

# Prognosis for Gross Motor Function in Cerebral Palsy

## Creation of Motor Development Curves

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CEREBRAL PALSY OCCURS IN EVERY 2/1000 TO 2.5/1000 live births.<sup>1</sup> It is “. . . an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development.”<sup>2</sup> Thus, whatever additional developmental difficulties individuals with cerebral palsy might have as a result of impairment of the developing central nervous system, the hallmark of these conditions is a disorder in the development of gross motor function.

When first told that their child has cerebral palsy (generally in the child's first 18 months of life), parents usually want to know its severity and whether their child will ever be able to walk. The evidence on which to base answers was, until recently, limited to observations about the association between constellations of reflex and early motor skills at age 2 years and walking at a later age<sup>3</sup>; or on motor

**Context** Lack of a valid classification of severity of cerebral palsy and the absence of longitudinal data on which to base an opinion have made it difficult to consider prognostic issues accurately.

**Objective** To describe patterns of gross motor development of children with cerebral palsy by severity, using longitudinal observations, as a basis for prognostic counseling with parents and for planning clinical management.

**Design** Longitudinal cohort study of children with cerebral palsy, stratified by age and severity of motor function and observed serially for up to 4 years during the period from 1996 to 2001.

**Setting** Nineteen publicly funded regional children's ambulatory rehabilitation programs in Ontario.

**Participants** A total of 657 children aged 1 to 13 years at study onset, representing the full spectrum of clinical severity of motor impairment in children with cerebral palsy.

**Main Outcome Measures** Severity of cerebral palsy, classified with the 5-level Gross Motor Function Classification System; function, formally assessed with the Gross Motor Function Measure (GMFM).

**Results** Based on a total of 2632 GMFM assessments, 5 distinct motor development curves were created; these describe important and significant differences in the rates and limits of gross motor development among children with cerebral palsy by severity. There is substantial within-stratum variation in gross motor development.

**Conclusions** Evidence-based prognostication about gross motor progress in children with cerebral palsy is now possible, providing parents and clinicians with a means to plan interventions and to judge progress over time. Further work is needed to describe motor function of adolescents with cerebral palsy.

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milestones such as sitting between the ages of 2 and 4 years and walking at a later age. However, the findings based on even these simple markers are conflicting.<sup>4,5</sup> Crude estimates of the probability of being able to walk 10 steps un-

aided at or after age 5 years vary for different clinical types of cerebral palsy.<sup>6</sup> These observations derive from clinic samples and are likely not representative of the entire population of children with cerebral palsy.

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For editorial comment see p 1399.

**Table 1.** Gross Motor Function Classification System (GMFCS)

	GMFCS Level					Total (N = 657)
	I (n = 183)	II (n = 80)	III (n = 122)	IV (n = 137)	V (n = 135)	
Age, y						
1-2	16	13	13	12	14	<b>68</b>
3-4	47	20	22	30	22	<b>141</b>
5-6	30	15	30	30	36	<b>141</b>
7-8	36	14	27	29	32	<b>138</b>
9-10	36	18	20	31	26	<b>131</b>
>10	18	0	10	5	5	<b>38</b>
Age, mean (SD) [median], y	6.90 (2.91) [6.82]	6.16 (2.75) [6.39]	6.88 (2.91) [6.85]	6.81 (2.71) [6.71]	6.76 (2.65) [6.62]	6.76 (2.80) [6.62]

Cross-sectional studies of motor behavior in children with cerebral palsy have demonstrated characteristic patterns of motor development according to severity of the condition,<sup>7</sup> although the descriptions of severity previously used have been crude and unsystematic. The motor growth curves created by Palisano et al,<sup>8</sup> which are based on cross-sectional population data stratified by severity using the validated Gross Motor Function Classification System (GMFCS) for cerebral palsy,<sup>9</sup> are an important improvement.

This article describes patterns of gross motor development of a community-based sample of children with cerebral palsy followed up prospectively. We used the GMFCS to longitudinally create curves charting the rates and limits of motor function by severity of motor impairment. These curves increase the prognostic information available to families and clinicians considerably.

**METHODS**

**Setting**

This study was made possible through a partnership between the *CanChild* Centre for Childhood Disability Research at McMaster University and the 19 publicly funded regional ambulatory children’s rehabilitation programs in Ontario. These programs provide a range of developmental therapies and services (predominantly physical, occupational, speech-language, and recreational therapies) by professionals trained and experienced in assessment and management of childhood disability. Because the centers are pub-

licly funded, each program serves the majority of eligible children in its area.

**Sample**

The sampling frame was created in early 1996 with 18 of the 19 centers and 1 hospital-based therapy program in a community without a regional center. Each center identified all the children who had been diagnosed as having cerebral palsy and who had been born in or after 1986. Children with neuromotor findings consistent with cerebral palsy, such as spasticity or reflex abnormalities, who had not been diagnosed as having cerebral palsy were included in the study. Children with other neuromotor disabilities, such as spina bifida or muscle diseases, were excluded. Children were also excluded if they had selective dorsal rhizotomy,<sup>10</sup> had received botulinum toxin injections in the lower limbs for spasticity management,<sup>11,12</sup> or were receiving intrathecal baclofen.<sup>13</sup> At the time the study started, it was not yet known how these relatively new interventions might affect gross motor function. None of these interventions was readily available in Ontario at the time of the study. To the best of our knowledge, no children were receiving hyperbaric oxygen therapy, an intervention that has since been shown to be of no added value for children with cerebral palsy.<sup>14</sup>

Sample size calculations were performed using data from Scutcheon and Rosenbaum.<sup>7</sup> Based on the Gross Motor Function Measure-88 (GMFM-88) and estimated score limits for a 10-year-old in each GMFCS stratum (98-100, 90-95, 60-80, 12-50 and <10), a

sample of 150 children per GMFCS stratum would provide a power of 0.85.

Of the sampling frame containing 2108 children, 1304 were stratified by age and GMFCS level and were randomly selected. Our target was 15 children in each combination of birth year and severity level. An initial sample was drawn from children with known severity level. We also drew a second random sample from those children whose severity level was initially unknown. Based on the required quota for each stratum, the centers established the severity level for a specified set of children. Once the level of a child in this set became known, he/she was added to the study sample for the appropriate stratum (TABLE 1).

Each of the sample sizes was calculated to achieve equal sampling fractions for children with initially known or unknown severity. We oversampled for each age and GMFCS stratum to try to achieve at least 15 children per predefined cell. A total of 366 children were ineligible or unavailable for various reasons. Of the remaining 938 children, 721 (77%) families consented and 682 (94.5%) provided data; 657 had fully useable data, after excluding children without cerebral palsy (FIGURE 1). The children ranged in age from 1 to 13 years at study entry.

At the first assessment, therapists reported the distribution of the child’s cerebral palsy as it was reported in the child’s clinic chart (hemisindrome, diplegia, triplegia, or quadriplegia). They also included any terms that had been used to describe the diagnosis. When no formal diagnosis had been given to the child,

therapists were asked whether the child's motor behavior and patterns "looked like" cerebral palsy. Males (n=369) comprised 56% of the group. Topographical distribution of cerebral palsy included 217 (33.0%) leg-dominant children, 62 (9.4%) 3 limb-dominant, 263 (40.0%) 4

limb-dominant, 98 (15.3 %) hemisymphromes, and 17 (2.8%) unknown.

### Outcome Measures

Severity of cerebral palsy was based solely on GMFCS level, which is a reliable and valid system that classifies children with cerebral palsy by their age-specific gross motor activity.<sup>8,9,15</sup> The GMFCS describes the major functional characteristics of children with cerebral palsy in each level within the following age windows: prior to second birthday; between age 2 years and fourth birthday; between age 4 years and sixth birthday; and between ages 6 and 12 years. The BOX outlines the main abilities of children aged 6 to 12 years in each GMFCS level. Use of the GMFCS requires familiarity with the child, but is not a test and requires no formal training.

Motor function was assessed with the GMFM.<sup>16</sup> The GMFM is a widely used, criterion-referenced, clinical observation tool with a scale from 0-100 that was developed and validated for children with cerebral palsy or Down syndrome.<sup>17</sup> It has excellent reliability and demonstrated ability to evaluate meaningful change in gross motor function in children diagnosed as having cerebral palsy.<sup>16,18,19</sup> The GMFM was not designed to compare the function of children with cerebral palsy to typically developing children. It measures gross motor function in lying and rolling, crawling and kneeling, sitting, standing, and walk-run-jump activities. It can be used with any child or adolescent diagnosed as having cerebral palsy. It focuses on the extent of achievement of a variety of gross motor activities (mainly mobility skills and activities requiring postural control such as sitting, kneeling, and standing on 1 foot) that a typically developing 5-year-old could accomplish. For data analyses, we used scores derived from the GMFM-66, a measure with interval levels that was developed by Rasch analysis of the original 88-item scale (GMFM-88).<sup>18-20</sup>

### Procedures and Quality Control

The ethics review boards of Hamilton Health Sciences Corp, the Bloorview

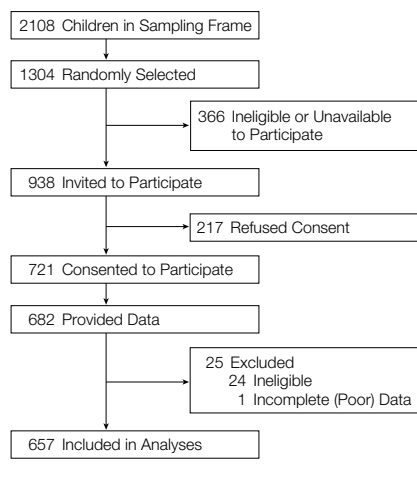
MacMillan Centre (Toronto, Ontario), and the Thames Valley Children's Centre (London, Ontario) approved the study. It was centrally managed at *CanChild*, with a site coordinator in each center, who was responsible for the day-to-day management of data collection. Before beginning to assess children, all therapists were trained on the administration and scoring of the GMFM.<sup>21</sup> Their reliability was assessed against a criterion tape at the end of training and reassessed annually over the 4 years of data collection to ensure that they continued to score the measure reliably.

To track individual gross motor development, children younger than 6 years were assessed with the GMFM-66 approximately every 6 months, and older children were assessed every 9 to 12 months. This timing was based on previous observations that led us to expect more rapid change in gross motor development in the preschool years.<sup>8</sup> On each occasion, therapists were also asked to classify the child's current GMFCS level.

### Analysis

To estimate the parameters of a nonlinear model of motor development, nonlinear mixed-effects modelling<sup>22</sup> was used for children in each of the 5 GMFCS levels. Importantly, in addition to describing the average pattern of development in each level, this analysis allows for orderly variations in the patterns of development. The degree of individual variations was estimated and individual motor development curves were fitted for each child. The model has 2 parameters—the estimated rate and limit of motor development—that have straightforward clinical interpretations. The model assumes that children have GMFM-66 scores near zero at birth. Subsequently, children are expected to acquire gross motor abilities rapidly, with the rate of development slowing as they approach the limit of their potential.<sup>7,8</sup> Based on clinical experience, the rate and limit of motor development are expected to vary substantially. Initial inspection of the data suggested that this model might fit these children well.

**Figure 1.** Sample Selection and Recruitment



### Box. Gross Motor Function Classification System Levels for Children With Cerebral Palsy Between the Ages of 6 and 12 Years<sup>9</sup>

#### Level I

Walks without restrictions; limitations in more advanced gross motor skills

#### Level II

Walks without assistive devices; limitations in walking outdoors and in the community

#### Level III

Walks with assistive mobility devices; limitations in walking outdoors and in the community

#### Level IV

Self-mobility with limitations; children are transported or use power mobility outdoors and in the community

#### Level V

Self-mobility is severely limited even with the use of assistive technology

**RESULTS**

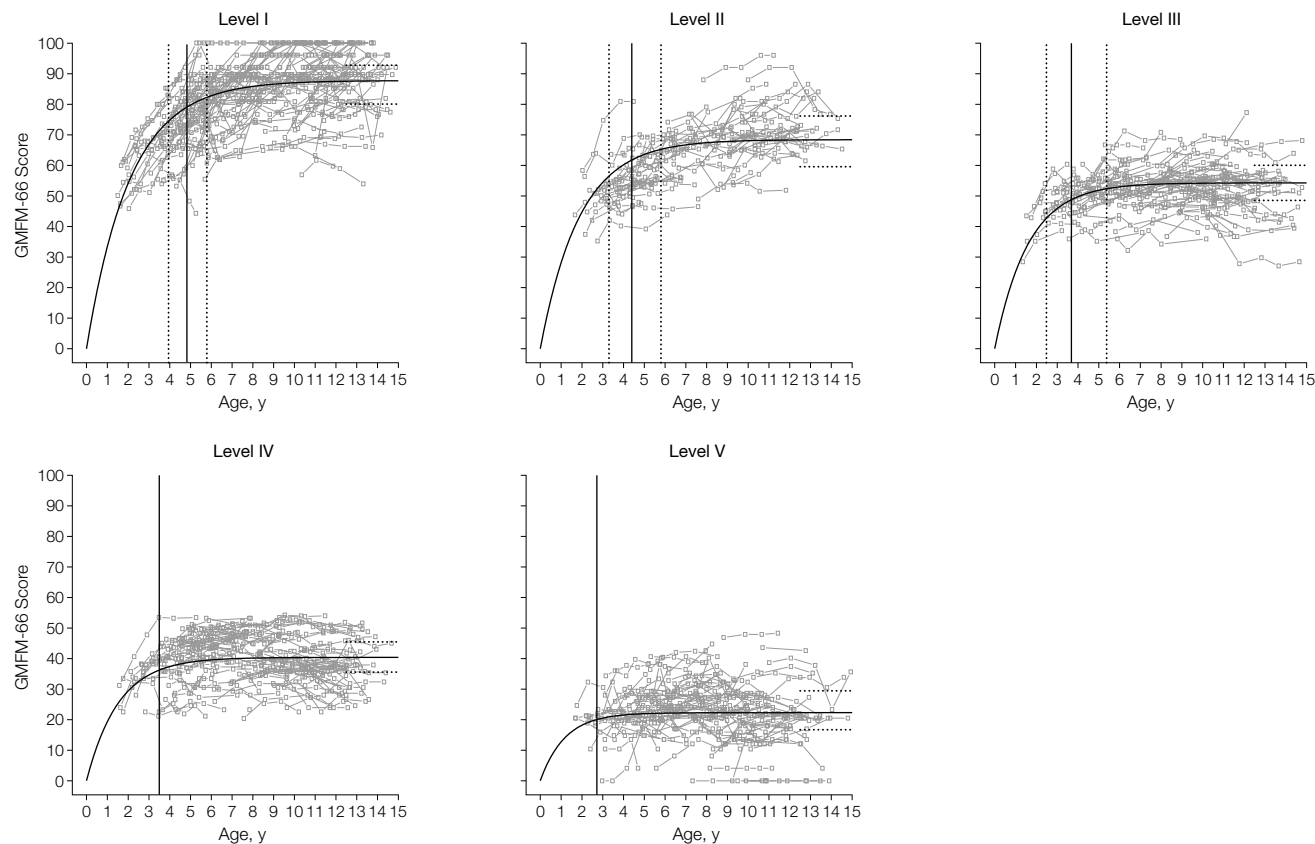
Over the course of the study, 657 children had a total of 2632 GMFM assessments, or an average of 4 observations per child. From these data, 5 distinct and significantly different motor growth curves, which described patterns of gross motor development by GMFCS level, were created (FIGURE 2 and FIGURE 3). Parameter estimates for the average GMFM-66 curve in each level are reported in TABLE 2. As expected, the estimated limit of development decreased as severity of impairment increased. Confidence intervals (95% CIs) for the limit parameters are tight and confirm that each level of severity is significantly different from the adjacent levels. For clinical purposes, the estimated variances in limit for each level

have been used to construct intervals that are expected to encompass 50% of the limits in the population. These individual differences in limit are plotted in Figure 2. The 95% CIs are conceptually different from and unrelated to the 50% bands. The 95% CIs provide an estimate of the precision of the point estimates of the mean limits, while the 50% bands provide clinical information about the degree to which individuals are expected to vary around that mean.

To enhance interpretation, the rate parameters from the nonlinear growth models have been transformed to age-90, the age in years by which children are expected to reach 90% of their motor development potential. Smaller values (in years) indicate faster progress toward motor development limits. Age-90

data in Table 2 suggest a trend for a faster progression to the limit as severity of impairment increases. However, the 95% CIs indicate that children in levels III through V progress significantly faster than children in level I, but children in level II do not progress faster than children in level I. An earlier (younger) age-90 does not indicate “better” developmental progress—only that a child is closer to his/her limit, whatever that limit may be. To aid in clinical interpretation, the variation in age-90 (50% range) is reported as the interval expected to encompass 50% of age-90 in the population. Positive correlations between limit and age-90 suggest that there is a tendency for children with lower motor development potential to reach their limit more quickly (ie, have a lower age-90)

**Figure 2.** Observed and Predicted Gross Motor Function Measure-66 (GMFM-66) Scores in Each Level of the Gross Motor Function Classification System



The curved solid lines indicate average performance. The horizontal dotted lines on the right of the figures indicate the band expected to encompass 50% of children's limits of development. The solid vertical lines indicate the average age-90. The dotted vertical lines indicate the bands expected to encompass 50% of age-90 values around the average. The absence of 50% bands in level IV and level V indicates low variation in age-90 values.

than children with higher potentials, even within GMFCS levels.

The estimates of the average patterns of motor development in each stratum and the degree of individual differences around them (Table 2) have straightforward clinical interpretations when combined with knowledge of children's initial GMFCS level. Thus, for example, the model predicts that the expected limit of a child's potential in level III is 54.3 points on the GMFM-66 (ie, the level III mean), with 50% of children's limits being between 48.5 and 60.0 points. In terms of the rate of development, children in level III are expected to have reached about 90% of their potential by about age 3.7 years. The positive correlation between limit and age-90 for children in level III suggests that a young child, who is performing at a higher level than expected on the basis of the average level III curve, is likely to level off sooner than his/her peers. A substantial amount of prognostic information can thus be derived on the basis of a single GMFM-66 assessment. The model incorporates possible classification errors within the GMFCS because these findings are based on children's initial classification with no effort to verify the child's "true" level if that happens to have changed over time.

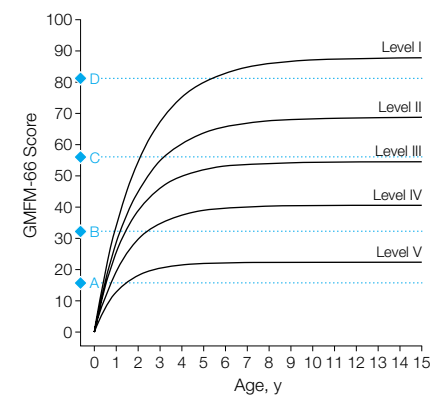
The residual SDs in Table 2 provide an indication of the degree to which the model fits for each GMFCS level, and are a measure of how much each child's GMFM-66 score can be expected to vary around their true ability over time. There

is a suggestion in Table 2 that SDs from the model predictions are larger in levels I and V than the middle levels. The raw residual SDs were plotted against predicted values and against children's ages in each GMFCS stratum to address the adequacy of the model fit. This revealed no tendency for the model errors to be systematically related to predicted value or age. The residual SDs in Table 2 suggest that the size of the expected within-child errors may be related to the GMFCS, which supports the use of separate models for each stratum.

To illustrate the clinical interpretation of these curves, 4 selected GMFM-66 items have been identified on the ordinate of the curves (Figure 3). The GMFM item 21 (diamond A) assesses whether a child can lift and maintain his/her head in a vertical position with trunk support by a therapist while sitting. A child with a GMFM-66 score of 16 would be expected to have a 50% chance of achieving this task.<sup>8</sup> This is something that would be seen relatively early in life among children in GMFCS levels I through IV, and only (on average) at about age 2 years in children in level V. The GMFM-66 item 24 (diamond B) assesses whether when in a sitting position on a mat, a child can maintain sitting unsupported by his/her arms for 3 seconds. Children would be expected to have a 50% chance of being successful at this task at an average GMFM-66 score of 32 points. This task would be relatively easily achieved by children in

GMFCS levels I through III, much later in children in level IV, and rarely by children in level V. The GMFM-66 item 69 (diamond C) measures a child's ability to walk forward 10 steps unsupported, a task associated with a mean GMFM-66 score of 56, and achievable (50% chance) predominantly by children in GMFCS levels I and II. Finally, the task of walking down 4 steps alternating feet with

**Figure 3.** Predicted Average Development by the Gross Motor Function Classification System Levels



The diamonds on the vertical axis identify 4 Gross Motor Function Measure-66 (GMFM-66) items that predict when children are expected to have a 50% chance of completing that item successfully. The GMFM-66 item 21 (diamond A) assesses whether a child can lift and maintain his/her head in a vertical position with trunk support by a therapist while sitting; item 24 (diamond B) assesses whether when in a sitting position on a mat, a child can maintain sitting unsupported by his/her arms for 3 seconds; item 69 (diamond C) measures a child's ability to walk forward 10 steps unsupported; and item 87 (diamond D) assesses the task of walking down 4 steps alternating feet with arms free.

**Table 2.** Parameters of Motor Development for Gross Motor Function Classification System (GMFCS)\*

	GMFCS Level				
	I (n = 183)	II (n = 80)	III (n = 122)	IV (n = 137)	V (n = 135)
Mean No. of observations per child	4.0	4.4	4.1	3.9	3.8
GMFM-66 limit	87.7	68.4	54.3	40.4	22.3
95% CI	86.0-89.3	65.5-71.2	52.6-55.8	39.1-41.7	20.7-24.0
50% range	80.1-92.8	59.6-76.1	48.5-60.0	35.6-45.4	16.6-29.2
Age-90, y†	4.8	4.4	3.7	3.5	2.7
95% CI	4.4-5.2	3.8-5.0	3.2-4.3	3.2-4.0	2.0-3.7
50% range	4.0-5.8	3.3-5.8	2.5-5.5	3.5‡	2.7‡
GMFM-66 limit/age-90 correlations	0.38	0.75	0.73	NA	NA
Residual SDs	3.9	2.8	2.0	2.4	3.1

\*GMFM-66 indicates Gross Motor Function Measure-66; CI, confidence interval; and NA, data not available because the variation in age-90 is near zero.

†Age-90 is the age in years at which children are expected to achieve 90% of their potential GMFM-66 score.

‡The variation in age-90 was near zero, so the 50% range is approximately equal to the population average.

arms free, which is GMFM-66 item 87 (diamond D), will be observed at an average GMFM-66 score of 81 points, and probably only by children in GMFCS level I.

## COMMENT

The patterns of motor development in children with cerebral palsy are the first to be based on longitudinal observations. They were created using a valid classification system of functional abilities and limitations of children with cerebral palsy and a systematic evaluation of gross motor function with an evaluative clinical instrument (GMFM). Data were collected from a large stratified random sample of children diagnosed as having cerebral palsy, who were receiving a range of accepted medical, orthopedic, and developmental therapy services. We believe the sample is representative of the population of children with cerebral palsy in Ontario, with results generalizable to populations elsewhere receiving similar types of mixed developmental therapies.

It is not clear whether children who are currently receiving newer therapeutic modalities (selective dorsal rhizotomy,<sup>10</sup> botulinum toxin,<sup>11,12</sup> intrathecal baclofen<sup>13</sup>) might perform substantially better than the children involved in this study, and if so, whether this would limit the generalizability of our findings. It should be noted that all of these recent therapeutic innovations are used only with highly selected subgroups of children with cerebral palsy, and that even the best results apply only to those specific groups and not to the whole population.

For example, following selective dorsal rhizotomy, the reported improvements in gross motor function are statistically significantly greater than those seen with physical therapy alone, but the actual measured GMFM-66 changes are still quite modest (mean measured added benefit in GMFM-66 change scores in the [selective dorsal rhizotomy plus therapy] group was 2.6)<sup>23</sup> and are unlikely to be associated with a change of GMFCS level. Similarly, while the effects of botulinum toxin injections have been well de-

scribed,<sup>11,12</sup> the mean measured change on the GMFM-88 was in the range of about 3%. Intrathecal baclofen is increasingly being used for the management of spasticity in individuals with cerebral palsy. Although individuals have shown improvements in spasticity and pain relief after receiving intrathecal baclofen, its effect on measured change in gross motor function is limited.<sup>24</sup> These comments are in no way meant to minimize the effectiveness of these interventions for specific subgroups of children with cerebral palsy, but rather to note that at this time these interventions do not, on average, have a major impact on function as assessed with the GMFM.

We expect that the findings from our study will help parents understand the outlook for their child's gross motor function, because an evidence-based estimate can now be made about gross motor prognosis based on age and GMFCS level. The data should prove equally useful to clinicians planning interventions, enabling clinicians and parents to make informed decisions about the most appropriate therapy goals for children. The curves also provide an effective way to assess whether a child's motor progress is consistent with patterns observed in children of similar age and severity.

Because the GMFM-66 assessments of children reported here were specifically made without the use of aids, such as walkers or crutches, these patterns of gross motor development probably represent the lower limit of what children in each level can, on average, accomplish in gross motor function. Furthermore, the curves appear to reach plateaus by about age 7 years. Children, on average, reach about 90% of their motor function (as measured by the GMFM-66) by around age 5 years or younger, depending on their GMFCS level.

However, the curves reveal nothing about the quality of motor control used to accomplish the activities, which is an aspect of motor development that appears to emerge later in childhood.<sup>25</sup> Nor do the curves show how children apply their motor function in the context of activity or participation in daily life, as formulated in the World Health Organiza-

tion's recent *International Classification of Functioning, Disability and Health* model.<sup>26</sup> Furthermore, the GMFM-66 assesses observed independent achievement of motor function tasks, but does not (at least in this study) attempt to evaluate the ways in which children's function is performed with or might be enhanced through the addition of augmentative and technical interventions such as aids, orthoses, or the use of powered mobility to increase day-to-day independence.<sup>27</sup> Children may change and improve their gross motor performance over the developing years through increased balance, stamina, energy efficiency, and quality of motor control—all features that are important and should be evaluated, but are beyond the scope of the GMFM-66.

Thus, it is extremely important that parents, physicians, therapists, program managers, third-party payers, and other decision makers not assume further therapy is unhelpful or unnecessary when the curves appear to level off. Continuing efforts should be made to address ways both to increase independent activity and to promote participation of children with disabilities, as well as to address secondary impairments that may arise. It should also be remembered that the children in the present study were receiving a range of contemporary developmental therapy services that we believe are representative of the therapies provided in the Western world. It is likely that as new therapies emerge, patterns of motor development in children diagnosed as having cerebral palsy may change and modifications to these models will be needed. We believe that the motor development curves will have important applications for the evaluation of specific interventions by permitting analysis of the extent to which these interventions improve a child's gross motor function beyond what is predicted based on age and GMFCS level.

Based on our previous work, an assumption of this study was that GMFCS levels are stable over time, making prognostication meaningful. Wood and Rosenbaum<sup>15</sup> demonstrated an overall reliability of GMFCS over time (from age

<2 years to >12 years) of 0.79, with higher values when one tracked the consistency of GMFCS levels from age 2 to 4 years to age 12 years (0.82) or from age 4 to 6 years to age 12 years (0.87). Children in our study were allocated to a GMFCS level at entry to the study, and data were analyzed according to that initial assignment. This was done to reflect the clinical reality that parents seek prognostication about their child's outlook from the time the disability is first diagnosed. As development progresses, children may be reclassified. If this occurs, it is important for clinicians to reformulate the prognosis, based on the most recent assessment of a child's motor activities and GMFCS stratum.

The present data can be used to explore the creation of motor growth curves for children with different distributions of cerebral palsy, as has been done by others.<sup>28</sup> These analyses are currently under way. However, there is reason to believe that in the absence of a systematic, protocol-driven classification of the topographical components of cerebral palsy, reliability of such categorizations is relatively poor.<sup>29</sup> For the same reason, we have not yet analyzed the findings according to the form of motor impairment (spastic, dystonic, ataxic, or mixed), which has been described elsewhere.<sup>30</sup> In fact, approximately 76% of the children in this study were described as having spastic cerebral palsy, with much smaller numbers in the other subgroups.

The curves describe patterns for groups of children. There is within-stratum variation in motor development, which is based on other aspects of each child's functional status.<sup>31,32</sup> More research is needed to understand, and to be able to measure accurately, the impact of factors such as a child's visual ability, cognitive capacity, motivation, parental encouragement, and the contribution of therapies that might be associated with individual variation in progress. It will also be important to continue to follow the motor development of these children through adolescence, because much remains to be learned

about the impact of puberty and the demands of secondary school on motor function and activity of adolescents with cerebral palsy. Finally, we expect that research by our group and others will provide validation of the accuracy and utility of these curves.

**Author Contributions:** *Study concept and design:* Rosenbaum, Walter, Palisano, Russell, Wood. *Acquisition of data:* Rosenbaum, Walter, Russell, Raina, Galuppi.

*Analysis and interpretation of data:* Rosenbaum, Walter, Hanna, Palisano, Raina, Bartlett.

*Drafting of the manuscript:* Rosenbaum, Walter, Hanna, Palisano, Raina.

*Critical revision of the manuscript for important intellectual content:* Rosenbaum, Walter, Hanna, Palisano, Russell, Raina, Wood, Bartlett, Galuppi.

*Statistical expertise:* Walter, Hanna, Raina.

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*Study supervision:* Rosenbaum, Russell.

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