Screening and methodological studies on Adolescent Idiopathic Scoliosis

Dissertation for the degree of Philosophiae doctor (PhD)

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“It always seems impossible until it’s done.” Nelson Mandela.

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List of papers

This doctorate dissertation is based on the following papers, referred to in the text by Roman numerals (Paper I-IV):

Paper I

**Repeatability, reliability, and concurrent validity of the Scoliosis Research Society-22 Questionnaire, and EuroQol in Patients with Adolescent Idiopathic Scoliosis.**

Adobor RD, Rimeslåtten S, Keller A, Brox JI.

*Spine* 2010; 35: 206-209

School screening and point prevalence of adolescent idiopathic scoliosis in 4000 Norwegian children aged 12 years.

Adobor RD, Rimeslåtten S, Steen H, Brox JI.

*Scoliosis* 2011, 6:23

Paper III

**Scoliosis detection, patient characteristics, referral patterns and treatment in the absence of a screening program Norway**

Adobor RD, Riise RB, Sørensen R, Kibsgård TJ, Steen H, Brox JI.

*Scoliosis* 2012, 7:18

**A health economic evaluation of screening and treatment in patients with adolescent idiopathic scoliosis**

Adobor RD, Joranger P, Steen H, Navrud S, Brox JI.

*Scoliosis* 2014, 9:21

Paper IV
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AAP</td>
<td>American Academy of Pediatrics</td>
</tr>
<tr>
<td>AAOS</td>
<td>American Academy of Orthopaedic Surgeons</td>
</tr>
<tr>
<td>AFBT</td>
<td>Adam Forward Bending Test</td>
</tr>
<tr>
<td>AIS</td>
<td>Adolescent idiopathic scoliosis</td>
</tr>
<tr>
<td>ATR</td>
<td>Angle of trunk rotation</td>
</tr>
<tr>
<td>CBA</td>
<td>Cost benefit analysis</td>
</tr>
<tr>
<td>CD</td>
<td>Cotrel-Dubousset</td>
</tr>
<tr>
<td>CEA</td>
<td>Cost effectiveness analysis</td>
</tr>
<tr>
<td>CHQ-CF87</td>
<td>Child Health Questionnaire CF 87</td>
</tr>
<tr>
<td>CHEERS</td>
<td>Consolidated Economic Evaluation Reporting Standards</td>
</tr>
<tr>
<td>CMA</td>
<td>Cost minimization analysis</td>
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<tr>
<td>CR</td>
<td>Coefficient of repeatability</td>
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<td>CUA</td>
<td>Cost-utility analysis</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>DRG</td>
<td>Diagnosis Related Group</td>
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<td>GWAS</td>
<td>Genome-wide association studies</td>
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<tr>
<td>ICC</td>
<td>Intraclass correlation coefficient</td>
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<tr>
<td>LOSP</td>
<td>Late operative site pain</td>
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<tr>
<td>LR+</td>
<td>Likelihood ratios positive</td>
</tr>
<tr>
<td>LR-</td>
<td>Likelihood ratios negative</td>
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<tr>
<td>MCD</td>
<td>Minimal detectable change</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
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<tr>
<td>MCD</td>
<td>Minimal clinical difference</td>
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<tr>
<td>MCID</td>
<td>Minimal clinically important difference</td>
</tr>
<tr>
<td>NCSS</td>
<td>Non clinically significant scoliosis</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institute of Health</td>
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<tr>
<td>NNT</td>
<td>Number needed to treat</td>
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<tr>
<td>NNS</td>
<td>Number needed to screen</td>
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<tr>
<td>HRQoL</td>
<td>Health-related quality of life</td>
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<tr>
<td>NPV</td>
<td>Negative predictive value</td>
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<td>OUS</td>
<td>Oslo University Hospital</td>
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<tr>
<td>PedsQL</td>
<td>Pediatric Quality of Life Inventory</td>
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<tr>
<td>POSNA</td>
<td>Pediatric Orthopaedic Society of North America</td>
</tr>
<tr>
<td>PPV</td>
<td>Positive predictive value</td>
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<tr>
<td>PSA</td>
<td>Probabilistic sensitivity analyses</td>
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<tr>
<td>QALY</td>
<td>Quality Adjusted Life Years</td>
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<tr>
<td>QLSDP</td>
<td>Quality of Life for Spine Deformities Profile</td>
</tr>
<tr>
<td>RA</td>
<td>Rasch analysis</td>
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<tr>
<td>SEM</td>
<td>Standard error of the mean</td>
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<tr>
<td>SOSORT</td>
<td>Society on Scoliosis Orthopaedic and Rehabilitation Treatment</td>
</tr>
<tr>
<td>SRS</td>
<td>Scoliosis Research Society</td>
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<td>SF-36</td>
<td>Medical Outcome Study Short Form-36</td>
</tr>
<tr>
<td>SSE</td>
<td>Scoliosis specific exercises</td>
</tr>
<tr>
<td>USPSTF</td>
<td>United States Preventive Services Task Force</td>
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<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
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</table>
Adolescent idiopathic scoliosis (AIS) is a complex three dimensional deformity of the spine that affects 2-3% of healthy adolescents. The cause is not known although genetic, hormonal, and environmental factors are involved. Idiopathic scoliosis in adolescents does normally not result in death, but affects health related quality of life. Brace treatment is recommended in growing adolescents with major curves >25° and surgery is recommended for curves > 45° in immature adolescents. Treatment outcomes were in the past mainly evaluated by radiological measures. In recent years, outcome evaluation is increasingly being based on the patient’s perspective in addition to evaluations of care providers. The Scoliosis Research Society 22 questionnaire (SRS-22) is widely used to evaluate health related quality of life (HRQoL) in AIS patients. We have trans-culturally translated, validated, and adapted the SRS-22 questionnaire for use in Norwegian patients. The Norwegian version of SRS-22 questionnaire has acceptable validity and repeatability. Scoliosis progression is associated with rapid growth of the spine. Early detection by screening allows for curve monitoring and timely initiation of brace treatment leading to reduced rates of surgery that may save costs, but its effectiveness is debated. Screening was abolished in Norway in 1994 presumably for lack of efficacy and rising costs. In 2007-2008 we conducted screening on 4000, 12 year-old children. The study was originally designed to screen 12000 children, but was not supported by the Directorate of Health. The point prevalence of scoliosis was 0.55%. We found acceptable sensitivity, specificity, and positive and negative predictive values. Screening performed once, was fast, simple and inexpensive, but did not detect any child suitable for bracing. During 2003-2011, 765 children were referred to our specialist clinic and their characteristics were evaluated. Close to 80% were detected by non-health care providers. More than 45% were detected and referred too late for brace treatment. Compared to the period 1976-1988 when screening was still performed, fewer patients are currently treated with brace and more patients operated. The detection of scoliosis in the absence of screening in Norway is suboptimal; two years later than internationally recommended. The HRQoL of patients treated for scoliosis with brace and surgery has been reported to be equal in the long term. We performed a cost minimization analysis comparing relative costs in screening and non-screening settings. Costs are comparable to similar programs in Europe. Screening was cost saving when leading to high rates of bracing and low surgical rates. Cost saving was higher when girls only are selectively screened.
Adolescent idiopatisk skoliose (AIS) er den vanligste formen for ryggskjever. De fleste tilfellene debuterer i forbindelse med puberteten, og skjevheten kan progrediere i takt med ryggvekst, kurvens størrelse og fleksibilitet. AIS forårsaker vanligvis ikke økt sykelighet og dødelighet, men påvirker helserelatert livskvalitet i form av smerte, fysisk funksjon, mental helse og selvfølelse. Tidlig diagnose er nødvendig for igangsetting av korsettbehandling som kan hindre prosessen og resultere i færre operasjoner. Tidligere ble AIS oppdaget ved skole screening for skoliose, men dette ble avskaffet i 1994, på grunn av antatte høye kostnader og tvil om screeningen førte til bedre behandling enn ikke-screening.

Effekt av skoliosebehandling ble tidligere kun målt med radiologiske mål, mens evaluering av behandlingseffekten ut fra pasientens egen vurdering nå i økende grad blir benyttet ved kliniske undersøkelser, bruk av kvalitetsregistrer, og ved helseøkonomiske overveielser. SRS-22 er et skoliose spesifikt spørreskjema som er akseptert internasjonalt som et viktig verktøy for å måle livskvalitet og «utility» som kan benyttes i helseøkonomiske analyser. I den første artikkelen i denne doktorgradsavhandlingen har vi oversatt og fastsatt målenøyaktigheten av SRS-22 spørreskjemaet, og sammenlignet dette med et globalt helse relatert livskvalitets måleskjema (EuroQol EQ5D). Den norske versjonen av SRS-22 spørreskjema har akseptabel validitet og repeterbarhet.

konsekvensene etter screeningen, og med de aktuelle behandlingsprosedyrene uten å kunne vurdere kostnadseffektiviteten.

Dette doktorgradsarbeidet har bidratt til økt oppdatert kunnskap om status når det gjelder forekomst og behandling av AIS i den norske befolkningen i vår samtid. Opplysningene er anvendt som grunnlagsmateriale for gjennomføring av en kostnadseffektivitets-analyse. En kostnad-nytte analyse er et redskap der bruk av resultatene vil kunne føre til praktiske konsekvenser med endring av rutiner og behandlingsprosedyrer, men dette vil være avhengig av hvordan pasienter og foreldre verdsetter tiltaket og hva samfunnet er villig til å betale. Arbeidene i denne avhandlingen vil kunne danne grunnlaget for fremtidige prospektive studier som kan måle livskvaliteten i QALY (quality adjusted life years) etter skoliose screening og behandling av AIS og derved utføre en fullstendig økonomisk evalueringsstudie.
# Dissertation at a glance

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<thead>
<tr>
<th>Paper</th>
<th>Research Question</th>
<th>Patients and methods</th>
<th>Measures</th>
<th>Results</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Is SRS-22 a valid tool for evaluation of health related quality of life in Norwegian patients with adolescent idiopathic scoliosis?</td>
<td>Cross-cultural adaptation of SRS-22 questionnaire. Test and retest in 55 patients.</td>
<td>Internal consistency, reliability and repeatability. Concurrent validity with EQ5D and EQ-VAS.</td>
<td>Moderate internal consistency, high reliability. Excellent repeatability. Poor concurrent validity with EQ-5D and EQ-VAS.</td>
<td>SRS-22 is a valid tool in evaluation of outcome measures in Norwegian patients with AIS.</td>
</tr>
<tr>
<td>II</td>
<td>Is the point prevalence of idiopathic scoliosis in 12 year old children in agreement with previous studies? Is screening for scoliosis effective at that age?</td>
<td>Screened 4000 children using forward bending test and scoliometer measurement &gt; 7°.</td>
<td>Scoliosis &gt; 10°, ATR &gt; 7°. Sensitivity, specificity, PPV, NPV, likelihood ratios.</td>
<td>Point prevalence was 0.55% for scoliosis &gt; 10°, and 0.13% for &gt; 20°. Sensitivity was 0.69, specificity 0.99, PPV 0.37, NPV 0.99, LHR+ 69, and LHR- 0.31.</td>
<td>Point prevalence was slightly lower. Screening model has acceptable sensitivity and specificity, but was not effective in detecting scoliosis with indication for bracing.</td>
</tr>
<tr>
<td>III</td>
<td>Is detection and referral rate of adolescent idiopathic scoliosis patients to specialist evaluation appropriate in the absence of a scoliosis screening program in Norway? Is rate of surgery higher and bracing lower without screening?</td>
<td>Prospective register of all patients referred for scoliosis evaluation from 2003 to 2011. Brace and surgical treatment records in screening period 1976-1988.</td>
<td>Patient demographics, maturity, family history of scoliosis, scoliosis detector, referral and treatments. Physical, radiological and neurological examinations.</td>
<td>752 patients registered. Mean detection age: 14.6 years. Risser 3.6. Post-menarche: 74%. Major curve: 38°. Lay people detected 71%. Rate of bracing was higher and surgery lower with screening.</td>
<td>Most patients were mature and had curves not suitable for bracing at first consultation. There is a delay of about 2 years from detection to referrals. Rate of surgery was higher, and bracing was reduced without screening.</td>
</tr>
<tr>
<td>IV</td>
<td>Is screening for adolescent idiopathic scoliosis cost saving?</td>
<td>Cost estimations of screening, brace and surgical treatments. Model based probabilistic analysis of non-screening scenarios.</td>
<td>Cost minimization analysis.</td>
<td>Incremental costs in non-screening scenarios with high treatment rates and high rates of surgery and lower rates of bracing.</td>
<td>Screening is cost saving when only girls are screened and when it leads to high rates of bracing and lower rates of surgery.</td>
</tr>
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1. Background

1.1 Adolescent Idiopathic Scoliosis

Idiopathic scoliosis is a complex three dimensional deformity of the spine in an otherwise healthy child. The deformity is characterized by lateral deviation, modification of the sagittal profile and axial rotation. Usual classification is based on the age of onset: infantile, before the age of 4 years; juvenile, age 4 to 9; and adolescent, from 10 years until the end of growth. Recent research has suggested that the longitudinal growth in the juvenile phase proceeds at an even pace rather that in a spurt. Accordingly, the juvenile type has been divided into early onset juvenile; 4-7 years, and late-onset juvenile; 7-10 years types. The adolescent type (AIS) is the most common form and it is often associated with rapid growth of the spine. A recent different classification has been proposed; early onset from birth to 5 years and late onset beyond 5 years based on the knowledge that most early onset idiopathic scoliosis might resolve, or progress to affect pulmonary function, but late onset idiopathic scoliosis is less likely to affect pulmonary function. With this terminology, AIS is increasingly referred to as “late-onset” idiopathic scoliosis.

Figure 1. AIS in a 12 year-old girl. a) Standing PA view, b) Adam forward bending position, c) standing PA X-ray view of the 63° right thoracic convex curve, d) sagittal X-ray view
1.1.1 **Etiology & Pathogenesis**

The etiology has not been fully elucidated as no single cause has been identified\(^{11-14}\). Biomechanically, abnormal growth and development, and asymmetrical growth of the vertebrae have been demonstrated, leading to vertebral rotation and the lateral curvature in idiopathic scoliosis\(^{15-18}\).

Genetic factors have been implicated as there is often a positive family history in AIS\(^{19-23}\). Researchers have mapped genetic locus for AIS to chromosome 8, 9, 17, and 19\(^{24-28}\). No single locus has however been identified, as there are phenotypic or genotypic heterogeneity, incomplete penetrance, and variable expressivity of the multiple genes involved. Since the pattern of susceptibility is not clear, AIS is best considered as a complex genetic trait disorder affected by multiple environmental factors\(^{29-33}\).

Historically, studies have linked altered activity of the hormone melatonin to development of scoliosis, but later studies have not supported this hypothesis and the possible mechanism involved remains unknown\(^{34-41}\). Estrogen and calmodulin have been evaluated in the etiology of idiopathic scoliosis, but the evidence remains inconclusive\(^{42-45}\). Studies have suggested increased levels of testosterone and growth hormones in pre-pubertal and pubertal children with idiopathic scoliosis. Recent advances in the research methodology include genomic-wide association studies (GWAS). It is proposed that 270 genes may be associated with AIS\(^{46}\). These genes point to AIS as an autosomal, multifactorial disorder that is not X-linked, and is not related to estrogen or melatonin receptors\(^{47}\).

1.1.2 **Epidemiology**

The reported prevalence of AIS varies widely from 0.5% to 4.5%\(^{10,48-52}\). These variations may reflect differences in the definition of scoliosis used and the patient population being studied. Differences found in specific populations may be due to genetic factors and possibly environmental factors\(^{50,53,54}\). Most studies using the definition of scoliosis defined as a radiographically measured Cobb angle of the primary curve $> 10^\circ$\(^{49,55}\), have reported the prevalence in the 2%-3% range\(^{48-50,52,56-62}\). Of all children with AIS, about 1.0-0.4% have primary curves $> 20^\circ$\(^{49,51,63,64}\), and only 0.1% have curves $> 40^\circ$\(^{49,65}\). Higher prevalence rates have been reported in the northern geographic latitudes in girls but not boys (Finland 12%, Singapore 0.9%)\(^{66}\), but those differences could be linked to environmental factors such as the difference in the onset of menses in the different geographic locations\(^{54}\). The exceptionally high prevalence rate of 12% reported in Finland was however not replicated in another study.
in Scandinavia reporting a prevalence rate of scoliosis > 20° of 1.1% for girls and 0.1% for boys\textsuperscript{67}. The prevalence of AIS is gender dependent, with the ratio of girls to boys being equal for minor curves, but rises for girls with curve magnitudes, reaching a ratio of 1:8 for those requiring brace treatment or surgery\textsuperscript{51,52,61,68-71}.

Point prevalence is a measure of the proportion of people in a population who has a disease or condition at a particular time or at a particular age, for example one-month prevalence of back pain or prevalence of scoliosis at school screening in 12 year-old children. Point prevalence rates of idiopathic scoliosis > 10° increases with age; from 0.1% in the age-group of six to eight years, to 0.3% in the age-group of nine to eleven years, and 1.2% in the age-group of twelve to fourteen years\textsuperscript{10}.

1.1.3 Natural history
Long term outcome studies on «untreated» patients with AIS do not show increased mortality\textsuperscript{72-74}, although progression of thoracic curves to > 80° might lead to cardiopulmonary problems and psychosocial concerns\textsuperscript{72,75,76}. The patients referred to in these studies were not strictly untreated; in one of the studies about half of the children had been braced\textsuperscript{72}. There are other limitations in those studies, including the inclusion of non-idiopathic etiologies, and or early onset scoliosis, lack of radiographic data, loss of patients and small numbers\textsuperscript{77}. The truly natural history is therefore difficult to obtain.

The risk of curve progression determines the natural history of AIS, which has been found to depend on gender, remaining growth, curve location, flexibility, magnitude and rotation\textsuperscript{68,72,78,79}. The more skeletally and sexually immature the patient is, the greater the probability of curve progression\textsuperscript{68,72,80,81}. Curves in girls progress more than in boys\textsuperscript{80}, and this risk is increased 3 to 10 times in girls compared with boys\textsuperscript{82,83}.

The remaining growth potential of the patient is estimated taking into consideration the patient’s age, growth spurt and radiographic parameters. Progression is most rapid during peak skeletal growth\textsuperscript{78,84}. Menarcheal status and skeletal age helps determine the growth spurt in girls. Peak growth velocity occurs approximately 6 to 12 months prior to the onset of menses in girls and the onset of axillary and facial hair in boys\textsuperscript{85}. In general, girls grow until 14 years of age, while boys grow until 16 years of age\textsuperscript{86}. Girls grow very rapidly until their first menstrual period, and then their growth generally slows down, but they continue to grow until 18 months to 2 years after their first menstrual period\textsuperscript{86}.
Several methods have been applied to estimate skeletal age including the Risser sign and the Greulich and Pyle left hand radiographic atlas which are in frequent use also in our hospital, but the subjective evaluation is encumbered with a relatively wide range of error. The Risser sign measures the amount of ossification and eventual fusion of the iliac apophysis, on a scale of 0 to 5 (Figure 2). Patients who are Risser 0 and 1 are growing rapidly, while patients who are 4 and 5 have stopped growing. Biological maturity can also be found from elbow radiographs (Sauvageain’s method). This method is simple, precise and reliable and allows skeletal age to be evaluated in regular six-month intervals during the phase of peak height velocity. Recently, a reliable method of correlating the maturity of the hand epiphyses (The Sanders digital maturity scale) to curve acceleration phase during the adolescent growth spurt has been developed from the Tanner-Whitehouse-III descriptors system. This system has been found to be reliable, and correlates more strongly with the behavior of idiopathic scoliosis than the Risser sign or the Greulich and Pyle radiographic atlas.

These markers of maturity are however variable and may not exactly identify the adolescent growth spurt. A recent critical review of the Risser sign has revealed its limitations and suggests that it should not be used as the sole maturity indicator. Closure of the tri-radiate cartilage of the acetabulum has been identified as a radiographic sign, which may closely approximates the time of peak growth velocity, but there is a large variation in growth and two years of adolescent growth may remain after the closure of the tri-radiate cartilage. It has therefore been suggested that the tri-radiate cartilage should be used in addition to the Risser sign in determining maturity. Larger curves at presentation have higher risks of progression both before, and after maturity. Curves > 50º at maturity are likely to progress into adulthood. Thoracic curves and double curves progress more than lumbar curves.
Figure 2. Markers of maturity X-ray images: a) Risser stages; b) not yet ossified tri-radiate cartilage; c) centers of ossification in the hand ©Trobisch P, Suess O, Schwab F

Figure 3. Spine development and scoliosis progression. The graph of Duval-Beaupeère represents the progression history of scoliosis. It has been developed for neuromuscular scoliosis, but it fits quite well also for idiopathic scoliosis, in which anyway generally the slope of each single tract of the graph is reduced.
1.1.4 **Effects on health related quality of life**

AIS may affect the social life, and the health related quality of life (HRQoL) of the affected patients. Few of the patients with AIS have risks of developing curves > 80° which may increase the risk of cardiopulmonary problems, and even death. There are few reports on marriage, childbearing, and sexual function of previously treated AIS patients. Since larger curves are more prevalent in girls than in boys, pregnancy, and childbearing are often a concern. One study reported that patients who previously had surgery or were braced functioned well with regard to marital status and number of children borne. A few had minor problems during pregnancy and delivery, but scoliosis did not increase as a result of childbearing. Some patients, however, experienced a slight negative effect in their sexual life compared to healthy controls. Studies in the past reported progression of scoliosis during pregnancy. Newer studies found no increase in curve magnitude, back pain or obstetrical outcome in scoliosis patients compared to controls who had never been pregnant.

Studies on the effect of adolescent scoliosis on the HRQoL have shown conflicting results. Some studies have reported poor self-image and poor social functioning in AIS patients. Others have shown lower scores on pain, general level of activity, self-image and mental health domains of SRS outcome questionnaires compared with controls. The pain is, however, usually not disabling, and there is minimal differences in function and physical disability between patients with AIS and controls due to back pain. The back pain is usually not associated with curve size, gender, family history of scoliosis, or limb-length discrepancy, but with mature age, skeletal maturity and overweight. Curve pattern may be associated with increased pain, where thoracolumbar curves seem more painful than double curves. In a large recent long term study from our department it was found that comorbidity significantly reduced HRQoL in adult life. Cultural differences are reported with respect to HRQoL. Studied on the other hand have reported that, patients with untreated AIS do not appear to have different outcome measures of work and disability than the normal population. Two recent Norwegian studies that included patients 24 years on average after bracing and a similar study from Sweden that included both braced and operated patients reported that long-term disability was comparable or just slightly lower than in the normal population.

Studies reporting minimal clinical important difference (MCID) when evaluating HRQoL in adolescents have been lacking. A recent review applying MCID of SRS outcome
questionnaire reported that AIS patients scored well in function/activity and mental health domains and differences from those unaffected rarely reached clinically significant values\textsuperscript{128}. Pain and self-image scores were statistically lower in patients with AIS than controls but only self-image was clinically significant.

1.1.5 Treatment options

Treatment of any disorder is an attempt to alter its natural history; therefore, long-term studies of both the natural history and treatment outcomes are necessary\textsuperscript{129}. The treatment of AIS is based on the knowledge of the risk of curve progression and patient maturity. Observation for curve progression, physical therapy, brace and surgery are the usual treatment modalities for AIS worldwide\textsuperscript{3;77;81;115;129;130}. Currently, there is lack of high quality evidence to support the effectiveness of physical therapy, chiropractic treatment, electrical stimulation or biofeedback in preventing progression of AIS\textsuperscript{131-134}.

Observation

Curves < 25° in immature patients are usually observed with regular X-ray-examinations for progression\textsuperscript{3;77}. Follow-ups depend on the patient’s rate of growth. Adolescents are observed every six months until growth is complete. Juveniles are observed every three to six to twelve months depending on their rate of growth. Because of concerns of radiation exposure, care is taken to limit the radiation exposure by replacing the anteroposterior view with the posteroanterior view thereby reducing the lifetime risks of breast and thyroid cancers\textsuperscript{135}. It is now known that the radiation exposure using current day radiographic techniques, including digital radiography, is significantly smaller than in the past\textsuperscript{136}. Some patients with curves > 50° on cessation of growth have the risk of progression into adulthood\textsuperscript{73}. Those patients are also observed with standing radiographs every few years in order to monitor the progression of the curves. Recently, the Society on Scoliosis and Rehabilitation Treatment (SOSORT) reached a consensus with recommendations to reduce x-ray exposures in patients with scoliosis\textsuperscript{137}.

Physical therapy

In some countries, comprehensive physical therapy programs are applied alone or in combination with bracing to prevent curve progression particularly for small curves (< 25°)
The evidence for effectiveness of physical therapy in preventing progression of AIS has been inconclusive. While some of the newer studies have provided low-quality evidence in favor of physical exercises in AIS, well-designed randomized controlled trials are lacking. A recent Cochrane systemic review found lack of high quality evidence to recommend the use of scoliosis specific exercise (SSE) for AIS. Because of tradition and the lack of evidence of effectiveness, physical therapy is not routinely used in Norway as a treatment modality to reduce progression of AIS, but physiotherapy is used in many patients for treatment of back pain and disability. It has however been estimated that 1/3 of all patients use physical therapy after surgery and for the treatment of small curves.

**Bracing**

The aim of brace treatment is to prevent and or limit progression and reduce surgery. Brace is usually recommended for growing adolescents with curves > 25°. The current recommended indication for brace treatment is age of 10 to 15 years, Risser grade of 0, 1, or 2, and a Cobb angle for the largest curve of 20° to 40°. Many different types of braces are available, but the thoracolumbar models are usually used. Prefabricated types such as the Boston brace is most commonly used in North America and Norway, whilst custom-made braces such as the Cheneau corset are common in Europe. The efficacy of brace treatment in limiting progression and reducing surgery has been investigated in numerous studies. But its effectiveness in the long term remained controversial until recently. A Cochrane review concluded that there was low evidence from well-designed scientific studies to support the use of braces to treat scoliosis as the majority consisted of prospective observational studies. But recently, a randomised study of high quality reported that bracing was effective in reducing curves to the threshold of surgery. The study also showed that the benefit increased with better compliance and that the success rate was > 90% in patients who used their brace 18 hours or more daily. The number needed to treat (NNT) in order to prevent surgery was 3.0 (95% CI, 2.0 to 6.2), and the reduction in relative risk with bracing was 56% (95% CI, 26 to 82). In addition, approximately 40 to 50% of adolescents assigned to observation or who wore their brace ≤6 hours per day also achieved treatment success (reduction to < 50°). It has therefore been suggested in the light of these findings that indications for bracing need to be refined to prevent unnecessary bracing of patients who are unlikely to benefit from it. A large long-term follow-up study from our department found out that the risk of surgery is markedly reduced in patients with good...
Other studies have also shown that compliant patients who wear the brace > 20 hours daily have reduced risks of curve progression and reduced rates of surgery.

**Figure 4.** Treatment with the Boston brace in a 12-year old girl with AIS. a) Standing PA X-ray before brace treatment of right convex thoracic curve of 42°, and left convex lumbar curve of 39°, b) standing PA X-ray in brace with reduction of the thoracic curve to 29° and the lumbar curve to 25°, c) front view of brace, d) posterior view of brace

**Surgery**

The generally agreed indication for surgery in adolescents is a primary curve > 45-50°. Objectives of scoliosis surgery are to stop progression, achieve correction of the deformity in three planes, balance the trunk, and reduce complications both in the short and long terms. Posterior instrumentation is the mainstay of treatment for most idiopathic curves. Anterior surgery is usually performed on thoracolumbar and lumbar major curves.

Modern instrumentation has evolved from the Harrington distractive rods, Cotrel-Dubousset (CD) system which introduced the hook system in the 1980s to the ISOLA hybrid system that combined pedicle screws, hooks and wires, and recently to the segmental all...
pedicle screws, originally pioneered by Suk\textsuperscript{167}, which allows stable correction in the coronal, sagittal and transverse planes\textsuperscript{168;169}. Surgery for AIS is effective in deformity correction and the magnitude of curve correction has increased from the Harrington rods to the all pedicle screw constructs\textsuperscript{167;170-174}.

There are risks associated with surgery for AIS. Complications with modern scoliosis surgery have however decreased substantially despite its complexity\textsuperscript{115;175-178}. Death is very unlikely but can occur, especially in patients operated as adults\textsuperscript{179}. Complete spinal cord injury is rare\textsuperscript{47}. SRS Morbidity and Mortality Database showed a 0.02\%, mortality rate and 0.8\% neurological complication rate for AIS patients\textsuperscript{180}. Others have reported 0.5\% rates of neurological deficit\textsuperscript{181}. SRS data also shows a reduction of the rate of neurological complications for all cases of spine deformity of 0.94\% from 1965–71 to 0.49\% in 2001–03 for AIS patients aged 10–17 years\textsuperscript{182;183}. The reduction in the neurological complication rates are mainly due to the use of intraoperative spinal cord monitoring during scoliosis surgery which can allow early recognition and treatment of spinal cord dysfunction\textsuperscript{184;185}.

Other complications include acute and delayed deep infection with reported rates between 0.5-10\%, pseudarthrosis, and implant prominence\textsuperscript{186}. Low-virulence organisms such as Propionibacterium acnes are usually the main cause of delayed infections following posterior spinal fusions. Instrumentation removal and a course of antibiotics is normally successful in eradicating the infections\textsuperscript{187;188}.

Rates of reoperations after primary posterior instrumentation, and fusion are reported to vary between 4 to 19\% mainly due to infections, pseudoarthrosis, postoperative curve progression of the adjacent unfused spine and implant removal due to pain or prominence\textsuperscript{147;175}. Reoperation due to late operative site pain (LOSP) of no apparent cause has been reported to be 19\% in the literature regardless of implant type (Harrington, CD, ISOLA). Implant removal was successful in pain relief in the majority of patients\textsuperscript{189}. All screw constructs have been reported to have lower revision rates than hooks and hybrid constructs\textsuperscript{190}.
Figure 5. Posterior surgery in AIS. a) Standing PA X-ray of 72° thoracic right convex, and lumbar left convex curve of 83° before surgery, b) sagittal view before surgery, c) standing PA view after posterior surgery with reduction of the thoracic curve to 25° and the lumbar curve to 15°, d) sagittal view after surgery, e) Standing PA view before surgery, f) AFBT position before surgery, showing a 10° ATR, g) standing PA view after surgery, h) AFBT position after surgery with normalising of the ATR.
Newer techniques

New techniques have evolved in recent years for the treatment of AIS. Convex-side vertebral stapling has been developed as an alternative to bracing\textsuperscript{191-195}. The indications and outcomes are not entirely clear, but it has been suggested that for thoracic and lumbar curves of \(< 35^\circ\), the results with vertebral body stapling are comparable with those of bracing. However, for thoracic curves of between \(35^\circ\) and \(44^\circ\), the results with vertebral body stapling are reported to be poor\textsuperscript{196}.

1.1.6 Outcome measurement

Health care costs are rising. Uncertainties exist in medical care, often because evidence of therapeutic efficacy is lacking. Selection of treatment options must therefore be based on standardized parameters designed to evaluate which treatment options produce the best patient outcome\textsuperscript{86}. There are different types of questionnaires to collect information from patients that can be used for useful and valid comparisons of different treatment methods. Both generic and disease specific questionnaires measure quality of life in a patient following a medical or surgical intervention. The Medical Outcome Study Short Form-36 (SF-36) is the most widely used generic outcome measuring HRQoL\textsuperscript{197}. EuroQol (EQ-5D and EQ-VAS) is a similar measure which includes a utility index that can be used in cost-benefit analyses\textsuperscript{198}. Another commonly used utility index; Short Form 6D (SF6D) has recently been reported to be better suited in evaluating spine treatment compared to the EQ-5D\textsuperscript{199}. The Pediatric Quality of Life Inventory (PedsQL), another generic quality-of-life instrument used in studies of acute and chronic illness, is also frequently used in accessing HRQoL in AIS treatment\textsuperscript{152;200;201}. The PedsQL is based on a modular approach, and consists of a 15-item core measure of global HRQoL and eight supplemental modules assessing specific symptom or treatment domains\textsuperscript{202}.

Patients with AIS were in the past commonly monitored by clinical evaluation and objective radiological measures\textsuperscript{203}. Clinical outcome research now focuses more on outcome from the patient’s perspective. Disease-specific outcome measurement assesses the results of treating a specific disease using a specific procedure\textsuperscript{86}. The SRS has developed a simple, practical, disease-specific, patient-based assessment for AIS\textsuperscript{118;204-208}. The SRS-22 questionnaire is currently accepted internationally for assessment of HRQoL in AIS. The SRS-22 has been translated and validated in Spanish, Turkish, Japanese, and Chinese and other languages\textsuperscript{209-223}, but not in Norwegian until Paper I of the present work. The SRS-22 has been concurrently validated against the generic questionnaire SF-36\textsuperscript{205;207;209;212;213;216;219;220;222-224}, the back-
specific Roland Morris Questionnaire, the Quality of Life for Spine Deformities Profile (QLSDP), and Child Health Questionnaire CF 87 (CHQ-CF87), and SF-12, but not the EuroQol. In the validation process of the SRS-22 questionnaire, the developers of the original questionnaire and subsequent validators have limited the assessment of reproducibility to calculation of intraclass correlation coefficient (ICC). This statistical measure of reliability describes the ability to discriminate between individuals, but agreement parameters are required for evaluation of measurement error in order to estimate if a real change has occurred in follow-ups. The SRS-22 is now the primary outcome measure of function of patients with AIS. The SRS-22 questionnaire has been also been tested in adults with scoliosis and found to be valid and responsive to surgical treatment. SRS-22 is also used for evaluating HRQoL in kyphosis, and secondary scoliosis. Recently, a short form (SRS-7) of the SRS-22 has been developed by the Rasch analysis (RA) with the aim of improving the HRQoL measures of AIS. RA is a statistical procedure which turns questionnaire ordinal scores into interval measures. Measures from Rasch-compatible questionnaires can be used, similar to body temperature or blood pressure, to quantify disease severity progression and treatment efficacy.

Outcome measurement in brace treatment

The outcome of brace treatment is usually measured in reduction of progression, surgical rates and on its effects on HRQoL. Outcome is usually measured at maturity defined as Risser grade 4 for girls or 5 for boys and a Sanders digital maturity stage of 7 (closure of all physes of the phalanges and curve progression to > 50° (treatment failure) or < 50° (treatment success). In the newly publisher randomized study on brace treatment, the rate of treatment success was 72% in the bracing group, and 48% in the observation group. When adjusted for propensity-score quintile and duration of follow-up, the odds ratio for a successful outcome associated with bracing was 1.93 (95% CI 1.08 to 3.46).

Studies in the past reporting the effects of bracing on HRQoL did not use measurements on validated questionnaires. These studies have suggested that bracing had a negative psychological impact, causing low self-esteem and a more negative self-image in the short term, but no psychological changes in the long term. Other studies found decreased mental health, perception of discrimination and lower satisfaction of overall wellbeing during the treatment phase of bracing but no difference between the patients and controls at final
follow-up 7 years later\textsuperscript{237}. Most of these studies have included patients with the Milwaukee brace and lack of adequate age-matched controls\textsuperscript{235,237}.

Current studies have measured the outcome of underarm brace treatment on HRQoL in the short term using the SRS-22 scores of patients with progressive curves, and matched with patients with similar curves who were observed. The patients who were observed had significantly better function and self-image domain scores than those braced, especially those with curves < 20°. The scores did not improve significantly with duration of brace wear, suggesting little adaptation\textsuperscript{239}. Studies based on the Boston brace did not however, produce a negative impact on body image and did not decrease the quality of life of adolescents compared with healthy controls\textsuperscript{240,241}. Differences may thus result from the type of brace used, as well as differences in culture and the attitudes of patients. In the newly published randomized brace study using mostly the Boston brace, there were no significant differences between bracing and observations groups measured by PedsQL scores or with respect to negative psychological impact, or other adverse effects like pain\textsuperscript{152}.

\textit{Outcome measurement in surgical treatment}

The role of surgery in AIS is to stop curve progression and improve the HRQoL in the affected patients. The rate of curve correction has improved from 40\% to over 70\% with modern surgery\textsuperscript{242,243}. The level of evidence is however weak on the improvement of HRQoL by scoliosis surgery\textsuperscript{129,244-249}. One study reported higher mental health scores on the SF-36 questionnaire but lower physical activity levels compared to normal controls, 2 years after surgery for AIS\textsuperscript{250}. Prospective studies suggest that the magnitude of surgical curve correction correlates with patient satisfaction and improvement in the self-image domain of SRS-22 questionnaire\textsuperscript{251-254}. However, other factors may play a role in patient’s self-image and satisfaction\textsuperscript{174,251,255}. Patient’s response on quality of life measures correlate more strongly with physical appearance than radiographic parameters. Multi-center studies of the outcome of surgical treatment of AIS using the SRS outcome instrument reported statistically significant improvement in pain, self-image, function and general level of activity in the short term, and 2 years after surgery\textsuperscript{203,252}. It was shown that, patients with pre-operative curves less than or equal to 54° were slightly more satisfied than those with pre-operative curves of > 55°, but at present there is no conclusive evidence that improved radiographic outcomes in patients with AIS correlate with enhanced function, self-image, or health\textsuperscript{196}.​
In general, the long term outcomes are favorable compared to control subjects at 15-20 years for segmental instrumentation\textsuperscript{180} and at 20-25 years for Harrington instrumentation\textsuperscript{101;102;256}. Spinal fusion may have an isolated negative effect on HRQoL measures mostly due to a decrease in “activity” domain scores, but an improvement in the HRQoL due to improvement in deformity correction\textsuperscript{257}.

The HRQoL however remains the same in AIS patients treated with brace or surgery both in the short term as well as the long term\textsuperscript{103;115;126;127}.

1.1.7 Screening
Screening for scoliosis allows for early detection, timely institution of brace treatment, leading to reduced surgical rates, and has been practiced for many years\textsuperscript{56;64;83;136;258-263}. School screening for scoliosis goes beyond its scope of early identification of AIS and has provided valuable knowledge about prevalence, etiology, natural history, and has contributed to the field of research on idiopathic scoliosis\textsuperscript{49;51;63;65}. Numerous factors that are implicated in the etiology of AIS including biological factors such as menarche, laterality of the brain, handedness, the thoracic cage, the intervertebral disc, and the role of melatonin have been studied in children referred from school screening programs\textsuperscript{264}.

The effectiveness of scoliosis screening has been debated in many studies\textsuperscript{58;64;65;136;258;264-279}. Some studies have reported decreased rates for surgery after the introduction of screening\textsuperscript{64;258;276;280}. Objections to scoliosis screening are largely based on the low prevalence rate of clinically significant scoliosis, the inverse relationship of sensitivity and specificity in the screening process, high rates of false-positive cases, high inter-observer variations and the costs involved mainly because of over-referrals\textsuperscript{281;282}. The challenge in scoliosis screening programs therefore is to achieve an acceptable rate of false positive results and to increase specificity at a low cost.

The policies of scoliosis screening vary considerably worldwide. Prior to the 1990’s, scoliosis was usually detected in Norway through school screening programs employing the forward bending procedure as a screening tool. In 1996, The United States Preventive Services Task Force (USPSTF) concluded that there was insufficient evidence to make a recommendation for, or against scoliosis screening\textsuperscript{265;266}. Their recommendation suggested that scoliosis screening did not meet established criteria for screening of diseases, because of over-referrals, high costs and little evidence that early treatment prevents surgery. Later publications suggest that they might not fully recognize data answering some of their objectives at the time of their
recommendation\textsuperscript{146}. In 2004, the USPSTF changed their position and recommended against routine screening of adolescents for idiopathic scoliosis\textsuperscript{267}. Based on the recommendations of the USPSTF, routine scoliosis school screening programs have been discontinued in many Western countries. In Scandinavian countries, Sweden has conducted school screening for many years and has an on-going scoliosis screening program\textsuperscript{81}. In Denmark, there has been an attempt to perform school screening, but screening programs have not been successfully implemented\textsuperscript{283}. In recent years, The SRS and the American Academy of Orthopaedic Surgeons, (AAOS), the Paediatric Orthopaedic Society of North America, (POSNA), and the American Academy of Paediatrics (AAP), have endorsed scoliosis screening as a means of preventing late presentation of large curves\textsuperscript{136;268;278;284}. In Canada, school scoliosis screening has been discontinued since 1979 when the Canadian Task Force on the Periodic Health Examination did not recommend screening\textsuperscript{285;286}. The British Orthopaedic Association and the British Scoliosis Society also do not recommend screening\textsuperscript{287}.

The international task force of the SRS on scoliosis screening recently found screening to be effective with regards to technical, program, and treatment dimensions, but lack studies on cost and economic valuations in order to make a statement on cost effectiveness\textsuperscript{288}. The impact of discontinuation of school scoliosis screening programs on detection and referral patterns of scoliosis has been studied in Canada, and in the United Kingdom\textsuperscript{226;289}. They reported that many patients were detected late mainly by laypersons, when curves were large and unsuitable for brace treatment. The discontinuation of the school screening programs was therefore followed by a suboptimal appropriateness of referrals for bracing. In Norway, the impact of discontinuation of school screening on the detection, patient characteristics, referral patterns, and treatment patterns has not been previously evaluated.

1.1.8 \textit{Health economic evaluation of screening}

There has been a growing interest for economic evaluation of health care interventions in recent years in view of limiting health resources in order to provide health care decision makers with information on the relative value of money offered by alternative treatments. Economic evaluations therefore seek to systematically compare the costs and health outcome options employed in the delivery of health care\textsuperscript{290}. As opponents of scoliosis screening mainly cite the costs involved and the lack of effectivity of the programs, it is therefore important to perform an appropriate economic analysis comparing costs and outcomes in settings where screening is performed compared to settings where screening is not performed. The results will enable health care providers and policy makers to determine whether to
recommend screening or not from a health economic perspective. There are several studies reporting on the cost of performing scoliosis screening\textsuperscript{70,275,277,282,291-296}, but few studies have reported the cost of bringing cases found on screening to treatment\textsuperscript{282,292-294}. There are no studies to date conducting partial or full economic evaluations according to recommended reporting standards of scoliosis screening and treatment.
2. Aims

As described in the background section, the consequence of the abolition of scoliosis screening in Norway in 1994 on current detection, patient characteristics, treatment, and referral patterns has not yet been studied. The methodology of scoliosis screening, its direct costs, and costs of follow-ups, treatment modalities, and economic evaluation is not known. The point prevalence of scoliosis in 12 year old children is also not known. The SRS-22 questionnaire has been internationally accepted as a valid instrument in measuring the HRQoL and outcome measure of treatment of patients with AIS. For SRS-22 to be used in Norwegian patients with AIS there is a need for it to be translated, validated and adapted into Norwegian language.

The specific aims of the study were therefore:

I. To evaluate the reliability, and the repeatability of the SRS-22 questionnaire and to evaluate its concurrent validity with EQ-5D for evaluation the HRQoL in AIS patients.

II. To evaluate the point prevalence of 12 year-old children in Norway, and to evaluate the validity of one single screening in detecting patients for bracing. To estimate the sensitivity, specificity, positive predictive value, and negative predictive value screening method employed.

III. To evaluate the patient characteristics at first presentation in the absence of scoliosis screening and to explore the appropriateness of referrals for idiopathic scoliosis. To compare the proportion of patients braced and operated in a time-period with and without scoliosis screening.

IV. To evaluate the cost of school screening, brace and surgical treatment of AIS in Norway, and to perform an economic evaluation of screening compared to non-screening.
3. Methods

3.1 Study design
Different study designs were used for specific aims in the study. Paper I was designed as a prospective study in order to conform to the guidelines on trans-cultural adaptation of HRQoL questionnaires. Paper II was designed as a cross-sectional study to screen 12 year olds once in combination with a vaccination program, and to determine the point prevalence of AIS in the age group. Paper III was designed as a prospective study to evaluate the characteristics of patients during the period 2003-2011 without screening, and to compare these with prospective data from the period 1976-1988 when screening was performed. The surgical rates were obtained retrospectively from surgical protocols for both periods. Paper IV was designed as a model based cost minimisation analysis (CMA) of screening and treatment modalities in screening and non-screening scenarios assuming equal outcomes in the patients.

Table 1. Summary of study designs, participants, inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Paper</th>
<th>Study design</th>
<th>Participants</th>
<th>Inclusion and exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Prospective study of cross-culture adaptation, validity, and reliability measurement of SRS-22 questionnaire</td>
<td>Answered first time: 76</td>
<td>Patients with AIS with previous brace and surgical treatment, or currently in brace treatment, or scheduled for surgery.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Answered second time: 57</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Cross-sectional study. Screening of 12 year olds once within a vaccination program</td>
<td>4000 school children</td>
<td>12 year old boys and girls in Health Region South of Norway</td>
</tr>
</tbody>
</table>
### III

Prospective study to evaluate the characteristics of AIS patients in 2003-2011 (without screening)

To compare treatment rates with control data during the period 1976-1988 with screening

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Late-juveniles and adolescents referred to idiopathic scoliosis evaluation for the first time. Patients with infantile and early juvenile idiopathic, neuromuscular, congenital or syndromic scoliosis were excluded</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### IV

A cost minimization analysis of scoliosis screening and treatment assuming equal outcomes

<table>
<thead>
<tr>
<th>Norway</th>
<th>Hong Kong</th>
</tr>
</thead>
<tbody>
<tr>
<td>4000 screened</td>
<td>115190 screened</td>
</tr>
<tr>
<td>16 year old school children participated in screening in 2006/2007</td>
<td>Norwegian and Hong Kong screening data. Treatment data in 2012 in Norway</td>
</tr>
</tbody>
</table>

### 3.2 Setting

Data was collected from hospital care only in Paper I and from primary, local and specialized hospital care in Papers II, III, and IV. In Paper II, public health/community health nurses and physical therapists in the study region were engaged as screeners. These were invited to a one-day intensive course at the Oslo University Hospital (OUS) - Rikshospitalet to improve their knowledge about AIS in preparation of the screening program. Additional courses were arranged at the various county centers for those who were not able to attend. The Norwegian Directorate of Health did not support the study with a recommendation, so participation was lower than expected.

The salary and social costs for hospital staff in Paper IV were estimated using the mean salary at the OUS. Salary and social costs of public health nurses were based on data from the Norwegian Nurses organization and data from the local communities in Norway. Estimates of the overhead were based on data from the Norwegian Central Bureau of Statistics.

### 3.3 Participants

Paper I included 57 AIS patients, 48 (84%) females and 9 (16%) males. Twelve (21%) had previous brace treatment, 6 (11%) had current brace treatment. Twenty-two (39%) had previous surgery and 17 (29%) were scheduled for surgery. In Paper II, 4000, 12 year old school children participated in screening in 2006/2007. Paper III included 752 patients.
registered from 2003-2011 when there was no screening. In the period of screening (1976-1988), data was based on 793 patients (on average, 41 were braced and 20 had surgery each year). Paper IV included screening of 4000, 12-year old children in Norway in 2006/2007, data from a screening study of 115190 children in Hong Kong and patients treated with brace or surgery at the orthopedic department, OUS-Rikshospitalet in Norway in 2006. Included additionally, were 122 adolescents who were treated for scoliosis in 2012 in Norway, according to administrative data from the three scoliosis clinics. Of these, 51(42%) were braced and 71(58%) had surgery, and about 10% of them having both brace and surgery.

3.4 Methodology
In Paper I, the English version of the SRS-22 was first translated into Norwegian and retranslated back to English by two independent bilingual translators–one whose mother tongue is English and the other whose mother tongue is Norwegian. A review committee composed of one specialist in physical medicine and rehabilitation, one public health nurse, two spine surgeons, and the two translators further assessed the forward and backward translations, and a consensus was achieved on the final translation. The EuroQol (EQ-5D) has already been cross-culturally adapted to Norwegian patients with back pain. The final version of the SRS-22, and the EQ-5D, and EQ-VAS questionnaires were mailed to AIS patients of various ages and severity of curves under treatment with a stamped return envelope.

In Paper II, screeners were taught about scoliosis and the screening procedure of Adam Forward Bending Test and measurement of the angle of inclination using the scoliometer. In addition, a scoliosis screening manual was provided to all participants and follow-up teachings were provided as needed. The screening procedure (Figures 2 & 3) combined the standing visual inspection of the back, the Adam Forward Bending Test and the scoliometer (OSI-scoliometer Orthopedic Systems Inc, Hayward, California, USA) measurement of angle of trunk rotation (ATR). Seven degrees of ATR was chosen as cut-off point for referral to radiography.

Radiographic results of screening from local hospitals were mailed to the Department of Orthopedics at OUS-Rikshospitalet.
In Paper III, data of patients referred to the specialized clinic for evaluation of AIS for the first time was registered by specialist orthopedic surgeons. Patient interviews, clinical examinations, radiological and neurological examinations were conducted.
Table 2. Characteristics registered from the patient interviews, clinical, neurological, and radiological examinations.

<table>
<thead>
<tr>
<th>Source</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient interview</td>
<td>Age, gender, menarcheal status, family history of scoliosis, age at detection, back pain and perception of muscle fatigue</td>
</tr>
<tr>
<td>Clinical examination</td>
<td>Adam forward bending test, angle of rotation, height and weight, shoulder, and truncal asymmetry, coronal balance.</td>
</tr>
<tr>
<td>Neurological examination</td>
<td>Muscle weakness, sensory weakness, reflexes</td>
</tr>
<tr>
<td>Radiology</td>
<td>Cobb angle, Risser sign</td>
</tr>
<tr>
<td>Recommended treatment (up to 6 months follow-up)</td>
<td>Brace, surgery, further observation, discharge</td>
</tr>
<tr>
<td>Hospital records</td>
<td>Referral patterns of primary physicians, physical therapist, chiropractors and hospital specialists. Duration from time of detection to referral and time to clinical evaluation. Actual number of patients who were operated yearly during the period 2003-2011, and estimates of the number of patients treated with brace or surgery during the years 1978-1988.</td>
</tr>
<tr>
<td>Surgical protocols</td>
<td></td>
</tr>
</tbody>
</table>

In Paper IV, we used a model approach to compare costs in screening with non-screening scenarios. The main mathematical equation on which the model was based is shown in Appendix Paper IV. Cost estimation was based on micro costing, case-mix, and market prices to estimate the cost of screening, bracing and surgery. The study perspective in relation to costs was based on a health sector budget perspective focusing on the costs related to orthopaedic treatment in hospital care, and in addition, we included costs for the society due to transportation and parents’ use of time during treatment of their children.
The strategies we compared were treatment in screening setting and estimated reduced treatment rates of 90%, 80%, and 70% of those treated in screening settings. This is based on the assumption that screening for scoliosis may lead to over-referrals to X-rays and outpatient evaluations, increased rates of bracing, but reduced surgical rates compared to settings when children are not screened. Additionally, in non-screening settings, many children are diagnosed late when they are matured, with curves not suitable for bracing.

In all non-screening scenarios, we simulated different distribution rates of brace and surgery based on the available non-screening data from Norway, (58% surgery and 42% brace). Since AIS is more prevalent in girls and 90% of those treated are girls, separate analyses were performed for girls.

Uncertainty was characterised by deterministic and probabilistic sensitivity analyses (PSA).

### 3.5 Outcome measures

In Paper I, the outcome measures were the SRS-22 and the EuroQol. In Paper II, outcome measures were asymmetry of the trunk on visual inspection of the back and an ATR ≥ 7° on the Adam forward bending test. In the hospital care setting the outcome measure were Cobb angle > 10° on standing radiographs, which is classified as AIS according to the criteria proposed by the SRS. Patients with scoliosis between 10° to 20° were classified as moderate, and referred to a new radiographic examination within 6 months at the local hospital. Patients with a Cobb angle > 20° were referred for physical, and clinical examinations and new standing X-rays including iliac crest exposure for Risser sign grading.

In Paper III, outcome was the characteristics outlined in Table 2.

In Paper IV, outcome measure was incremental cost which was defined as the cost of treatment in a non-screening scenario minus the cost of treatment and cost incurred in conducting the screening. Hence, a positive incremental cost implies that screening is more cost saving compared to the non-screening scenario. We also estimated incremental cost changes by varying the ratio of bracing to surgery in the non-screening scenarios. The probability of the incremental cost being > 0 was estimated in all cases.

**Cost estimations**

Costs were estimated for screening, brace and surgical treatments.
Screening

All activities directly involved in the screening and follow-up of patients were measured, valued, and costs calculated.

Bracing and surgery

Two hospital health economics, assisted by one orthopedic surgeon, a physical medicine specialist and one nurse estimated the costs of brace and surgical treatments based on data extracted from hospital treatment records. For bracing, we estimated the costs of the brace equipment, transportation, radiographic and clinical examinations during the period of brace wear, hospital hotel services for 4 days for the child and one parent during brace fitting. Additionally, the costs of reimbursements for wear and tear of clothing and beddings from the National Insurance Scheme were included.

For surgery, we estimated the costs of implants, salaries of anaesthesiologists and staff at the theatre, intensive care, intermediate postoperative care, and regular ward costs. Surgery was usually performed using either a hybrid construct with an average of 5 pedicle screws, 8 hooks, and 5 to 6 sublaminar wires or an all pedicle-screw construct using 15 to 17 pedicle screws. Two surgeons usually performed the surgery using an estimated average time of 180 minutes. One anesthesiologist, one anesthesiologist nurse and two scrub nurses assisted them working on average for 300 minutes. After surgery, patients stayed in hospital for an average of 10 days. No braces were used postoperatively. During the first postoperative year, patients had two follow-up consultations. In addition, costs of radiological examinations, outpatient visits for follow-ups, transportation, and costs of complications and re-operations during the first year were measured. Costs were estimated using micro costing (MI), case-mix group (CA) and market price (MA) methods. For MI, the cost per hour for different health professionals was included by multiplying the salary (inclusive income tax), other social costs (pension, insurance, sick-leave, training etc) of employment (27%) and overhead (40%).

Currency, price date and conversion

All prices and costs were converted from 2006 to 2012 NOK (Norwegian kroner) by using an inflation rate of 3.21% per year based on the yearly rate of change of one unit value within the Diagnosis –Related Group(DRG) System in Norway. The exchange rate was pegged at 8NOK = 1Euro.
Time horizon for cost estimations

The time horizon for estimating costs was six years from the first screening at 11 years. We assumed two screenings per child, based on the recommendations of the SRS\textsuperscript{136} at the age of 11 and 13 years, and anticipated that 60% of the scoliosis cases were detected at the first screening and the rest at the second. For the non-screening scenarios we also assumed a dispersion of the expected cost (bracing and surgery) of 10%, 15%, 20%, 20%, 15% 10%, and 10% for each age group from 11 to 17 respectively. When aggregating costs over time, we used an annual social discount rate of 4% as recommended by the Norwegian Directorate of Health to calculate the present value of costs. The social discount rate is an interest rate used to bring future value into the present when considering the time value of money\textsuperscript{290}

Table 3. Outcome parameters. Summary of independent variables and scales

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Scale</th>
<th>Used in Paper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>Years</td>
<td>I, III</td>
</tr>
<tr>
<td>Gender</td>
<td>Male / Female</td>
<td>I, II III IV</td>
</tr>
<tr>
<td>Menarcheal status (age)</td>
<td>Yes / No (Years)</td>
<td>II, III</td>
</tr>
<tr>
<td>Age at scoliosis detection</td>
<td>Years</td>
<td>III</td>
</tr>
<tr>
<td>Clinical examination</td>
<td></td>
<td>III</td>
</tr>
<tr>
<td>Adam forward bending test</td>
<td>Positive / Negative</td>
<td>II, III</td>
</tr>
<tr>
<td>Angle of rotation</td>
<td>Degrees (Scoliometer) or Centimeter(ruler)</td>
<td>II, III</td>
</tr>
<tr>
<td>BMI</td>
<td>Kg/m(^2)</td>
<td>III</td>
</tr>
<tr>
<td>Physical examination of truncal asymmetry</td>
<td>Inspection / Description Plumb line deviation</td>
<td>II,III</td>
</tr>
<tr>
<td>Truncal shift</td>
<td>Cm</td>
<td>III</td>
</tr>
<tr>
<td>Back pain and perception of muscle fatigue</td>
<td>Point scale: 0 to 5 Verbal scale: no pain to pain all the time</td>
<td>III</td>
</tr>
</tbody>
</table>
Neurological examination

<table>
<thead>
<tr>
<th></th>
<th>Sensory</th>
<th>Motor</th>
<th>Reflexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present/ absent</td>
<td>Present/ absent</td>
<td>Present/absent</td>
<td>III</td>
</tr>
</tbody>
</table>

Treatment options

<table>
<thead>
<tr>
<th></th>
<th>Observation</th>
<th>Brace</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>I, II, III, IV</td>
<td>I, II, III, IV</td>
<td>I, II, III, IV</td>
</tr>
</tbody>
</table>

Patient Outcome

<table>
<thead>
<tr>
<th></th>
<th>SRS-22</th>
<th>EuroQol EQ5D</th>
<th>EQ5D-VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>III</td>
<td>0-10-100</td>
<td>0-100</td>
</tr>
</tbody>
</table>

Radiology

<table>
<thead>
<tr>
<th></th>
<th>Cobb angles</th>
<th>Risser sign</th>
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</thead>
<tbody>
<tr>
<td>Degrees</td>
<td>I, II, III</td>
<td>I, II, III</td>
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<tr>
<td>0-5</td>
<td></td>
<td></td>
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</table>

Health economic evaluation

<table>
<thead>
<tr>
<th></th>
<th>Costs and resources</th>
<th>Incremental costs and outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euro</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>Euro</td>
<td>IV</td>
<td>IV</td>
</tr>
</tbody>
</table>

### 3.6 Statistical methods

Descriptive statistics of means, standard deviations, and frequencies were measured for numerical data, to evaluate the construct validity, internal consistency, repeatability, and reliability of the SRS-22 questionnaire in Paper I, and to evaluate test reliability of screening by estimating sensitivity, specificity, PPV, NPV, likelihood ratios (LH+, LH-) in Paper II. Descriptive statistics in Papers III and IV included numbers, or percentages, means and mean differences (95% confidential interval).

Chi-square statistics was employed to compare the differences in the rate of treatment during periods of screening to non-screening (categorical variables in two independent samples) in Paper III. The proportions of the treatment modalities in the two periods, mean difference between the proportions, odd ratio (OR) and 95% confidential intervals were calculated.

Multivariable logistic regression was applied to estimate the association between back pain as the outcome variable, with gender, curve size, and BMI as predictor variables. Included covariates in the regression analysis were curve size and BMI as possible confounding factors on the assumed association between back pain and gender. The Hosmer-Lemeshow test was
used to assess the logistic model adequacy. Effect sizes were measured by OR (95% confidential intervals).

Uncertainty of the input variables in Paper IV was assessed by one-way and multi-way sensitivity analyses. Parametric uncertainty was also analysed by means of PSA, where all uncertainties in the relevant parameters were accounted for simultaneously\(^{290,300}\). The PSA was used to analyse the distribution of incremental cost estimations in all scenarios (100000 interactions), to estimate the confidential intervals for total incremental costs, and formed the basis for the Tornado diagram. In the PSA, we used gamma distributions for estimation of unit cost, beta distributions for the number of hours used and probabilities. Poisson distributions were used for the number of children treated with brace or surgery.

Analyses were performed using Statistical Package for Social Science (SPSS), version 14.0 (SPSS Inc., Chicago, IL) except in the evaluation of repeatability where Altman plots were constructed using MedCalc 9. The model simulations in Paper IV were performed using The Decision Tools Suite software component "@risk6".

Table 4. Overview of statistic methods used in the studies

<table>
<thead>
<tr>
<th>Paper</th>
<th>Measure</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Construct validity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Internal consistency</td>
<td>Cronbach alpha</td>
</tr>
<tr>
<td></td>
<td>Reliability</td>
<td>Intraclass correlation coefficient</td>
</tr>
<tr>
<td></td>
<td>Repeatability</td>
<td>Altman Bland plots, repeatability coefficient</td>
</tr>
<tr>
<td></td>
<td>Concurrent validity</td>
<td>Pearson’s ( r ) correlation coefficient</td>
</tr>
<tr>
<td>II</td>
<td>Test effectivity</td>
<td>Sensitivity, specificity, PPV, NPV, likelihood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ratios (LH+, LH-)</td>
</tr>
</tbody>
</table>


### III Association between back pain and other characteristics
- Logistic model adequacy
- Effect size
- Comparison of brace and surgical treatment during two periods

<table>
<thead>
<tr>
<th>Methodology</th>
<th>Multivariable logistic regression</th>
<th>Hosmer-Lemeshow</th>
<th>Odds ratio, Chi-square statistics</th>
</tr>
</thead>
</table>

### IV Estimation of costs and resources
- Analysis of uncertainty
- Methodological uncertainty
- Parametric uncertainty

<table>
<thead>
<tr>
<th>Methodology</th>
<th>Micro-costing (MI), case-mix group (MI), market price (MA) methods</th>
<th>One-way and multi-way sensitivity analysis</th>
<th>Probabilistic sensitivity analysis (PSA) and Tornado diagrams. PSA used to estimate confidential intervals for cost of treatment alternatives, and incremental costs. Gamma distributions for unit cost estimation, beta distributions for no. of hours used, probabilities and Poisson distributions for no. of children treated for scoliosis</th>
</tr>
</thead>
</table>

### 3.7 Ethical considerations
All studies were conducted in conformity with the Helsinki Declaration. The study design in all parts and protocols were approved by the Regional Ethical Committee for Medical Research in Norway, and Ethic committee of OUS-Rikshospitalet. Where applicable, patients or parents received oral and written information about the project and gave their informed consent.

In Paper II, written information about the screening, and the results were provided to the children and their parents (Appendix Paper II). Signed consent forms from parents were received before screening was performed. Parents of those with confirmed scoliosis on X-rays were also informed about the results and follow-up regimes. No children or parents declined to partake in the screening program.
4. Synopsis

4.1 Paper I

**Background:** SRS-22 is widely used for evaluation of health-related quality of life in AIS. Its repeatability, which is essential for use in follow-up studies, and concurrent validity with EuroQol, which can be used for cost-utility analysis, has not yet been assessed. The objective was to evaluate the repeatability, reliability, internal consistency, and concurrent validity of an adapted Norwegian version of the Scoliosis Research Society 22 questionnaire (SRS-22) and the generic health-related quality of life instrument EuroQol (EQ-5D and EQ-VAS).

**Methods:** The forward-backward translation of the English version of the SRS-22 was performed according to the guidelines for cross-cultural adaptation of outcome questionnaires. Fifty-seven patients with AIS of various ages and severity of deformity completed questionnaires including SRS-22, EQ-5D, and EQ-VAS twice with a two-week interval.

**Results:** The study demonstrated moderate internal consistency and high reliability of the SRS-22 questionnaire, with Cronbach alpha and ICC ranging from 0.76 to 0.93 for the 5 domains. Repeatability was excellent for all domains of SRS-22, with repeatability coefficients < 1. Concurrent validity with EQ-5D was poor to moderate, with Pearson’s r ranging from 0.01 to 0.58. However, total scores of the two instruments showed satisfactory agreement.

**Conclusions:** The SRS-22 outcome instrument has satisfactory repeatability, but the poor to moderate concurrent validity of the SRS-22 with EQ-5D suggests that the disease specific and the generic questionnaires measure different parameters.
4.2 Paper II
School screening and point prevalence of adolescent idiopathic scoliosis in 4000 Norwegian children aged 12 years. Adobor RD, Rimeslåtten S, Steen H, Brox JI.

*Scoliosis* 2011; 6:23

**Background:** Early diagnosis of idiopathic scoliosis allows for observation and timely initiation of brace treatment in order to halt progression. Screening allows for the early detection and has contributed to the study of the etiology of idiopathic scoliosis, but its effectiveness is debated. The prevalence of idiopathic scoliosis in adolescents is variable. The aim of the study was to describe the point prevalence of AIS and to evaluate the effectiveness of school screening in 12-year-old children.

**Methods:** Community nurses and physical therapists in the Southern Health region were the screeners. They fulfilled an educational course to improve their knowledge about AIS and to learn the screening procedure, including the Adam Forward Bending Test and measurement of angle of rotation using a scoliometer.

**Results:** There were 12000 twelve year old children in the study population. About 4000 were screened. The prevalence of idiopathic scoliosis defined as a positive Adam Forward Bending Test, ATR > 7° and primary major curve on radiographs > 10°, was 0.55%. Five children (0.13%) had a major curve > 20°. Bracing was not indicated in any child; all children were post menarche; four had Risser sign of 4, and one with Risser 1 did not have curve progression > 5° at later follow-up. In one of these 5 children however, the major curve progressed to 45° within 7 months after screening and the girl was operated.

**Conclusions:** The point prevalence of AIS in 12-year old children is in agreement or slightly lower than found in previous studies. The screening model employed demonstrates acceptable sensitivity and specificity and low referral rates. Screening at the age of 12 years only was not effective for detecting patients with indication for brace treatment.
4.3 Paper III

**Background:** School scoliosis screening programs were abolished in Norway in 1994 for lack of efficacy and for the costs involved. The objective of the study was to evaluate the detection, patient characteristics, referral patterns and treatment of idiopathic scoliosis at a scoliosis clinic during the period 2003-2011, when there was no screening, and to compare treatment modalities to the period 1976-1988 when screening was performed.

**Methods:** Patient demographics, age at detection, family history, clinical and radiological charts of consecutive patients referred for scoliosis evaluation during the period 2003-2011, were registered. Maturity was estimated according to Risser sign and menarcheal status. Severity of pain was recorded by a verbal 5-point scale from no pain to pain at all times. Referral patterns were recorded. Treatment modalities in the current period were compared to the period 1976-1988.

**Results:** We registered 752 patients from 2003-2011. Eighty-six percent were girls. Mean age at detection was 14.6 (±1.9) years. Sixty percent had Risser sign 3, whilst 74% were post menarche with a mean age at menarche of 13.2 years. The mean major curve at first consultation was 38° (10°-95°). About 40% had a major curve > 40°. Seventy-one percent were detected by patients, close relatives, and friends. Orthopedic surgeons referred 61% of the patients. The mean duration from detection to the first consultation was 20 (0-27) months. The proportion of the average number of patients braced each year was 68% during the period with screening compared to 38% in the period without screening, while the proportion for those operated was 32% and 62%, respectively (p=0.002, OR 3.5, (95% CI 1.6 to 7.5).

**Conclusions:** In the absence of scoliosis screening, lay persons most often detect scoliosis. Many patients presented with a mean Cobb angle approaching the upper limit for brace treatment indications. The frequency of brace treatment has been reduced and surgery is increased during the recent period without screening compared with the period in the past when screening was still conducted.
4.4 Paper IV


Scoliosis 2014, 9:21

Study design: Model based cost minimisation analysis using hospital’s costs and administrative data, and market prices to estimate costs in screening, bracing and surgical treatment. Uncertainty was characterised by deterministic and probabilistic sensitivity analyses. Time horizon was 6 years from first screening at 11 years of age.

Objective: To compare estimated costs in screening and non-screening scenarios (reduced treatment rates of 90%, 80%, 70% of screening, and non-screening Norway 2012). Summary of background data: Adolescent idiopathic scoliosis can progress and affect the health related quality of life of the patients. Research shows that screening is effective in early detection, allowing for bracing, and reduced surgical rates, and may save costs, but still controversial from a health economic perspective.

Methods: Data was based on screening and treatment costs in primary health care and in hospital care settings. Participants were 4000, 12-year old children screened in Norway, 115190 children screened in Hong Kong and 112 children treated for scoliosis in Norway in 2012. We assumed equivalent outcome of health related quality of life, and compare only relative costs in screening and non-screening settings. Incremental cost was defined as positive when a non-screening scenario was more expensive relative to screening.

Results: Screening per child was € 8.4 (95% CI 6.6 to 10.6), € 10350 (8690 to 12180) per patient braced, and € 41690 (35250 to 49480) per child operated. Incremental cost per child in non-screening scenario of 90% treatment rate was € 12.3 (2 to 25), increasing from € 0.3 (-7 to 8) to € 27.0 (14 to 42) as surgical rates increased from 40% to 80%. For the 80% treatment rate non-screening scenario, incremental cost was € 4.8 (-5 to 16) compared to screening all, and € 10.7 (3 to 20) compared to screening girls only. For the non-screening Norwegian scenario, incremental cost per child was € -3.1 (-16 to 11). Bracing and surgery were the main cost drivers and contributed most to uncertainty.

Conclusions: With the assumptions in the present study, screening is cost saving when performed in girls only, and when it leads to reduced treatment rates. Cost of surgery was dominating in non-screening whilst cost of bracing was dominating in screening. The economic gain of screening increases when it leads to higher rates of bracing and reduced surgical rates.
5. Discussion

5.1 Methodological considerations

5.1.1 Cross-cultural adaptation of the SRS-22 questionnaire

It has been recommended that clinicians and researchers who lack a suitable health-related quality of life measure in their own language either develop a new measure, or translate and evaluate a measure previously validated in another language, known as a cross-cultural adaptation. Specific guidelines have been proposed for the cross-cultural adaptation process which includes recommendations for obtaining semantic, idiomatic, experiential and conceptual equivalence in translation by using back-translation techniques and committee review, pre-testing techniques and re-examining the weights of scores. It has also been suggested that health related quality of life measures should have three objectives: discriminate between individuals and groups, predict outcome, and evaluate change in health status over time. In Paper I, the recommended methodology was followed. The study was conducted in a clinical setting and AIS patients under different treatment phases were included.

Construct validity and reliability

The strength of the psychometric attributes such as validity, reliability and responsiveness determine the overall quality of an instrument. Construct validity of a questionnaire relates to the question of what the instrument is measuring. Reliability addresses how much of the variation that is attributed to chance or random errors, and describes the ability to discriminate between individuals. In Paper I, two measures of reliability were estimated: internal consistency by Cronbach alpha, and Intraclass Correlation Coefficient (ICC: 2, 1).

Repeatability

Developers of the original SRS-22 questionnaire and subsequent validators have limited the assessment of reproducibility to calculation of intraclass correlation coefficient (ICC). Agreement parameters are required for evaluation of measurement error. We therefore employed the statistical measure proposed by Altman and Bland to estimate repeatability, which is a measure based on the variation within individuals. We based the measurement of repeatability on the standard error of measurement (SEM) which is calculated by extracting the square root of the mean within subject variance term in...
the one-way analysis of variance table. The coefficient of repeatability (CR) is then calculated from the formula: $CR = SEM \times 1.96\sqrt{2}$. The difference between two measurements for the same subject is expected to be less than the CR for 95% of pairs of observations. This measure defines the smallest detectable change between two measurements on the same individual and has been designated the minimal detectable change (MDC)\textsuperscript{227,310}. Diagrammatically, plots of the difference between test and retest against the mean of the sum scores were constructed for detecting any evidence of increasing variability with higher mean scores (heteroscedasticity). The SD of the difference was subtracted or added to the mean difference to create limits of agreement which were drawn as lines in the plots, as recommended by Bland and Altman\textsuperscript{308,309}.

Few other studies have assessed the smallest detectable change measured on the SRS-22. One study determined the MCD, and based on that, determined the MCID, which is the threshold that is clinically relevant to the patient on a 90% probability level\textsuperscript{311}. Another study determined the MCD based on 95% probability\textsuperscript{312} as in Paper I. In this study, two methods were used to calculate the MID. The anchor-based MID defined as the mean preoperative/follow-up difference in SRS-22 scores in the group of patients who stated they were much better than before surgery. They used the same anchor criterion, the optimal cut-off value to identify patients that had improved from the receiver operating characteristic (ROC) curve. Additionally, the distribution-based MID was calculated by using the standard error of measurement method\textsuperscript{312}.

5.1.2 Validity of scoliosis screening

Sensitivity and specificity

The sensitivity and specificity measures the efficiency of a screening test. Combining the Adam forward bending test with the scoliometer increases specificity and sensitivity\textsuperscript{313}. The use of the scoliometer has been shown to increase the sensitivity and the specificity in detecting a Cobb angle of $> 20^\circ$ in one report\textsuperscript{313}. A scoliometer reading of $5^\circ$ has been shown to have a sensitivity of 100%, but only 47% specificity, whereas a scoliometer reading of $7^\circ$ increases the specificity to 86% and decreases the sensitivity to 83%\textsuperscript{314}. A scoliometer reading of $7^\circ$ has therefore been recommended as cut-off point for referral to radiography\textsuperscript{298,315,316}. In Paper II, we designed our screening to conform to these recommendations.
Predictive validity

The positive predictive value (PPV) of visual inspection and the forward-bending test varies with the degree of curvature by which a true positive is defined, the prevalence of scoliosis in the screened population, and the skills of the examiners. In order to increase the PPV of the screening test in Paper II, we designed the study by organizing courses for the examiners thereby improving their skills. In addition, likelihood ratios (LH) ratios were calculated to increase the predictive validity of the screening test.

WHO criteria

Supporters of screening programs suggest that earlier detection allows for bracing that can reduce the need for surgery. Whilst opponents of screening programs suggest that AIS lacks the characteristics that render a disease as a good candidate for screening. These characteristics include high prevalence, high burden of suffering, preclinical phase, acceptable test and treatment, and reasonable costs. It is hereby discussed whether AIS satisfy the 10 specific criteria laid down by WHO that a screening program must satisfy.

1. The condition should be an important health problem

AIS is an important health problem that affects the teenage population during their most vulnerable years. Scoliosis > 10° affect 2.0-3.0% of teenagers. However, curves > 20° affect only 1.0-0.4%, and curves > 40° are present in only 0.1%, of the affected population. The deformity may represent a burden both physically and psychologically in the affected patients. AIS patients have increased suicidal thoughts and increased concerns related to body development and peer interactions compared to age matched controls. Patients’ views of their condition are usually influenced by culture, environment, peer groups and their own experience. They also have decreased perception of their health status, even after brace and surgical treatment. Long-term studies from Scandinavia in the past have reported that untreated scoliosis may lead to poor self-image, back pain, and psychological problems during both childhood and limited job opportunities, and lower marriage rate in adulthood. But these studies lack internal controls and it is likely that many patients with spinal conditions other than AIS were included. Other long-term studies suggest a poor correlation between the magnitude of curves and the extent of psychosocial complaints. Current data on the psychosocial effects of scoliosis and poor cosmetics are however limited.
Outcome studies increasingly suggest that scoliosis affects the HRQoL aspects of disability, pain, mental health and self-image of the affected adolescents both in the short term and in the long term\(^{72;73;101-106}\) as described in the background chapter.

2. There should be a treatment for the condition

Treatment of any condition is an attempt to alter its natural history\(^{73}\). Long-term studies of both the natural history and treatment outcomes are therefore necessary in evaluating the efficacy of the treatment of AIS. The treatment of AIS is based on the knowledge of the risk of curve progression and the maturity of the patient. Three main treatment options: observation, bracing, surgery are used in treatment of AIS as discussed in the background section.

3. Facilities for diagnosis and treatment should be available

The diagnosis of AIS requires clinical and radiological examination\(^{333}\). Radiographs are required to confirm cases of AIS suspected on clinical examination, or scoliosis screening in order to determine the severity of the curves, and to evaluate the skeletal maturity (risk of progression) of the patients. The diagnosis of AIS is confirmed if the primary curve is \(> 10^\circ\) and other reasons for scoliosis are excluded\(^{83;334}\). Facilities for scoliosis diagnosis and treatment are available in Norway, and worldwide.

4. There should be a latent stage of the disease

Screening identifies unrecognized disease in individuals without signs and symptoms. Screening for scoliosis is performed in apparently normal children without signs or symptoms of scoliosis. The latent stage of a disease is the time from onset to the first symptoms or signs appear and the patient seeks medical care. This depends on the population’s awareness of the disease and the available access to health care. Scoliosis can develop quickly in some adolescents, and may be missed without a specific screening program. The scoliosis curvature itself may be too subtle to be noticed, even by observant parents. Early manifestations of underlying scoliosis like asymmetries of the neck, shoulder, ribs, waistline and hips may be noticed earlier by screening. Waistline asymmetry may be observed as straightening or excessive indentation of the waistline on one side, increasing hip prominence, tilting of the hem or waistband of a skirt, or uneven alignment of leg pant legs that may be evident to the dressmaker\(^{86}\). Other early manifestations of underlying scoliosis could be breast asymmetry in girls\(^{335}\) or prominence of lower coastal margins that will be most noticeable to the patient.
In the absence of a screening program, scoliosis is most likely to be detected by patients themselves, close family and friends or other lay persons when curves are larger and the surface deformity is evident, but patients are not suitable for brace treatment as reported in Paper III.

Screening is reported to detect scoliosis at a younger age with smaller curves, leading to brace treatment and reduction of surgical rates. In a case control study in the Netherlands involving 108 patients who were operated for idiopathic scoliosis and 216 controls demonstrated that patients detected through screening had significantly smaller Cobb angles at diagnosis, compared to otherwise-detected patients (34° versus 46°, p<0.01). Patients were also diagnosed at a significantly younger age than otherwise detected patients (10.8 versus 13.4 years). In that study, patients detected through screening had a threefold greater chance of being treated with brace before surgery (OR = 3.1; 95% CI =1.3 to 7.0). Similar findings were demonstrated in their cross sectional study involving 125 patients who had completed treatment with brace or surgery or with brace followed by surgery. They found in that study also that patients detected through screening had significantly smaller Cobb angles at diagnosis, and younger at detection compared to otherwise-detected patients (28° versus 40°, p<0.01 and 9.9 versus 12.6 years, p<0.01).

5. There should be a test or examination for the condition

The Adam forward bending test and a surface device measuring the angle of rotation like the scoliometer is normally applied in the screening test of AIS. There is a large variation of detection rates of scoliosis because of different standards of various examiners, and this is thought to be one of the main causes of the ineffectiveness of school screening for scoliosis. The use of the Adam Forward Bending Test alone has low sensitivity and specificity and is thus insufficient. Higher referral rates and lower PPV’s are reported. The Moiré topography has also been applied to the screening program in the past, but has led to a large number of false positive findings. The use of the scoliometer to measure the ATR was introduced to increase the effectiveness of the screening programs.

6. The test should be acceptable to the population

For a screening test to be acceptable to the population, it should cause no harm, and have benefits. The screening procedure of scoliosis is safe, and non-invasive. There is however a
concern that the screening test might cause stress, psychological labeling, anxiety, discomfort, and radiation exposure. The latter is generally reduced with the current techniques of shielding, the use of special films, and digital radiography\textsuperscript{136}. In Paper II, 38 children were falsely diagnosed as AIS. They had positive screening, but a normal spine on radiography. If screening was performed yearly nationwide, the total estimated number of children with negative radiographs (Cobb angle < 10°) in 60000 children aged 12 years in the Norwegian population is estimated to about 570, which might be a concern for health authorities. In Paper II, the concern of safety has been addressed by making attempts to limit psychological labeling through provision of adequate verbal and written information to children and parents before and after screening, informing them about the results and follow-up regimes. We applied a relatively high cut-off angle ATR of 7° as indication to referral to radiography, and applied the accepted SRS’s definition of curvature > 10° as scoliosis\textsuperscript{299}, thereby reducing over-referrals and limiting the exposure to radiation and reducing costs. The acceptability of screening in patients and their parents has however not been systematically evaluated.

7. The natural history of the disease should be adequately understood

The risk of progression of scoliosis and its effects on HRQoL and pulmonary function in patients with large curves is of concern for patients, parents, and care providers. Knowledge of the natural history of AIS will enable these to make informed decisions about the treatment options available. The main risks of progression of AIS, its effects on HRQoL and pulmonary functions have been already discussed in the background section.

8. There should be an agreed policy on whom to treat

The policy on whom to treat for AIS is based on the available knowledge of the risk of curve progression, the natural history and effects on HRQoL, and pulmonary functions discussed above. It is generally agreed that, children whose curves are < 25° and still growing, should be observed for curve progression. Brace treatment should be initiated when curves are > 25°-40° in patients who are growing. Curves > 50° in patients who are mature will continue to slowly progress over time\textsuperscript{72,73,94,97-99}, and these patients are recommended surgery\textsuperscript{47}. The evidence for effectiveness of physical therapy in preventing progression of AIS has been inconclusive, and the policy on treatment of AIS with physical therapy and other alternative
methods varies worldwide. In some countries, comprehensive physical therapy programs are applied alone or in combination with bracing to prevent curve progression, particularly for small curves (< 25°). 

9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole

There are concerns that screening can involve costs and use of medical resources on a majority of people who do not need treatment (over-referrals). Scoliosis screening will be cost saving in relation to medical expenditure as a whole if early diagnosis through screening results in bracing and costs saved by reduced surgical rates as suggested in Paper IV. In Paper III, we reported higher rates of bracing and reduced surgical rates during a period of screening. Other studies have reported similar results.

There are reports from several countries that have estimated the cost involved in scoliosis screening. These estimates vary considerably and are not easily comparable. Programs have been conducted under different settings, variable scoliosis definitions have been employed with some programs performing multiple screenings in different age groups. Some studies have reported only the direct costs associated with the screening, whilst others have reported the costs of diagnosis and follow-ups in addition, and some have reported costs of treatment of cases detected through screening. In these studies, the cost of screening per child varied from $0.07 to $43.7 and $149 per child and up to $4000 for each case brought to treatment depending on how the costs were calculated. Studies that assessed the economic impact of school scoliosis screening programs by only examining the costs paid by the school have generally reported lower costs. The few studies that included total costs, as in Paper IV, suggest long-term cost saving if early detection leads to brace treatment, and reduced surgical rates. It has been postulated that the costs involved with scoliosis screening are relatively low on a societal level and may justify the procedure to detect those children who will be at risk for developing scoliosis. In screening for scoliosis, there is an added value not necessarily linked to improvement in health state, but to the value of information and reassurance about the absence of scoliosis in those found negative on screening. There is currently a debate about whether there is a value from the process of receiving information and care, independent of the outcome.
10. Case-finding should be a continuous process, not just a “once and for all” project

Based on the knowledge of age and sex-specific prevalence of scoliosis, and the length of time between detection and treatment, it has been suggested that scoliosis screening programs should be planned as a continuous process and not just a once and for all project\(^{65}\). There is a possibility of missing out some cases if screening is performed once, since the screening test lacks complete accuracy.

A single screening test can however be used to establish the diagnostic sensitivity and specificity for example by the use of the scoliometer\(^{313}\). However, the effectiveness of scoliosis screening is best determined by evaluating the complete school screening program, including the sensitivity and PPV and reproducibility of the series of screening tests for scoliosis diagnosis and treatment\(^{349;350}\). The optimal age for scoliosis screening is under debate. A recent international task force of the SRS found the literature difficult to interpret on the optimal age of screening\(^{288}\). They agreed that ideally screening should be performed in girls before the onset of menses, and 1-2 years later for boys as females achieve adolescence about two years before males and AIS is more prevalent in girls. Previously, the SRS recommended that school screenings should be performed annually between the ages 10 to 14 years in conjunction with a school health examination. The AAP has recommended scoliosis screening at routine health supervision visits at ages 10, 12, 14, and 16\(^{351}\). In recent years, the AAOS, SRS, POSNA, and AAP all suggest screening girls twice at ages 10 and 12 years, and boys once at age 13 or 14 years\(^{136}\).

In paper II, we performed prevalence screening in 12 year-old children once in conjunction with a vaccination program, and this was not effective in detecting cases for bracing. In this study, the screeners were public health nurses and physical therapist. It is possible that other health professionals like physical education teachers could be engaged as screeners to perform the screening as a continuous process.

5.1.3 Characteristics of scoliosis detected in the absence of screening

In Paper III, we designed a prospective study, in which a standardized simple scoring sheet was used to evaluate patients with late juvenile and adolescent scoliosis patients referred for scoliosis evaluation for the first time at the specialist clinic during the period 2003–2011. The study appropriately included only late-juveniles (7 years and older) and adolescents, and excluded patients with non-idiopathic aetiology. Relevant aspects including patient
demographics, scoliosis detector, family history, perception of pain and muscle fatigue, was registered. Clinical and neurological examinations were performed in order to exclude non idiopathic scoliosis. Referral patterns of primary physicians, physical therapists and community health nurses, chiropractors, and hospital specialists to the scoliosis clinic were noted. The duration from time of detection to referral and evaluation was also recorded. Recommended treatment was appropriately registered.

Surgical protocols were used to validate the number operated during both periods and the number braced during the years 1976–1988 was registered prospectively. The results of brace treatment in these patients has been reported in 3 publications126;127;153. The indications for bracing and surgery were the same during the two observation periods.

The number obtained from surgical protocols was considered as the best estimate of the true number of actually operated patients.

5.1.4 Health economic evaluation of scoliosis screening

The most appropriate economic evaluation method of analysis depends on the problem being tackled, the institutional framework, the practical measurement challenges, and the perspective of the analyst290;352. It is important to perform appropriate economic evaluation of treatment options in relation to costs of scoliosis screening. AIS as a deformity in teenagers, can lead to increased morbidity, and may affect the social and the HRQoL of the affected patients72;73;101-106, but rarely death7;75;76;106. There is however, lack of validated utility measures in AIS in order to perform a full cost-effectiveness analysis (CEA), cost-utility analysis (CUA) or cost-benefit analysis (CBA). Paper IV was not designed as a prospective trial using utility measures in order to perform a full economic evaluation analysis. We therefore performed a partial economic evaluation of cost minimization analysis (CMA), assuming that long term effects of treatment options (brace and surgery) are not different in patients whose scoliosis was detected through screening or otherwise, and compared only relative costs.

CMA being a partial health economic evaluation has been criticized for not answering the effectiveness questions290;352. Compared with CEA, the CMA is more prone to bias and overestimation or underestimation of the value of information and the probability that treatment is cost effective353.
In Paper IV, many of the input variables had uncertainties. We assumed equal prevalence and natural history of scoliosis in Hong Kong and Norway and based the evaluation on data from both Hong Kong and Norway. The uncertainty of input variables was assessed by one-way and multi-way sensitivity analyses. Parametric uncertainty was also analyzed by means of probabilistic sensitivity analysis (PSA), where all uncertainties in the relevant parameters were accounted for simultaneously\(^{290,300}\). We also performed sensitivity analyses for the most uncertain variables. Total costs were estimated for screening and treatment based on our own data when available, otherwise we supplemented data from the largest reported longitudinal study of screening cohorts\(^{354}\).

### 5.2 Statistical methods

The choice of statistical methods in Papers I to III have been discussed. In Paper IV, we appropriately applied the recommended reporting standards and statistical analyses\(^{355}\). We used PSA to estimate the confidence intervals for total and incremental costs, and performed sensitivity analysis as illustrated in the Tornado diagram. In a tornado diagram, the categories appear from the top to the bottom according to the magnitude of contribution to uncertainty. This enables a decision maker to focus on the variables that contribute most to the variability of outcome\(^{356}\). In the PSA, we used gamma distributions for estimation of unit cost, beta distributions for the number of hours used, and probabilities. Poisson distributions were used for the number of children treated with brace or surgery. Boot-strapping based on 100000 interactions was used to analyse the distribution of incremental cost estimations in all scenarios.

### 5.3 Methodological strengths

The main strengths in Paper I were adequately sized population of patients and presuming that the condition was unchanged between questionnaire administrations. Patient data was collected and evaluated using the recommended methods.

In Paper II, screeners were adequately prepared and educated in order to improve their skills, as the sensitivity and specificity depends largely on the skills of the examiner. Studies have shown that adequate preparation and teaching of the screeners increase sensitivity and specificity of scoliosis screening\(^{314}\). The combination of the Adam forward bending test and a scoliometer reading of 7\(^{\circ}\) most likely increased test effectivity. Screening was combined with a vaccination program in order to reduce costs. The accepted definition of scoliosis of 10\(^{\circ}\)
primary curve was employed. Statistical tests included LH ratios which are commonly used for evaluating a screening test.

The main strengths of Paper III were the prospective design, the large sample size, and the use of data from periods with and without screening and the prospective registration on bracing.

The main strength of Paper IV was the recommendations developed by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) which were applied. This gives more transparency, and complete reporting of methods and findings that will facilitate interpretation and comparison of similar studies. In addition, analyses were performed to characterize uncertainty. Input data was based on Norwegian data (Paper II) and from the largest reported longitudinal study of screening cohorts which may increase the generalizability of the findings of study.

5.4 Methodological limitations

In Paper I, the Consensus-based Standards for the selection of health measurement Instruments (COSMIN) checklist which contains standards for design requirements and preferred statistical methods of studies on the measurement properties of health measurement instruments, was not rigorously followed. The checklist is usually used to check if a study on measurement properties meets the standards for good methodological quality. In Paper I, aspects of construct validity were estimated, but hypothesis testing was not used and responsiveness was not evaluated. The coefficient alpha could not be adjusted for errors caused by factors external to the instrument such as differences in testing situations and responders over time.

The main limitation in Paper II is that the true point prevalence in Norwegian school children aged 12 year could not be calculated because only those with a positive screening test were referred to X-ray examination. The Scoliometer has good measurement reproducibility, but lacks a correlation between the ATR measured by the Scoliometer and the size of lateral deviation measured on a radiograph using the Cobb angle. A lower threshold value for the Scoliometer test would have increased the number referred to X-rays, but because of the poor correlation between lateral deviation and spinal rotation in the younger age group, as in Paper II, the effect of lowering the threshold is questionable. In Paper II, we found a relatively high number of false positive screens and the number of false negative screens is
suspected to be considerably lower. Nevertheless, the point prevalence estimated in Paper II is most likely lower than the true point prevalence.

The general limitations to screening of scoliosis are the low prevalence of AIS requiring treatment\(^{56,115;129;259;261;262;361}\), which increases the likelihood that a positive screen could be false positive. There is also the likelihood of negative screen for people who will develop scoliosis later (false negative). False positive screening might cause unnecessary anxiety, and stress, time lost from school or work for follow-up or specialty care, radiation exposure, and adverse psychosocial effects (for example related to brace wear)\(^{3,265;267}\). In one study, 450 children were screened to detect one child who needed treatment\(^{62}\). Some studies question the benefit of preclinical detection of scoliosis through screening, and argue that most cases detected through screening do not progress to the point of surgery, and that most cases requiring surgery were detected without screening\(^{267;336;362;363}\). In general, the number needed to screen (NNTS) to identify a child with a Cobb angle of > 10° ranges from 48 to 58, and to identify one child who subsequently need treatment (> 20-25°) ranges from 429 to 466\(^{48;52;56;58;59;61;62;71;342}\).

If the screening population is selected for any reason, the selection bias can make the screening test look better or worse than it is for a random sample. In Paper II, 12-year olds were selected. Time biases are perceived with screening when a disease is diagnosed earlier by screening than without screening. Without screening, the disease may be discovered later, when symptoms or signs appear more clearly. As discussed earlier, screening leads to early detection\(^{280;336}\) which allows for more bracing and less surgery\(^{258;280}\) if compliance with brace treatment is good\(^{148;156;159-161}\). It has been suggested that there will be an added burden for patients who must live with knowledge of scoliosis longer because of earlier detection through screening.

In Paper II we planned to include 12000 children in the screening program and follow them in a cohort study and compare treatments with those referred from other regions (from a similar population of about 30000 in Health Region East and Northern Norway) referred to the scoliosis clinic at the OUS-Rikshospitalet. We were however able to screen only 4000 out of the 12000. Since screening has been discontinued in Norway, the Directory of Health in Norway was not willing to support the program with a recommendation. Many community health nurses and physical therapists were therefore not willing to conduct a task that was not recommended by the health authorities and participation in the program was therefore lower than anticipated.
In Paper III, resident orthopedic surgeons with variable experience in scoliosis management participated in the study. The inter-tester reliability was not tested. This variability in experience most likely influences evaluation of patient characteristics and the recommended treatment options. The physician filled in registration chart has not been validated. Back pain recorded by a physician is likely to be less valid than self-assessment by patients. At the beginning of the study the validated adapted version of the Norwegian SRS-22 questionnaire (Paper I) was not available for evaluation of baseline HRQoL.

Findings in Paper III suggest that the absence of screening for scoliosis has resulted in less patients being treated with brace and more patients having surgery. However, technical advances in scoliosis surgery in recent years coupled with changes in surgeon attitudes may contribute to the observed variation in treatment trends exhibited over the two periods. Surgical treatment of scoliosis has evolved from the one-dimensional Harrington distraction rods to the three-dimensional CD instrumentation and later third generation instrumentation with segmental all pedicle screws construct. During the period of screening, bracing was administered by one spine surgeon, while different spine surgeons were involved in brace treatment during the period without screening. There was probably less enthusiasm for bracing in the last period. These factors are possible confounders contributing to the observed difference in bracing and surgery during the two periods.

There are limitations to the use of CMA as a health economic evaluation method as in Paper IV. In order to use CMA as an appropriate health economic method, it is necessary to generate unambiguous evidence of clinical equivalence between the alternatives being compared. However, high quality evidence evaluating HRQoL in patients detected by scoliosis screening versus no screening is lacking. Ideally, randomised studies or controlled prospective studies are needed to compare outcome in scoliosis treatment with or without screening. Since the prevalence of scoliosis is low it is difficult to include an adequate study sample even within a large country or internationally. Utility scores may differ in shorter periods during treatment, for example by wearing a rigid brace, or postoperatively, and there are no long-term results from controlled studies. Another limitation is the assumption of equal prevalence and natural history of AIS in Norway and Hong Kong in performing the analysis. However studies show regional variations in the prevalence of AIS, like higher prevalence in girls but not boys in higher latitudes than in lower latitudes. But those differences could be linked to environmental factors such as the difference in the onset of menses in different geographic locations and different cultures and not related to genetics. It is also likely that
mechanisms of referral may be very different in the two settings and different countries due to healthcare systems structures and barriers to access. The presentation of AIS has also been reported to be linked to socioeconomic status and race\textsuperscript{365}. A recent study however found equal prevalence of AIS in 12 years old children in Malaysia and Norway\textsuperscript{366;367}. In performing the CMA; we limited our the study perspective to only costs related to expenses in an orthopedic department. We did not include costs related to primary health care, paramedics and alternative costs in relation to referred patients. In addition, we did not systematically register costs of patients’ out of pocket expenses like transportation in relation to adjuvant treatment for scoliosis. These could underestimate our total costs.

5.5 General discussion of the findings

5.5.1 Reliability and agreement of outcome questionnaire in AIS
Outcome data are considered reliable when measurements are reproducible with low levels of random error. An instrument is considered valid if it measures what it is intended to measure.

In Paper I, we found satisfactory score distribution, internal consistency, reliability, and repeatability for all domains of SRS-22 and for EQ-5D and EQ-VAS. Internal consistency (Table 5) for the function domain was higher compared with the Turkish\textsuperscript{209}, Spanish\textsuperscript{211} and German\textsuperscript{221} versions, and in agreement with the original version\textsuperscript{118;204}. The inconsistencies have previously been traced to question 15 (Are you and/or your family experiencing financial difficulties because of your back?) and question 18 (Does your back condition limit your going out with friends/family?). In Paper I, we pointed out that, these questions may reflect socio-cultural aspects (economy and participation) which may differ from function in terms of the ability to perform activities of daily living. The Cronbach alpha for the remaining questions of the function domain compare well with the original version\textsuperscript{118;204}. Later modification and refinement of question 15 and 18 has resulted in a higher Cronbach alpha value for the function domain\textsuperscript{207}.

SRS-22 scores in normal adolescents of various ages, gender and race without scoliosis have been published\textsuperscript{212;368;369}. In the study from the USA, scores were lower as age increased from 11 to 19 years. Females had lower mental scores than males, and Caucasians scored higher in function, pain and self-image than other groups\textsuperscript{368}. Also, in the study from China, females were reported to have lower scores for self-image and pain domains than males. Function domain was higher for males aged $>15.9$ than females\textsuperscript{369}. One study in the validation studies of the SRS-22 questionnaire included healthy adolescents and patients with non-clinically
significant scoliosis, and the SRS-22 discriminated between patients with AIS and controls\textsuperscript{212}. Boys had higher scores than girls and scores worsened with age, and with increasing body mass index\textsuperscript{212}. The ICCs in Paper I are in agreement with previous studies and support the conclusion that SRS-22 is a useful instrument for discrimination between patients\textsuperscript{204;205;209;211;213;214;216}.

In evaluating the concurrent validity of the SRS-22, it has shown high correlation coefficients to the corresponding domains of the various generic outcome instruments SF-36\textsuperscript{205;207;209;213;216;219;220;222-224}, SF-12\textsuperscript{212}, the Child Health Questionnaire CF 87\textsuperscript{225}, and the Roland Morris Questionnaire\textsuperscript{221}. We found poor correlations between SRS-22 and EQ-5D for the domains of pain, mobility, function, and mental health. The self-image and satisfaction to treatment domains are not comparable between the two instruments. The low correlation coefficient observed in Paper I may reflect poor intrinsic correlation between the two instruments rather than a validity problem of the translated questionnaire. Another possible reason is that the EuroQol has been validated for use in adult populations with back pain in Norway\textsuperscript{370}, but not in the younger population with spine deformity as in the study population in Paper I.

\textit{Repeatability}

While reliability parameters are recommended for instruments that are used for discriminative purposes, agreement parameters are required for use in follow-up studies. In Paper I, we calculated the repeatability coefficient using 95\% probability. Other authors have evaluated the minimal detectable change (MDC) of the SRS-22 questionnaire using 90\% probability\textsuperscript{311}. Bago et al also estimated the MDC (but called it the minimal important difference (MID) using a 95\% probability\textsuperscript{312}. Their results ranged from 0.3 to 0.8 for the function, pain, self-image, and mental health domains and are lower than the results in Paper I. We found the coefficients of repeatability for the 5 domains of pain, self-image, function/activity, mental health, and satisfaction with treatment, to vary from 0.7 to 1.0. The practical interpretation is that the lowest detectable average change for each domain is slightly lower than one step on verbal scales with response categories from 1 to 5. This means that the measurement error for an individual patient ranges from about 15 to 20\% for the different domains. A smaller change between two subsequent measurements is indistinguishable from the measurement error, and the given limit represents the minimum detectable difference. The variation between two measurements in the same individual should be considered when assessing
follow-up results after treatment and in the planning of prospective studies. Repeated measurements may reduce the measurement error and increase the validity of observations \(^{371}\). The estimates of both agreement and reliability parameters reported in Paper I supplement current knowledge of clinometric properties of questionnaires for use in patients with AIS.

**Table 5. Overview of psychometric properties of the SRS-22 in various languages.**

P= Pain, F= Function, MH= Mental health, SI= Self-image, S= Satisfaction with treatment
NCSS= Non clinically significant scoliosis
QLSDP= Quality of Life for Spine Deformities Profile

<table>
<thead>
<tr>
<th>Language/Author/ Publication year</th>
<th>Internal consistency (Cronbach (\alpha))</th>
<th>Reliability ICC</th>
<th>Concurrent reliability Global outcome measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original article in English Hafer)</td>
<td>P= 0.80, SI= 0.70, F= 0.71, S= 0.78</td>
<td>1.0, 0.98, N/AN/A, 0.69, 1.0N/A</td>
<td>SF-36</td>
</tr>
<tr>
<td>English, Asher 2003 (original reliability study)</td>
<td>P= 0.92, SI= 0.75, F= 0.86, MH= 0.90, S= 0.88</td>
<td>P= 0.96, SI= 0.90, F= 0.90, MH= 0.87, S= 0.85</td>
<td>SF-36</td>
</tr>
<tr>
<td>English, Asher, 2005</td>
<td>P= 0.80, SI= 0.81, F= 0.77, MH= 0.89, S= 0.88</td>
<td>Not examined</td>
<td>SF-36</td>
</tr>
<tr>
<td>Spanish, Bago 2004 Climent 2005</td>
<td>P= 0.81, SI= 0.73, F= 0.67, MH= 0.83, S= 0.78</td>
<td>P= 0.93, SI= 0.94, F= 0.83, MH= 0.94, S= 0.98</td>
<td>QLSDP (Climent)</td>
</tr>
<tr>
<td>Turkish Alanay, 2005</td>
<td>P= 0.72, SI= 0.80, F= 0.48, MH= 0.72, S= 0.83</td>
<td>P= 0.80, SI= 0.82, F= 0.76, MH= 0.78, S= 0.81</td>
<td>SF-36</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Language</th>
<th>Source</th>
<th>P</th>
<th>SI</th>
<th>F</th>
<th>MH</th>
<th>S</th>
<th>Examined</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese</td>
<td>Hashimoto, 2007</td>
<td>0.88</td>
<td>0.79</td>
<td>0.75</td>
<td>0.85</td>
<td>Not</td>
<td>SF-36</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>(Hong Kong) Chenug, 2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.87</td>
<td>SF-36</td>
<td></td>
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<tr>
<td>German</td>
<td>Niemeyer, 2009</td>
<td>0.75</td>
<td>0.84</td>
<td>0.67</td>
<td>0.88</td>
<td>0.67</td>
<td>Roland Morris</td>
<td></td>
</tr>
<tr>
<td>French Canadian</td>
<td>Beausejour, 2009</td>
<td>AIS=</td>
<td>0.88</td>
<td>NCSS=</td>
<td>0.81</td>
<td>C=</td>
<td>SF-12</td>
<td></td>
</tr>
<tr>
<td>Greek</td>
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<td>0.87</td>
<td>0.72</td>
<td>0.87</td>
<td>0.67</td>
<td>Not examined</td>
<td>Not examined</td>
</tr>
<tr>
<td>Polish</td>
<td>Glowacki, 2009</td>
<td>0.81</td>
<td>0.77</td>
<td>0.81</td>
<td>0.80</td>
<td>0.69</td>
<td>Not examined</td>
<td>Not examined</td>
</tr>
<tr>
<td>Norwegian</td>
<td>Adobor, 2010 (Paper I)</td>
<td>0.93</td>
<td>0.93</td>
<td>0.87</td>
<td>0.89</td>
<td>0.90</td>
<td>EuroQol</td>
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<td>0.78</td>
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<td></td>
<td>0.79 to 0.87</td>
<td>SF36</td>
<td></td>
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<tr>
<td>Brazilian</td>
<td>Rosanova, 2010</td>
<td>Not</td>
<td></td>
<td></td>
<td></td>
<td>Not</td>
<td>SF-36</td>
<td></td>
</tr>
<tr>
<td>Korean Lee, 2011</td>
<td>P= 0.83</td>
<td>F= 0.85</td>
<td>SI= 0.75</td>
<td>MH= 0.81</td>
<td>S= 0.61</td>
<td>Not examined</td>
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<tr>
<th>Tai Sathira-Angkura, 2012</th>
<th>P= 0.78</th>
<th>F= 0.74</th>
<th>SI= 0.80</th>
<th>MH= 0.83</th>
<th>S= 0.87</th>
<th>SF-36</th>
</tr>
</thead>
</table>

Repeatability examined only in the study by Adobor (Paper I).

5.5.2 Reliability of scoliosis screening

The sensitivity and specificity of scoliosis screening depends largely on the skills of the examiner and the magnitude of the scoliosis being sought. The use of scoliometer has been shown to increase the sensitivity and the specificity in detecting a Cobb angle of > 20°. In Paper II, using a scoliometer reading of 7°, an estimated point prevalence rate of scoliosis of 0.8%, and a scoliosis definition of > 10° in 12 year-old children, we found sensitivity of 69% and specificity of 99% in detecting AIS in the study population. A scoliometer reading of 5° has been shown to have a sensitivity of 100%, and 47% specificity for identification of scoliosis, whereas a scoliometer reading of 7° increases the specificity to 86% but decreases the sensitivity to 83%. The reliability of screening procedure in Paper II is thus satisfactory, although the sensitivity was low.

The PPV of visual inspection and the forward-bending test varies with the degree of curvature by which a “true positive” is defined, the prevalence of scoliosis in the screened population, and the skills of the examiners. In Paper II, we found the PPV to be 37%. A study found PPV of 54% for curves > 10° with a predicted prevalence of 2%, and 24% for curves > 20° with an estimated prevalence rate of 0.3%. The magnitude of PPV is thus inversely related to the degree of curvature used to define scoliosis since the prevalence of small curves is greater than large curves. In a study from Australia, the PPV was 78% for curves > 5° in a population with an estimated prevalence of 3%. A meta-analysis of the clinical effectiveness of school scoliosis screening citing 34 studies reported that the pooled PPV for curves > 10°, curves > 20°, and treatment were 28.0%, 5.6% and 2.6%, respectively.

A LH ratio > 1 indicates that a test result is associated with a disease and a LH ratio < 1 indicates that a test result is associated with the absence of a disease. It is when the positive
LH ratio is > 5 or the negative LH ratio is < 0.2 that LH ratios can be applied to the pre-test probability of a patient having a specific diagnosis. In Paper II, the LH+ ratio was calculated to be 69 and the LH- ratio was 0.3. The screening model was sensitive enough to reduce the number of false positive results. However, since the number of abnormal radiographs of Cobb angle > 10° (true scoliosis) is not known in the study population, the true PPV cannot be known.

5.5.3 Prevalence rates in screening
In Paper II, using the scoliometer and radiographic examination of those who had a positive screening, at age 12 we found a point prevalence rate of 0.55% of scoliosis > 10°; 0.40% in girls and 0.15% in boys. Point-prevalence is the prevalence based on a single examination of the target population at one point in time, which will probably underestimate the true prevalence of AIS. The prevalence of AIS has been reported to vary from 0.5% to 5% \(^{10,48-52}\). The variation is mostly due to different definitions of scoliosis being used and different ages being examined. Prevalence rates are higher (5%) when a spine deformity of 5° is being sought\(^{58}\). Using a Cobb angle of 10° for the definition of scoliosis\(^{49,55}\), prevalence rates for AIS ranges from 2% - 3% range\(^{48-50,52,56-62}\), 1.0% for curves > 20°\(^{49,51,63,64}\), and only 0.1% have curves > 40°\(^{49,65}\).

There are few reports of age-specific prevalence of idiopathic scoliosis in the literature\(^{10,71,293}\). These studies report a low prevalence in children between six to ten years, increasing to 1.37% for girls at age 11 to 12 years and 2.22% for girls aged 13 to 14 years. The point prevalence specifically in 12 year old children has not been reported in the literature. One study reported a point prevalence rate of 0.35% in the 9-11 year group, and 1.2% in the 12-14 year group\(^{10}\). The low prevalence rate in our study could be due to the large variety of the start of puberty and scoliosis, which could underestimate the true prevalence of AIS. The true prevalence of AIS is not known since false negative cases cannot be detected without an X-ray examination of the study population. In addition, only 12-year-old children were examined once, and there are inaccuracies in the screening test employed. As reported in earlier studies, we also found a higher prevalence of scoliosis in girls compared with boys\(^{52,56,70,71}\).

5.5.4 Characteristics of scoliosis detected in the absence of screening
In the absence of scoliosis screening, the majority of patients detected with scoliosis in Paper III were skeletally mature and had curves that were not suitable for brace treatment. The mean
chronological age at detection was 14 years, which is 2 years older than the ideal age148;276. Other signs of maturity were consistent with this observation: 60% had Risser sign > 3 and 78% of the girls were post menarche. A large proportion of patients also had curves > 40° at first presentation, which is beyond the international recommendation for initiation of brace treatment148;150. Findings are in agreement with two previous studies that have assessed the impact of discontinuation of scoliosis programs on detection, referral patterns and management. In a Canadian study, 32% of patients with AIS were referred too late for brace treatment226. Another study conducted in England, showed that about 70% of the patients were detected by non-health care providers, either by patients themselves, close family members, or friends, and that 56% were detected with primary curves > 40° and therefore were not suitable for brace treatment289. Contrary to previous studies, we found no differences between patient maturity and curve sizes in scoliosis detected by patient and families compared to those detected by healthcare providers.

In Paper III, 59% of all patients reported some, but not disabling back pain and only between 1-3% had back pain almost all the time. Our findings are consistent with other studies on back pain in AIS73;97;116-118. We found a significant association between back pain and gender, with girls reporting more pain compared with boys, but no association between back pain, curve size, and BMI. This is in agreement with one previous study reporting less postoperative pain in male patients with AIS372.

5.5.5 Referral rates in screening

The use of objective criteria was introduced to increase the effectiveness of screening programs. Without the use of objective criteria, referral rates have been reported to be as high as 21%, but reduced to about 2% by the use of the scoliometer274;315;333. In Paper II we found a referral rate of 1.5% using a Scoliometer reading of 7°. Generally, a referral rate of 12% has been predicted using 5° Scoliometer reading, and 3% referral rate using 7° Scoliometer reading315. A meta-analysis that included 34 studies reported a pooled referral rate to radiography of 5%271. It is an agreement that referral rates should be in the range of 2% to 3% in school screening for scoliosis274;281;315;373.

Referral rates are high in scoliosis screening because screening for scoliosis using the Scoliometer, or any surface topographic measurement devise does not reveal scoliosis per se, but detects thoracic deformity281;360. The radiographic measured thoracic Cobb angle is better correlated to the rib-index in the 14-18 years age group than in smaller curves usually found.
in the younger age group\textsuperscript{360}. Thus, it is not possible to reliably predict the Cobb angle from surface topography in the age group that is screened\textsuperscript{315,360}. This lack of association of the surface asymmetry (hump) and Cobb angle in the younger group such as in Paper II, creates a burden of false positive referrals in school screening programs\textsuperscript{360}. It has been reported that, in typical screening settings where the prevalence and positive predictive value are relatively low, for every curve > 10° detected, there are 1-5 false positives; similarly, for every curve > 20° detected, there are 3-24 false-positives\textsuperscript{265,360}. In practical terms, in order to detect 10 patients with scoliosis > 20° there would be 60 to 240 negative X-ray examinations. This number of false positive children on screening must be accepted if those with asymmetry, who might develop scoliosis should be detected. The high number of false positive children referred for x-ray examination is a concern of harm in screening.

5.5.6 Referrals of scoliosis detected without screening

The detection and referrals of scoliosis patients to specialised scoliosis clinics for evaluation is suboptimal in many countries without a screening program\textsuperscript{226,289,360}. In Paper III, similar findings were reported as discussed above. In order to ensure uniformity and quality of care for scoliosis patients, it is important that persons involved in child health care like physical therapists, community health nurses, chiropractors, sports instructors, primary physicians and orthopaedic surgeons be better informed about guidelines for scoliosis detection, and prompt referrals to specialised scoliosis clinics without unnecessary delay\textsuperscript{226}. In Paper III, 2/3 of all patients were first observed by orthopedic surgeons at local hospitals on average 16 months before being referred to the specialist clinic for scoliosis. One third of patients were referred directly by primary physicians, physical therapists or community health nurses to the specialist clinic. The mean waiting time from referral to specialist evaluation was only 4 months, which is at an acceptable level for a specialist’s evaluation of pediatric cases.

In Norway, the general guideline for primary physicians is to refer suspect cases of AIS to local orthopaedic surgeons for diagnosis or refer directly to specialist evaluation of high risk patients for progression. Recommended guidelines for referrals to orthopaedic surgeons in general include ATR \geq 7°, Cobb angle \geq 20°, and a progression of \geq 5° Cobb angle\textsuperscript{3,316}. Orthopaedic surgeons at local clinics are authorized to diagnose and observe AIS patients for progression and to refer without unnecessary delay progressive curves > 20° in immature patients to specialist clinics for evaluation. Results in Paper III suggest that this strategy caused a delay in the referrals to specialist evaluation either due to the non-awareness of
existing guidelines, or failure of education on these guidelines. In the absence of or as an alternative to school screening, direct referral to specialist clinics should be considered as a more appropriate strategy for young patients with scoliosis. However, without objective screening test, proper training and clear guidelines for referrals, there is a risk of inappropriate referrals to the specialized care setting if community health nurses, physical therapists, chiropractors, sports instructors, refer patients directly to scoliosis specialist evaluation without first referring to local orthopaedic surgeons. The magnitude of the eventual inappropriate referrals is not known. Local orthopaedic surgeons still play important roles as gatekeepers while offering reassurances to the families and proper follow-up for mild cases. The emphasis is to better inform all persons involved with child health care about the guidelines for scoliosis detection. This includes the examination of asymmetries of the back in the routine examination of the child\textsuperscript{226}, and in cases of confirmed scoliosis in immature patients, refer to specialized evaluation without unnecessary delay.

5.5.7 Health economic evaluation of scoliosis screening

Scoliosis screening programs are often criticized for high costs due to over referrals and lack of efficacy of the programs. The effectiveness of a screening program thus depends on the costs involved and the number of cases detected early that results in bracing and less surgery compared to a non-screening setting. Results of Paper III and other studies have shown that discontinuation of screening has led to late detection and high rates of surgery\textsuperscript{226,289,374}. In Paper IV, we used model based analysis to compare costs of screening and treatment in screening and non-screening settings assuming equivalent long term outcomes of brace and surgical treatment. We found that screening may be cost saving when it leads to high bracing and low surgical rates. Results also suggest that the cost saving of screening is larger when only girls are screened. Selective screening of girls is most cost saving because they constitute about 90% of those treated for scoliosis. The model applied in the present study show positive incremental costs in non-screening scenarios with high rates of surgery and lower rates of bracing suggesting that screening is cost saving in these scenarios. Screening only increases costs compared to non-screening when both treatment rates and surgical rates are very low in comparative non-screening scenarios. In the extreme non-screening scenarios where treatment rates are approaching those of screening, screening both boys and girls was not cost saving. Likewise in the extreme non-screening scenario where treatment rates were very low approaching 60% of those treated in screening, non-screening becomes cost saving. However,
these scenarios are the least likely to occur. In the non-screening scenarios where treatment levels are 90-100% of those in screening, patients are probably younger at detection, and according to guidelines and the results of the recent RCT study on bracing, these patients are likely to be recommended bracing. This implies that the ratio of bracing/surgery is likely to be >1 and bracing will be the dominating treatment option. On the contrary, when treatment levels in non-screening scenarios are in the 60% to 70% range of that of screening, patients are likely to be older and curves too large and not suitable for bracing and surgery is most likely to be the dominating treatment option (ratio of brace to surgery likely to be < 1). These findings are in agreement with one previous study that found screening to be cost effective. The researchers recommended screening only for high-risk groups such as girls. They argued that this will reduce over-referrals and over-treatment. The most recent systemic review on cost analysis of screening on the other hand could not conclude from the seven studies in the review whether screening was cost effective or not. Both reviews however did not adhere to the recommended health economic evaluation principles in conducting and reporting of the studies. Other publications from various countries have reported studies with information related to costs and cost effectiveness without following the recommended guidelines on conducting and reporting health economic evaluations. The reported costs vary widely in these studies depending on whether all cost items were included or not. In Paper IV, we based our evaluations on total costs and performed a health economic evaluation of scoliosis screening. Thus, to date prior to our study (Paper IV) has no researchers performed partial or full economic evaluation of cost effectiveness of scoliosis screening following recommended health economic evaluation principles.

Results of our study indicate that the cost of scoliosis screening was low. Combining screening with a vaccination program and only referring children with significant curves for specialist evaluation most likely reduced costs. Costs were only increased compared to non-screening scenarios with unrealistically low treatment rates, high bracing, and low surgical rates.
6. Conclusions

From the specific aims of the present dissertation, the following conclusions are drawn:

I. SRS-22 is a valid tool for evaluation of Norwegian patients with AIS. The Norwegian version of the SRS-22 has satisfactory reliability, repeatability, and concurrent validity with the EuroQol.

II. The point prevalence of AIS in school children aged 12 years in Norway was slightly lower compared with studies from other countries. The screening model applied had acceptable sensitivity and specificity and was neither time consuming nor expensive compared to similar screening programs in Europe. A single screening at 12 years of age was not effective in detecting scoliosis with indication for bracing.

III. In the absence of screening in Norway, most patients were detected late by close family members and friends and were not suitable for brace treatment. There was a delay of about 2 years from detection to specialist evaluation. Rates of surgery were increased and bracing reduced in a period without screening compared to a period of screening.

IV. Screening is not likely to increase costs unless both treatment and surgical rates are very low in settings when screening is not performed. Screening may save costs when girls are selectively screened, and when it leads to high rates of bracing and lower rates of surgery.
7. Implications of the findings in the study

The translated, validated and the adopted Norwegian version of the SRS-22 questionnaire has been used in Norwegian studies¹²⁵-¹²⁷,¹⁵³ and is used in the Norwegian Quality Registry for Surgery of Spinal Deformities.

In the absence of scoliosis screening in Norway today, there is a delayed detection of scoliosis, and inappropriate and non-uniform referral practices of child health-care providers cause a delay in specialists’ evaluation. To ensure uniformity and quality of care for scoliosis patients, the study suggests that persons involved in child health should be better informed about guidelines for scoliosis detection. Immature patients with radiographically confirmed scoliosis should be referred to specialized clinics without unnecessary delay.

The establishment of a screening procedure and the analysis of the cost of scoliosis screening and treatment modalities provide valuable information to health authorities and policy makers to consider the reintroduction of screening in Norway. The modeling used in the economic evaluation study (Paper IV) could be employed worldwide with local cost estimate variations. The results provide the economic evidence for health policy makers and healthcare providers to consider reintroduction of scoliosis screening worldwide.
8. Recommendations for future research

The responsiveness to change of SRS-22 with brace and surgical treatments should be evaluated in future studies. As the quality of the EQ-5D as a utility index for cost-benefit analyses is questioned, other measures should be evaluated. We suggest a full health economic evaluation comparing costs and outcomes as cost-benefit evaluation or cost utility evaluation and parents’ willingness-to-pay for screening and gain in QALY to be assessed.
9. Reference List


(39) Qiu XS, Tang NL, Yeung HY, Qiu Y, Qin L, Lee KM et al. The role of melatonin receptor 1B gene (MTNR1B) in adolescent idiopathic scoliosis—a genetic association study. Stud Health Technol Inform 2006; 123:3-8.


(283) Andersen MO. 2006. Personal Communication


Appendix I

Norwegian Version of SRS-22 Questionnaire (Paper I)
Alle svar vil bli behandlet konfidensielt

Del 1: Besvares av alle pasienter.

1. Hvilket av de følgende utsagn passer best til din smerte opplevelse de siste 6 månedene?
   - Ingen
   - Mild
   - Moderat
   - Moderat til sterk
   - Sterk

2. Hvilket av de følgende utsagnene beskriver din smerte opplevelse den siste måneden?
   - Ingen
   - Svak
   - Moderat
   - Moderat til sterk
   - Sterk

3. Har du vært nervøs i løpet av de 6 siste månedene?
   - Aldri
   - Litt av tiden
   - Noe av tiden
   - Mesteparten av tiden
   - Hele tiden

4. Hva ville du synes om å måtte tilbringe resten av livet med ryggen slik den er nå?
   - Svært tilfreds
   - Ganske tilfreds
   - Verken tilfreds eller utilfreds
   - Litt utilfreds
   - Svært utilfreds

5. Hva er ditt nåværende aktivitetsnivå?
Sengeliggende/rullestol
Hovedsaklig ikke i aktivitet
Lett arbeid, slik som daglige gjøremål i hjemmet
Moderat manuelt arbeid og moderate sportsaktiviteter, som gå-turer og sykling
Full aktivitet uten begrensinger

6. Hvordan tar du deg ut i klær?

- Svært godt
- Godt
- Akseptabelt
- Dårlig
- Svært dårlig

7. Har du følt deg så nedfor de 6 siste månedene at ingenting kan muntre deg opp?

- Veldig ofte
- Ofte
- Noen ganger
- Sjelden
- Aldri

8. Har du vondt i ryggen i hvile?

- Svært ofte
- Ofte
- Noen ganger
- Sjelden
- Aldri

9. Hva er ditt nåværende aktivitetsnivå, jobb eller skole?

- 100%
- 75%
- 50%
10. Hvilket av disse utsagnene beskriver best utseende av overkoppen din, definert som kroppen med unntak av hodet, bena og armene?

☐ Svært godt
☐ Godt
☐ Akseptabelt
☐ Dårlig
☐ Svært dårlig

11. Hvilke medisiner tar du for tiden mot ryggsmertene? (marker alle relevante)

☐ Jeg tar ingen medisiner
☐ Reseptfrie medisiner ukentlig eller sjeldnere (Feks Ibux eller Paracet)
☐ Reseptfrie medisiner daglig
☐ Sterke medisiner ukentlig eller sjeldnere (Feks Paralgin Forte / Pinex Forte / Nobligan)
☐ Sterke medisiner daglig
☐ Andre (angi nedenfor)

Medisiner:

______________________________

Hvor ofte:(Brukt ukentlig/sjeldent/daglig)

______________________________

12. Begrenser ryggen deg med hensyn til aktiviteter og gjøremål hjemme?

☐ Aldri
☐ Sjelden
☐ Av og til
☐ Ofte
☐ Veldig ofte

13. Har du følt deg rolig og harmonisk de siste 6 månedene?
Hele tiden
Nesten hele tiden
Noe av tiden
Litt av tiden
Ingen følelse av ro og harmoni

14. Føler du at helsetilstanden din innvirker negativt på ditt forhold til andre mennesker?
   □ Nei
   □ Ubetydelig
   □ Lett grad
   □ Moderat grad
   □ Betydelig grad

15. Har du eller din familie økonomiske problemer som følge av din rygg?
   □ Betydelig
   □ I moderat grad
   □ I lett grad
   □ Ubetydelig
   □ Ingen

16. Har du følt deg nedstemt og deprimert i løpet av de 6 siste månedene?
   □ Aldri
   □ Sjeldent
   □ Noen ganger
   □ Ofte
   □ Veldig ofte

17. Hvor mange dager har du vært borte fra jobb eller skole på grunn av ryggsmarter de siste 3 månedene?
   □ 0
   □ 1
   □ 2
18. Går du ut like mye som dine venner?
   - Mye mer
   - Mer
   - Like mye
   - Mindre
   - Mye mindre

19. Føler du deg attraktiv med ryggen slik den er?
   - Ja, svært
   - Ja, litt
   - Verken attraktiv eller ikke
   - Nei, ikke særlig
   - Nei, overhodet ikke

20. På en skala fra 1 til 9, hvor 1 er svært dårlig og 9 er svært godt, hvordan vil du beskrive ditt selvbilde?
   - 9
   - 8
   - 7
   - 6
   - 5
   - 4
   - 3
   - 2
   - 1

Del 2: Besvares kun dersom du har fått behandling.

21. Er du fornøyd med resultatet av behandlingen?
   - Svært godt fornøyd
☐ Ganske fornøyd
☐ Verken fornøyd eller misfornøyd
☐ Litt misfornøyd
☐ Veldig misfornøyd

22. Ville du ønsket samme behandling på nytt dersom du hadde de samme plagene?
☐ Definitivt ja
☐ Sannsynligvis ja
☐ Usikker
☐ Sannsynligvis ikke
☐ Definitivt ikke
Informasjonsbrev om SRS-22 spørsmål skjema
Kjære…………………………………………….

Vi vurderer din ryggskjevhet ved hjelp av røntgenbilder og vi spør deg om hvordan ryggskjevheten påvirker din helsetilstand. Det finnes flere spørreskjemaer som er spesielt utviklet for pasienter med skoliose. Vi har fått oversatt det mest brukte til norsk og vi ønsker å teste ut om det egner seg for norske pasienter. Vi har i tillegg tatt med noen spørsmål som brukes for ulike andre pasientgrupper. Vi vil be deg om å besvare vedlagte spørsmål så godt du kan.

Etter 14 dager får du tilsendt et nytt skjema som vi ber deg besvare.

Du kan når som helst trekke deg fra undersøkelsen.

Oslo,………………..

Vennlig hilsen

Raphael Adobor            Silje Rimeslåtten            Jens Ivar Brox
Prosjektlege               Prosjektsykepleier          Seksjonsoverlege
Appendix III

Information and Consent form/ Informert samtykke skjema (Paper II)
Informert samtykke

Til foreldre og foresatte

Rikshospitalet er i gang med et forsknings-prosjekt i Helse-Sør. ”Vil screening for skoliose ved 12-års alder i Helse Sør bidra til å senke alder for førstegangskonsultasjon ved ortopedisk poliklinikk?” Hvor vi vil undersøke om screening (i dette tilfelle; visuell undersøkelse av ryggen) i 12-års alder vil gjøre at skoliose (skjevhet i ryggen) oppdages på et tidligere tidspunkt enn pr dags dato.

Tidligere ble skoliose oppdaget i forbindelse med screening av alle skolebarn. I dag er skolehelsetjenesten i stor del falt bort på dette området og skoliose oppdages mer eller mindre tilfeldig og ofte for sent.


Det mistanke om at _____________________________ kan være skjev i ryggen. Han/hun vil derfor få tilsendt time til røntgen for å avkrefte /bekrefte dette. Han/hun vil også få oppfølging ved Rikshospitalet hvis det er behov for dette.


Databehandleransvarlig er Rikshospitalet - Radiumhospitalet HF. Opplysningene vil ikke bli utlevert til andre. Prosjektet er godkjent av personverneombudet ved RH-RR HF.

Ansvarlige for prosjektet:

   Jens Ivar Brox, Seksjonsoverlege, Prosjektveileder
   Raphael Adobor, Spesialist i ortopedi, Prosjektleder
   Silje Rimeslåtten, spesial sykepleier, Prosjektmedarbeider
   Ryggseksjonen, ØPO-klinikken, Rikshospitalet-Radiumhospitalet HF

Kontakt informasjon:

   Silje Rimeslåtten, Ortopedisk avdeling
Samtykke

Jeg har lest og forstått informasjonen, og gir mitt/vårt samtykke til å delta i undersøkelsen.

__________________________              ________________               ____________

Underskrift (foreldre/foresatte)              Sted                              Dato
Informasjonsbrev til foreldre etter screening
I forbindelse med skole screening for skoliose, var det misanke om ryggsjevhet hos barnet ditt.

Røntgen fotografering viser
- ingen ryggsjevhet
- liten grad av ryggsjevhet
- moderat grad av ryggsjevhet
- storstør grad av ryggsjevhet.

Vurdert etter behandlingsopplegg for ryggsjevhet ved ortopedisk avdeling Rikshospitalet:
- Trenger barnet ditt ingen behandling eller oppfølgjing ved ortopedisk avd, Rikshospitalet
- Trenger barnet ikke behandling nå, men vil få oppfølgjing ved vår avdeling.
- Barnet få derfor time for poliklinisk undersøkelse under 110ke om ………… uker.

Mvh
Raphael Adobor
Prosjektlege
Patient questionnaire at first consultation/ Registreringsskjema for 1.gangsvurdering av skoliose (Paper III)
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<td><strong>SKULDERASSYMETRI:</strong></td>
<td><strong>Balanse:</strong></td>
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<td>Akillessenereflaks</td>
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<td><strong>HØYRE/VENSTREKONVEKS SKOLIOSE</strong></td>
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<td><strong>VENSTRE</strong></td>
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<td><strong>COBB 2:</strong></td>
<td>Fylles kun inn ved dobbeltkurve</td>
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<tr>
<td><strong>COBB ØVRE KOMPENSATORISKE KURVE:</strong></td>
<td><strong>COBB NEDRE KOMPENSATORISKE KURVE:</strong></td>
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<td><strong>SPONDYLOLISTESE:</strong></td>
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Registreringskjema for 1. gangsvurdering av skoliose.


På forhånd takk.

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<th>Aldri</th>
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KING-MOE Klassifikasjon. Vennligst sett et kryss ved aktuelle kurve.

(Fylles ut av lege)
Appendix VI

The mathematical model (Paper IV)
A.1: Introduction

In this supplementary data, we show the core equation on which the simulation model was based. We begun by presenting the equations for estimating the cost of the different interventions: screening, diagnosis of scoliosis, confirming scoliosis > 20º, brace treatment and surgery. Then we estimated the fraction of children receiving the each category of interventions in the various scenarios. In the end we merged the estimated costs and the estimated fractions to estimate the cost per child for each category of intervention and for the different scenarios.

The methodology used in the cost-minimizing analysis and discounting are presented in the main text of the manuscript and based on general literature on health economic evaluation. Methods for performing decision models probabilistic are based on Briggs et al. The simulation model was built in Microsoft Excel. For the probabilistic sensitivity analysis we used the software @risk which is a part of the Decision Tools Suite software. The software @risk works is an extension to Excel.

A2: Estimation of cost of screening, brace treatment and surgery – all scenarios

Estimating the cost of the school screening:
\[ C_s = (u_1 \cdot u_{c1}) + m + s \]

- \( u_1 \) = Number of minutes (units) used per child per examiner (se row 1 in table 4).
- \( u_{c1} \) = Cost per minute (unit cost) used per examiner (se row 1 in table 4).
- \( m \) = Cost of materials and supplies.
- \( s \) = Cost of scoliometer.

Estimating the cost of diagnosis scoliosis:
\[ C_{\text{con}} = t_{\text{con}} + \text{rad}_{\text{con}} \]

- \( t_{\text{con}} \) = Cost of transportation to/from X-ray exam (se row 4 in table 4).
- \( \text{rad}_{\text{con}} \) = Cost of radiographs (se row 5 in table 4).

Estimating the cost of the confirming scoliosis > 20º:
\[ C_{\text{con}>20} = t_{\text{con}>20} + q_{\text{con}>20} + \text{rad}_{\text{con}>20} \]

- \( t_{\text{con}>20} \) = Transport to/from specialist evaluation (se row 6 in table 4).
- \( q_{\text{con}>20} \) = Specialist evaluation (se row 7 in table 4).
- \( \text{rad}_{\text{con}>20} \) = Radiographs (se row 8 in table 4).

Estimating the cost of brace treatment:
\[ C_b = \sum (u_j \cdot u_{cj}) \]

Where \( j = 9 \) to \( 16 \) in table 4.

Estimating the cost of surgery:

\[ C_{su} = im + t + \sum (hi \cdot hei) + \sum (u_j \cdot u_{cj}) \]

\( im \) = Utilities/implants cost per operation

\( t \) = Cost for transportation home after surgery.

\( hi \) = Hour used of health personal category \( i \).

\( hei \) = Cost pr hour pr person of health personal in category \( i \).

\( u_j \) = Number of units used of category \( j \).

\( u_{cj} \) = Cost pr unit of category \( j \).

Where \( i = 18 \) to \( 21 \) in table 4, and \( j = 22 \) to \( 30 \) in table 4.

For each child receiving surgery, 15% were assumed to be re-operated.

A3: Estimating the fraction of children receiving each category of interventions

A3.1 The screened group

The fraction of the screened children receiving the different category of interventions:

\[ F_{scj} = \frac{TrHKj}{ChHK} \]

\( F_{scj} \) = the fraction of children in the screening group receiving intervention category \( j \).

\( TrHKj \) = the number of children in the Hong Kong study receiving intervention category \( j \).

\( ChHK \) = the number of children participating in the Hong Kong study.

Here, \( j = 31 \) to \( 34 \), were 31 means diagnosis scoliosis, 32 means confirming scoliosis > 20º, 33 means brace treatment and 34 means surgery.

A3.2 The non-screening group

A3.2.1 Non-screening scenario Norway

The fraction of children receiving surgery or brace treatment:

\[ F_{nscNj} = \frac{TrNj}{ChN} \]

\( F_{nscNj} \) = the fraction of children receiving intervention category \( j \).

\( TrNj \) = the number of children 2012 in the Norway receiving intervention category \( j \).
StN = the number of children in the age cohort in year 2012.
Here, j = 33 and 34, were 33 means brace treatment and 34 means surgery.

The fraction of children confirmed for scoliosis or scoliosis > 20º:
\[ \text{FnscNj} = \left( \frac{\text{TrHKj} / \text{ChHK} \cdot \text{ChN}}{\text{ChN}} \right) \cdot \text{Fr-conf} \]

Fr-conf = the fraction of the screened children confirmed for scoliosis or scoliosis > 20º, who also would be confirmed for scoliosis or scoliosis > 20º if the same group was not screened.
Here, j = 31 and 32, were 31 means confirmed for scoliosis and 32 means confirmed for scoliosis > 20º.

A3.2.2: Non-screening scenario 70%, 80% and 90%
We illustrate by using the 80% non-screening scenario. The same type of equations was used for the 70% and 90% scenarios.

The fraction of children in a year cohort receiving surgery or brace treatment for the 80% non-screening scenarios:
\[ \text{Fnsc80j} = \frac{\text{Tr80j}}{\text{ChN}} \]

Fnsc80j = the fraction of children receiving category j treatment for the 80% non-screening scenario.
Tr80j = the number of children receiving category j of treatment in the 80% non-screening scenario.
Here, j = 33 and 34, were 33 means brace treatment and 34 means surgery.

In the 80% non-screening scenario, number receiving brace treatment and surgery, respectively:
\[ \text{Tr8033} = ((\text{TrN33} / (\text{TrN33} + \text{TrN34})) \cdot \text{TrNifHK}) \cdot 0.8 \]
\[ \text{Tr8034} = ((\text{TrN34} / (\text{TrN33} + \text{TrN34})) \cdot \text{TrNifHK}) \cdot 0.8 \]
Tr8033 = the number receiving brace treatment for the 80% non-screening scenario
Tr8034 = the number receiving surgery for the 80% non-screening scenario
TrNifHK = Total number treated with brace or surgery

\[ \text{TrNifHK} = \sum ((\text{TrHKj} / \text{ChHK}) \cdot \text{ChN}) \]
Here, j = 33 and 34, were 33 means brace treatment and 34 means surgery.

A4: Estimating the cost pr child

A4.1: The screened group

Here we estimate the cost pr child in a cohort (here defined as the selected one year cohort) for the different interventions.

\[
\begin{align*}
C_{\text{ChSsc}} &= 1 \times Cs \\
C_{\text{ChScon}} &= F_{\text{sc31}} \times C_{\text{con}} \\
C_{\text{ChScon>20}} &= F_{\text{sc32}} \times C_{\text{con>20}} \\
C_{\text{ChSb}} &= F_{\text{sc33}} \times C_{b} \\
C_{\text{ChSsu}} &= F_{\text{sc34}} \times C_{su}
\end{align*}
\]

\(C_{\text{ChSsc}}\) = Cost of school screening pr child screened.
\(C_{\text{ChScon}}\) = Cost of confirming scoliosis pr child screened.
\(C_{\text{ChScon>20}}\) = Cost of confirming scoliosis > 20\(^\circ\) pr child screened.
\(C_{\text{ChSb}}\) = Cost of bracing pr child screened.
\(C_{\text{ChSsu}}\) = Cost of surgery pr child screened.

A4.2: The non-screening group

Here we use the 80% scenario as an example.

\[
\begin{align*}
C_{\text{ChN-Scon}} &= F_{\text{nc31}} \times C_{\text{con}} \\
C_{\text{ChN-Scon>20}} &= F_{\text{nc32}} \times C_{\text{con>20}} \\
C_{\text{ChN-Sb}} &= F_{\text{nc8033}} \times C_{b} \\
C_{\text{ChN-Ssu}} &= F_{\text{nc8034}} \times C_{su}
\end{align*}
\]

\(C_{\text{ChN-Scon}}\) = Cost of confirming scoliosis pr child not screened.
\(C_{\text{ChN-Scon>20}}\) = Cost of confirming scoliosis > 20\(^\circ\) pr child not screened.
\(C_{\text{ChN-Sb}}\) = Cost of bracing pr child not screened.
\(C_{\text{ChN-Ssu}}\) = Cost of surgery pr child screened.

\(F_{\text{nc31}}\) and \(F_{\text{nc32}}\) were, as a simplification used in the model, the same as we used for the Norwegian non-screening scenario.
These cost per child per intervention was dispersed over a 6 year period as described in the main text of the manuscript. The incremental cost was estimated by subtracting the total discounted cost per non-screened child from the total discounted cost per screened child.
School screening and point prevalence of adolescent idiopathic scoliosis in 4000 Norwegian children aged 12 years

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Abstract

Background: School screening for adolescent idiopathic scoliosis (AIS) is discussed. The aim of the present study was to describe the point prevalence of AIS and to evaluate the effectiveness of school screening in 12-year-old children.

Methods: Community nurses and physical therapists in the Southern Health region of Norway including about 12000 school children aged 12 years were invited to participate. All participating community nurses and physical therapists fulfilled an educational course to improve their knowledge about AIS and learn the screening procedure including the Adam Forward Bending Test and measurement of gibbus using a scoliometer.

Results: Sub-regions including 4000 school children participated. The prevalence of idiopathic scoliosis defined as a positive Adam Forward Bending Test, gibbus > 7° and primary major curve on radiographs > 10°, was 0.55%. Five children (0.13%) had a major curve > 20°. Bracing was not indicated in any child; all children were post menarche; four had Risser sign of 4, and one with Risser 1 did not have curve progression > 5° at later follow-up. In one of these 5 children however, the major curve progressed to 45° within 7 months after screening and the girl was operated.

Conclusion: The point prevalence of AIS in 12-year-old children is in agreement or slightly lower than previous studies. The screening model employed demonstrates acceptable sensitivity and specificity and low referral rates. Screening at the age of 12 years only was not effective for detecting patients with indication for brace treatment.

Background

There is a wide variation in the reported prevalence of adolescent idiopathic scoliosis (AIS). One study suggests that about 2.0% of adolescent children are found with screening to have scoliosis with a Cobb angle of > 10°, about 0.5% > 20°, and only 0.1% > 40°[1]. A review of twenty peer-reviewed papers shows a wide range variation of AIS prevalence in different countries with higher prevalence rates in the northern geographic latitudes and lower prevalence rates as the latitude is approaching the equator. (Finland 12%, Singapore 0.9%). [2]. The prevalence of scoliosis > 20° in Scandinavia is reported to be 1.1% for girls and 0.1% for boys in another study [3]. Point prevalence is a measure of the proportion of people in a population who has a disease or condition at a particular time or at a particular age, by example one-month prevalence of back pain or prevalence of scoliosis at school screening in 12 year-old children. Point prevalence rates of AIS have been shown to increase with age; from 0.1% in the age-group of six to eight years, to 0.3% in the age-group of nine to eleven years, and 1.2% in the age-group of twelve to fourteen years [4].

Screening for scoliosis has been practiced worldwide for many years and has provided valuable knowledge about prevalence, aetiology and the natural history of idiopathic scoliosis. School screening for scoliosis beyond its scope of early identification of AIS has contributed to the field of research for aetiology of idiopathic scoliosis. Numerous factors that are implicated in the aetiology of AIS including biological factors such as menarche, lateralisation of the brain, handedness, the thoracic cage, the intervertebral disc, and the role of melatonin have been
studied in children referred from school screening programmes [5]. Early diagnosis allows for bracing that is reported to be effective by numerous outcome studies [6-8], although the evidence is weak according to a recent Cochrane report [9]. In 1995, The United States Preventive Services Task Force advised against scoliosis screening [10,11]. Later publications suggest that they might not fully recognise data answering some of their objectives at the time of their recommendation [6]. In recent years, The Scoliosis Research Society and the American Academy of Orthopaedic Surgeons, the Paediatric Orthopaedic Society of North America, and the American Academy of Paediatrics have endorsed scoliosis screening while The Canadian Task Force on the Periodic Health Examination, the British Orthopaedic Association, and the British Scoliosis Society do not recommend screening [12,13].

The effectiveness of scoliosis screening is therefore still under debate. Objections to scoliosis screening are largely based on the low prevalence rate of clinically significant scoliosis, the inverse relationship of sensitivity and specificity in the screening process, high rates of false-positive cases, high inter-observer variations and the costs involved mainly because of over-referrals [14,15]. The challenge in scoliosis screening programmes therefore is to decrease the sensitivity to an acceptable rate of false positive results and to increase specificity in order to reduce over-referrals thereby reducing costs for the patients and society.

Based on the recommendations from 1995, routine scoliosis school screening programmes have been discontinued in many Western countries including Norway in the last 10-15 years. In Scandinavian countries, Sweden has conducted school screening for many years and has an ongoing scoliosis screening programme [7]. In Denmark, there have been attempts to perform school screening, but no specific scoliosis screening programmes have been successfully implemented (personal communication with Andersen, M.O.)

The effects of the discontinuation of scoliosis school screening programmes in Norway have not been thoroughly evaluated. However, a preliminary review of the referral records at the Oslo University Hospital suggests that fewer children with AIS are being detected early enough to benefit from brace treatment (unpublished data).

In Canada, school scoliosis screening has been discontinued since 1979 when the Canadian Task Force on the Periodic Health Examination did not recommend screening. The impact of this discontinuation has recently been examined. This report shows that, in subjects with confirmed AIS, 32% were classified as too late referrals with regards to brace treatment. The discontinuation of the school screening programmes was therefore followed by a suboptimal appropriateness of referrals for bracing [16].

The optimal age for scoliosis screening is still under debate. School screening has generally been performed between the ages of 10 to 14 years in conjunction with a school health examination [10,17]. The Scoliosis Research Society has recommended annual screening of all children aged 10-14 years. The American Academy of Orthopaedic Surgeons has recommended screening girls at 11 and 13 years and screening boys at age 13 or 14 years. The American Academy of Paediatrics has recommended annual scoliosis screening with the forward bending test at routine health supervision visits.

The combination of the Adam forward bending test and the scoliometer measurement of the angle of trunk rotation (ATR) has been shown to be the simplest, quickest, most reliable, and least expensive objective measure of trunk deformity [18]. It has been recommended that an inclination above 7° or ATR > 1 cm is a positive screening sign and should be followed-up with an X-ray for further evaluation of the curve [19].

The present study was designed to evaluate the point prevalence, and the effectiveness of school screening of AIS in a Norwegian population of 12000 children aged 12 years.

Methods
Study design
Screening of idiopathic scoliosis was performed in conjunction with the ordinary school health examination and vaccine programme in 12 year-old children in the Health Region South of Norway which has a population of about 12000 children at this age.

Sample selection
There is a similar distribution of girls and boys in the population at target and in the population screened. The sex distribution in the group with positive screening and in those with scoliosis at x-ray examination, are reported in the results section.

Preparation for school screening
Public health/community nurses and physical therapists in the study region were engaged as screeners. They were invited to a one-day intensive course at the Oslo University Hospital, Rikshospitalet to improve their knowledge about AIS. Additional courses were arranged at the various county centres for those who were not able to attend. Participants were taught about scoliosis and the screening procedure of Adam Forward Bending Test and measurement of the angle of inclination using the scoliometer. In addition, a scoliosis screening manual was provided to all participants and follow-up teachings were provided as needed.
Screening technique
The screening procedure combined the standing visual inspection of the back, the Adam Forward Bending Test and the scoliometer (OSI-scoliometer Orthopaedic Systems Inc, Hayward, California, USA) measurement of angle of trunk rotation (ATR). Seven degrees of ATR was chosen as cut-off point for referral to radiography [20-22].

Referral criteria and treatment
Radiographic results from screening at local hospitals were mailed to the Department of Orthopaedics at Oslo University Hospital-Rikshospitalet. A Cobb angle > 10° on standing radiographs were classified as AIS according to the criteria proposed by the Scoliosis Research Society [23].

Scoliosis between 10° to 20° were referred to a new radiographic exposure within 6 months and Cobb angles > 20° were referred for physical examination and new standing X-rays including crista crest exposure for Risser sign grading.

Statistical analysis
We estimated that the population of boys and girls were equal in the examined population and calculated the point prevalence of AIS. We also estimated the point prevalence of scoliosis > 10° from the reported prevalence in two previous epidemiological studies [24]. Based on these studies, we used 0.8% as the point prevalence rate of scoliosis in the study population to estimate the sensitivity and specificity of the screening procedure used.

Sensitivity is a measure of a test's ability to identify positive results. It is calculated from the ratio of true positives to combined true positive and false negatives. Specificity measures a test's ability to identify negative results. Specificity is calculated from the ratio of true negatives to combined true negatives and false positives.

Additional parameters determining reliability of the screening procedure such as positive predictive value, (PPV), negative predictive values, (NPV) and likelihood ratios (LR+, and LR-) were also calculated [25].

Positive predictive value (PPV) is the proportion of patients with positive test results who are correctly diagnosed, and negative predictive value (NPV) is the proportion of patients with negative test results who are correctly diagnosed.

Likelihood ratios are normally used for assessing the value of performing a diagnostic test. They use the sensitivity and specificity of the test to determine whether a test result usefully changes the probability that a condition exists. Two versions of the likelihood ratio exist, one for positive and one for negative results.

Results
Of the 12000 twelve year-old children living in different regions of Health Region South, we were able to screen only sub-regions including 4000 twelve year old school children. Since screening has been discontinued in Norway, the Directory of Healthy in Norway was not willing to support the programme with a recommendation. Many community nurses and physical therapists were not willing to conduct a task that was not recommended and participation in the programme was therefore lower than expected.

Sixty pupils were found positive on both standing, forward bending test and scoliometer measurements > 7°. There were 39 (65%) girls and 21 (35%) boys. Twenty-two were confirmed with scoliosis on standing radiographs, 16 (73%) girls and 6 (27%) boys. Thirty-eight of which 23 (60%) girls and 15 (40%) boys had normal spine curvatures on X-ray examination (false positive). These were followed up until maturity and none progressed to > 25°. The referral rate to radiography from screening was 1.5% and point prevalence of confirmed scoliosis was 0.55%.

Five girls with clinical and radiographic significant scoliosis (> 20°) were discovered with screening, (Table 1). All were post menarche. Four had Risser sign of 4 and were more than 1 year post menarche. Brace treatment was therefore not indicated in any of them. One girl had Risser 1, but was more than one year post menarche; the major curve did not progress > 5° within 6 months, and brace treatment was therefore not indicated. Scoliosis in four of the girls did not progress > 5° during long-term follow-up. In one of them the scoliosis progressed from 37° to 45° within 7 months after screening and she was operated. The point prevalence of curves > 20° was 0.13% in girls and 0.0% in boys.

Eleven girls and 6 boys had curves between 10° and 20° and they were observed for further progression until maturity. None of them progressed to > 25°.

With an estimated point prevalence rate of scoliosis of 0.8% in 12 year-old children, the sensitivity was calculated to be 69%, the specificity was 99%, positive predictive value was 37%, and the negative predictive value was 99%. The positive likelihood ratio (LR+) was 46 and the negative likelihood ratio (LR-) was 0.55 (Table 2).

Discussion
There is a wide variation in the reported prevalence of AIS. Most studies have reported that about 2.0% of adolescent children are found on screening to have scoliosis with a Cobb angle > 10°[1]. Point-prevalence is the prevalence based on a single examination of everyone in the population at one point in time which will probably underestimate the true prevalence of AIS.

The point prevalence applied in the present study was based on examination in 12 year-old children and because there is a large variety of the start of puberty and scoliosis, the study could underestimate the true prevalence of AIS.
The present study has shown a point prevalence of 0.55% for scoliosis. The observed point prevalence rate in 12-year-old children in the current study corresponds well with previous studies reporting the age-specific prevalence for 9-11 and 12-14 years. The prevalence rates in previous studies however are not easily comparable because they do not exclusively refer to AIS and different age groups are usually included. The prevalence rate could be different if various Cobb angles of > 5°, 10° or 20° were used and if non-structural scoliosis were included. The point prevalence of AIS in 12-year-old children in the present study was 0.40% in girls and 0.15% in boys which reflects the later onset of puberty in boys.

Optimal age of screening
The optimal age for scoliosis screening is still under debate. School screening has generally been performed between the ages of 10 to 14 years in conjunction with a school health examination. Ideally screening should be performed in girls before the onset of menses and 1-2 years later for boys. The challenge in screening is to detect clinically significant curves in immature children which have the potential of progression.

The girls with a significant scoliosis curve of > 20° in the present study were all judged to be too mature for brace treatment. This suggests that screening should have been performed one year earlier. The prevalence rate of 0.55% in the present study as compared with 1.1% in girls in previous studies most likely reflects the wide range of onset of puberty [3], and the fact that only 12-year-old children were examined. Age at menarche is considered a reliable prognostic factor for AIS and varies in different geographic latitudes. AIS prevalence has also been reported to be different in various latitudes, with higher values in northern countries. The point prevalence of AIS in 12 year-children in the present study does not compare well with the reported 12% prevalence of AIS in Finland [2], but rather with the 1.1% rate found in another report about of AIS prevalence in the Scandinavian countries [3].

Radiological skeletal maturity was evaluated by Risser sign only in the present study, while bone age assessment from the left hand (Greulich & Pyle, 1959) or elbow (Sauvegrain) is most used world-wide [26]. In one of the girls with Risser sign of 4, and 1 year post-menarche at screening, her major curve progressed from 37° to 45° within 7 months. Additional assessment of skeletal age at screening might have provided important supplemental information.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at screening</th>
<th>Major curve at screening</th>
<th>Risser sign</th>
<th>Post Menarche</th>
<th>Major curve at follow up</th>
<th>Treatment status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>37° thoracic, 32° lumbar</td>
<td>4</td>
<td>12 months</td>
<td>45° thoracic, 43° lumbar</td>
<td>Posterior fusion</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>27° thoracic, 16° lumbar</td>
<td>1</td>
<td>16 months</td>
<td>27° thoracic, 21° lumbar</td>
<td>Observation</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>16° thoracic, 24° lumbar</td>
<td>4</td>
<td>16 months</td>
<td>19° thoracic, 24° lumbar</td>
<td>Observation</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>30° thoracolumbar</td>
<td>4</td>
<td>2 months</td>
<td>30° thoracolumbar</td>
<td>Observation</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>29° thoracic</td>
<td>4</td>
<td>24 months</td>
<td>29° thoracic</td>
<td>Observation</td>
</tr>
</tbody>
</table>

Table 2 Contingency table showing the calculations of parameters of reliability of the screening test

<table>
<thead>
<tr>
<th></th>
<th>Children with Scoliosis</th>
<th>Children without Scoliosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Screening</td>
<td>True Positive (TP): 22</td>
<td>False Positive (FP): 38</td>
</tr>
<tr>
<td>Negative Screening</td>
<td>False Negative (FN): 10</td>
<td>True Negative (TN): 3962</td>
</tr>
</tbody>
</table>

Sensitivity = TP/(TP+FN) = 22/32 = 0.69
Specificity = TN/(FP+TN) = 3962/4000 = 0.99
PPV (positive predictive value) = TP/(TP+FP) = 22/60 = 0.37
NPV (negative predictive value) = TN/(FN+TN) = 3962/3962 = 0.99
LR+ (positive likelihood ratio) = Sensitivity/(1-specificity) = 0.69/0.01 = 69
LR- (negative likelihood ratio) = 1-sensitivity/(specificity) = 0.31/0.99 = 0.31

The prediction of scoliosis progression depends largely on skeletal maturity and curve magnitude. Larger curves in immature patients have higher risks of progression than smaller curves in more mature patients. The rationale behind screening is therefore to enable early detection of curves > 20° in immature patients that permits initiation of bracing which may halt progression, or allow surgery at appropriate time and avoid the complications of surgery of advanced scoliosis.

Effectiveness of scoliosis screening
Direct evidence of the effectiveness of scoliosis screening would require controlled prospective studies demonstrating that persons who receive screening have better outcomes than those who are not screened. Documentation is limited, but few studies including a recent study
from the Netherlands, have demonstrated that scoliosis cases detected through screening had lower chances of having surgery than otherwise detected patients [27,28]. There are some studies reporting that patients with scoliosis detected by screening are younger than referred cases, have smaller curve size, and reduced risk to progress to > 45°, and thereby having surgery. On the other hand, the number of referrals to local scoliosis clinics is increased by screening [29-32].

The current study was designed to screen 12000, twelve year old children but we were able to screen only 4000. Since screening has been discontinued in Norway, the health authorities did not support the study with a recommendation that could have boosted participation in the study. The study did neither include sufficient school children nor a follow up to evaluate whether those children screened have a better outcome than those not screened.

**Accuracy of screening tests**

The sensitivity and specificity of scoliosis screening depends largely on the skills of the examiner and the magnitude of the scoliosis being sought. The use of scoliometer has been shown to increase the sensitivity and the specificity in detecting a Cobb angle of > 20° [33]. A scoliometer reading of 5° has been shown to have a sensitivity of 100%, and 47% specificity for identification of scoliosis, whereas a scoliometer reading of 7° increases the specificity to 86% but decreases the sensitivity to 83% [34]. In the present study, using a scoliometer reading of 7°, the sensitivity was 69% and the specificity was 99% in detecting AIS in the study population.

The positive predictive value of visual inspection and the forward-bending test varies with the degree of curvature by which a “true positive” is defined, the prevalence of scoliosis in the screened population, and the skills of the examiners [35,36]. The magnitude of PPV is thus inversely related to the degree of curvature used to define scoliosis since the prevalence of small curves is greater than large curves. In a study from Australia, the PPV was 78% for curves > 5° in a population with an estimated prevalence of 3% [37]. In another study, the PPV was 54% for curves > 10° with a predicted prevalence of 2%, and 24% for curves > 20° with an estimated prevalence rate of 0.3% [36]. A meta-analysis of the clinical effectiveness of school scoliosis screening citing 34 studies reported that the pooled PPV for curves > 10°, curves > 20°, and treatment were 28.0%, 5.6% and 2.6%, respectively [38]. In the present study, the PPV was found to be 37% applying the accepted > 10° definition of scoliosis and an estimated point prevalence of 0.8% in 12-year-old children.

A likelihood ratio > 1 indicates that a test result is associated with a disease and a likelihood ratio < 1 indicates that a test result is associated with the absence of a disease. It is when the positive likelihood ratio is > 5 or the negative likelihood ratio is < 0.2 that likelihood ratios can be applied to the pre-test probability of a patient having a specific diagnosis. In this present study, the positive likelihood ratio was calculated to be 69 and the negative likelihood ratio was 0.3. The screening model was sensitive enough to reduce the number of false positive results. However, since the number of abnormal radiographs of Cobb angle > 10° (true scoliosis) is not known in the study population, the true PPV cannot be known.

**Referral rates**

Referral rates have been reported to be as high as 21% without the use of objective criteria, but reduced as much as 90% by the use of objective criteria [20,39,40]. A 3% referral rate has been predicted using 7° scoliometer reading, as compared to a referral rate of 12% using 5° scoliometer reading [20]. A Meta-analysis of the clinical effectiveness of school scoliosis screening citing 34 studies reported the pooled referral rate to radiography of 5% [38]. It is now widely agreed upon that referral rates should be in the range of 2% to 3% in school screening for scoliosis [20,39,41,42]. In the present screening study the referral rate was 1.5% based on a scoliometer reading of 7° which may reflect that screening was conducted on 12-year-old children only.

In the present study, 38 children were falsely diagnosed as AIS (positive on screening but had normal spine on radiography). If screening was performed yearly nationwide, the total estimated number of children with negative radiographs (Cobb angle < 10°) in 60000 children of 12 years in the Norwegian population of 5 million inhabitants will be 570 which might be a concern for health authorities.

Screening for scoliosis using the scoliometer does not reveal scoliosis per se but detects thoracic deformity. The radiographic measured thoracic Cobb angle has been shown not to correlated to the rib-index (that is the surface deformity) in the younger group but only in the 14-18 years-old age group [43]. This lack of association of the surface asymmetry (hump) and radiological asymmetry (Cobb angle) in the younger group such as in our study, is creating the burden of false positive referrals and the negative attitude of several health decision boards to discontinue school screening programs in the various countries. Thus, it is not possible to reliably predict the degree of curvature from surface topography in the age group that are screened [6]. It has been reported that, in typical screening settings where the prevalence and positive predictive value are relatively low, for every curve > 10° detected, there are 1-5 false-positives; similarly, for every curve > 20° detected, there are 3-24 false-positives [11,43]. This number of false positive children on screening must be accepted if those
with asymmetry, who might develop scoliosis should be detected.

The goal of screening is to detect those who will be at risk for developing scoliosis in the school-age population. In evaluation of the effectiveness of screening for scoliosis it should also be taken into account the knowledge gained and contribution it offers in clinical research of idiopathic scoliosis aetiology. The lack of a deeper insight on school screening issue, its value and negative impact of its discontinuation in some countries was the trigger for a recent decision of the Scoliosis Research Society (SRS) presidential line to create an International task Force for the better study of the school screening issue and creation of a “white paper” with recommendations based on recent knowledge on the topic [42].

Potential adverse effects
It has been argued that screening could have psychological labelling effects to subjects, and increase exposure to radiographs. In the present study, attempts have been made to limit psychological labelling by providing adequate verbal and written information to children and parents before and after screening. We also tried to limit exposure to radiography by choosing a high cut-off ATR of 4° and providing adequate training for our screeners thereby reducing false positive findings which in turn reduce unnecessary exposure to radiography.

Conclusion
The point prevalence of AIS in the present study is in agreement or slightly lower than results from earlier studies. The screening model employed demonstrates acceptable sensitivity and specificity, and low referral rates. The calculated likelihood ratios are acceptable for a screening test. In the present study screening for scoliosis at the age of 12 years only was not effective for detecting patients with indication for brace treatment. Screening should probably be initiated one year earlier for girls and one year later for boys, or be conducted more than once. The costs and the use of health care resources and the radiation exposure should be considered when the screening criterion is chosen.

Acknowledgements
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Authors’ contributions
JIB and RDA designed the study. RDA and SR designed the screening programme and performed the educational courses for the screeners. RDA, JIB and SR were involved in the collection of the data for the manuscript. RDA examined all referred patients. RDA, JIB and HS were involved in the analysis and the interpretation of results, drafting and critical review of the manuscript. All authors have given final approval to the version to be published.

Competing interests
None of the authors have received benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this manuscript e.g., royalties, stocks, stock options, decision making positions.

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Scoliosis detection, patient characteristics, referral patterns and treatment in the absence of a screening program in Norway

Raphael Dziwornu Adobor1*, Rolf Bjarne Riise1, Roger Sørensen1, Thomas Johan Kibsgård1, Harald Steen2 and Jens Ivar Brox1

Abstract

Background: Early diagnosis of idiopathic scoliosis allows for observation and timely initiation of brace treatment in order to halt progression. School scoliosis screening programs were abolished in Norway in 1994 for lack of evidence that the programs improved outcome and for the costs involved. The consequences of this decision are discussed.

Objectives: To describe the detection, patient characteristics, referral patterns and treatment of idiopathic scoliosis at a scoliosis clinic during the period 2003–2011, when there was no screening and to compare treatment modalities to the period 1976–1988 when screening was performed.

Methods: Patient demographics, age at detection, family history, clinical and radiological charts of consecutive patients referred for scoliosis evaluation during the period 2003–2011, were prospectively registered. Patients were recruited from a catchment area of about 500000 teenagers. Maturity was estimated according to Risser sign and menarchal status. Severity of pain was recorded by a verbal 5-point scale from no pain to pain at all times. Physical and neurological examinations were conducted. The detector and patient characteristics were recorded. Referral patterns of orthopedic surgeons at local hospitals and other health care providers were recorded. Patient data was obtained by spine surgeons. Treatment modalities in the current period were compared to the period 1976–1988.

Results: We registered 752 patients with late onset juvenile and adolescent idiopathic scoliosis from 2003–2011. There were 644 (86%) girls and 108 (14%) boys. Mean age at detection was 14.6 (7–19) years. Sixty percent had Risser sign ≥3, whilst 74% were post menarche with a mean age at menarche of 13.2 years. Thirty-one percent had a family history of scoliosis. The mean major curve at first consultation at our clinic was 38° (10°-95°). About 40% had a major curve >40°. Seventy-one percent were detected by patients, close relatives, and friends. Orthopaedic surgeons referred 61% of the patients. The mean duration from detection to the first consultation was 20(0–27) months. The proportion of the average number of patients braced each year was 68% during the period with screening compared to 38% in the period without screening, while the proportion for those operated was 32% and 62%, respectively (p=0.002, OR 3.5, (95%CI 1.6 to 7.5).

Conclusion: In the absence of scoliosis screening, lay persons most often detect scoliosis. Many patients presented with a mean Cobb angle approaching the upper limit for brace treatment indications. The frequency of brace treatment has been reduced and surgery is increased during the recent period without screening compared with the period in the past when screening was still conducted.
Background
Idiopathic scoliosis is a complex three-dimensional deformity of the spine characterized by a lateral deviation and axial rotation [1-3]. Classification is according to the age of onset; infantile, from birth to 3 years; juvenile from 3 to 8 years, and adolescent from 10 years to maturity [4]. Idiopathic scoliosis is also classified into early onset (<5 years) or late onset (>5 years) [5]. Adolescent idiopathic scoliosis (AIS) is the most common form and is often associated with rapid growth [4]. The prevalence rate of idiopathic scoliosis as proposed by the Scoliosis Research Society (Cobb angle >10°) [6] is reported from 0.5% to 3%, but only 5% of these patients have curve progression to >30° [7,8]. We recently performed screening in 4000 twelve years old Norwegian children and found a 0.55% point prevalence of AIS [9]. The ratio of girls to boys is equal for minor curves, but rises for girls as the curve magnitudes, reaching a ratio of 1:8 for those requiring treatment [10]. The etiology is not known, but several genetic predisposing factors have been described [11-16].

Early detection of scoliosis allows for monitoring of the development and progression of the deformity, and timely initiation of bracing that is reported to be effective by non-randomised studies [17-21], although the scientific evidence is weak according to a recent Cochrane Review [7]. After scoliosis has been detected, skeletal growth (Risser sign 0 and 1) gender and curve location has consistently been reported to increase the risk of progression [2,4,22-24], while conflicting risk is reported for curve magnitude with some studies reporting larger curves increasing the risk of progression, whilst some studies do not [10]. Curve flexibility (initial correction in brace) is reported to reduce the risk of progression in braced patients [25]. Progression is most rapid during peak skeletal growth, which precedes menarche in girls and occurs 6 to 12 months after the onset of axillary and facial hair in boys [26]. Several methods have been applied to estimate skeletal age including the Risser sign and Greulich and Pyle radiographic atlas [27]. The Risser sign is the most common method used to assess remaining growth in patients with idiopathic scoliosis [28].

Bracing to prevent or limit scoliosis progression is usually recommended for progressive curves >25° [19]. Surgical treatment is considered for curves >45°-50° to limit further progression, and correct the deformity [29-31]. Screening for scoliosis allows for early detection and has in addition, provided valuable knowledge about prevalence, etiology and the natural history [32,33]. However, there are objections to scoliosis screening based largely on the low specificity of the screening test and the costs involved because of over-referrals [8,34,35]. In our recently published screening program, we found a specificity of 0.99 and a positive predictive value of 0.37 [9].
2003, and included all new referred patients to the specialist clinic at the orthopaedic department, Oslo University Hospital, Rikshospitalet. Norway has a public universal healthcare system in which waiting times for specialists’ evaluation of paediatric cases are generally at an acceptable level. Rikshospitalet is a tertiary referral centre designated to offer specialized services to the Norwegian population of 4.7 million inhabitants. It is estimated that the specialist clinic offered scoliosis services to approximately 80% of the Norwegian population representing about 500,000 teenagers during the study periods [49]. The surgeons filled in a standardised 2 page chart based on patient data from interview, clinical examination and radiological measures. The inter-observer agreement of the methods used for collecting data in the standardized chart has not been evaluated. The inclusion criteria was late-juveniles (7 years and older) and adolescents referred to idiopathic scoliosis evaluation for the first time. Patients with infantile and early-onset juvenile idiopathic, neuromuscular, congenital or syndromic scoliosis were excluded.

Patient records and surgical protocols during the years 1976–1988 were reviewed to estimate the number of late-onset juvenile and adolescent idiopathic scoliosis patients that were treated with Boston brace or operated with Harrington’s rods at the Sophies Minde Hospital. The Sophies Minde Hospital was the name of the orthopedic department of the Rikshospitalet during that period, and provided scoliosis services to the same segment of Norwegian population as at now. The results of brace treatment in these patients were previously reported in 3 publications [50-52]. Indication for bracing was a major scoliotic curve >20° with an observed progression >5° and the Risser sign <3, and the indication for surgery was progressive curves >20° with an observed progression >5° and the Risser sign obtained from a postero-anterior radiograph at the level of the iliac crest ossification [28]. The convexity and magnitude of the curves were measured according to the Cobb method from the radiographs of full postero-anterior films by 2 experienced radiologists [53]. Scoliosis was classified by the orthopedic surgeons according to the King Moe types [54]. Interrater agreement of Cobb measurements and King-Moe classifications was not evaluated in the present study.

Demographics
Age at scoliosis detection, at evaluation and at menarche was recorded. Family history of idiopathic scoliosis was obtained from the parents of the affected child based on questioning them if any family member had consulted or been braced or operated for scoliosis. The originator of detection was classified into six groups: 1) the patient himself/herself; 2) parents, family, siblings, grandparents, aunt/uncles and friends; 3) primary physicians; 4) hospital specialists (orthopedic specialist, radiologist); 5) allied health care provider (physician therapist community health nurse, chiropractor, osteopath and 6) non-health care provider (dressmaker, sports instructor or hairdresser).

Referral patterns
Referral patterns of primary physicians, physical therapists community health nurse, chiropractors and hospital specialists to the scoliosis clinic were noted. The duration from time of detection to referral and evaluation was also recorded.

Clinical assessment
Physical examination was conducted by observing the patient standing for assessment of asymmetries of the shoulder, ribs, scapula, waist and hips. Shoulder symmetry was assessed by the relative position of both shoulders and recorded as normal, asymmetry < 2 cm or asymmetry > 2 cm. Decompensation of the trunk over pelvis was recorded as positive truncal shift. Coronal balance was measured by the plumb line in cm as the lateralizing position of the cervico-thoracic junction in relation to the left or right of the gluteal cleft. Height and body weight were measured by a nurse for calculation of body mass index (BMI kg/m²). In the Adams forward bending position, the thoracic rib cage prominence (angel of thoracic rotation (ATR) or prominence of the paraspinal muscles in the thoracolumbar/lumbar area was measured either in degrees using a scoliometer or in centimeters using a ruler. Half of the patients were measured using the scoliometer and half measured in centimeters. Back pain and perception of fatigue of the back muscles were recorded by a verbal 5-point scale: never had pain, seldom pain, sometimes pain, often pain, always pain.

Neurological assessment was performed by evaluating the spinal reflexes, extremity weakness, hyper-reflexia and abdominal reflexes to eliminate neurological etiology.

Radiological measures
Skeletal age was estimated by a radiologist using Risser sign obtained from a postero-anterior radiograph at the level of the iliac crest ossification [28]. The convexity and magnitude of the curves were measured according to the Cobb method from the radiographs of full postero-anterior films by 2 experienced radiologists [53]. Scoliosis was classified by the orthopedic surgeons according to the King Moe types [54]. Interrater agreement of Cobb measurements and King-Moe classifications was not evaluated in the present study.

Recommended treatment
Prescribed or recommended treatment up to 6 months follow-up after the first consultation was recorded as further observation, brace treatment, surgery or discharge. We assumed that additional patients had surgery either after brace treatment was initiated or after further follow-up. We therefore also reviewed surgical protocols in order to estimate the actual number of patients who were operated yearly during the period of the study.

Statistical analysis
Descriptive statistics of mean, median, standard deviation, range, and frequencies were calculated using the
Statistical Package for Social Science (SPSS), version 14.0 (SPSS Inc., Chicago, IL. We categorized curve size (10.0° – 24.9°; 25.0° – 34.9°; 35.0° – 39.9°; 40.0° – 44.9°; > 45.0°), BMI (<30 and >30) kg/m², age (7–12 years; 13 and 14 years; 15 and 16 years; 17 years and older), and back pain (absent, seldom, sometimes, often and all the time). We applied multivariable logistic regression to estimate the association between back pain as the outcome variable, with gender, curve size, and BMI as predictor variables. Regression analysis was performed in order to examine the confounding effect of curve size, and BMI on the assumed association between back pain and gender. The Hosmer-Lemeshow test was used to assess the logistic model adequacy. Effect sizes were measured by odds ratio (OR) and 95% confidential intervals were calculated.

One-way ANOVA with correction for multiple tests assuming non-equal variance was performed to analyse differences between originator of detection in relation to age and curve size. In addition, the non-parametric Kruskal–Wallis test was used to test differences in patient treatments, and Risser signs between various originators of scoliosis detection. If significance was observed, the non-parametric Mann–Whitney U test was used to detect differences between two groups of originators.

The average number of patients treated with brace and those operated in the two periods were calculated from the prospective data and the administrative data (surgical protocols). Chi-squared statistics was used to compare whether the number of those treated with brace and those operated in the two periods differ from one another. The proportions of the treatment modalities in the two periods, mean difference between the proportions, odds ratio (OR) and 95% confidential intervals were calculated.

The study was approved by the Ethic Committee of the Oslo University Hospital (reference number 12/11063).

Results

Demographics

There were 752 patients, 644 (85%) girls and 108 (14%) boys. The age distribution is shown in Table 1. Mean age at scoliosis detection was 14.6± 2.1 (7–20) years. Mean age for girls was 14.5±2.1 and 15.5± 2.1 for boys. Thirty-one percent had a family history of scoliosis with 9% being first degree (parents or siblings) or second degree relations, respectively.

Originator of scoliosis detection

The originator of detection is shown in Table 1. Seventy-one percent were detected by patients, family members or friends, 27% by health care providers, and 2% by non-health care providers. The distribution of patient

<table>
<thead>
<tr>
<th>Table 1 Main patient characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td>Gender (n=752)</td>
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<tr>
<td>Girls</td>
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<tr>
<td>Boys</td>
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<tr>
<td>Age/years</td>
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<tr>
<td>7-12</td>
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<td>13-14</td>
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<tr>
<td>15-16</td>
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<tr>
<td>17 and older</td>
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<tr>
<td>Scoliosis detector</td>
</tr>
<tr>
<td>Patient him/herself</td>
</tr>
<tr>
<td>Parents/family/ friends</td>
</tr>
<tr>
<td>Primary physicians</td>
</tr>
<tr>
<td>Hospital specialists</td>
</tr>
<tr>
<td>Allied health care provider</td>
</tr>
<tr>
<td>Non-health care provider</td>
</tr>
<tr>
<td>Risser sign1</td>
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<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<td>3</td>
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<td>4</td>
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<tr>
<td>5</td>
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<tr>
<td>Cobb angle2°</td>
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<tr>
<td>10 - 24.9</td>
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<tr>
<td>25 - 34.9</td>
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<tr>
<td>35 - 39.9</td>
</tr>
<tr>
<td>40 - 44.9</td>
</tr>
<tr>
<td>&gt;45</td>
</tr>
<tr>
<td>King Moe Classification3</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>Back pain3</td>
</tr>
<tr>
<td>Absent</td>
</tr>
<tr>
<td>Seldom</td>
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<tr>
<td>Sometimes</td>
</tr>
<tr>
<td>Often</td>
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<tr>
<td>All the time</td>
</tr>
<tr>
<td>Treatment recommendations</td>
</tr>
<tr>
<td>Brace</td>
</tr>
<tr>
<td>Surgery</td>
</tr>
<tr>
<td>Further observation</td>
</tr>
<tr>
<td>Discharged</td>
</tr>
</tbody>
</table>

1Not reported, n = 3 2Not reported, n = 60 3Not reported n = 20.
maturity, curve sizes and treatment modalities according to the various originators of detection is shown in Table 2.

Patients whose scoliosis were detected by parents, family and friends were statistically younger compared to those detected by the patients themselves (p=0.01). Risser sign was lower in patients whose scoliosis were detected by parents, family and friends compared to those detected by patients themselves (p=0.005) or those detected by primary physicians (p=0.019). There were no differences in the curve size according to the originator of detection. Community health nurses and physical therapist detected patients with scoliosis that were suitable for brace treatment more than when the patients detect scoliosis themselves (p=0.005).

**Referral patterns**

Sixty-one percent of patients were referred by orthopaedic surgeons, 33% by primary physicians, and 5% by physical therapists community health nurses or chiropractors. The mean duration from detection to referral was 16±16.9 (0–27) months and the mean duration from referral to first consultation at our clinic was 4.0 ± 2.6 months.

**Maturity**

The distribution of Risser sign is shown in Table 1. Sixty percent were ≥ Risser 3. Seventy-eight percent of the girls had had menarche at the time of the first visit with 36% of them ≥ 2 years earlier. Mean age at menarche was 13.2±1.2 years.

**Physical examination**

Mean body mass index (BMI) was 19.7±3.2 (range 11.9 - 41.0) kg/m². BMI was 19.7±3.2 in girls and 19.9±3.3 in boys. Asymmetries of the shoulders were registered in 52%. Twenty-eight percent had coronal imbalance, but only 10% were > 2 cm. Truncal shift was registered in 35%. The mean ATR was 8.4° in the thoracic region and 7.9° in the lumbar region of those measured with the scoliometer, and 1.5 cm in the thoracic region, and 1.2 cm in lumbar region of those measured in centimeters. All patients had normal neurological examination except one girl who had an abnormal superficial abdominal reflex. A supplementary MRI revealed a Chiari malformation and syringomyelia.

**Back pain**

Boys reported more often (75%) that they seldom or never had back pain compared with girls (58%), 7% of the boys reported that they have pain often or almost all the time compared with 18% of the girls. There is a significant association between back pain and girls compared with boys (p = 0.006, OR 2.88, 95%CI (1.36 to 6.19).

**Radiological measures**

The mean major curve at first consultation was 37.8°± 14.5° (range 10.95°); 37.8°±14.1° in girls and 37.5°±16.8° in boys. Seventy-five percent of the primary curves had convexity towards the right. The curve magnitude and classification according to King-Moe are shown in Table 1.

**Treatment modalities**

At the initial consultation, brace treatment was recommended in 18%, surgery in 20%, 8% were discharged, and 54% were scheduled for further observation. Curve size, age, and Risser sign of these patients are shown in Table 3. After 6 months observation, an additional 3% were recommended for brace treatment, 6% for surgery, 35% were discharged, and 48% recommended further follow-up. The recommended treatment modalities at the first consultation and at 6 months observation are shown in Table 1. This means that at the outpatient clinic the yearly average number of patients recommended for brace was 19, and 22 for surgery. The additional review of surgical protocols reflecting a longer follow-up period revealed that on average, 32 patients were operated yearly during the study period.

**Table 2 Age in years, Risser sign, curve size in degrees, and percentage of treatment modalities according to originator of detection**

<table>
<thead>
<tr>
<th>Originator of detection</th>
<th>Age Mean±SD</th>
<th>Risser sign Median(range)</th>
<th>Curve size Mean±SD</th>
<th>Treatment modalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient him/herself</td>
<td>15.4±1.9</td>
<td>4 (0 to 5)</td>
<td>40.6±15.6</td>
<td>Brace 8.0, Surgery 24.5, Observation 24.0, Discharged 36.0</td>
</tr>
<tr>
<td>Parents/family/friends</td>
<td>14.5±2.0</td>
<td>3 (0 to 5)</td>
<td>38.8±14.5</td>
<td>Brace 21.9, Surgery 27.5, Observation 26.7, Discharged 24.0</td>
</tr>
<tr>
<td>Primary physicians</td>
<td>14.8±2.1</td>
<td>4 (0 to 5)</td>
<td>35.8±14.4</td>
<td>Brace 18.1, Surgery 24.5, Observation 23.4, Discharged 34.0</td>
</tr>
<tr>
<td>Hospital specialists</td>
<td>15.6±2.4</td>
<td>4 (0 to 5)</td>
<td>39.2±15.8</td>
<td>Brace 16.7, Surgery 25.0, Observation 16.7, Discharged 41.7</td>
</tr>
<tr>
<td>Allied health care provider</td>
<td>14.5±2.5</td>
<td>4 (0 to 5)</td>
<td>35.3±13.5</td>
<td>Brace 28.1, Surgery 17.7, Observation 24.0, Discharged 30.2</td>
</tr>
<tr>
<td>Non-allied health care provider</td>
<td>14.5±2.1</td>
<td>4 (0 to 5)</td>
<td>38.3±15.8</td>
<td>Brace 6.3, Surgery 31.3, Observation 43.8, Discharged 18.8</td>
</tr>
</tbody>
</table>

* After 6 months observation.
Table 3 Age in years and Risser sign and curve size in degrees, at first consultation

<table>
<thead>
<tr>
<th></th>
<th>Age (Mean±SD)</th>
<th>Risser sign (Median(range))</th>
<th>Curve size (Mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brace treatment</td>
<td>12.8±1.9</td>
<td>0(0 to 4)</td>
<td>36.0±8.7</td>
</tr>
<tr>
<td>Surgery</td>
<td>14.4±1.7</td>
<td>3(0 to 5)</td>
<td>58.3±10.9</td>
</tr>
<tr>
<td>Further observation</td>
<td>15.0±2.0</td>
<td>4(0 to 5)</td>
<td>32.4±9.8</td>
</tr>
<tr>
<td>Discharge</td>
<td>16.2±2.0</td>
<td>5(0 to 5)</td>
<td>25.4±8.1</td>
</tr>
</tbody>
</table>

Brace and surgical treatment 1976–1988
During the period 1976–1988, an average of 41 patients were treated with the Boston Brace each year [51,52]. According to the surgical protocols, an average of 20 patients was operated each year with Harrington’s rods for late-juvenile or adolescent idiopathic scoliosis during the same period.

Comparison of treatment modalities
The number of patients treated with brace relative to those operated during 1976–1988 was 41/19 and 20/32 during 2003–2011. The proportion of patients treated with brace during 1976–1988 (68%) was higher than during 2003–2011 (38%) and vice-versa for surgical treatment (p=0.002, OR 3.5 95% CI 1.6 to 7.5). The mean difference was 30% 95% CI (10 to 47).

Discussion
The majority of patients detected with scoliosis in the absence of screening were skeletally mature and had curves that were not suitable for brace treatment. According to internationally accepted guidelines brace treatment is recommended in growing children with progressive curves >25°, who has at least one year growth potential [19]. The mean chronological age at detection in the present study was 14 years, which is 2 years older than the ideal age [19,55]. At the first presentation, 60% had Risser sign ≥3, and 78% of the girls were post menarche, indicating that most patients were detected late, and not suitable for brace treatment. A large proportion of patients also had curves ≥40° at first presentation which is beyond the international recommendation for initiation of brace treatment [43]. The present results are in agreement with two previous studies that have assessed the impact of discontinuation of scoliosis program on detection, referral patterns and management. In a Canadian study, 32% of patients with AIS were referred too late with regard to brace treatment [48] and in a study conducted in London, United Kingdom, 56% of cases were detected when the primary curve was >40° and not suitable for brace treatment [47].

About 71% of cases were detected by non health care providers either by patients themselves, close family members or friends. It has been suggested that parents should be educated to perceive asymmetries of the back, shoulders, waistline, hips, and breast in their children as early signs of scoliosis and seek early and appropriate medical evaluation [42,48]. In the present study, only 27% of cases were detected by healthcare providers. We found statistical differences in patient maturity, and treatment modalities between different originators of scoliosis detection. Close family members and friends detected patients with scoliosis at a younger age compared to scoliosis detected by the patients themselves. Since majority of curves were large at detection, we found no differences in the curve size according to the originator of detection.

Community health nurses and physical therapists detected patients with scoliosis that were suitable for brace treatment more than when the patients detect scoliosis themselves.

Referral patterns
Two thirds of all patients were first observed by orthopedic surgeons at local hospitals on average 16 months before being referred and only 1/3 of patients were referred directly by primary physicians or physical therapists or community health nurses to the specialist clinic. Norway, with its public universal healthcare system, promotes referrals to specialized care and waiting times are generally at an acceptable level for a specialist’s evaluation of pediatric cases as shown in this study where the mean waiting time from referral to specialist evaluation was 4 months. A general guideline for primary physicians is to refer suspected cases of AIS to local orthopedic surgeons for diagnosis or refer directly to specialist evaluation of high risk patients for progression. Orthopedic surgeons at local clinics are authorized to diagnose and observe AIS patients for progression and to refer without unnecessary delay progressive curves >20° in immature patients to specialist clinics for evaluation. These orthopedic surgeons downstream the specialists’ clinics are however not authorized to prescribe brace treatment. There is either a late detection of AIS in the community in the absence of screening, or there is a delay in the referral practices of health care providers to specialist evaluation due to their non- awareness of existing guidelines, or failure of education on these guidelines. The result is that many patients with AIS in the present study were referred when mature, and with curves approaching the upper limit of brace treatment indications.

To ensure uniformity and quality of care for scoliosis patients, we suggest that persons involved in child health care like physical therapists community health nurses, chiropractors, sports instructors, primary physicians and orthopedic surgeons be better informed about guidelines.
for scoliosis detection. This includes the examination of asymmetries of the back in the routine examination of the child [48]. Without objective screening test, proper training and clear guidelines for referrals, there is a risk of inappropriate referrals to the specialized care setting if one will suggest that community health nurses, physical therapists, chiropractors, sports instructors, refer patients directly to scoliosis specialist evaluation without first referring to local orthopedic surgeons. However, the magnitude of the eventual inappropriate referrals is not known. Local orthopedic surgeons still play important roles as gatekeepers while offering reassurances to the families and proper follow-up for mild cases. We emphasize therefore that in cases of confirmed scoliosis in immature patients, those involved in child health care should refer to specialized evaluation without unnecessary delay.

**Patient characteristics**

The majority of the patients were girls as reported before [56]. The average angle of trunk rotation (ATR) is in agreement with a previous report [57]. Family history of scoliosis is consistent with earlier studies [11,12,14-16]. Curve classification according to King-Moe compares well with the original publication reporting that type 2 curves were most common and type 5 were the least common [54]. Neurological examination to eliminate underlying neurological pathology was normal in all patients except one patient who was subsequently referred for neurosurgical treatment before brace treatment commenced.

**Scoliosis and back pain**

Previous studies have reported slightly increased back pain in adolescents with idiopathic scoliosis compared to the normal population, but the pain is not usually disabling [58,59]. These studies have not showed any association between back pain and curve size, gender, family history of scoliosis, or limb-length discrepancy, but significant association between back pain and maturity, overweight and larger proximal thoracic curves [61]. In the present study an association between pain and maturity, overweight and larger proximal thoracic curves [61]. In the present study most patients (59%) reported some, but not disabling back pain and only between 1-3% had back pain almost all the time. One previous study reported less postoperative pain in male patients with AIS [62]. In the present study, we also found a significant association between back pain and girls compared with boys but no association between back pain, curve size, and BMI.

**Comparison of treatment modalities during screening years versus non-screening years**

The efficacy of scoliosis screening is under debate [40-44]. To justify screening, it should lead to early detection and initiation of brace treatment at the appropriate time to optimize its efficacy and reduce the option of surgery. Earlier studies suggest that screening may improve the outcome of bracing and either reduce the surgical rate or optimize timing for surgery [43,45,63,64]. A recent case control study reported that screening does not reduce surgery in scoliosis patients [46]. In the present study, we found that the average number of patients braced each year during the period of screening was significantly higher than in the period without screening. Authors clearly acknowledge the methodological weakness, when numbers of those operated were not retrieved from prospectively collected data, but from administrative count data (surgical protocols) over both periods. The Norwegian population has increased during the study years from an average of 4.1 million inhabitants during the screening years to 4.7 million during the non-screening periods, but the population segment of 10–19 year olds who represent the risk population in the study has remained relatively the same (634229 in 1976–1988 to 616715 during 2003–2011) [49]. Within the relatively close periods in comparison, we assume that the prevalence, natural history, and the indications for idiopathic scoliosis treatment have not changed [48]. The p-value in the chi-square statistics comparing the proportions of brace and surgical treatment was statistically significant. Our results therefore suggest that the absence of screening for scoliosis has resulted in less patients being treated with brace and more patients having surgery. However, technical advances in scoliosis surgery in recent years coupled with surgeon attitudes may also contribute to the observed change in treatment trends exhibited over the two periods. The Boston brace has remained the choice of brace type at our institution, but surgical treatment of scoliosis has evolved from the Harrington distraction rods to third generation instrumentation with segmental all pedicle screws construct in the course of the two periods. In addition, during the screening period bracing was administered by one spine surgeon, while different spine surgeons were involved in brace treatment during the period when there was no screening. The issue of non-uniform health care provision has the potential of introducing another bias in the comparison of treatment rates in the two periods.

**Limitations of the study**

Resident orthopaedic surgeons with variable experience in scoliosis management participated in the study. The inter-tester reliability was not tested. This variability in experience could influence evaluation of
patient characteristics and the recommended treatment. The assessment of back pain applied has not been validated and recording by a surgeon may be less valid than self-assessment by patients. The estimation of surgical rates in the two treatment periods was based on surgical protocols and not on the registration chart at the outpatient clinic. There is an indication that, the number obtained from in the surgical protocol is a more valid estimate of the true number of actually operated than the recorded recommendations. It is also likely that some patients were not registered at the outpatient clinic. In view of the methodological weaknesses and other limitations which the authors clearly acknowledge in the manuscript, the results of the comparison of the rate of brace and surgery treatments during the two periods should be interpreted with caution.

Conclusion
In the absence of a scoliosis screening program, many patients were referred late and presented with a mean Cobb angle approaching the upper limit of brace treatment indication. The present study suggests that fewer patients are being braced, and more patients are having surgery. However, we acknowledge methodological limitations in comparing treatment from the two periods, and cannot exclude factors other than screening to have contributed to the observed changes. The majority of cases were detected by lay persons and referred too late for specialist evaluation. Scoliosis detected by parents, family and friends were younger than scoliosis detected by the patients themselves. Better dissemination of guidelines for scoliosis referrals are suggested to improve referral timing in the absence of school scoliosis screening programs. The reintroduction of scoliosis screening may be considered in Norway in order to detect idiopathic scoliosis earlier than we do today.

Competing interests
None of the authors have received benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this manuscript e.g., royalties, stocks, stock options, decision making positions.

Authors' contributions
RR, RS and JIB designed the study. RA wrote the drafted manuscript. JIB analyzed the data statistically. All authors were involved in the collection of the data, interpretation of the results, drafting and critical review of the manuscript. All authors have given approval to the final version to be published.

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A health economic evaluation of screening and treatment in patients with adolescent idiopathic scoliosis


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Abstract

Summary of background data

Adolescent idiopathic scoliosis can progress and affect the health related quality of life of the patients. Research shows that screening is effective in early detection, which allows for bracing and reduced surgical rates, and may save costs, but is still controversial from a health economic perspective.

Study design

Model based cost minimisation analysis using hospital’s costs, administrative data, and market prices to estimate costs in screening, bracing and surgical treatment. Uncertainty was characterised by deterministic and probabilistic sensitivity analyses. Time horizon was 6 years from first screening at 11 years of age.
Objective

To compare estimated costs in screening and non-screening scenarios (reduced treatment rates of 90%, 80%, 70% of screening, and non-screening Norway 2012).

Methods

Data was based on screening and treatment costs in primary health care and in hospital care settings. Participants were 4000, 12-year old children screened in Norway, 115190 children screened in Hong Kong and 112 children treated for scoliosis in Norway in 2012. We assumed equivalent outcome of health related quality of life, and compared only relative costs in screening and non-screening settings. Incremental cost was defined as positive when a non-screening scenario was more expensive relative to screening.

Results

Screening per child was € 8.4 (95% CrI 6.6 to10.6), € 10350 (8690 to 12180) per patient braced, and € 45880 (39040 to 55400) per child operated. Incremental cost per child in non-screening scenario of 90% treatment rate was € 13.3 (1 to 27), increasing from € 1.3 (−8 to 11) to € 27.6 (14 to 44) as surgical rates relative to bracing increased from 40% to 80%. For the 80% treatment rate non-screening scenario, incremental cost was € 5.5 (−6 to 18) when screening all, and € 11.3 (2 to 22) when screening girls only. For the non-screening Norwegian scenario, incremental cost per child was € -0.1(−14 to 16). Bracing and surgery were the main cost drivers and contributed most to uncertainty.

Conclusions

With the assumptions applied in the present study, screening is cost saving when performed in girls only, and when it leads to reduced treatment rates. Cost of surgery was dominating in non-screening whilst cost of bracing was dominating in screening. The economic gain of screening increases when it leads to higher rates of bracing and reduced surgical rates.

Keywords

Cost minimisation analysis, Scoliosis screening, Scoliosis treatment, Health related quality of life

Introduction

Adolescent idiopathic scoliosis (AIS) is a complex three dimensional deformity of the spine, characterized by lateral curvature >10° and axial rotation, which affects 2-3% of otherwise healthy teenagers [1-3]. The deformity usually progresses with rapid growth of the spine and can affect health related quality of life of the patients [4]. Conventional treatment options are bracing and surgery [1-3]. Bracing is normally recommended for progressive curves of 20-40° in immature patients to prevent progression and reduce surgery, whilst surgery is considered for curves >45°-50° to stop progression and correct the deformity [1]. In patients with AIS, only a minority have progressive curves requiring treatment [5], and 90% of those treated are girls [6,7]. Treatment outcomes are usually measured by radiographic changes of
the curves, but increasingly also by changes in health related quality of life. Early detection by screening allows for monitoring curve progression, and timely initiation of bracing. A recent randomised study found bracing to reduce curves which progress to the threshold of surgery [5].

Screening is controversial and practices vary worldwide [8-10]. Opponents cite mainly increased costs and lack of effectiveness of the programs. Some previous studies have supported whilst others have discouraged screening [11,12]. The United States Preventive Services Task Force neither supported nor opposed screening in 1993 [12,13], but recommended against routine screening in 2004 [14]. Discontinuation of screening programs has led to late detection and high rates of surgeries in various countries [15-17]. Currently, most international scoliosis and child health societies support and recommend screening [18]. The Scoliosis Research Society’s International task force recently reported even before the BRAIST study [5] was published, that screening was effective in technical, clinical, program, and treatment efficacy, but could not make a statement on cost effectiveness due to lack of studies evaluating costs and health economic analyses [19].

Reviews and long-term studies suggest that health related quality of life of patients treated with brace or surgery are not different [1,2,6]. The aim of the present study was therefore to perform a cost minimization analysis (CMA) comparing only costs in screening and non-screening settings, while assuming equal long term health related quality of life of patients whose scoliosis are detected through screening or without.

**Methods**

We used a model approach to compare costs in screening with non-screening scenarios. The main mathematical equation on which the model was based is shown in Additional file 1. Input model parameters were collected from screening and hospital care. Screening in Norway was performed once in 12-year old children, and did not detect patients suitable for bracing [20]. We assumed similar epidemiology and natural history of AIS in Hong Kong and Norway, and used suitable data from a large population-based cohort longitudinal screening study by Lee et al. from Hong Kong in 2010 as model input for screening [21]. In this study, 115190 children were screened: 3158 received X-rays, 59 had out-patient visits for further assessment only, 264 were braced, 10 had surgery, and 29 had both brace and surgery (85% brace and 15% surgery). The percent treated in Hong Kong was thus 2.63 per 1000 children.

Screening is no longer performed in Norway. According to administrative data from the three scoliosis clinics in Norway, 122 adolescents were treated for scoliosis in 2012, of which 51(42%) were braced and 71(58%) had surgery, with about 10% of them having both brace and surgery. These 122 children, aged 11 to 17 is the number of patients out of the cohort of 63421 children who were the target group for scoliosis treatment in Norway for that year. Thus, the percent of children treated in Norway in 2012 was 1.92 per 1000 children.

Model input for the non-screening scenarios were based on Norwegian data when available. Otherwise, inputs were estimated from the Hong Kong data.
Study perspective in relation to costs

We used a health sector budget perspective focusing on the costs related to orthopaedic treatment in hospital care [22], and in addition, we included costs for the society due to transportation and parents’ opportunity cost of time during treatment of their children.

Strategies being compared

Screening for scoliosis may lead to over-referrals to X-rays and outpatient evaluations, increased rates of bracing, but reduced surgical rates compared to settings when children are not screened [23,24]. In non-screening settings, many children are diagnosed late when they are matured, with curves not suitable for bracing [15-17,23]. We therefore assumed that reduced numbers of children are treated for scoliosis in non-screening settings and estimated reduced treatment rates of 90%, 80%, and 70%, respectively of those treated in screening by Lee et al. We compared costs in these reduced treatment rates to costs in the screening setting in Hong Kong. Treatment in this context includes the percentage of children who have X-rays for diagnosis, those treated with brace or surgery, and those who have further follow-ups. The estimated treatment rate of non-screening in Norway 2012 was 73% of that in Hong Kong. We also compared costs in non-screening scenario in Norway 2012 with the costs in the screening setting in Hong Kong. Since AIS is more prevalent in girls, and 90% of those treated for AIS are girls [5,6], we performed separate analyses in girls.

In all non-screening scenarios, we simulated different distribution rates of brace and surgery based on the available non-screening data from Norway (58% surgery and 42% brace), since this is the only available data on the distribution of brace and surgery in a non-screening setting. We used data from Hong Kong to estimate the frequency of X-ray examination and referrals since non-screening Norwegian data was not available (see Additional file 1). Based on this study, we estimated that about 15% of patients required referrals to X-ray and to specialist’s examinations. In all non-screening scenarios, these rates were adjusted accordingly.

Incremental cost was defined as the cost of treatment in a non-screening scenario minus the cost of treatment and cost incurred in conducting the screening. A positive incremental cost therefore implies that screening is more cost saving compared to the non-screening scenario. How incremental cost change by varying the ratio of bracing to surgery was estimated for all the non-screening scenarios. The probability of the incremental cost being positive was estimated for all cases.

Time horizon for cost estimations, discount rate

The time horizon for estimating costs was six years from the first screening at 11 years of age. We assumed two screenings per child, based on the recommendations of the Scoliosis Research Society [18] at the age of 11 and 13 years, and anticipated that 60% of the scoliosis cases were detected at the first screening and the rest at the second. We based our assumption on the knowledge of age and gender- specific prevalence of scoliosis, as well as the length of time between detection and treatment. Since screening tests are not fully accurate, it has also been suggested that scoliosis screening programs should be planned as a continuous process and not just a once and for all project as there is a possibility of missing out on some cases if screening is performed only once. For the non-screening scenarios we also assumed a dispersion of the expected cost (bracing and surgery) of 10%, 15%, 20%, 20%, 15% 10%,...
and 10% for each age group from 11 to 17 respectively. The literature is scarce with regards to the true dispersion of expected costs in scoliosis treatment, but shows a peak of treatment around 13–14 years of age. We therefore assumed 25% expected costs before, and 35% after the peak years [2,5,6,25]. When aggregating costs over time, we used an annual social discount rate of 4% (as recommended by the Norwegian Directorate of Health [26]) to calculate the present value of costs. The social discount rate is an interest rate used to bring future value into the present when considering the time value of money [22].

**Estimating costs and resources**

We used hospital’s costs and administrative data, and market prices to estimate the cost of screening, bracing and surgery.

**Screening**

Screening was performed once in 4000 twelve year old children as part of a vaccine and physical examination program from autumn 2006 to spring 2007 [20]. Community nurses and physical therapists performed the screening. All activities directly involved in the screening and follow-up of patients were identified, measured, and costs estimated (Table 1).
<table>
<thead>
<tr>
<th>No.</th>
<th>Variables</th>
<th>Unit cost (€)</th>
<th>Range (±%), cost</th>
<th>Units</th>
<th>Range (±%), units</th>
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<td>Transportation to X-ray exam</td>
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<td>5</td>
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<td></td>
<td>For confirmed scoliosis &gt;20°</td>
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<td>30</td>
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<tr>
<td>12</td>
<td>Out-patient consultations</td>
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<td>30</td>
<td>4</td>
<td>20</td>
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<td>Physical therapy</td>
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<td>20</td>
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<tr>
<td>14</td>
<td>Radiographs</td>
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<td>30</td>
<td>4</td>
<td>20</td>
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<td>15</td>
<td>Time used by one parent (days)</td>
<td>289</td>
<td>30</td>
<td>4</td>
<td>30</td>
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<td>Implants/utilities (per operation)</td>
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<td>Time used by one parent (days)</td>
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<td>15</td>
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<tr>
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<td>Taxi from home to school after treatment (days)</td>
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<td>50</td>
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</table>

*Two surgeons and two scrub nurses were involved in each surgery.

All items in each category of interventions were identified, measured, and costs estimated. Percentage of uncertainty was estimated for each item. The percentages of the uncertainty of the PSA’s are also given.
Bracing and surgery

We estimated the costs of bracing and surgery based on data from hospital records. For bracing, we estimated the costs of the brace equipment, transportation, radiographic and clinical examinations during the period of brace wear, 3 days hospital hotel services for the child and one parent during brace fitting. Additionally, the costs of reimbursements for wear and tear of clothing and beddings from the National Insurance Scheme were included. For surgery, we estimated the costs of implants, salaries of the staff at the theatre, intensive care, intermediate postoperative care, regular ward costs, and costs of re-operations (Table 1).

Surgery was usually performed using either a hybrid construct with an average of 5 pedicle screws, 8 hooks, and 5 to 6 sublaminar wires or an all pedicle-screw construct using 15 to 17 pedicle screws. Two surgeons usually performed the surgery using an estimated average time of 180 minutes. One anesthesiologist, one anesthesiology nurse and two scrub nurses assisted them working on average for 300 minutes. After surgery, patients stayed in hospital for an average of 10 days. No braces were used postoperatively. During the first postoperative year, patients had two follow-up consultations. In addition, costs of radiological examinations, outpatient visits for follow-ups, transportation, and costs of complications and re-operations during the first year were measured.

With the public universal healthcare system in Norway, there are no hospital fees for parents when children are braced or surgically treated. Cost per hour for different health professionals was estimated by adding social costs of employment (pension, insurance, sick-leave, and training) and overhead to the salary (inclusive income tax). The salary and social costs for hospital staff were estimated using the mean salary at the Oslo University Hospital and the estimates of the overhead costs were based on data from the Norwegian Central Bureau of Statistics [27]. Salary and social costs of public health nurses were based on data from the Norwegian Nurses organization, and local community administrations.

Currency, price date and conversion

All prices and costs were converted from 2006 to 2012NOK (Norwegian kroner) by using an inflation rate of 3.21% per year based on the yearly rate of change of one unit value within the Diagnosis –Related Group System (DRG) in Norway. The exchange rate used was 8 NOK =1 € (Euro).

Statistical analysis

Values are given as numbers, percentages, means and mean differences. Results are presented with a 95% credibility interval (CrI), which show the 2.5th and 97.5th percentile of the outcome distribution. The uncertainty of input variables was assessed by one-way and multi-way sensitivity analyses. Parametric uncertainty was analyzed by probabilistic sensitivity analysis (PSA), where all uncertainties in the relevant parameters were accounted for simultaneously [22,28]. The PSA was used to analyse the distribution of incremental cost estimations in all scenarios (100000 interactions) and to estimate the CrI for total incremental costs, which forms the basis for the Tornado diagram in Figure 1. In the PSA, we used gamma distributions for estimation of unit costs, beta distributions for the number of hours used and their probabilities. Poisson distributions were used for the number of children treated.
The screening study was approved by the Regional Ethical Committee for Medical Research in Norway.

Results

Cost estimations

For all the relevant scenarios, the total estimated costs were € 8.4 (95% CrI 6.6 to 10.6) per child screened, € 10350 (8690 to 12180) per patient braced, and € 45880 (38040 to 55400) per surgery (re-operations included). The average time used to screen a child was 9 minutes (Table 1).

Incremental costs and outcomes

The incremental cost per child in a non-screening scenario of 90% treatment rate compared with screening was € 13.3 (1 to 27). The probability of the incremental cost being positive was 99%. In the 80% treatment rate non-screening scenario, incremental cost was € 5.5 (−6 to 18) with the probability of the incremental cost being positive was 82%. When comparing non-screening scenarios to screening for girls only: the incremental cost was € 11.3 (2 to 22) for the 80% treatment rate scenario and € 4.3 (−4 to 14) for the 70% treatment rate scenario. The probability of the incremental cost being positive was 99% and 82%, respectively. The incremental cost per child in the non-screening Norwegian scenario compared with screening was € 0.1 (−14 to 16), and the probability of the costs being positive was 50% (Table 2).
<table>
<thead>
<tr>
<th></th>
<th>Screening boys and girls</th>
<th>Screening girls only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cost per child</td>
<td>Incremental cost per child</td>
</tr>
<tr>
<td>Screening</td>
<td>57.0 (49 to 66)</td>
<td>-</td>
</tr>
<tr>
<td>Non-screening Norway</td>
<td>57.1 (44 to 73)</td>
<td>0.1 (−14 to 16)</td>
</tr>
<tr>
<td>Non-screening 90%</td>
<td>70.3 (59 to 84)</td>
<td>13.3 (1 to 27)</td>
</tr>
<tr>
<td>treatment rate of Lee et al.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non- screening 80%</td>
<td>62.5 (52 to 75)</td>
<td>5.5 (−6 to 18)</td>
</tr>
<tr>
<td>treatment rate of Lee et al.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non- screening 70%</td>
<td>54.7 (46 to 66)</td>
<td>−2.3 (−13 to 9)</td>
</tr>
<tr>
<td>treatment rate of Lee et al.</td>
<td></td>
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</tbody>
</table>

The incremental cost was highest in the 90% treatment rate non-screening scenario with probability of being > 0 close to 100%. Incremental cost in non-screening Norway 2012 is close to the 70% treatment rate scenario. Incremental costs were higher in all non-screening scenarios when comparing screening of girls only than when comparing to screening of both boys and girls. The probabilities of incremental costs being >0 are also higher when comparing non-screening scenarios to screening of girls only than for both boys and girls combined.
Comparing the undiscounted cost per child in the non-screening scenario of 80% treatment rate, to screening, the cost of bracing per child of €26.0 (21 to 33) was dominating in the screening scenario, whilst the cost of surgery per child of €60.2 (48 to 75) was dominating in the non-screened scenario.

Incremental cost in the non-screening 90% treatment rate scenario varied from €-6.3 (−13 to 3) to €27.6(14 to 44) as the percentage of surgery increased from 30% to 80%. For the 80% treatment rate scenario with 30% surgery, and 70% bracing, incremental cost was €-11.0 (−19 to −3) favouring non-screening. With 80% surgery, and 20% bracing, incremental cost was €18.2 (6 to 33) favouring screening (Table 3).
<table>
<thead>
<tr>
<th>Ratios of brace / surgery in non-screening scenarios</th>
<th>20/80</th>
<th>30/70</th>
<th>40/60</th>
<th>50/50</th>
<th>60/40</th>
<th>70/30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment rates in non-screening scenarios compared to screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>37.0</td>
<td>29.7</td>
<td>22.4</td>
<td>15.1</td>
<td>7.8</td>
<td>-0.5</td>
</tr>
<tr>
<td>(22 to 55)</td>
<td>(16 to 45)</td>
<td>(10 to 36)</td>
<td>(4 to 27)</td>
<td>(−2 to 18)</td>
<td>(−8 to 9)</td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td>27.6</td>
<td>21.0</td>
<td>14.5</td>
<td>7.9</td>
<td>1.3</td>
<td>-5.3</td>
</tr>
<tr>
<td>(14 to 44)</td>
<td>(9 to 35)</td>
<td>(3 to 27)</td>
<td>(−2 to 19)</td>
<td>(−8 to 11)</td>
<td>(−13 to 3)</td>
<td></td>
</tr>
<tr>
<td>80%</td>
<td>18.2</td>
<td>12.4</td>
<td>6.5</td>
<td>0.7</td>
<td>-5.2</td>
<td>-11.0</td>
</tr>
<tr>
<td>(6 to 33)</td>
<td>(1 to 25)</td>
<td>(−4 to 18)</td>
<td>(−9 to 11)</td>
<td>(−14 to 4)</td>
<td>(−19 to −3)</td>
<td></td>
</tr>
<tr>
<td>70%</td>
<td>8.8</td>
<td>3.7</td>
<td>-1.4</td>
<td>-6.5</td>
<td>-11.6</td>
<td>-16.8</td>
</tr>
<tr>
<td>(−3 to 22)</td>
<td>(−7 to 15)</td>
<td>(−11 to 9)</td>
<td>(−15 to 3)</td>
<td>(−20 to −3)</td>
<td>(−24 to −9)</td>
<td></td>
</tr>
<tr>
<td>60%</td>
<td>-0.6</td>
<td>-5.0</td>
<td>-9.3</td>
<td>-13.7</td>
<td>-18.0</td>
<td>-22.5</td>
</tr>
<tr>
<td>(−11 to 11)</td>
<td>(−15 to 5)</td>
<td>(−18 to 0)</td>
<td>(−22 to −5)</td>
<td>(−26 to −10)</td>
<td>(−30 to −15)</td>
<td></td>
</tr>
</tbody>
</table>

Mean 95%CrI are given for non screening scenarios with treatment rates from 60% to 100% combined with different ratios of bracing to surgery from 20/80 to 70/30.

Non-screening is more expensive with higher treatment rates and higher surgical rates compared with screening. Non-screening is less expensive with lower treatment rates and higher bracing rates compared to screening.
**Characterizing uncertainty**

The expected incremental cost estimates are shown in Figure 2. In the non-screening scenario of 90% treatment rates, the probability of a positive incremental cost was close to 100%. Results comparing non-screening scenarios to screening in girls are shown in Figure 3. Uncertainty is also illustrated in a tornado diagram for the non-screening scenario of 80% treatment rate. The most important contributor to uncertainty was the percent braced, followed by the probability of being re-operated (Figure 1).

**Figure 2 Incremental cost estimations in four non screening scenarios compared to screening both boys and girls.**

**Figure 3 Incremental cost estimations in four non screening scenarios compared to screening of girls only.**

**Discussion**

Scoliosis screening programs are considered to be beneficial from a clinical point of view [19], but are criticized for high costs due to high referral and treatment rates [8,11,13]. In the present study we used data from a large longitudinal screening study, and detailed costing of all activities in performing the analyses. Results suggest that screening is cost saving, unless both treatment rates and surgical rates are very low in comparative non-screening scenarios. In agreement with previously published studies reporting that discontinuation of screening has led to late detection and high rates of surgery [15-17], the model applied in the present study indicates that costs increase in non-screening scenarios with high rates of surgery and lower rates of bracing.

The effectiveness of a screening program thus depends on the costs involved and the number of cases detected early that result in bracing and less surgery compared to a non-screening setting. In a recent clinical trial, bracing reduced the number of children with curve progression to the threshold of surgery [5].

The results of the present study show that, screening has a large potential of cost saving if only girls are screened. Selective screening of girls is most cost saving because they constitute about 90% of those treated for scoliosis. In Table 2, we showed that there is a high probability of cost saving when only girls are screened compared to non-screening scenarios with treatment rates widely ranging from 70% to 100% of those of screening.

Table 3 shows that in the extreme non-screening scenario where treatment rates are approaching those of screening, screening both boys and girls was not cost saving. Likewise in the extreme non-screening scenario where treatment rates were very low approaching 60% of those treated in screening, non-screening becomes cost saving. However, these scenarios are the least likely to occur. In the non-screening scenarios where treatment levels are 90-100% of those in screening, patients are probably younger at detection, and likely to be recommended bracing according to guidelines and the results of the recent RCT study on bracing [5]. This implies that the ratio of bracing/surgery is likely to be >1 and bracing will be the dominating treatment option. On the contrary, when treatment levels in non-screening scenarios are in the 60% to 70% range of that of screening, patients are likely to be older and
curves too large and not suitable for bracing [15], and surgery is most likely to be the dominating treatment option (i.e. ratio of brace to surgery likely to be <1).

In the Hong Kong study, about 15% of those detected by screening ended up having surgery compared to about 60% in non-screening Norway. Obviously, screening is not cost saving if the number treated in non-screening approximates that with screening and the surgical rate is 15%. However, this scenario is very unlikely to occur and was therefore not included in our analyses.

An interesting finding according to Table 3 is that screening both boys and girls tends to increase costs if the distribution of brace/surgery is 70/30 or 60/40 in a non-screening scenario. This scenario is also unlikely to occur. According to a previous Norwegian study, non-screening scenarios of 30/70 or 40/60 are more likely to occur [15].

Our findings are in agreement with a review [29] on cost effectiveness of screening that found screening to be cost effective in one study [30], and recommended screening only for high-risk groups such as girls at twelve years of age in order to reduce over-referrals and over-treatment. However, the most recent review was not able to conclude whether screening was cost effective or not [31]. None of the studies cited in these reviews, however, applied recommended health economic evaluation principles [32].

Simulations in the present study suggest that the economic gain of screening increases when screening leads to higher rates of bracing and reduced rates of surgery. In a previous study, we reported higher rates of bracing and reduced surgical rates during a period of screening compared to a period without [15]. Similar findings have been reported from the Netherlands, Sweden and USA [23,24,33]. Bracing has been shown to reduce progression of curves to the threshold of surgery. In the recently published RCT study on bracing, the success rate was >70% and about 90% in those with high compliance [5]. Similar results were observed at long-term in a large Norwegian cohort study [6]. The current evidence of efficacy of bracing in the short term and good results at long-term indicates that patients with AIS should be detected early to allow for bracing. In addition, bracing avoids the complications of surgery, keeps the spine mobile, and might have positive long term effects. These benefits should be considered when interpreting the results of the present study. There has however been a lack of enthusiasm for bracing in the past amongst care providers. This is presumably due to the absence of high level of evidence of efficacy on bracing, and concerns of negative psychological impact on the patients. The results from the recent RCT study [5] on bracing do not however support this view.

With the assumptions made in the current study, screening of both boys and girls would neither have increased nor decreased costs compared to the treatment of AIS in Norway in 2012 where the estimated treatment rate was 73% compared to screening in Hong Kong, and 58% had surgery. However, selective screening of girls only would have been cost saving in Norway; as shown in Table 2 above.

Studies in the past have reported varying costs of scoliosis screening, and costs of bringing cases detected on screening to treatment, depending on how costs are measured [30,34-39]. The cost of screening in the current study is comparable to similar programs in Europe where total costs were included [34-36]. The estimated cost was based on two screenings per child, and community nurses performed the screening in conjunction with a vaccine program. Transportation costs and salaries of health professionals would have increased if screening
had been performed in a different and isolated setting and not by community nurses. The estimated costs of bracing and surgery are comparable to those reported in the literature [40]. Many factors may influence the validity of our cost estimations. Treatment costs are likely to be underestimated in our study as bone grafts and intra-operative neuromonitoring were not used during surgeries, as compared with a study from the USA [40]. Our study perspective was limited to costs related only to expenses in an orthopedic department. We did not include costs related to primary health care, paramedics and alternative costs in relation to referred patients. In addition, we did not systematically register costs of patients’ out-of-pocket expenses like transportation in relation to adjuvant treatment for scoliosis. Though physical therapy and counseling are not routinely offered to AIS patients in Norway, it is estimated that 1/3 of the patients use physiotherapy whilst under brace treatment or postoperatively [6,41].

Several input parameters contribute to uncertainties in our analysis. The cost of regular wards in surgical treatment was difficult to estimate accurately despite considerable effort. AIS patients undergoing surgical treatment require increased nursing resources compared to caring for ordinary pediatric patients at the orthopedic ward. The main analyses may also underestimate the cost of surgery.

The probabilities of positive incremental costs varied widely in the current study. There was however higher certainty in the incremental cost estimates when comparing non-screening scenarios to screening of girls only, as opposed to boys and girls combined. More research is warranted in order to reduce the uncertainties in future health economic evaluations of scoliosis treatment.

**Limitations and strengths**

Ideally, randomised studies or controlled prospective studies are needed to compare outcome in scoliosis treatment detected through screening or otherwise. However since the prevalence of scoliosis is low, it is difficult to include an adequate study sample even within a large country or internationally. Clinical trials including utility comparisons of bracing and surgery in both short and long terms are lacking. Utility scores may differ in shorter periods during treatment, for example by wearing a rigid brace, or postoperatively.

We assumed similar prevalence and natural history of AIS in Hong Kong and Norway in performing the analysis. Studies, however, show regional variations in the prevalence of AIS, like higher prevalence in girls but not boys in higher latitudes than in lower latitudes [42]. However, those differences could be linked to environmental factors such as the difference in the onset of menses in different geographic locations [43], and different cultures and not related to genetics. It is also likely that mechanisms of referral may be very different in the two settings, and in various countries, due to healthcare systems structures and barriers to access. The presentation of AIS has also been reported to be linked to socioeconomic status and race [44]. A recent study however found equal prevalence of AIS in 12-year old children in Malaysia and Norway [20,45].

The main strength of the present work is the application of current recommended standards for reporting health economic evaluations in conducting the study [32]. This gives more transparency and complete reporting of methods and findings which will facilitate interpretation and comparison of similar studies. We also used data from the largest reported longitudinal study of screening cohorts [21]. Analyses were performed to assess the
uncertainties. The percentage detected for bracing, costs of surgery, and re-operations were the major contributors to uncertainty. More accurate estimates of these factors could improve the reliability and applicability of future analyses.

Generalisability

The model approach used in the current study could be employed worldwide with local cost estimate variations. Our results provide the missing economic evidence for health policy makers and healthcare providers to consider reintroduction of scoliosis screening.

In providing health services, policy makers are concerned about costs in view of limited healthcare resources, whereas patients and their families value the best treatment option available independent of costs. At present, there is a gap in the knowledge of the patient’s preference in choosing treatment options. In a recently published trial, bracing was preferred to observation by patients and their families leading to the interruption of the trial and subsequently continued as a preference study [5].

Conclusions

Early detection through screening leading to bracing and fewer surgeries may save costs. Selective screening of high-risk groups like girls should probably be preferred. Screening is not likely to increase costs unless both treatment and surgical rates are very low in comparable settings where screening is not performed.

Consent

Written informed consent was obtained from all patients for the publication of this report and any accompanying images.

Competing interests

None of the authors have received benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this manuscript e.g., royalties, stocks, stock options, decision making positions.

Authors’ contributions

RDA, PJ and JIB designed the study. RDA, HS, and JIB were involved in the collection of the data for the manuscript. PJ and SN collected data and performed the health economic analysis. PJ built and ran the simulation model for the study. RDA, PJ, HS, SN and JIB took part in the analysis and the interpretation of results, drafting and critical review of the manuscript. All authors have given final approval to the version to be published.
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45. Khindarli T: Prevalence of Scoliosis in Primary School Students in Marang District, Terengganu. www.researchgate.net. 2014. Ref Type: Electronic Citation.
Percent braced as first treatment
Probability of re-operation
No. operated among screened
Cost per day regular ward
Days at regular ward
Minutes per screened
No. braced among screened
Examiner cost per hour
Implant cost per operation

Change in incremental cost (euro)
Additional files provided with this submission:

Additional file 1. The mathematical model (516k)
http://www.scoliosisjournal.com/content-supplementary/s13013-014-0021-8-s1.pdf