), loss of correction, re-operation</td>
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<tr>
<td>• Quality of life</td>
<td>Harms that cannot be attributed to screening (KQ5) or treatment (KQ6)</td>
</tr>
<tr>
<td>• Pain</td>
<td>All KQs:</td>
</tr>
<tr>
<td>• Functional outcomes</td>
<td>• Studies rated as poor quality; case reports; cross-sectional studies</td>
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<tr>
<td>Harms</td>
<td>KQs 1–4: Case series; cost-effectiveness studies; qualitative study designs</td>
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<tr>
<td>Any screening or treatment harm present at 6 months or more after screening, surgery, or treatment initiation including but not limited to:</td>
<td>KQs 1–4: Randomized clinical trials; controlled trials; cohort studies; registry-based observational studies</td>
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<td>physiologic harm, psychosocial harm, labeling or radiation exposure</td>
<td>KQs 5, 6: Randomized clinical trials; controlled trials; cohort studies; registry-based observational studies case series, case-control</td>
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<tr>
<td>Mortality or neurologic damage at any time point</td>
<td>All KQs:</td>
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*operationalized as screen “detectable,” meaning the study has data on the population before curve reached 45-50 degrees (for example, bracing before surgery)*

Abbreviations: KQ = key question; AIS = adolescent idiopathic scoliosis
### Table 2. Quality Assessment Criteria

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Quality criteria</th>
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| Randomized controlled trials USPSTF methods\(^2\) | • Valid random assignment?  
• Was allocation concealed?  
• Was eligibility criteria specified?  
• Were groups similar at baseline?  
• Were measurements equal, valid, and reliable?  
• Was there intervention fidelity?  
• Was there adequate adherence to the intervention?  
• Were outcome assessors blinded?  
• Was there acceptable followup?  
• Were the statistical methods acceptable?  
• Was the handling of missing data appropriate?  
• Was there evidence of selective reporting of outcomes?  
• Was the device calibration and/or maintenance reported? |
| Observational studies (e.g., prospective cohort studies), adapted from the Newcastle-Ottawa Scale (NOS)\(^3\) | • Was the cohort systematically selected to avoid bias?  
• Was eligibility criteria specified?  
• Were groups similar at baseline?  
• Was the outcome of interest not present at baseline?  
• Were measurements equal, valid, and reliable?  
• Were outcome assessors blinded?  
• Was there acceptable followup?  
• Were the statistical methods acceptable?  
• Was the handling of missing data appropriate? |

Abbreviation: USPSTF = U.S. Preventive Services Task Force

### References

Appendix B. Ongoing Studies

We identified two potentially relevant ongoing or recently completed randomized clinical trials (RCTs) through two registries: ClinicalTrials.gov (http://clinicaltrials.gov), and the World Health Organization’s International Clinical Trials Registry Platform (http://www.who.int/ictrp).

The “Multicenter Schroth Exercise Trial for Scoliosis,” or MultiSETS (NCT01610908),\(^1\) is a Canadian RCT of exercise for treatment of adolescent idiopathic scoliosis (AIS). The study will examine the effectiveness of the Schroth approach, which uses scoliosis-specific exercises to strengthen postural muscles and improve posture motor control. The study population is female adolescents with AIS aged 10 to 16 who have not yet reached skeletal maturity (Risser sign 0 to 3). One group is receiving usual care plus a 6-month Schroth exercise program involving five individual sessions with a Schroth therapist, daily exercises to complete at home, and weekly group therapy sessions. The control group will receive usual care. The final data collection was expected to occur in August 2016, and the estimated study completion date is in January 2017.

Another ongoing study, called “CONservative TReatment for Adolescent Idiopathic Scoliosis,” or CONTRAIS (NCT01761305),\(^2,3\) is a Swedish RCT designed to compare the effectiveness of nighttime bracing, scoliosis-specific exercises, and physical activity in adolescents with AIS. The study population is male and female adolescents with AIS aged 9 to 17 who have not yet reached skeletal maturity. Patients will be randomized into one of three groups. All groups will receive a prescription for physical activity; one group additionally will engage in scoliosis-specific exercises, the second group additionally will receive nighttime bracing, and the third group (physical activity-only) will serve as the comparator. The final data collection is expected to occur in January 2019, and the estimated study completion date is December 2021.

References
Appendix C. Excluded Studies

<table>
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<th>Code</th>
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<td>E2</td>
<td>Not original research in a peer-reviewed journal</td>
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<td>E3</td>
<td>Publication date</td>
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<td>E4</td>
<td>Ineligible SETTING</td>
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<td>E5</td>
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<td>1.</td>
<td>[Commentary on] Spinal range of motion, muscle endurance and back pain and function at least 20 years after fusion, or brace treatment for adolescent idiopathic scoliosis: a case control study. D.C. Tracts. 2007;191:8-11 4p. PMID: 106176098. KQ1E12, KQ2E12, KQ3E9, KQ4E12, KQ5E12, KQ6E9.</td>
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<tr>
<td>10.</td>
<td>Abbott A,Moller H,Gerdhem P CONTRAIS: CONservative TRTreatement for Adolescent Idiopathic Scoliosis: A randomised controlled trial protocol. BMC musculoskeletal disorders. 2013;14:. PMID: 0. KQ1E12, KQ2E12, KQ3E6e, KQ4E12, KQ5E12, KQ6E6e.</td>
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Appendix C. Excluded Studies


36. Andersen MO, Christensen SB, Thomsen K. Outcome at 10 years after treatment for adolescent idiopathic scoliosis. Spine (03622436). 2006;313:350-354 5p. PMID: 0. KQ1E12, KQ2E12, KQ3E6, KQ4E12, KQ5E12, KQ6E6c.
Appendix C. Excluded Studies


Appendix C. Excluded Studies


Appendix C. Excluded Studies


Appendix C. Excluded Studies


Appendix C. Excluded Studies


Appendix C. Excluded Studies


Appendix C. Excluded Studies

118. Bunge EM, Habbema JDF, de Koning HJ. A randomised controlled trial on the effectiveness of bracing patients with idiopathic scoliosis: failure to include patients and lessons to be learnt. Eur Spine J. 2010;195:747-53. PMID: 20195651. KQ1E12, KQ2E12, KQ3E6e, KQ4E12, KQ5E12, KQ6E6e.

119. Bunge EM, Juttmann RE, de Koning HJ. Screening for scoliosis: do we have indications for effectiveness?. Journal of Medical Screening. 2006;131:29-33 5p. PMID: 0. KQ1E9, KQ2E6, KQ3E12, KQ4E12, KQ5E6, KQ6E12.


122. Bunge Em, Juttmann Re, Kleuver M, Biezen Fc, Koning Hj. Bracing patients with idiopathic scoliosis: design of the Dutch randomized controlled treatment trial. BMC musculoskeletal disorders. 2008;9:57. PMID: 0. KQ1E12, KQ2E12, KQ3E6e, KQ4E12, KQ5E12, KQ6E6e.


130. Burwell RG, Dangerfield PH. The NOTOM hypothesis for idiopathic scoliosis: is it nullified by the delayed puberty of female rhythmic gymnasts and ballet dancers with scoliosis?. Studies in Health Technology & Informatics. 2002;910:42708. PMID: 15457686. KQ1E12, KQ2E12, KQ3E12, KQ4E2, KQ5E12, KQ6E12.

Appendix C. Excluded Studies


Appendix C. Excluded Studies

KQ1E12, KQ2E12, KQ3E9, KQ4E6a, KQ5E12, KQ6E9.

KQ1E12, KQ2E12, KQ3E6, KQ4E12, KQ5E12, KQ6E6.

KQ1E12, KQ2E12, KQ3E9, KQ4E12, KQ5E12, KQ6E6.

KQ1E12, KQ2E12, KQ3E2, KQ4E12, KQ5E12, KQ6E2.


KQ1E12, KQ2E12, KQ3E9, KQ4E12, KQ5E12, KQ6E6a.

KQ1E12, KQ2E12, KQ3E12, KQ4E6, KQ5E12, KQ6E12.

KQ1E12, KQ2E12, KQ3E6, KQ4E12, KQ5E12, KQ6E6.

KQ1E12, KQ2E12, KQ3E12, KQ4E6, KQ5E12, KQ6E12.

KQ1E12, KQ2E12, KQ3E12, KQ4E9, KQ5E12, KQ6E12.

KQ1E12, KQ2E12, KQ3E12, KQ4E12, KQ5E12, KQ6E12.

KQ1E12, KQ2E12, KQ3E12, KQ4E6, KQ5E12, KQ6E12.

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Appendix C. Excluded Studies


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   KQ1E12, KQ2E12, KQ3E12, KQ4E9, KQ5E12, KQ6E12.

   KQ1E12, KQ2E12, KQ3E12, KQ4E6b, KQ5E12, KQ6E12.

   KQ1E12, KQ2E12, KQ3E5, KQ4E12, KQ5E12, KQ6E12.

   KQ1E12, KQ2E12, KQ3E10, KQ4E12, KQ5E12, KQ6E6.

   KQ1E12, KQ2E12, KQ3E6, KQ4E12, KQ5E12, KQ6E6.

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   KQ1E12, KQ2E12, KQ3E2, KQ4E12, KQ5E12, KQ6E2.

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   KQ1E12, KQ2E12, KQ3E6, KQ4E12, KQ5E12, KQ6E6.

   KQ1E12, KQ2E12, KQ3E2, KQ4E12, KQ5E12, KQ6E2.

   KQ1E12, KQ2E12, KQ3E9, KQ4E12, KQ5E12, KQ6E6.

   KQ1E12, KQ2E12, KQ3E10, KQ4E12, KQ5E12, KQ6E6.
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Appendix C. Excluded Studies


Appendix D Table 1. Adverse Events in Primary Analysis Population (As-Treated) of BrAIST Trial

<table>
<thead>
<tr>
<th></th>
<th>Skin bruising/lacerations (on the trunk)</th>
<th>Ulcers/pressure sores (on the trunk)</th>
<th>Rash (on the trunk)</th>
<th>Back pain</th>
<th>Abnormal breast development</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Other – as listed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Braced group (n=146)</td>
<td>Non-serious (related)*</td>
<td>4 (4)</td>
<td>3 (3)</td>
<td>5 (5)</td>
<td>33 (32)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>30 (24)</td>
</tr>
<tr>
<td>Number of events = 79</td>
<td>Serious (related)*</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Observed group (n=96)</td>
<td>Non-serious (related)*</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>30 (22)</td>
<td>1 (1)</td>
<td>--</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Number of events = 41</td>
<td>Serious (related)*</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Source: Appendix of Weinstein 2013

* The number in parentheses indicates the number of events related to BrAIST or AIS. Events were considered “related” based on the judgment of the investigator or research coordinator.

† Events were considered “serious” if the event was related to the protocol and resulted in any of the following: intervention required to prevent permanent impairment or damage, hospitalization, persistent disability, life-threatening experience or death.

‡ “Other” events listed on next page

“Other” Adverse Events: Brace (n=31)

**Serious Adverse Event**
# Anxiety and depression

**Non-Serious Adverse Event**
# Gastric discomfort/nausea after eating
# Asymmetrical patellar reflex.
# Right scapular pain.
# Self-reported depression, patient no longer participates in usual activities because of his insecurity regarding his back/appearance.
# Numbness in left shoulder blade area of back.
# Sharp, shooting pain down right arm from shoulder to elbow, numbness in forearm.
# Hip pain
# Midback pain
# Shoulder pain
# Knee pain
# Neck Pain
# Brace causing a lot of hip pain. Rubbing rubs off layer of skin so limits brace wear.
# Shoulder and under arm pain after adjustments were made to brace
# Pain near the inferior aspect of the right scapula radiating to the axillary region. Area has mild redness. Pt believes the pain is related to brace wear
# Right hip goes numb when standing or walking for a long length of time
# Asthma flair up
Appendix D Table 1. Adverse Events in Primary Analysis Population (As-Treated) of BrAIST Trial

# Occasional numbness in arms and legs and occasional spasms in arms only.
# Tingling, poking sensation on right rib area where temperature monitor in brace.
# Right arm/shoulder pain
# Participant is having back pain all the time and is no longer wearing a brace.
# Headaches while wearing the brace
# Pt. reports having suicidal thoughts
# Numbness/tingling or weakness of arms or legs, limits activity.
# Side pain, limits activity
Vasovagal response and fainting during a school field trip
Numbness occasionally in arms and legs
Salter-Harris I fracture distal phalanx of the right great toe
Abdominal pain
Injured ankle - small fracture to growth plate lateral side
Dislocated patella

“Other” Adverse Events: Observed (n=9)
# Buttock, hip and thigh pain
# Hand & feet numbness
# Numbness/tingling in fingers
# Shoulder pain
Hip pain from gymnastics
Fracture right great toe
Mild pain in right foot most likely due to clubfeet
Right heel pain due to motor vehicle accident
Uneven shoulders, pain (ache)

# Events were considered “related” based on the judgment of the investigator or research coordinator.

Reference