Short Stature and Functional Impairment

A Systematic Review

Patricia G. Wheeler, MD; Karen Bresnahan, MD; Barbara A. Shephard, MD; Joseph Lau, MD; Ethan M. Balk, MD, MPH

Objective: To review the available evidence on the association between primary short stature and intellectual and physical dysfunction among children.

Methods: Systematic searches were performed through October 2001 of English-language studies of children with short stature and functional limitations. Included studies evaluated children with isolated short stature, constitutional growth delay, growth hormone deficiency, or multiple hormone deficiency. Evaluated outcomes included intelligence, academic achievement, visual-motor skills, psychomotor development, and behavior problems.

Results: Eleven studies evaluated academic achievement, and 22 evaluated intelligence. No substantial deviation from normal was seen among short children, but many studies found that children with short stature had significantly lower intelligence and academic achievement scores than controls. Three studies found significant visual-motor skill reduction among short children. One study of psychomotor development found a delay in meeting early developmental landmarks among children with Russell-Silver syndrome. Five studies evaluating teacher-rated behavior found that short children had no more behavior problems than controls.

Conclusions: While, on average, children with short stature score lower than their peers on functional tests, few short children scored outside the normal range. Furthermore, there is no evidence to explain the cause of any deficits, and limited data suggest that treatment of short stature does not improve children's functional status. Nevertheless, treatment may be warranted in children with severe short stature to alleviate restrictions on activities of daily living. Further research focusing on physical limitations due to short stature is needed to address these issues.


Short stature is a common finding in the general population, with between 0.1% and 2.5% of the population affected, based on height 2 to 3 SDs below the population mean. The causes of short stature are multiple and are associated with a wide range of clinical, emotional, and practical effects in children. At one extreme, a variety of skeletal dysplasias can result in extreme short stature that is occasionally associated with early death and severe musculoskeletal abnormalities. Short stature may also be associated with, and may possibly be a marker for, severe medical diseases, such as diabetes, celiac disease, or chronic kidney disease. More commonly, short children have isolated or idiopathic short stature (ISS) either because of a genetic tendency toward short stature (familial short stature) or a constitutional growth delay (CGD) caused by delayed onset of puberty.

A small number of children with short stature have abnormalities in the growth hormone (GH) axis. Related endocrine abnormalities, such as hypothyroidism and Cushing disease, may also lead to short stature. In addition, a variety of genetic disorders, including chromosomal disorders, metabolic disorders, and single gene disorders, can result in short stature.1

We summarize the scientific evidence about the association between short stature in children due to specific conditions and functional impairment. We focused on short stature due either to ISS or to a medically determinable impairment, excluding skeletal dysplasias and conditions in which short stature is a small aspect of a larger problem. We will henceforth refer to this definition of short stature as primary short stature, to emphasize our aim of separating out the association of short stature alone with potential intellectual or physical dysfunction. We did not attempt to address the

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cause of any functional impairment in these children. This analysis was part of a larger systematic review sponsored by the Social Security Administration to assist with updating disability definitions. In addition to the evidence summarized here, the review included analyses of children with Russell-Silver syndrome and Turner syndrome and examined both functional impairment among children with skeletal dysplasias and the relationship between height velocity and severity of common chronic diseases in children.²

METHODS

The population of interest included boys and girls with primary short stature, aged 17 years or younger, from all racial/ethnic and socioeconomic groups.

CAUSES OF SHORT STATURE

To best elucidate any association between short stature and functional impairment, we focused on conditions in which ISS was reported to be the primary problem. This avoided potential confounders with regard to the cause of functional impairment. The primary causes of short stature considered were ISS, CGD, GH deficiency (GHD), and multiple hormone deficiency (MHD). We excluded studies that specifically focused on children with Russell-Silver syndrome or Turner syndrome to remove potential confounding factors, such as clinical heterogeneity within Russell-Silver syndrome, and the mosaic chromosome abnormalities, which may be associated with increased intellectual impairment in Turner syndrome. Down syndrome and other syndromes that may result in short stature as part of the underlying disorder were not included because children with these conditions are considered to be disabled based on their primary diagnosis alone, and the associated physical and intellectual disabilities are well understood.³ Except for the definition of short stature, no predetermined definitions for each of the causes of short stature were used. Instead, definitions used by study authors were generally accepted.

Studies of children with ISS and CGD were included if affected individuals had heights less than the fifth percentile and no determining cause had been found other than delay in skeletal maturity. Children with GHD have partial or complete absence of GH. Those with MHD have absence of 1 or more other pituitary hormones in addition to GH.

FUNCTIONAL IMPAIRMENT

According to the Social Security Administration a child younger than 18 years will be considered disabled if he or she has a medically determinable physical or mental impairment or combination of impairments that causes marked and severe functional limitations and that can be expected to cause death, or that has lasted or can be expected to last for a continuous period of at least 12 months.³ However, the Social Security Administration’s definition of disability is an administrative one, which is not commonly used by clinicians or researchers. In general, disability is defined differently by different researchers for different diseases. Furthermore, studies of children with short stature frequently focus on differences of ability rather than on disability per se. Evaluation of the association between short stature and functional impairment was complicated by the difficulty in distinguishing whether an impairment was due directly to short stature or to the underlying medical condition. Choosing to concentrate on conditions such as GHD where the primary problem is short stature, helped to minimize the effects of the underlying medical condition.

Based on the Social Security Administration’s definitions of disability and on the abilities evaluated by researchers, we reviewed the following outcomes: (1) intelligence, (2) academic achievement, (3) visual-motor skills, and (4) teacher-rated behavior problems. Various other possible outcomes were not evaluated because of limited clinical relevance, lack of availability of studies, or subjectivity of assessment. These included social functioning, psychomotor development, and parent-rated behavior problems, among others.

SEARCH STRATEGY AND STUDY SELECTION

We conducted a systematic search of the English language literature on short stature and functional impairment in MEDLINE from 1966 through October 2001. Supplemental searches were performed in ERIC, PsycInfo, Healthstar, and Embase. Additional studies were identified from reference lists of review and primary articles, and from domain experts. The search strategy retrieved articles with the following key words or text words: developmental bone diseases, growth disorders, body height, short stature, disability, limitation, handicap, and impairment. Abstracts and, subsequently, potentially relevant full articles were screened by us.

We included studies that reported original data on the association between primary short stature in children younger than 18 years and the outcomes of interest. We excluded studies with fewer than 10 children with one of the causes of short stature listed above, case reports, review articles, commentaries, letters, and abstracts. Studies could be cross-sectional or longitudinal, prospective or retrospective, and comparative (with unaffected children) or not.

DATA EXTRACTION

Data extraction forms were developed by physician methodologists and pediatrician domain experts. Forms included study setting, demographics, study eligibility criteria, study size, study design, funding source, relevant measurements and outcomes evaluated, statistical methods, results, and potential biases. Study quality was assessed on a 3-point scale, based on study methods and reporting.² Pediatricians with domain expertise in genomics, growth disorders, and functional impairment performed data extraction. All extracted data were reviewed by methodologists. No statistical analyses were performed.

RESULTS

A total of 13 537 citations were reviewed. For the analysis of functional impairment among children with primary short stature, 20 articles provided unique data from 19 studies.³⁻²⁴ Five other articles reported duplicate data.²⁵⁻²⁸ An additional 89 studies were reviewed for other topics. All studies reported a level of intellectual or physical function among children with short stature. No study analyzed the correlation between height and function specifically among short children. Complete evidence tables that include all relevant extracted data can be found at http://www.ahrq.gov/clinic/epcsums/shortsum.htm.²

INTELLIGENCE

Seventeen studies evaluated IQ in approximately 900 children with short stature as a result of ISS, CGD, GHD, or MHD (Table 1).³⁻¹⁰,¹²,¹³,¹⁸,¹⁹,²² Overall, children with short stature tended to have IQs within 1 SD of the population norm. All but 3 studies evaluated children who had previously been referred to specialty clinics; however, the ranges of
mean IQs were similar in both referred and nonreferred children.

### ISS or CGD

Nine studies evaluated intelligence among children with ISS or CGD. All but 2 found that short children scored at or above the population means on IQ tests. An analysis of the National Health Examination Survey from the 1960s by Wilson et al.\(^2\) found that children with heights less than the fifth percentile had a mean IQ lower than 100, which was significantly lower than controls. This study also found a significant correlation between normalized height and IQ scores across children of all heights, but notably, that the change in children's height percentiles did not correlate with change in IQ during a 2- to 5-year period. Skuse et al.\(^1\) who also included children with Russell-Silver syndrome, found that these children had a mean IQ lower than 100, but not significantly different from average-height controls. Two other studies found that short children had significantly lower, although still normal, IQs than average-height controls.\(^5,6\) An additional study reported that 6 times as many short children as controls reached IQs greater than 90.\(^1\) Several studies found that short children with ISS and with GHD had mean IQs lower than 90.\(^6,7\)

### Table 1. Mean IQ of Children With Short Stature\(^a\)

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Sample</th>
<th>Mean Height SDS</th>
<th>Mean IQ(^b)</th>
<th>Sample Source</th>
<th>Bias(^c)</th>
<th>Quality(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Downie et al.(^4) 1997</td>
<td>106 (119)</td>
<td>&lt;−2</td>
<td>103 (109)</td>
<td>Population</td>
<td>...</td>
<td>A</td>
</tr>
<tr>
<td>Wilson et al.(^2) 1986</td>
<td>−335 (−6430)(^*)</td>
<td>&lt;−1.6</td>
<td>92 (97-105)(^*)</td>
<td>Population</td>
<td>...</td>
<td>B</td>
</tr>
<tr>
<td>Rovet et al.(^*) 1986</td>
<td>25</td>
<td>&lt;−2</td>
<td>101</td>
<td>Clinic</td>
<td>No stat</td>
<td>B</td>
</tr>
<tr>
<td>Siegel et al.(^4) 1994</td>
<td>90 (90)</td>
<td>−2.8</td>
<td>107; 18%&lt;90 (^*)</td>
<td>...</td>
<td>...</td>
<td>C</td>
</tr>
<tr>
<td>(116; 3%&lt;90)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kranzler et al.(^5) 2000</td>
<td>34 (29)</td>
<td>−1.7</td>
<td>105 (112)</td>
<td>Population</td>
<td>&gt;IQ</td>
<td>C</td>
</tr>
<tr>
<td>Gordon et al.(^9) 1984</td>
<td>24 (23)</td>
<td>&lt;−1.6</td>
<td>108 (110)</td>
<td>Clinic</td>
<td>Matched</td>
<td>C</td>
</tr>
<tr>
<td>Skuse et al.(^4) 1994</td>
<td>22 (22)</td>
<td>−2.5</td>
<td>96 (105)</td>
<td>Clinic</td>
<td>&gt;IQ</td>
<td>C</td>
</tr>
<tr>
<td>Holmes et al.(^9) 1985</td>
<td>21</td>
<td>&lt;−2</td>
<td>...</td>
<td>Clinic</td>
<td>No stat</td>
<td>C</td>
</tr>
<tr>
<td>McCauley et al.(^4) 1987</td>
<td>16</td>
<td>−4.5</td>
<td>...</td>
<td>Clinic</td>
<td>&gt;IQ No stat</td>
<td>C</td>
</tr>
<tr>
<td>Siegel et al.(^4) 1994</td>
<td>42</td>
<td>&lt;−2</td>
<td>...</td>
<td>Clinic</td>
<td>&gt;IQ</td>
<td>B</td>
</tr>
<tr>
<td>Frisch et al.(^9) 1990</td>
<td>23</td>
<td>−2.5</td>
<td>115</td>
<td>Clinic</td>
<td>...</td>
<td>B</td>
</tr>
<tr>
<td>Meyer-Bahlburg et al.(^17), 1978</td>
<td>13 w/GHD(^8)</td>
<td>−3.7</td>
<td>101</td>
<td>...</td>
<td>...</td>
<td>B</td>
</tr>
<tr>
<td>Abbott et al.(^3) 1982</td>
<td>9 w/MHD(^8)</td>
<td>−4.0</td>
<td>102</td>
<td>No stat</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Siegel et al.(^4) 1994</td>
<td>87 (90)</td>
<td>−2.7</td>
<td>110; 9%&lt;90 (^*)</td>
<td>...</td>
<td>...</td>
<td>C</td>
</tr>
<tr>
<td>(116; 3%&lt;90)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holmes et al.(^3) 1985</td>
<td>17</td>
<td>&lt;−2</td>
<td>...</td>
<td>Clinic</td>
<td>...</td>
<td>C</td>
</tr>
<tr>
<td>Siegel et al.(^16) 1998</td>
<td>25 (25)</td>
<td>−3.1</td>
<td>105 (109)</td>
<td>...</td>
<td>...</td>
<td>A</td>
</tr>
<tr>
<td>Steinhausen and Stahnke,(^18) 1976</td>
<td>32</td>
<td>−3.7</td>
<td>103</td>
<td>Clinic</td>
<td>No stat</td>
<td>B</td>
</tr>
<tr>
<td>Pollitt and Money,(^17) 1984</td>
<td>13</td>
<td>−6.9</td>
<td>103</td>
<td>Clinic</td>
<td>...</td>
<td>B</td>
</tr>
<tr>
<td>Young-Hyman,(^24) 1986</td>
<td>27</td>
<td>&lt;−2</td>
<td>110</td>
<td>Clinic</td>
<td>&gt;IQ</td>
<td>C</td>
</tr>
</tbody>
</table>

Abbreviations: CGD, constitutional growth delay; GHD, growth hormone deficiency; ISS, isolated short stature; MHD, multiple hormone deficiency; SDS, standard deviation score (standard deviations from population mean height); ellipses, no data.

\(^a\)Parentheses indicate values for the control group.

\(^b\)Mean scores in bold were significantly different from controls or population norms.

\(^c\)Studies noted with “Matched” used controls that were matched for IQ among other factors.

\(^d\)A = good quality, least bias; B = fair quality, susceptible to some bias; and C = poor quality, substantial bias likely.

\(^*\)Significant correlation between height and IQ. IQ value was reported graphically.

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### Table 2. Mean Academic Achievement Scores of Children With Short Staturea

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Sample</th>
<th>Mean Height SDS</th>
<th>Test</th>
<th>Math</th>
<th>Reading</th>
<th>Comprehension</th>
<th>Spelling</th>
<th>Sample Source</th>
<th>Bias</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Downie et al,1997</td>
<td>106 (119)</td>
<td>−2</td>
<td>BAS1</td>
<td>40 (44)</td>
<td>44 (48)</td>
<td>...</td>
<td>...</td>
<td>Population</td>
<td>...</td>
<td>A</td>
</tr>
<tr>
<td>Wilson et al,1986</td>
<td>335 (-640)</td>
<td>−1.6</td>
<td>WRAT</td>
<td>91 (96-106)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>Population</td>
<td>...</td>
<td>B</td>
</tr>
<tr>
<td>Stathis et al,1989</td>
<td>113 (3178)</td>
<td>−2</td>
<td>PPVT-R</td>
<td>92 (97)</td>
<td>...</td>
<td>98 (103)</td>
<td>98 (103)</td>
<td>Clinic &gt;IQ</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Siegel et al,1994</td>
<td>90 (90)</td>
<td>−2.8</td>
<td>WRAT</td>
<td>96.22%&lt; 80%</td>
<td>102 (105)</td>
<td>...</td>
<td>...</td>
<td>Population &gt;IQ</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Kranzler et al,2000</td>
<td>34 (29)</td>
<td>−1.7</td>
<td>KTEA</td>
<td>105 (121)</td>
<td>106 (115)</td>
<td>107 (114)</td>
<td>104 (101)</td>
<td>Population &gt;IQ</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Gordon et al,1984</td>
<td>24 (23)</td>
<td>−1.6</td>
<td>PIAT</td>
<td>103 (103)</td>
<td>102 (102)</td>
<td>102 (103)</td>
<td>...</td>
<td>Clinic Matched</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Siegel and Hopwood,1986</td>
<td>42</td>
<td>−2</td>
<td>WRAT</td>
<td>85 (85)</td>
<td>96 (96)</td>
<td>...</td>
<td>...</td>
<td>Clinic &gt;IQ</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Abbott et al,1982</td>
<td>11</td>
<td>ND</td>
<td>WRAT</td>
<td>83 (83)</td>
<td>88 (88)</td>
<td>...</td>
<td>85 (85)</td>
<td>Clinic No stat</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Siegel et al,1994</td>
<td>87 (90)</td>
<td>−2.7</td>
<td>WRAT</td>
<td>99 (105)</td>
<td>103 (105)</td>
<td>98 (103)</td>
<td>98 (103)</td>
<td>Clinic &gt;IQ</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Siegel et al,1998</td>
<td>25 (25)</td>
<td>−3.1</td>
<td>WRAT</td>
<td>102 (99)</td>
<td>105 (98)</td>
<td>...</td>
<td>99 (100)</td>
<td>Clinic ...</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

**GHD or MHD**

Six studies evaluated intelligence among children with GHD or MHD referred from specialty clinics. Five of the studies found that short children with hormone deficiencies had, on average, IQs near or greater than the population mean, including one study by Frisch et al7 that found these children to have significantly higher IQs. However, of these, 1 study found that children with GHD had significantly lower than average IQs,15 and a second study by the same authors found that these children were 3 times more likely to have an IQ less than 90, similar to their analysis of children with ISS.15 A small study by Abbott et al,5 of children with a variety of hormone deficiencies, including panhypopituitarism and congenital goiter, found that these children had a mean IQ near 1 SD below population mean.

**Combined Causes of Short Stature**

Four studies evaluated intelligence among children with ISS, CGD, or GHD. All found that, overall, short children referred to specialty clinics had IQs that were near or above population norms.

**ACADEMIC ACHIEVEMENT**

Nine studies evaluated academic achievement in approximately 900 children with short stature as a result of ISS, CGD, GHD, or MHD.9,10,15-17,19,23 Academic achievement was assessed by a variety of standardized studies (Table 2). Overall, 4 of the studies found academic achievement scores at or above the population norm, while the other 5 studies reported scores up to 1 SD below the population norm. While the studies found small, if any, decrement in academic achievement, no definitive conclusions can be made because of the small numbers of studies, frequent exclusion of children with low IQs, and lack of statistical analyses.

**ISS or CGD**

Among 6 studies examining academic achievement in children with ISS or CGD, all short children scored either above population norms or within approximately 1 SD of normal scores. However, most studies found that children with short stature were more likely to have lower academic achievement scores than children of average height. Four studies found that short children had significantly lower...
scores on various tests of academic achievement than controls, although in one study, the mean score of the short children was greater than the population norm. In the other 3 studies, the differences in test scores between children of short and average height were reduced but not eliminated after controlling for factors such as socioeconomic background, parental education, and non–English speaking parent. As with their evaluation of IQ, Wilson et al found that change in height percentile did not correlate with change in academic achievement. An additional study by Siegel et al found that even though mean scores were similar, short children were significantly more likely to have a skill deficit in mathematics than average-height children. The final study found that short children had similar scores as average-height controls; however, this study is of limited value because the subjects were matched by IQ. Importantly, 3 of the studies explicitly excluded children with low IQs. Notably, all 4 population-based groups of short children had statistically significantly lower academic achievement scores than average-height children in contrast with 2 of 3 of the groups who were recruited from specialty clinics. However, Kranzler et al found no difference in academic achievement scores between children with short stature recruited from schools and those recruited from a pediatric endocrinology clinic.

### GHD or MHD

Three studies examined academic achievement among children with GHD or MHD. A fourth study included children with either ISS or GHD. One study of 11 children found achievement scores ranging from 83 to 88 (population average of 100), but found that lower achievement scores were associated with lower than average IQ, which was, in turn, related to socioeconomic level and physical dysfunctions in this population. Another study of 42 children with GHD or MHD found a similar decrease in academic achievement scores (particularly in mathematics), but reported no correlation with physical dysfunctions, such as a history of prematurity, anoxia, and seizures, in a subset of the children studied. All 3 studies found that test scores among short children were within 1 SD of population means. However, 2 studies explicitly excluded children with low IQs. In the study that included children with ISS, children scored at or above population means. All children were referred from specialty clinics.

### VISUAL-MOTOR SKILLS

Three studies evaluated 81 patients with ISS, GHD, or MHD for visual-motor skills with either the Developmental Test of Visual-Motor Integration or the Bender Visual-Motor Gestalt Test (Table 3). The tests are designed to estimate a child's level of perceptual-motor integration as evaluated by their ability to copy a series of designs. All 3 studies found that short children referred to specialty clinics were significantly more likely to have a reduction in visual-motor skills than historical controls.

Two studies of children with ISS reported a significant delay in visual-motor skills. The children were, on average, 2 to 3 years behind what is expected for their chronological age. The study that evaluated children with GHD or MHD also found a significant delay in visual-motor skills, with one quarter of the children having a score less than the 16th percentile. However, the degree of functional deficit or impairment in visual-motor skills was not reported.

### BEHAVIOR

Six articles reported data from 5 studies evaluating behavior in children with primary short stature by a variety of tests (Table 4). Only results of teacher-rated tests were evaluated to minimize biases related to reporting from family members. A total of 274 children were evaluated and compared with controls. Overall, children with short stature had a similar likelihood of behavioral problems as children with average height. No study described any functional limitations or disabilities based on behavior.

### Isolated Short Stature

Four studies evaluated behavior among children with ISS, one of which included several children with Russell-
extraversion scores were similar among short children either GHD or CGD and found that neuroticism and overall, few children had been tested by relatively objective methods (ie, teacher instead of parent rating). Overall, the evidence implies that short stature may be associated with increased behavioral problems; however, the latter did not meet statistical significance. The study, which included children with Russell-Silver syndrome, found that short children had significantly higher total behavior scores than controls, suggesting more abnormal behavior. The authors also reported that the short children had significantly more social and attention problems. Other tests of behavior did not suggest significant differences between children with short and average height. Across studies, there was no apparent difference in behavior between short children either referred or not referred to specialty clinics. Kranzler et al found no difference in teacher-rated behavior between referred and nonreferred short children.

**Combined Causes of Short Stature**

One study evaluated behavior among children with either GHD or CGD and found that neuroticism and extraversion scores were similar among short children and controls.20

Table 4. Teacher-Rated Behavior Problems Among Children With Short Stature

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Sample Height</th>
<th>Teacher-Rated Behavior Scores</th>
<th>Sample Source Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voss et al,21 1991</td>
<td>140 (140) &lt;−2.0 RBQ Disturbance: 29%&gt;9 Activity: 1.7 (1.1) Hyperactivity: 16%&gt;3</td>
<td>. . . . . . Population A</td>
<td></td>
</tr>
<tr>
<td>Voss and Mulligan,22 1994</td>
<td>132 (132) &lt;−2.0 RBQ Total: 6.2 (5.1) Activity: 1.7 (1.1) Hyperactive: 13.7 (11.9)</td>
<td>. . . . . . Population A</td>
<td></td>
</tr>
<tr>
<td>Gordon et al,4 1984</td>
<td>24 (23) −1.7 CBCL Total: 31.2 (27.5) Activity: 22.6 (24.1) Hyperactive: 13.7 (11.9)</td>
<td>. . . . . . Clinic B</td>
<td></td>
</tr>
<tr>
<td>Kranzler et al10 2000</td>
<td>34 (29) −1.7 BASC . . . . . . Externalizing: 46.9 (47.8) School Problems: 12.7 (12.1)</td>
<td>Population C</td>
<td></td>
</tr>
<tr>
<td>Skuse et al,18 1994</td>
<td>27 (29) −2.7 BASC Total: 49 (42) Internalization: NS</td>
<td>. . . . . . Clinic C</td>
<td></td>
</tr>
</tbody>
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**COMMENT**

This systematic review evaluated functional limitations in children with primary short stature not due to skeletal dysplasias. Most reports found that children with short stature have mean test scores within the range of normal for intelligence, academic achievement, and behavior (ie, within 1 SD of the mean). However, among the studies that directly compared short children with average-height controls—who were otherwise similar to the short children—most found that short children had significantly lower academic achievement test scores or a greater likelihood of low scores than controls. Similar results were found in a number of studies that evaluated intelligence. Substantial deficits were found in the visual-motor skills of children with ISS or hormone deficiency, although conclusions are limited due to small sample sizes. In most studies evaluating behavior, there were no significant differences between short children and controls. There was little uniformity, however, in how behavior problems among short children were measured; overall, few children had been tested by relatively objective methods (ie, teacher instead of parent rating). Therefore, the evidence implies that short stature may be asso-

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An association between short stature and functional impairment (such as decreased intelligence, poor academic achievement, and behavior problems) has long been postulated, and a variety of studies have looked for such an association. The specific functional impairments evaluated as well as the extent and cause of the short stature have been varied; thus, no consensus has arisen on the connection, if any, between short stature and functional impairments. This systematic review summarizes the state of the evidence regarding the association of primary short stature and functional impairments. Studies found that most children with primary short stature scored within the normal range of functional tests; however, within studies, short stature was often associated with decreased intelligence, academic achievement, and visual-motor skills. Importantly, there is no evidence regarding whether treatment of short stature improves function.

What This Study Adds

An association between short stature and functional impairment (such as decreased intelligence, poor academic achievement, and behavior problems) has long been postulated, and a variety of studies have looked for such an association. The specific functional impairments evaluated as well as the extent and cause of the short stature have been varied; thus, no consensus has arisen on the connection, if any, between short stature and functional impairments. This systematic review summarizes the state of the evidence regarding the association of primary short stature and functional impairments. Studies found that most children with primary short stature scored within the normal range of functional tests; however, within studies, short stature was often associated with decreased intelligence, academic achievement, and visual-motor skills. Importantly, there is no evidence regarding whether treatment of short stature improves function.

The applicability of many of the studies that evaluated IQ and visual-motor skill to short children who are not being followed in endocrinology or growth clinics may be somewhat limited since few studies included non-referred children. However, no differences in IQ were seen across studies, and one study found no difference in IQ, academic achievement, or teacher-rated behavior between short children recruited from a school and those recruited from an endocrinology clinic. It was more common that academic achievement scores were significantly lower in short children compared with controls in population-based studies than in clinic-based studies, possibly speaking to motivational differences among referred and nonreferred children and families.

The small number of studies and small sample sizes of most studies limit our conclusions. In addition, many of the studies evaluating intellectual function either implicitly or explicitly excluded children with very low IQs. Therefore, the true prevalence of intellectual impairment among children with primary short stature cannot be estimated. Even in the biased sample of children evaluated, the prevalence of abnormal test scores was rarely reported. Only 2 studies reported the frequency of abnormal test results; the remainder reported only average test scores, although a few comment that the range of test scores was similar for short and average-height children. Furthermore, none of the studies examined whether short stature is the cause of the reduced scores for academic achievement and intelligence.

One explanation for poorer test scores for intelligence and academic achievement in children with short stature might be an underlying condition that has caused both the short stature and cognitive impairment. It is noteworthy that of 1074 genetic syndromes with short stature as a feature listed in a major genetics database, POSSUM, two thirds are associated with mental retardation.30 Thus, it is possible that an underlying genetic abnormality may be responsible for an increased risk for children with short stature to have decreased intelligence and academic achievement. Similarly, nongenetic causes, such as chronic disease, may lead to the same combination of problems. It should be noted that most of the studies reviewed excluded children with obvious genetic conditions or chronic disease, but such problems may be very subtle and not readily identifiable to the clinician.

Importantly, studies for the most part do not address many specific questions that are likely to be of interest to physicians, such as the association between short stature and mental retardation, or outcomes that are likely to be of interest to children and their families. In particular, children who are more than about 4 to 5 SDs below the mean for height may potentially face numerous physical restrictions (eg, inability to use school bathrooms or reach elevator buttons). However, such limitations have not been reported in clinical studies. Instead, the primary purpose of most studies was to compare the average function of children with short stature with those with average height. Even among the functional abilities evaluated, very few studies attempted to estimate the prevalence of any actual impairment or disability among short children. The few that did tended to suffer either from biases due to eligibility criteria or due to poor, incomplete reporting of methods and results.

Future studies should focus on functional deficits instead of solely on functional level. Studies should report and analyze the prevalence of limitations rather than report only comparisons of mean scores. It is not clear that more studies of intellectual function are needed. More helpful would be studies that look at physical limitations due to height per se, such as difficulties in climbing stairs. In addition, to improve the clarity and value of findings, and to reduce bias, studies should focus on specific causes of short stature, ensure that subjects are not excluded based on outcomes of interest, such as intelligence, and should be as broad-based as possible to avoid biases due to evaluating only children referred to a clinic. The potentially confounding effect of conditions that can result in both short stature and dysfunction needs to be accounted for clearly.

The information detailed in this report has important clinical ramifications. While many of the studies found that children with short stature were at greater risk to have test scores lower than their peers, most short children still had IQs, academic achievement, and behavior within the normal range. The reason for this discrepancy is not clear. Despite a large number of studies looking at intelligence, academic achievement, behavior, and other skills in short children, no study found a direct causal link between short stature and functional impairment. In studies that compared short children who were treated with GH therapy with those not treated, no difference was found in cognitive function between the groups.18 Currently, there is no evidence that deficits in intelligence, academic achievement, or behavior would improve if short children gained additional height. The evidence thus does not support a functional benefit from GH treatment in non-GHD children. There are, though, some non-GHD chil-
children who do benefit from GH treatment, specifically, children with severe short stature (typically >4.5 SD below the mean). Growth hormone treatment in these children may help relieve practical restrictions in activities of daily living; although, again, the data on this is not clear, owing to a paucity of studies that look at functional limitations caused by short stature.

Accepted for publication September 11, 2003.

This study was conducted by the Tufts-New England Medical Center Evidence-Based Practice Center under contract to the Agency for Healthcare Research and Quality, Rockville, Md, contract 290-97-0019.

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REFERENCES