

# Motor Development in Very Preterm and Very Low-Birth-Weight Children From Birth to Adolescence

## A Meta-analysis

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**W**ITH ADVANCES IN NEONATAL intensive care, the survival of very preterm (born  $\leq 32$  weeks of gestation) and very low-birth-weight (VLBW) (weighing  $\leq 1500$  g) children has improved considerably. However, these children are at risk for poor developmental outcomes due to a variety of risk factors associated with preterm birth.<sup>1</sup> Over the last 2 decades, a body of research using a variety of methods and study designs has reported significant motor impairment in very preterm and VLBW children. Importantly, the presence of motor dysfunction may crucially affect the child's exploration of the world, attainment of handwriting skills, and involvement in social activities.<sup>2-4</sup> Because of this effect on adaptive functioning, impaired motor development is a risk factor for later poor cognitive performance, learning disabilities, and behavior problems,<sup>5-7</sup> which are present in very preterm and VLBW children.<sup>8,9</sup> This highlights the clinical relevance and need for an accurate prediction of motor consequences of very premature birth and VLBW.

**For editorial comment see p 2257.**

**Context** Infants who are very preterm (born  $\leq 32$  weeks of gestation) and very low birth weight (VLBW) (weighing  $\leq 1500$  g) are at risk for poor developmental outcomes. There is increasing evidence that very preterm birth and VLBW have a considerable effect on motor development, although findings are inconsistent.

**Objective** To investigate the relationship between very preterm birth and VLBW and motor development.

**Data Sources** The computerized databases EMBASE, PubMed, and Web of Knowledge were used to search for English-language peer-reviewed articles published between January 1992 and August 2009.

**Study Selection** Studies were included if they reported motor scores of very preterm and VLBW children without congenital anomalies using 1 of 3 established and widely used motor tests: the Bayley Scales of Infant Development II (BSID-II), the Movement Assessment Battery for Children (MABC), and the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP). Forty-one articles were identified, encompassing 9653 children.

**Results** In comparison with term-born peers, very preterm and VLBW children obtained significantly lower scores on all 3 motor tests: BSID-II:  $d = -0.88$  (95% confidence interval [CI],  $-0.96$  to  $-0.80$ ;  $P < .001$ ), MABC:  $d = -0.65$  (95% CI,  $-0.70$  to  $-0.60$ ;  $P < .001$ ), and BOTMP:  $d = -0.57$  (95% CI,  $-0.68$  to  $-0.46$ ;  $P < .001$ ). Whereas motor outcomes on the BSID-II show a catch-up effect in the first years of development ( $r = 0.50$ ,  $P = .01$ ), the results on the MABC demonstrate a nonsignificantly greater deficit with increasing age during elementary school and early adolescence ( $r = -0.59$ ,  $P = .07$ ).

**Conclusion** Being born preterm or VLBW is associated with significant motor impairment persisting throughout childhood.

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This meta-analysis aimed to determine the motor abilities of very preterm and VLBW children as measured by 3 reliable, validated, and widely used tests<sup>10</sup>: the Bayley Scales of Infant Development version II (BSID-II),<sup>11</sup> the Movement Assessment Battery for Children (MABC),<sup>12</sup> and the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP).<sup>13</sup> Together, these measures

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focus on a broad spectrum of motor skills, measured from birth to 15 years of age. A second aim was to study the association of age at assessment, birth weight, and gestational age with motor outcomes to enhance the prediction of motor development from infancy to adolescence.

## METHODS

### Selection of Studies

This meta-analysis used the guidelines outlined by Stroup et al.<sup>14</sup> The computerized databases EMBASE, PubMed, and Web of Knowledge were used to search for articles by combining the search terms *prematu\**, *preterm*, *low birth weight*, *gestational age*, and *motor\** or *movement*. Furthermore, reference lists of published articles were used to locate other relevant studies.

The following inclusion criteria were used: (1) the study included children born very preterm ( $\leq 32$  weeks) and/or with VLBW ( $\leq 1500$  g); (2) the article was published between January 1992 and August 2009 (to coincide with the release of the BSID-II); (3) the study reported average or median motor development outcomes; (4) the study included only data of children without congenital anomalies; (5) when a study included subgroups with additional perinatal complications, only the group of very preterm and VLBW children without complications was included; and (6) the study was published in an English-language peer-reviewed journal.

We contacted authors for additional data if necessary. To ensure stability of results, we excluded studies using the Alberta Infant Motor Scale, Peabody Developmental Motor Scales, Griffiths test, or Touwen examination as a measure of motor proficiency because fewer than 4 studies used these tests.<sup>15</sup> Most studies using the BSID-II and BOTMP did not include a term-born comparison group and interpreted findings for very preterm and VLBW children using normative data. In contrast, the majority of studies using the MABC did include a comparison

group of term-born children. To enhance comparability of studies, for the BSID-II and BOTMP, only studies using normative data were included; for the MABC, the presence of a control term-born group was set as an additional inclusion criterion. If multiple studies were published using the same participants, only the most recent study reporting motor development was included to prevent the use of correlated data that would inflate homogeneity.

### Outcome Measures

The BSID-II consists of a mental developmental index, psychomotor developmental index (PDI), and behavioral rating scale. It is considered "the best measure for the assessment of infants."<sup>10</sup> In this meta-analysis, the PDI score was used as the dependent variable, assessing both fine and gross motor skills. Norms were based on 1700 infants aged 1 to 42 months. Scores on this test are normalized and have a mean (SD) of 100 (15). Higher PDI scores indicate better psychomotor development.

The MABC is recognized as one of the most commonly used tests of motor impairment.<sup>10</sup> It consists of 32 tasks divided into 4 age categories, each containing 8 items covering 3 subscales: manual dexterity, ball skills, and balance skills. An overall motor impairment score is calculated by combining scores on all 3 subscales, ranging from 0 to 40. Scores on the 3 subscales separately and the overall motor impairment score were used as dependent variables. Norms were based on 1234 children aged 4 to 12 years. In 5 studies median scores were reported.<sup>3,16-19</sup> In the other studies means and standard deviations were used. For ease of interpretation, the direction of scores was inverted when calculating effect sizes such that higher scores indicate better performance.

The BOTMP is considered the next most frequently used test of motor impairment after the MABC<sup>10</sup> and consists of 46 items that are divided into 8 subtests: running speed and agility, bal-

ance, bilateral coordination, strength, upper limb coordination, response speed, visual motor control, and upper limb speed and dexterity. A composite score can be obtained for gross and fine motor subscales separately, and the scores may be summed to yield a battery composite measuring general motor proficiency. All 3 composite scores were included as dependent variables. Normative data were compiled on 765 typically developing children aged 4.5 to 14.5 years. Scores on this test are normalized with a mean (SD) of 50 (10). Higher scores indicate better motor proficiency.

Mean age at assessment, birth weight, and gestational age were obtained from each study and defined in months, grams, and weeks, respectively.

### Quality Assessment

Two authors (J.F.d.K. and C.S.A.-M.) independently assessed the quality of each included study using the Newcastle-Ottawa Scale.<sup>20</sup> This instrument assesses the quality of observational studies in terms of the selection of children (4 criteria), comparability of study groups (1 criterion), and outcome assessment (3 criteria). Total rating scores range from 1 to 9, with 9 being the most favorable. Differences in assessment between both authors were resolved by consensus.

### Statistical Analyses

Statistical calculations were carried out using the computer programs SPSS version 14.0 (SPSS Inc, Chicago, Illinois) and Comprehensive Meta-Analysis version 2.2.<sup>21</sup> Techniques by Hozo et al<sup>22</sup> were used to convert medians into means and standard deviations if necessary. Effect sizes (Cohen  $d$ <sup>23</sup>) for dependent measures derived from the 3 motor tests were determined for each study separately. An overall effect size for each dependent variable was computed by weighting each study's effect size by the study's sample size. To test heterogeneity of the effect sizes,  $Q$  and  $I^2$  tests were conducted.<sup>24-26</sup> Possible differences between the combined effect sizes of subscales of the MABC and

BOTMP were assessed using  $Q$  test statistics.

Several studies separately reported the results for very preterm and VLBW children with and without perinatal complications. The perinatal complications studied differed greatly between studies, including bronchopulmonary dysplasia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage, atrophy, or subependymal cysts. While the main meta-analysis compared the study means for the PDI scores of the BSID-II between very preterm and VLBW children without perinatal complications, an exploratory analysis considered children with complications. In this analysis, no distinction was made between perinatal complications.

To study the association with birth weight, age at assessment, and gestational age, Pearson correlation coefficients were calculated between each of these variables and the studies' effect sizes of the BSID-II and the MABC. These correlation analyses were not conducted for the BOTMP and all subscales because of the limited number of studies available and accompanying low levels of statistical power. For the interpretation of the correlation coefficients and effect sizes, Cohen's<sup>23</sup> guidelines were used.

To study the possibility of publication bias, Rosenthal's<sup>15</sup> fail-safe  $N$  was calculated, which measures the necessary number of studies to nullify the overall effect. Furthermore, we investigated the correlation between sample sizes and effect sizes for each dependent variable. The tendency that significant results in small samples are easier to publish in comparison with nonsignificant results in small samples would become evident by a significant negative correlation between sample size and effect size. In addition, we used linear regression methods proposed by Egger et al<sup>27</sup> to investigate the degree of funnel plot asymmetry. To study the association of study quality with effect sizes, correlation between quality score and effect size was calculated. In all studies using the BSID-II, age of par-

**Table.** Description of the Meta-analytic Sample of Very Premature and VLBW Children

	All Children	By Age			
		0 to <4 y	4 to <8 y	8 to <12 y	12 to <16 y
Sample size, No. (%)	9653 (100)	7855 (81)	856 (9)	803 (8)	139 (2)
Sex, No. (%)					
Male	3830 (40)	3266 (42)	214 (25)	325 (40)	16 (12)
Female	4385 (45)	3801 (48)	204 (24)	356 (44)	18 (13)
NA	1453 (15)	788 (10)	438 (51)	126 (16)	105 (75)
Birth weight, mean (SD), g	1060 (207)	1037 (204)	1152 (258)	991 (196)	1162 (92)
Gestational age, mean (SD), wk	28.2 (1.5)	28.0 (1.5)	28.5 (1.4)	27.8 (1.5)	29.5 (1.6)

Abbreviations: NA, not available; VLBW, very low birth weight.

ticipants was corrected for gestational age. Significance testing was 2-sided and  $\alpha$  set at .05.

## RESULTS

A total of 111 potentially relevant studies were identified. Of these, 21 articles were removed due to overlap with the study samples reported in more recent studies. Another 15 studies did not meet the criteria used to define very preterm and VLBW children. Of the remaining 75 articles, 7 used motor tasks not included in this meta-analysis and 6 used an old version of the motor tasks used in this meta-analysis. Twenty-one articles were excluded because means or median scores for the dependent variables were not reported or could not be calculated from the available information. Finally, 41 studies were included in the analysis: 24 using the BSID-II,<sup>28-51</sup> 10 using the MABC,<sup>3,16-19,52-56</sup> and 7 using the BOTMP.<sup>4,57-61</sup> Results for subscales of the MABC and BOTMP were reported by 5 and 3 studies, respectively. The final meta-analytic sample contained a total of 9653 children with a mean birth weight of 1060 g and mean gestational age of 28.2 weeks (TABLE).

### Bayley Scales of Infant Development II

The BSID-II was used in 24 studies (eTable; see <http://www.jama.com>). Children born very preterm and VLBW children had significantly poorer PDI scores compared with the normative sample, as indicated by the combined

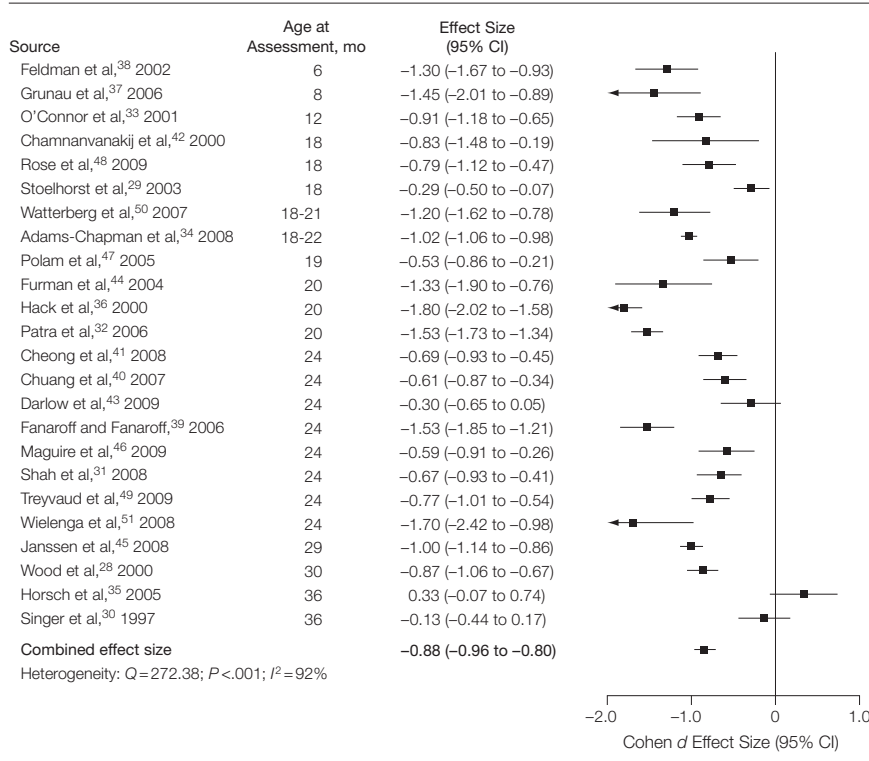
random effect size of  $-0.88$  (95% confidence interval [CI],  $-0.96$  to  $-0.80$ ,  $P < .001$ ) (FIGURE 1). Only random-effect size could be calculated due to heterogeneously distributed data ( $P < .001$ ).

All but 1 study<sup>35</sup> found that very preterm and VLBW children had poorer psychomotor development than the normative sample. One study<sup>34</sup> had a relatively large sample size and therefore heavily influenced the combined effect size, although removal of this study from the analysis did not change the result ( $d = -0.88$ , 95% CI,  $-0.98$  to  $-0.78$ ;  $P < .001$ ). Fail-safe  $N$  for the PDI scores of the BSID-II was 8865, and there was a nonsignificant negative correlation between sample size and effect size ( $r = -0.06$ ,  $P = .79$ ). Furthermore, the Egger degree of funnel plot asymmetry was not significant ( $P = .25$ ), together indicating that there was no evidence for publication bias.

### Exploratory Analyses

Seven studies reported PDI scores of very preterm and VLBW children with and without perinatal complications. These studies encompassed 1120 very preterm and VLBW children with perinatal complications and 5810 very preterm and VLBW children without perinatal complications.<sup>30-32,34,35,40,42</sup>

Compared with very preterm and VLBW control children without perinatal complications, those with additional perinatal complications showed a further significant decrease in their PDI scores of 0.51 SD (95% CI,  $-0.66$

**Figure 1.** Effect Size and Heterogeneity Statistics for Bayley Scales of Infant Development II Ordered by Age at Assessment

CI indicates confidence interval.

to  $-0.36$ ;  $P<.001$ ). PDI scores in those with additional perinatal complications were significantly lower than in children born at term ( $d=-1.30$ ; 95% CI,  $-1.84$  to  $-0.76$ ;  $P<.001$ ) and results were heterogeneously distributed ( $P=.008$ ). Fail-safe  $N$  was 355, and there was a positive and nonsignificant correlation between sample size and effect size ( $r=0.31$ ,  $P=.41$ ). Furthermore, the degree of funnel plot asymmetry was not significant ( $P=.65$ ), together indicating no evidence of publication bias.

### Movement Assessment Battery for Children

There were 10 studies using the MABC (eTable). The overall motor impairment score was consistently higher in very preterm children and VLBW children compared with term-born peers, with a combined effect of  $d=-0.65$  (95% CI,  $-0.70$  to  $-0.60$ ;  $P<.001$ ) (FIGURE 2). Data were

homogeneously distributed ( $P=.62$ ). Fail-safe  $N$  for the combined effect size was 437. There was a moderate nonsignificant positive correlation ( $r=0.46$ ,  $P=.18$ ) between sample size and effect size and a nonsignificant degree of funnel plot asymmetry ( $P=.36$ ), indicating that there was no evidence of publication bias.

Five studies reported outcomes for the MABC subscales (Figure 2).<sup>16-18,55,56</sup> Effect sizes were significant for balance skills ( $d=-0.77$ ; 95% CI,  $-1.08$  to  $-0.45$ ;  $P=.02$ ), ball skills ( $d=-0.34$ ; 95% CI,  $-0.40$  to  $-0.27$ ;  $P<.001$ ), and manual dexterity ( $d=-0.62$ ; 95% CI,  $-0.69$  to  $-0.55$ ;  $P<.001$ ), indicating poorer motor skills in very preterm and VLBW children. Balance skills were more impaired compared with both ball skills ( $Q_1=52.85$ ,  $P<.001$ ) and manual dexterity ( $Q_1=20.19$ ,  $P<.001$ ). In addition, ball skills were less impaired than manual dexterity ( $Q_1=8.03$ ,  $P=.005$ ). Data were homogeneously

distributed for ball skills and manual dexterity ( $P=.21$  and  $P=.35$ , respectively) but heterogeneously distributed for balance skills ( $P<.001$ ). Fail-safe  $N$ s were 165, 24, and 82 for balance skills, ball skills, and manual dexterity, respectively, and all correlations with sample size were not significant ( $r=-0.56$ ,  $P=.33$ ;  $r=-0.26$ ,  $P=.68$ ; and  $r=0.05$ ,  $P=.94$ , respectively). In addition, no significant degree of funnel plot asymmetry was present for ball skills and manual dexterity ( $P=.78$  and  $P=.92$ , respectively), indicating no evidence of publication bias. However, there was a significant degree of asymmetry in the funnel plot for balance skills ( $P=.01$ ), indicating a possibility for publication bias and the necessity to interpret outcomes for the balance subscale cautiously.

### Bruininks-Oseretsky Test of Motor Proficiency

Four studies assessed motor skills with the BOTMP (eTable). Motor proficiency was consistently poorer in very preterm and VLBW children than in the normative sample.<sup>58-61</sup> The combined effect size  $d$  was  $-0.57$  (95% CI,  $-0.68$  to  $-0.46$ ;  $P<.001$ ) and data were homogeneously distributed ( $P=.65$ ) (FIGURE 3). Fail-safe  $N$  for the battery composite was 28, and there was a positive nonsignificant correlation between sample size and effect size ( $r=0.28$ ,  $P=.72$ ) and a nonsignificant degree of funnel plot asymmetry ( $P=.39$ ), together indicating no evidence of publication bias.

Two studies reported findings for the fine motor as well as the gross motor subscales (Figure 3).<sup>58,62</sup> In addition, 1 other study<sup>4</sup> reported findings for the fine motor subscale and another study<sup>57</sup> for the gross motor subscale. Very preterm and VLBW children had poorer outcomes for both fine motor ( $d=-0.86$ ; 95% CI,  $-0.99$  to  $-0.73$ ;  $P<.001$ ) and gross motor subscales ( $d=-0.53$ ; 95% CI,  $-0.60$  to  $-0.46$ ;  $P<.001$ ) as compared with the normative sample. No difference was found between the combined effect size for the fine and gross motor subscales ( $Q_1=1.68$ ,  $P=.19$ ), and

data were homogeneously distributed ( $P=.10$  and  $P=.17$  for fine and gross motor skills, respectively). Fail-safe  $N$ s were 30 for both subscales, and there was a negative but nonsignificant correlation between sample size and effect size for both fine motor skills ( $r=-0.58$ ,  $P=.61$ ) and gross motor skills ( $r=-0.23$ ,  $P=.85$ ). The degree of funnel plot asymmetry was not significant for both subscales as well ( $P=.89$  and  $P=.96$ , respectively), indicating no evidence of publication bias.

**Age at Assessment, Birth Weight, and Gestational Age**

There was a significant positive correlation between mean age at assessment and the studies' effect sizes for the PDI scores of the BSID-II ( $r=0.50$ ,  $P=.01$ ) and a nonsignificant negative correlation between mean age at assessment and the studies' effect sizes as measured by the MABC ( $r=-0.59$ ,  $P=.07$ ). These results suggest that differences in motor outcomes of very preterm and VLBW infants as compared with the normative sample and term-born controls decrease in the first years of development but may be stable or increase later in development.

An increase in birth weight was related to better psychomotor development outcomes as measured by the PDI scores of the BSID-II ( $r=0.54$ ,  $P=.008$ ). In contrast, increased birth weight was not significantly related with less overall motor impairment as measured by the MABC ( $r=0.25$ ,  $P=.53$ ). Similarly, there was a significant relationship between gestational age and psychomotor development outcome as measured by the PDI scale of the BSID-II ( $r=0.42$ ,  $P=.05$ ), but no significant relation between gestational age and motor outcomes as measured by the MABC ( $r=0.21$ ,  $P=.58$ ). These findings indicate that having a lower birth weight or a lower gestational age is only related with poorer motor outcomes in the first years of development.

No association was found between study quality and effect size for all scales on the 3 motor measures ( $r=0.01$ ,  $P=.98$ ).

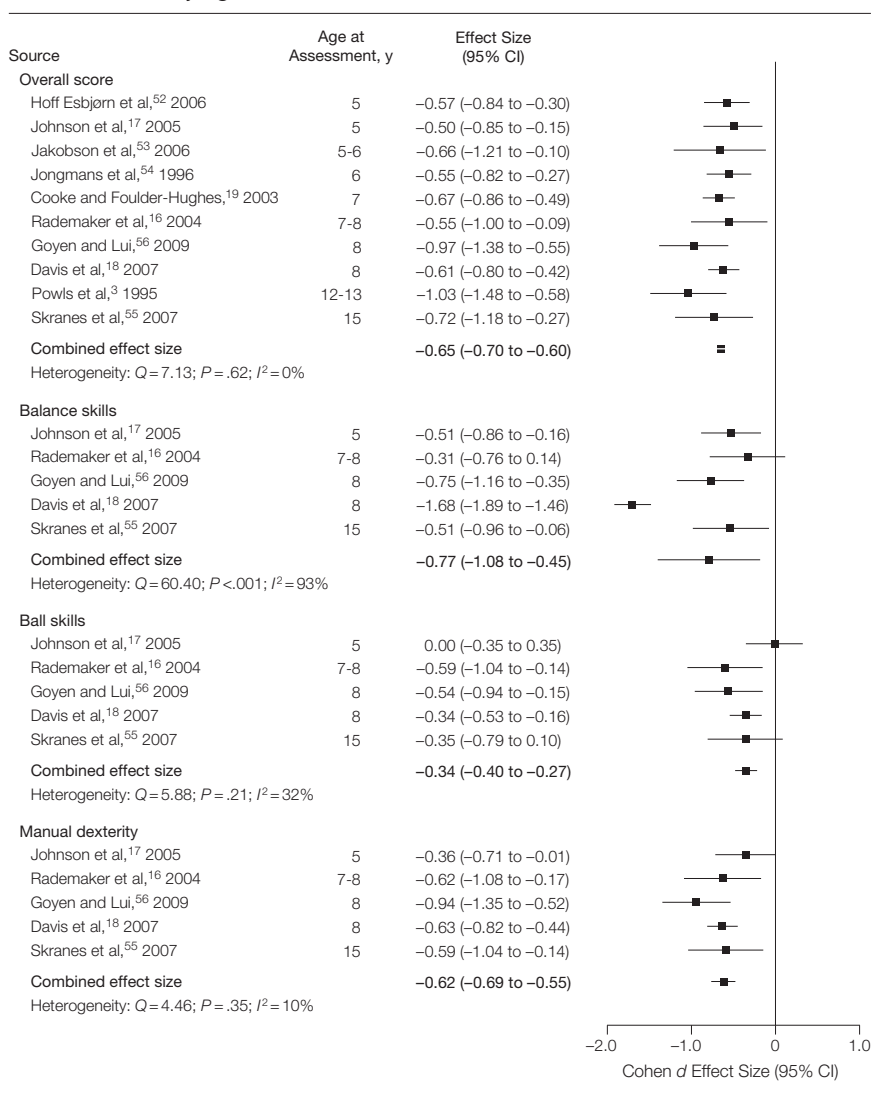
**COMMENT**

This meta-analysis demonstrates clear evidence for substantial motor impairment in very preterm and VLBW children from infancy to 15 years of age. Results indicate that these children are on average  $-0.57$  to  $-0.88$  SD behind their term-born peers or typically developing children in motor development, as measured by 3 psychometrically sound and widely used motor tests. Perinatal complications in very preterm and VLBW children increase the degree of motor impairment even further. Motor problems were evident

in balance skills, ball skills, manual dexterity, and fine and gross motor development as measured by subscales of the MABC and the BOTMP. Although previous research has suggested that motor problems were apparent in very preterm and VLBW children,<sup>3,57,63</sup> the current study qualifies the extent of these motor difficulties.

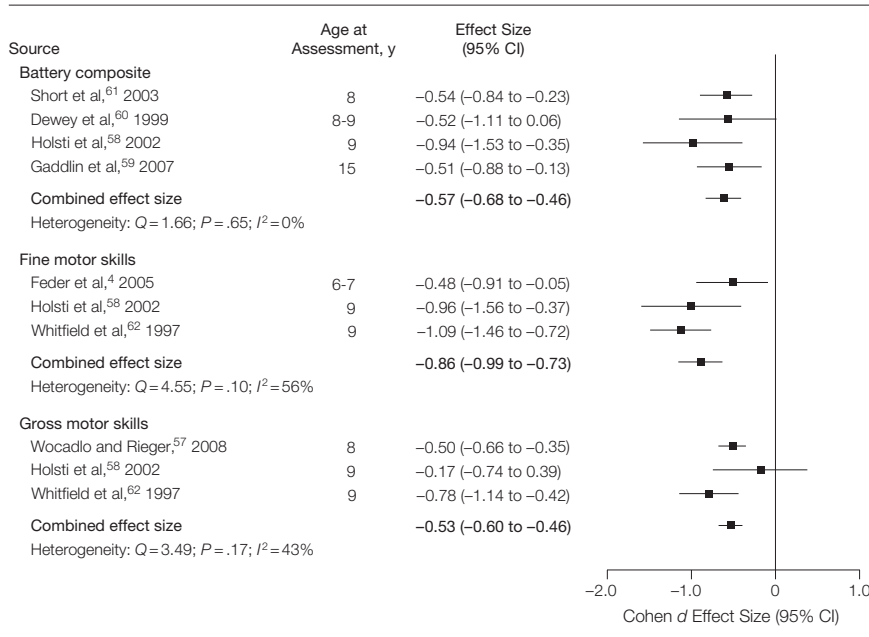
Variability in motor outcomes between very preterm or VLBW children is common, for instance due to sex differences,<sup>45,57</sup> but still poorly understood.<sup>64</sup> This meta-analytic study aggregates studies on different aspects of

**Figure 2.** Effect Sizes and Heterogeneity Statistics for the Movement Assessment Battery for Children Ordered by Age at Assessment



CI indicates confidence interval.

**Figure 3.** Effect Sizes and Heterogeneity Statistics for the Bruininks-Oseretsky Test of Motor Proficiency Ordered by Age at Assessment



CI indicates confidence interval.

motor development, showing that very preterm and VLBW children have significantly more difficulties in keeping their balance than handling a ball and, albeit to a somewhat lesser extent, performing skillful actions with their hands and fingers. This finding stresses the importance of further investigating motor tasks that isolate diverse aspects of motor functioning.

Correlation analyses showed divergent effects of age at assessment on motor functioning as measured by the BSID-II and MABC. Remarkably, motor outcomes on the BSID-II show a catch-up effect in the first years of childhood, whereas the results on the MABC demonstrate nonsignificantly greater deficit with increasing age during elementary school and early adolescence. This finding suggests that motor milestones, as measured by the BSID-II, are easier to attain than more advanced motor skills, as measured by the MABC. Indeed, advanced motor skills put a high load on affected brain structures in very preterm and VLBW children.<sup>55</sup> Interestingly, the divergent effects of age at assessment on the

development of motor skills co-occur with huge changes in the circumstances of children at the age of 5 years. At this age, motor development in very preterm and VLBW children may not be sufficient to compete with the increasing demands of elementary school,<sup>4</sup> thereby propelling further deterioration of motor skills. This highlights the clinical importance of a full assessment of motor skills at early ages in these children and the need for developing early interventions to address motor problems.<sup>65</sup>

In line with previous research, having a lower birth weight or lower gestational age is strongly related to poorer motor outcomes in the first years of development as measured by the BSID-II,<sup>1,3,54</sup> which corresponds with the effects of birth weight and gestational age on cognitive and behavioral outcomes for very preterm and VLBW children.<sup>8</sup> At later stages of development, less robust relations between birth weight, gestational age, and motor scores were obtained for the MABC. The absence of a clear relation at school age and during adoles-

cence is supported by other studies<sup>3,54</sup> and may indicate a decrease in the effect of perinatal factors such as birth weight and gestational age on motor development as age increases.

This study has some limitations that need to be taken into account. The majority of studies using the BSID-II or BOTMP did not include a control group of term-born children; however, these studies compared very preterm and VLBW children with large and representative normative samples. Furthermore, all 3 included motor tests rely on subjective observations and classification by examiners for determining motor scores. Although this could have influenced the outcomes, motor tests were administered by experienced and trained examiners. In addition, interrater reliabilities have been extensively tested and found to be satisfactory.<sup>66,67</sup> Another limitation is the heterogeneously distributed PDI scores of the BSID-II. However, this heterogeneity is likely caused by the rapid rate of motor development in young children, which is supported by findings that test scores of the BSID-II only have moderate stability over time.<sup>67</sup> Finally, unpublished and non-English-language studies were not included in the meta-analysis, which might have caused bias.

This meta-analysis highlights the substantial impairment in motor development of very preterm and VLBW children and the persistence of this impairment into adolescence. While young infants are able to catch up with their peers in reaching important motor milestones, more subtle motor problems are likely to increase when greater demands are put on these vulnerable children at elementary school age and beyond. Future research should elucidate the exact effect of these motor dysfunctions on the impaired behavioral and cognitive development of very preterm and VLBW children, for instance by using motor paradigms that isolate diverse aspects of motor functioning combined with cognitive and behavioral measures.

**Author Contributions:** Dr Oosterlaan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** de Kieviet, Piek, Aarnoudse-Moens, Oosterlaan.

**Acquisition of data:** de Kieviet.

**Analysis and interpretation of data:** de Kieviet, Oosterlaan.

**Drafting of the manuscript:** de Kieviet.

**Critical revision of the manuscript for important intellectual content:** Piek, Aarnoudse-Moens, Oosterlaan.

**Statistical analysis:** de Kieviet.

**Administrative, technical, or material support:** Oosterlaan.

**Study supervision:** Aarnoudse-Moens, Oosterlaan.

**Financial Disclosures:** None reported.

**Additional Information:** The eTable is available at <http://www.jama.com>.

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What is success? I think it is a mixture of having a flair for the thing that you are doing; knowing that it is not enough, that you have got to have hard work and a certain sense of purpose.

—Margaret Thatcher (1925- )