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Medical Policy Manual

Topic: DNA-Based Testing for Adolescent Idiopathic Scoliosis

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Section: Genetic Testing

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Adolescent idiopathic scoliosis (AIS) is a disease of unknown etiology that causes mild to severe spinal deformity in approximately 1% to 3% of adolescents.[1] Diagnosis of AIS is established by radiologic observation in adolescents (age 10 years until the age of skeletal maturity) of a lateral spine curvature of 10 degrees or more, as measured using the Cobb angle (spinal curve).[2] Curvature is considered mild (less than 25º), moderate (25º to 40º), or severe (more than 40º) in an individual still growing. While there is controversy about the value of both screening and treatment, once diagnosed, patients must be monitored over several years, usually with serial radiographs for curve progression. If the curve progresses, spinal bracing is the generally accepted first-line treatment. If the curve progresses in spite of bracing, spinal fusion may be recommended.

Classification tables for likelihood of progressive disease have been constructed to assist in managing patients, but these have not proven to be highly reliable and the impact of their use on outcomes is unknown.[3,4] A recent testing algorithm has been developed to identify patients unlikely to exhibit severe progression in curvature versus those at considerable risk for severe progression.[5] The ScoliScore™ AIS (adolescent idiopathic scoliosis) prognostic DNA-based test uses an algorithm incorporating results from 53 SNP genetic markers with a Cobb score to produce a general risk score. A suggested use of this test to predict the likelihood of spinal curve progression is to triage patients who would benefit from individualized treatment regimens based upon their given risk score. The test

is intended for Caucasian patients with a primary diagnosis of AIS between the ages of 9 and 13 years with a mild scoliotic curve (defined as <25º).

Regulatory Status

The ScoliScore™ AIS (adolescent idiopathic scoliosis) prognostic DNA-based test (Axial Biotech) has not been approved or cleared by the U.S Food and Drug Administration (FDA) but is being offered as a laboratory-developed test. The laboratory performing this test is accredited by the Centers for Medicare and Medicaid (CMS) under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).

MEDICAL POLICY CRITERIA

DNA-based prognostic testing for adolescent idiopathic scoliosis is considered **investigational**.

SCIENTIFIC EVIDENCE

Validation of the clinical use of any genetic test focuses on 3 main principles:

1. The analytic validity of the test, which refers to the technical accuracy of the test in detecting a mutation that is present or in excluding a mutation that is absent;
2. The clinical validity of the test, which refers to the diagnostic performance of the test (sensitivity, specificity, positive and negative predictive values) in detecting clinical disease; and
3. The clinical utility of the test, i.e., how the results of the diagnostic test will be used to change management of the patient and whether these changes in management lead to clinically important improvements in health outcomes.

Literature Appraisal

Randomized Controlled Trials (RCTs)

There are no published randomized controlled trials which examine the analytic validity, clinical validity, or clinical utility of prognostic DNA testing algorithms to predict spinal curve progression.

Nonrandomized Trials

Current evidence is limited to the following three retrospective validation studies:

- In 2010, Ward et al. published a company-sponsored clinical validation study of the ScoliScore™ AIS test.[2] The genome-wide association study (GWAS) was used to develop a 1 to 200 scoring system. An analysis of patients with scores of 190 or greater was performed to determine risk for developing severe curves. Cases were preselected by curvature severity (mild, moderate, or severe) and assigned into three cohorts identified as:

    1. a screening cohort of white females (n=176);
    2. a spinal surgery practice cohort of white females (n=133); and
    3. a male cohort (n=163).

Inclusion/exclusion criteria were cited as being used, but not explicitly provided, although a component of cohort development was matching of prevalence of disease by severity according to that expected from review of the literature or survey of clinical practices. There is minimal information provided about the demographics of patients assigned to each cohort.

The predictive value of a negative test (defined as identification of patients without severe curve progression) for the screening cohort, the spinal surgery practice cohort, and the male cohort was 100% (95% confidence intervals [CI]: 98.6 to100%), 99% (95% CI: 95.4 to 99.6%), and 97% (95% CI: 93.3 to 99%), respectively. No analysis was performed to demonstrate whether this was a statistically significant improvement in prediction of negatives, given the low initial prevalence of patients expected to exhibit severe progression. Although there is a description of positive predictive value in patients exhibiting high-risk score values, recruitment of patients into this category appears to be derived from patients pooled from different and undescribed sources, making interpretation difficult.

- A subsequent GWAS evaluation of 327,000 SNPs in 419 families with AIS failed to duplicate the associations reported in the study by Ward et al.[6]

- In 2013, Ogura and colleagues evaluated the 53 SNPs used in the ScoliScore test with curve progression in 2117 Japanese patients with AIS. No association with curve progression was identified.[7]

- In 2012, Roye et al. reported results in 91 patients evaluated with the ScoliScore.[8] Although they noted a positive correlation between Cobb angle and ScoliScore results (r-.581, p<0.001), ScoliScore appeared to be providing information very different from that observed using standard risk score with a marked increase in low-risk patients and decrease in high-risk patients. However, no clinical endpoints were examined in association with classification results, and so the interpretation of results observed remains unclear.

Clinical Practice Guidelines

There are no evidence-based clinical practice guidelines which recommend DNA-based testing to predict the risk of progression of scoliosis in patients with AIS.

Summary

The current evidence on DNA-based testing for adolescent idiopathic scoliosis (AIS) is limited to preliminary clinical validity studies. It is not clear if the increase in predictive accuracy provided by testing is statistically or clinically meaningful. There is little evidence on the analytic performance of this test, nor is there any direct evidence demonstrating that use of this test results in improve health care outcomes. Furthermore, the value of early identification and intervention(s) for individuals at risk for progression to severe spinal curvature is unclear. As a result, DNA-based testing for adolescent idiopathic scoliosis is considered investigational. Further research is needed on both clinical validity and clinical utility.

REFERENCES

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8. Roye, BD, Wright, ML, Williams, BA, et al. Does ScoliScore Provide More Information Than Traditional Clinical Estimates Of Curve Progression? *Spine (Phila Pa 1976)*. 2012 May 18. PMID: 22614798
9. BlueCross BlueShield Association Medical Policy Reference Manual "DNA-Based Testing for Adolescent Idiopathic Scoliosis." 2.04.74

CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score
	81599	Unlisted multianalyte assay with algorithmic analysis
HCPCS	None	