A prospective, longitudinal study of growth, nutrition and physical activity in young children with cerebral palsy

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Abstract

**Background:** Cerebral Palsy is the most common cause of physical disability in childhood, occurring in one in 500 children. It is caused by a static brain lesion in the neonatal period leading to a range of activity limitations. Oral motor and swallowing dysfunction, poor nutritional status and poor growth are reported frequently in young children with cerebral palsy and may impact detrimentally on physical and cognitive development, health care utilisation, participation and quality of life in later childhood. The impact of modifiable factors (dietary intake and physical activity) on growth, nutritional status, and body composition (taking into account motor severity) in this population is poorly understood. This study aims to investigate the relationship between a range of factors – linear growth, body composition, oral motor and feeding dysfunction, dietary intake, and physical activity (adjusting for motor severity) – and health outcomes, health care utilisation, participation and quality of life in young children with cerebral palsy (from corrected age of 18 months to 5 years).

**Design/Methods:** This prospective, longitudinal, population-based study aims to recruit a total of 240 young children with cerebral palsy born in Queensland, Australia between 1st September 2006 and 31st December 2009 (80 from each birth year). Data collection will occur at three time points for each child: 17 – 25 months corrected age, 36 ± 1 months and 60 ± 1 months. Outcomes to be assessed include linear growth, body weight, body composition, dietary intake, oral motor function and feeding ability, time spent sedentary, participation, medical resource use and quality of life.

**Discussion:** This protocol describes a study that will provide the first longitudinal description of the relationship between functional attainment and modifiable lifestyle factors (dietary intake and habitual physical activity) on the growth, body composition and nutritional status of young children with cerebral palsy across all levels of functional ability.
Background

Cerebral palsy (CP) is the most common cause of physical disability in childhood occurring in 1 in 500 children [1]. It is a group of permanent disorders of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain [2]. Damage to the structure of the brain is static and permanent; however, the consequent symptoms are variable and may change over time [2]. In addition to disordered movement or posture, children may have a range of associated disabilities, including intellectual disability, hearing and visual deficits, nutrition, feeding and swallowing problems, respiratory infections and epilepsy [1]. Cerebral palsy has substantial life long effects on daily function and quality of life for children and their families with an estimated economic cost of over AUD $115,000 per person per annum [3].

Growth and nutritional status of children with CP

Poor growth and nutritional status are commonly reported in children with CP [4, 5]. Conversely, there is evidence to suggest that certain children with CP are at risk of obesity, particularly those with marked spasticity and who are relatively inactive [6]. Poor growth is frequently considered a ‘normal’, untreatable side-effect of CP, however, the impact of poor growth on health, participation and quality of life is an area that requires further investigation [7]. Most studies have concentrated on severely impaired children and are frequently flawed by a lack of valid and repeatable methods for assessing linear growth and body composition in this population [8].

The largest study to date into the growth parameters of children and adolescents with CP was based on retrospective data relating to height and weight obtained from the patient records of 24,920 children and adolescents aged 2 – 20 years. The 10th, 50th and 90th percentile curves for body weight, height and body mass index (BMI) were developed from over 141,900 measurements of weight and height [8]. This study confirmed that children with moderate to severe motor
impairment are growth impaired. Trends for lower weight and height for age were apparent for the lower functioning groups and deviated further from those of the general population with increasing functional impairment. The largest differences in weight and height were seen in those with the most severe motor impairment. Interestingly, in the lowest functioning groups (groups 4 and 5), the presence of a feeding tube was associated with greater weight and height (group 5), in comparison to children in group 4 who did not have a feeding tube. The major strengths of this study were the large sample and the development of growth curves stratified by gross motor skills and mode of feeding. The most significant limitations of the study were that the methods utilised to measure height were of unknown validity and reliability in this population, non validated tools were used to determine functional severity and the sample was largely cross sectional with only a portion having repeated measures.

Importantly, the growth curves presented in this study are purely descriptive of growth within the study population and have not been related to health outcomes [8]. Any representative sample of children with CP will include a large number of undernourished subjects, as such, these population specific growth charts are not a prescription for desirable growth in this group. This study raises two key questions related to growth and nutrition for children with CP: what is desirable growth and, what is the relationship between growth, nutritional status and health related outcomes and quality of life in this population?

**Causes of poor growth in CP**

It has been hypothesised that poor growth in children with CP may be related to nutritional factors, physical factors or factors related to the brain lesion itself. Nutritional factors include inadequate dietary intake, secondary to impaired oral motor and swallowing competence and poor nutritional status and may impact directly on growth [4, 9, 10]. Physical factors result in decreased mechanical stress on bones due to immobility or lack of weight bearing [11]. Bone growth studies have
suggested that immobilisation decreases bone formation and longitudinal bone growth and increases bone resorption, which suppresses certain growth-stimulating hormones [11]. Factors related to the brain lesion itself may impact on growth either directly (via a negative neurotrophic effect on linear growth) or indirectly (via the endocrine system) [4, 10]. Growth differences between impaired and unimpaired limbs in children with hemiplegia, support the hypothesis that non-nutritional factors play a significant role in reducing growth in children with CP [12].

Cross-sectional studies have identified links between feeding ability and measures of growth and nutritional status [13, 14]. Longitudinal investigations have found that early nutritional supplementation by gastrostomy results in improved linear growth in children with severe CP if commenced early in life [10, 15, 16]. Swallowing difficulties have been reported in up to 99% of children with CP classified as GMFCS IV or V, the majority of which exhibit moderate to severe (76%) or profound (15%) dysphagia [17]. The prevalence of dysphagia in children with more mild motor impairment (GMFCS scores I-III) is unknown, as is the point at which oral motor dysfunction begins impacting on dietary intake and growth. Specific issues related to oral motor and swallowing problems in CP include poor saliva control and drooling [18]; difficulty sucking, chewing and swallowing [19-21]; and oropharyngeal aspiration [22-24], all of which impact on lifestyle. Poor saliva control has been associated with health and lifestyle impacts such as poor hygiene, reduced social acceptability of anterior drooling, reduced social interaction and self-esteem, increased daily cares [25-27] and aspiration of posterior drooling with associated pulmonary complications [28]. The impact of oral motor impairment on feeding and swallowing has been associated with reduced dietary intake leading to suboptimal nutritional status and requirement for tube feeding [13, 14]. Other health issues related to oral motor and swallowing problems include pulmonary complications and pneumonia associated with oropharyngeal aspiration requiring multiple hospitalisations [29, 30] [28], and lifestyle impacts on the child and family such as parent reported extended length of mealtimes [31].
In a sample of 171 children with CP, Stevenson and colleagues [4] found that children with severe gross motor impairment had significantly lower height $Z$-scores than less impaired children and that mid arm circumference and tricep skinfold thickness highly correlated with both height and weight $Z$-scores. This study suggests that growth is related to body composition and severity of CP. Stallings and colleagues [9] found that disease severity variables (oral motor function, ambulatory status, and gastrostomy feeding) and non-disease variables (age, pubertal status, gender, and mid parental height) explained approximately 70–75% of the variability in length of 142 children with quadriplegic CP. After controlling for these, body composition (upper arm muscle area and percent body fat) explained 10–15% of the remaining variation. The magnitude of the impact of body composition on linear growth was similar to that of disease severity. Importantly, body composition had a stronger effect on the growth of younger children compared to older children. Both of these studies were cross sectional and therefore the strength of evidence is low.

The cross-sectional multi-centred study North American Growth in CP Project (NAGCPP) showed a significant relationship between functional severity and nutritional status in a group of 235 moderately to severely impaired children (GMFCS III-V) [32, 33]. These children, aged 2-18 years, had lower fat-stores, shorter stature, and decreased muscle mass compared to typically developing children. In addition, these studies demonstrated an association between overall growth status and increased health care use and impaired participation [7, 32]. The NAGCPP did not include an entire population based sample, few children were less than 3 years and only children with moderate to severe motor impairment (Gross Motor Function Classification System (GMFCS) III-V) were included. In addition, lifestyle factors (dietary intake and time spent sedentary) were not assessed.

*Physical activity in children with CP*
Habitual physical activity is an established determinant of health and, in Australia, the cost of illness directly attributable to insufficient activity is AUD$377m per annum across the entire population [35]. The best available evidence indicates that people with mobility impairment are among the least physically active groups in society and consequently children with CP have increased risk of inactivity related illness [36, 37]. While it is likely that physical activity enhances health and wellbeing in young children with CP, empirical evidence of this relationship has not been reported. To date, studies have focused on the use of step monitors to monitor ambulatory activity in older (> 5yrs) children with CP. Studies evaluating activity in young children with CP who are frequently unable to walk have not been conducted. Studies which accurately document patterns of physical activity and sedentary behaviour in this population and relate the data to health outcomes are urgently needed. Such studies require the development and evaluation of methods for assessing activity and inactivity in children who move in a range of different ways including crawling, cruising, rolling and bottom shuffling. Results will permit ascertainment of the importance of inactivity prevention and physical activity promotion strategies in the management of children with CP, as well as the identification of high need groups.

**Difficulties with the assessment of growth and nutritional status in CP**

The neuromuscular complications associated with CP make accurate anthropometric and body composition measurements difficult and sometimes impossible in this population. Our group, and others, have overcome this issue by using segmental limb measures which provide reliable, valid and clinically useful alternatives to measuring height in children with CP [38-40]. For evaluation of body composition, the use of deuterium-oxide is considered a “gold-standard-technique” due to its reliability, accuracy and the limited assumptions required with its use compared to other more commonly used and widely available measures such as skinfold thicknesses; however, its limited availability, cost and time required for analysis result in a technique that is generally prohibitive for routine clinical use. When used in combination with published hydration constants [41, 42],
deuterium-oxide can be used to determine fat free mass and hence fat mass in children, using the two component model of body composition. It is a safe, non-radioactive, naturally occurring, isotope that has been used to measure total body water in a wide range of groups including pregnant women, infants and the elderly [43, 44].

Current investigations into the growth, oral motor and feeding difficulties and nutritional status of children with CP have focused on cross sectional data at one time point or diverse samples across a broad age range. They concentrate on only the most severely impaired children without use of validated measures of height, body composition, gross motor function and health status. Measures of feeding ability and oral motor dysfunction have been most commonly derived from parent questionnaires rather than the use of validated clinical tools. There have been no longitudinal investigations into the impact of lifestyle factors (dietary intake and habitual physical activity) on growth, body composition, nutritional status and their impact on health outcomes in children with CP. The paucity of such information reduces capacity to develop and implement effective management strategies for this population.

**Aims and hypotheses**

This study will investigate the influence of growth, body composition, dietary intake, oral motor and swallowing function and physical activity (adjusted for motor severity) on health outcomes, participation and quality of life in a prospective population based study of young children with CP (from corrected age (ca) of 18 months to 5 years). The hypothesized interaction between these factors is represented graphically in the conceptual model (see **figure 1**).

This broad aim will be addressed by the following four hypotheses (H):
H1: Growth status, nutritional status and growth velocity, from 18 months of age will be related to the level of gross motor functional attainment (GMFCS) at 5 years of age.

H2: Body composition (fat free mass and fat mass) will be related to the level of gross motor functional attainment at 5 years of age.

H3a: For a given GMFCS level, dietary intake, oral motor/swallowing function and time spent sedentary at 3 and 5 years of age will be significantly related to growth velocity and body composition.

H3b: The relationship between dietary intake, oral motor/swallowing function & time spent sedentary at 18 months will predict growth status, nutritional status and body composition at 5 years of age.

H4: Controlling for functional severity, children with slower growth, suboptimal body composition (fat free mass and fat mass), lower levels of oral motor/swallowing function and greater time spent sedentary will have:

(i) higher health care utilisation and direct medical costs at 3 and 5 years.

(ii) lower levels of participation in school, leisure and community at 3 and 5 years.

(iii) poorer quality of life of life at 5 years.

Study significance

This study will be the first longitudinal, population based study to enable more accurate prediction of the early natural history of nutritional and growth problems in young children with CP linked to dietary intake, time spent sedentary, health outcomes and resource utilization. Specifically this project will:
• Determine the nature and timing of nutritional, feeding and growth abnormalities.
• Enable better prediction of the likelihood and impact of sub-optimal dietary intake from an earlier age.
• Enable planning of nutritional treatment options at optimal times.
• Develop and validate methods for measuring sedentary behaviour in young children with CP, including those who do not walk as their primary means of locomotion.
• Highlight the relative contribution of poor dietary intake, oral motor and feeding difficulties and sedentary behaviour on growth and body composition taking into account severity of disability.
• Quantify the impact of dietary intake and physical activity on medical resource use to inform service provision planning.
• Define the relationship between habitual physical activity levels and functional abilities to predict eventual functional attainment.
• Define the relationship between oromotor/swallow dysfunction and gross motor attainment.
• Quantify the impact of poor nutrition and low levels of physical activity on participation in society and quality of life (QOL).
• Allow interpretation of data derived from clinical methods for the assessment of body size and composition (eg body mass index (BMI) and skin-fold thickness).

Methods/ Design

This prospective, population based longitudinal study aims to recruit a total of 240 young children with CP born in Queensland, Australia, between 1st September 2006 and 31st December 2009. It is being conducted in conjunction with another study: Queensland CP Child Study of Motor Function and Brain Development (NHMRC 465128). Ethics approvals have been received from the University of Queensland Medical Research Ethics Committee (2008002260), the Children’s Health Services District Ethics Committee (HREC08/QRCH/112/AM01), the Cerebral Palsy League of Queensland (CPLQ 2008/2010 1029), Gold Coast Health Service District Human
Research Ethics Committee (HREC/09/QGC/88), and the Townsville Health Service District Human Research Ethics Committee (HREC/09/QTHS/96). Further ethics approvals are being sought from additional paediatric and regional centres throughout Queensland.

**Selection criteria**

**Inclusion criteria:**

All Queensland born children diagnosed with CP, born between 1\textsuperscript{st} September 2006 and 31\textsuperscript{st} December, 2009. We define CP as a group of permanent disorders of movement and posture that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain [2]. The characteristic signs are spasticity, movement disorders, muscle weakness, ataxia and rigidity [45].

**Exclusion criteria:**

Children with a progressive or neurodegenerative lesion will be excluded from the study.

**Recruitment**

Recruitment for this study commenced in April 2009 and state-wide recruitment has been established in collaboration with the Queensland CP Register, the Queensland CP League, the Queensland Children’s Health Services District, the Queensland CP Health Service (QCPHS), and other regional hospitals and health service districts throughout Queensland. Community awareness has been generated through paediatricians, general practitioners, allied health professionals, child health nurses, and neonatal follow-up clinics. These groups have been encouraged to refer children with motor delay (not sitting at 10 months, not standing at 12 months or walking at 24 months) for confirmation of a diagnosis of CP. Specialist clinics have been established within the Children’s Health Services District where suitability for the study can be confirmed.
**Study entry**

Eligible children will enter the study from 18 months corrected age. They will be assessed for diagnostic criteria, co-morbidities and for differential neurological assessment by a Paediatric Rehabilitation Specialist and/or a Paediatric Neurologist. All measures will be performed on three occasions at 17 to 25 months (according to study entry); 36 ± 1 months and 60 ± 1 months corrected age (see Figure 2 flow chart for details). Children diagnosed after 25 months of age may enter the study at either 30 ± 1 months or 36 ± 1 months. To ensure collection of data at three time periods, these children will have their second assessment conducted at 48 ± 1 months.

**Feasibility**

Children who are detected after 18 months of age will be entered into the study at the time of diagnosis, will receive assessment at entry and be followed up until outcome at 5 years. According to the Queensland CP Register there are 80-120 new children with CP born in Queensland each year. We propose recruitment of at least 80 children each year (total 240 children from 360 potential children). High ascertainment is expected for children with moderate to marked motor delay (GMFCS III to IV) and this has been the case for children born preterm and children referred to the QCPHS. Children born at term with mild motor delay (GMFCS I and II) and predominant lower limb involvement (diplegia) are typically identified through the Qld CP Health Service and CP Orthopaedic services at the Royal Children’s and Mater Children’s Hospitals.

Recruitment and data collection for this study is being conducted in conjunction with the Queensland CP Child Study of Motor Function and Brain Development (NHMRC 465128). This is a population based prospective cohort study (n=240) which aims to determine the pathway(s) to motor outcome (gross and fine motor) from diagnosis at 18 months to outcome at 5 years in relation to the nature of the brain lesion (using structural MRI). Children enter the study at 18 months of age.
with assessments conducted every six months until 3 years of age then again at 4 years and final outcomes are assessed at 5 years.

**Measurements and procedures**

**Gross motor function**

Gross Motor Function will be determined using the Gross Motor Function Measure (GMFM 66). The GMFM 66 has been shown to be valid and reliable and has been rasch analysed to enable improved scaling [46]. Gross motor function assessment will be conducted by two experienced paediatric physiotherapists whom have criterion rating with the study developers (Boyd). All GMFM assessments will be video taped to enable scoring of the accelerometry data for validation of the Actigraph for the identification of time spent sedentary.

**Motor type:**

Type of cerebral palsy (eg, spastic, dystonic, or hypotonic) and motor distribution (unilateral, bilateral, number of limbs involved) will be determined by two independent physiotherapists at each assessment according to Sanger [45] and the internationally accepted classification system on the European CP Register [47]. The classification of motor type will be recorded for both physiotherapists, independently, at each assessment and common agreement will be assessed for rating motor type at a young age.

**Functional severity:**

Functional severity will be determined using the internationally accepted Gross Motor Function Classification System (GMFCS) [34] by two independent physiotherapists trained in performing the gross motor function assessment. Children will be classified as being in one of five functional categories for the age bands under two years, two to four years and four to six years. The GMFCS
has established validity and reliability for use in young children with CP [34, 48]. Inter rater reliability for the current study will be determined.

**Anthropometry:**

Weight will be measured to the nearest 100 grams using chair scales (Seca Ltd, Germany). Height or length will be measured to the last completed millimetre with a portable stadiometer/length measuring board (Shorr Productions, LLC, Maryland, USA). Knee height and upper-arm length will be measured with an anthropometer (Holtain Ltd, Dyfed, UK). Intraobserver reliability has technical errors of 0.23cm for upper-arm length and 0.16cm for knee height with coefficients of variation of 1.22% and 0.56% respectively [38]. Height estimates will be predicted from knee height and upper arm length using published validated equations [38]. Body mass index will be calculated as weight (kg) divided by height (m) squared. Head circumference and mid arm circumference will be measured to the last completed millimetre using a steel flexible measuring tape.

Duplicate measurements of tricep skin-fold thickness and subscapular skin-fold thickness will be measured using callipers (Holtain Ltd, Dyfed, UK) by trained investigators. By convention, all measurements will be conducted on the left side of the body. This protocol is modelled on the convention used for development the National Centre for Health Statistics charts [49]. Data from skin-fold thicknesses have been found to be useful when assessing the nutritional status of children with CP [14]. Reliabilities have technical errors for intraobserver and interobserver measures of tricep skin-fold thickness of 0.60mm and 0.55mm with coefficients of variation of 5.93% and 6.98% respectively [7].
Anthropometric and body composition data will be converted to Z-scores using age and gender specific reference data for the general population [50, 51]. Between-group comparisons will be conducted across GMFCS levels (I–V).

**Body composition:**

Total body water (TBW) will be measured non-invasively, using the deuterium-dilution technique [52]. Children will be given a dose of deuterium in the form of water either orally or via feeding tube. In the absence of a feeding tube in children with feeding difficulties, children will be assessed to determine the most suitable technique to enable the consumption of the isotope with minimal risk of spillage. Any spillage that may occur will be collected in an absorbent cloth which will be weighed before and after dosing to accurately determine how much fluid has been lost [53]. A single baseline urine sample will be collected prior to administration of the dose to determine natural baseline enrichments of the isotopes and a second urine sample will be collected at approximately five hours after dosing. Measurement of the isotopic enrichment of a sample of body fluids at this time enables calculation of the body water pool using standard equations [54].

Collection of urine samples from children with poor or no bladder control will involve the inclusion of an absorbent liner in their nappy from which urine will be extracted for analysis [53]. Analyses of the urine samples will be performed using an isotope ratio mass spectrometer. Similar procedures have been used by our group in infants, children following severe traumatic brain injury and children with mild and severe CP [52, 55-57]. The accuracy of TBW measured using the deuterium dilution technique is excellent at approximately 1% [58], and 1 – 2% for repeated measurements [59, 60]. Fat free mass (FFM) will be determined through division of TBW by age and gender specific hydration factors [41, 42].

**Bioelectrical impedance analysis**
Impedance (Ohm) will be measured using a Body Stat 1500MDD (Isle of Mann, UK) at 800\(\mu\)A and a fixed frequency of 50KHz. Children will be required to lie in a supine position with arms and legs slightly abducted from the trunk. The electrical current will be applied through two non-polarizing surface electrodes placed at the dorsal surfaces of the hand and foot over the distal aspect of the second and third metacarpals and metatarsals. The voltage drop will be measured by two further electrodes placed at the right pisiform prominence of the wrist and between the lateral and medial malleoli of the ankle. The proximal and distal electrodes will be a minimum of 5 cm apart. All measurements will be taken twice, with a third measurement taken if the difference is greater than 5 Ohm. The mean of the two closest values will be used for analysis. Total body water will be estimated from measurement of impedance and height or length using previously published equations [61-63]. The relationship between height\(^2\)/impedance and TBW measured using deuterium dilution will be examined using regression analysis. An equation for the estimation of TBW from measures of height or length and impedance, specific for young children with CP, will be developed [52]. Reliability of measurements of impedance in this population will be determined.

**Habitual time spent sedentary:**

The time that children spend sedentary in their own free-living environment will be measured using the ActiGraph GT3M accelerometer (Shalimar, FL). The GT3M is a small (3.8 x 3.7 x 1.8 cm), lightweight (27 g) triaxial accelerometer that detects accelerations of a magnitude and frequency that correspond with human movement, filtering out other forms of motion (e.g. vibration). Raw acceleration data is recorded in real time as counts per minute. Output from the device can be used to indicate when the wearer was active, as well as when they were sedentary.

Accelerometry is the most appropriate method for measurement of sedentary behaviour in this study. Self-report is inappropriate in this age-group as our pilot data demonstrate that parental reporting correlates poorly with criterion measures in the target population [64]. Pedometers
measure only steps and are therefore inappropriate for use with children who do not walk, and
doubly labelled water, while considered the gold standard for the measurement of physical activity,
is prohibitively expensive and will not provide data on patterns of activity. Additionally, the
ActiGraph has demonstrated cross-validity with criterion measures of activity in populations, age
groups and activities relevant to the current study including: hip worn ActiGraphs for walking
people with brain injury (r = 0.74) [65]; for measuring free play in young children (r = 0.72) [66];
and wrist worn ActiGraphs for measuring wheelchair activity in people with disabilities (r = 0.66)
[67].

**Time spent sedentary vs time spent active:** While both time spent active and sedentary behaviour
have established links with child health outcomes [68], our study will focus on measurement of
sedentary behaviour. Time spent active will not be used as an outcome measure because young
children with CP move in a variety of ways including walking, running, crawling, creeping, rolling,
and bottom-shuffling. In combination with disordered movement kinematics and kinetics, these
diverse modes of movement make the relationship between counts per minute and activity intensity
for children with CP unpredictable. As a consequence, identification of time spent in moderate to
vigorous physical activity (the intensity recommended for maintaining good health [68]) is
impossible to derive from accelerometer output in this population. In contrast to accelerometer-
based measurement of activity, we can be confident that, providing a child is wearing the monitor,
if counts per minute are zero, the child is sedentary.

**Identification of cut points for sedentary behaviour:** There is a methodological challenge in
choosing to measure sedentary behaviour: when counts per minute are greater than zero it does not
necessarily follow that the child is active (e.g., very low but non-zero counts per minute will be
registered with regular weight-shift that occurs with prolonged sitting). Therefore, in order to
validly determine when a child has been sedentary, a criterion validity study will be conducted to
determine cut-points for differentiating between sedentary behaviour and non-sedentary behaviour. The method used will be based on those described by Welk et al [69].

Participants in the criterion validation study for the Actigraph will be 100 children with CP participating in the Queensland CP Child Study of Motor Function and Brain Development, with a minimum of two children in each of the 15 possible combinations of age (17 to 25 months, 36 ± 1 months and 60 ± 1 months) and GMFCS level (I-V) in our sample. As part of their evaluation, children in the Queensland CP Child: Brain and Motor Development Study complete the Gross Motor Function Measure 66 [46], a standardised motor assessment battery which takes between 40-60 min to complete and requires the children to complete a range of motor tasks (e.g., sitting, standing, rolling, crawling etc). During these assessments, children will wear an Actigraph GT3M and will also be video taped. The video of the assessment will subsequently be coded using BEST direct observation software to provide a real-time criterion measure of when the child was active and when they were inactive. Active behaviour is defined as either positional change where the centre of gravity is moved (e.g., sit to stand, stand to sit, bending down) or translocation of any description (e.g., walking, crawling, rolling). Sedentary behaviour is defined as the child being stationary with or without limb or head movement. To derive unique sedentary cut-points (count per minute) which maximize sensitivity and specificity in each of the 15 cells, a receiver operator characteristic curve analysis will be conducted. For this analysis, counts per minute will serve as the independent variable, with a (1,0) indicator variable corresponding to 1= sedentary (as determined from direct observation) versus 0 = non-sedentary activity (again, as determined from direct observation) serving as the dependent variable.

Measurement of habitual time spent sedentary: To measure free-living sedentary behaviour at each of the three planned data collection points, ActiGraphs will be set for 15 second epochs and worn at the centre of the child’s back [70], for a period of 3 days, the minimum required for a valid estimate
of habitual activity in children [70]. Children will be required to wear the Actigraph during waking hours only and parents will be given instructions for wear and logging wear-time. After 3 days, the ActiGraph will be returned by courier for data extraction and analysis. Following return, output will be analysed for periods of non-wear and the data converted to mean counts per minute for the monitoring period. Analysis will be performed according to functional severity (GMFCS) with mean counts per minute used to stratify participants into high, medium and low levels of sedentary behaviour.

**Dietary intake:**

Usual dietary intake will be determined using a three day weighed food record [71]. Parents will be instructed to weigh all food and fluids offered to the child before and after consumption. Parents will also be instructed to record information regarding the amount of food and fluids lost due to spillage as well as the time taken (in minutes) for the child to consume each meal, snack or drink. Food records will be reviewed by the Research Dietician with the caregiver present to clarify any ambiguous information. Food records will be analysed using the Foodworks™ dietary analysis software program (Xyris Software (Australia) Pty Ltd). Mean energy intake will be expressed as a percentage of age and gender specific recommendations [72].

**Feeding ability:**

Oral motor and swallowing function will be assessed using a number of measures obtained from a parent completed feeding questionnaire, direct observation during a clinical feeding evaluation of a regular meal and from ratings derived from the video taped clinical feeding evaluation. Saliva control and drooling measures were derived from parent report and clinician’s rating during the clinical feeding evaluation using a five point scale for severity and four point scale for frequency described by Thomas-Stonell and Greenberg [73]. A subset of clinical signs suggestive of aspiration will be noted from parent report in the feeding questionnaire and during the clinical
feeding evaluation [74]. Objective measurement of oral motor function during feeding will be rated from the videotaped clinical feeding evaluation using the Schedule for Oral Motor Assessment (SOMA). The SOMA was normalised on 127 young infants aged 8-24 months with 10% of the population having CP. It has a positive predictive validity of 90% and sensitivity greater than 85% to detect clinically significant oral-motor dysfunction in infants and young children. This assessment has also been used to evaluate children of older ages. The SOMA has excellent levels of inter-rater reliability (kappa > 0.75) and intra-rater reliability (85%) [75-77]. Oral motor and swallowing function will also be formally rated using the Feeding and Swallowing Competency Subtest (Part 2) of the Dysphagia Disorders Survey (DDS) – Pediatric [17, 78]. The DDS was developed as a screening tool to assess feeding and swallowing function in children and adults with developmental disability [3-78 years; mean 31.71 years] with 5% of the population (n=31) 3-17 years. It has more recently been used in a group of 166 children (2 years 1 month – 19 years 1 month; mean 9 years 4 months) with moderate to severe CP and intellectual disability [17, 78]. Test validity and inter-item reliability were determined from a sample of 626 people with developmental disability. Inter-rater reliability was undertaken on a sample of 21 participants by 6 speech pathologists and achieved excellent reliability of 97% [17, 78]. Inter-rater reliability of direct ratings for the SOMA and DDS will be compared for 10% of the participants in our study.

**Participation:**

Participation will be determined using parent-report on the domains of self-care, mobility and social functioning using the scaled scores (rasch analysed) of the Pediatric Evaluation of Disability Inventory (PEDI) [79]. The PEDI is a generic standardised instrument of functional performance in children with disabilities that has been found to be both valid and reliable. It has been standardised on a sample of 412 able bodied American children between the ages of 0.5 and 7.5 years [79]. There are three independent domains of the PEDI (participation in self-care, mobility and social function) that are rated by parent report as capable (score =1) or incapable to perform (score = 0).
The PEDI has been found to be a valid and reliable assessment of functional performance in children with disabilities [79].

The mobility and self-care domain of the PEDI will be completed by the caregiver to assess the child's participation in activities of daily living. On the first occasion the PEDI will be administered as an interview (15-20 mins). On subsequent occasions it will be provided as a questionnaire mailed to the family for completion prior to the study visit, and will be checked by the researcher at the study visit. The PEDI raw aggregate scores can be converted into normative standard scores and scaled scores using conversion tables provided in the manual [79]. Scaled scores provide an indication of the child's performance along a continuum of item difficulty or complexity in a particular domain. The range of possible scores (0-100) represents increasing levels of function. In the present study, all raw scores will be converted to scaled scores (Rasch analysed) to compare the entire group (age range 18 months to five years) of all children across the self-care domain for capability, without the difficulties of 'ceiling and floor' effects due to age limitation in the normative standard scores.

**Quality of life:**

Parent perception of quality of life will be assessed using the condition specific tool CP Quality of Life-child (CP QOL–Child) from 4 years of age [80]. The CP QOL–Child assesses aspects of life that parents and children have identified as important including physical wellbeing, social wellbeing, emotional wellbeing, school, access to services, and acceptance by others. The psychometric properties of the CP QOL - Child are excellent with Cronbach’s Alpha range from 0.74-0.92 for parent-proxy report [80]. Test re-test is adequate, where ICC 0.76-0.89 and it is moderately correlated with generic QOL and health (r=0.30-0.51) [80]

**Resource use and the direct costs of treatment:**
In order to determine the relationship between motor prognosis and resource use, medical and allied health resource use and the direct costs of treatment will be monitored and compared to outcomes with adjustment for confounders such as disease severity using cost and consequences analysis [81].

**Sample size calculations:**

240 children will be studied with three measurements planned for each participant between 18 months and 5 years of age. For hypothesis 1, a sample size of 45 per group (GMFCS I-V, totalling 225 patients) will have 80% power and 5% significance of detecting a between group difference in height of 6 cm (assuming a standard deviation of change of 10 cm) between 18 months and 5 years of age, between functional groups and non-CP infants [51]. To allow for attrition we will enrol 240 infants in total.

**Statistical considerations:**

Primary analysis will use the intention to treat principle, using the Last Observation Carried Forward principle for participants who withdraw before the end of the study period. Differences between participants who complete and withdraw will be assessed using t-tests for continuous variables, after transformations of non-normally distributed variables, and Fisher’s Exact Test for categorical variables. Baseline characteristics of the GMFCS groups will be compared similarly. Details for the statistical models that will be used to analyse data to address each hypothesis are as described below.

H1: Outcome is attainment of GMFCS, a 5-level categorical variable at 5 yrs. We will consider the explanatory variables growth and nutritional status in separate models. Individual Z-scores for height or predicted height from knee height or upper arm length will be measured at 18, 36 and 5 yrs and modelled using mixed-effects models. These models are used as they incorporate both fixed and random variables in the analysis. We will model using a random-intercept and slope for
each participant. We will test potential covariates (eg sex) and include them as fixed effects if appropriate.

H2: Outcome is attainment of GMFCS at 5 years. Explanatory variables are fat free mass (FFM) and fat mass at 18, 36 and 5 years. We will investigate the association between explanatory and outcome variables using separate mixed-effects models.

H3a: Outcome variables are growth status and body composition. We will investigate the association with explanatory variables dietary intake and habitual physical activity at 3 years and 5 years. We will use mixed-effects models with random intercept and slope for each participation, with GMFCS as a fixed effect and with appropriate interaction terms.

H3b: Outcome variables are growth status, nutritional status and body composition at 5 years of age. Explanatory variables are dietary intake and habitual physical activity at 18 months of age. We will investigate the ability of the explanatory variables to predict the outcome variables using mixed-effects models.

H4: Outcomes are health care utilization and direct medical costs, participation (PEDI) at 3 and 5 years and QOL at 5 yrs. Explanatory variables are growth, body composition and physical activity at 18 months and 36 months. We will investigate the association between explanatory and outcome variables using mixed-effects models with a random intercept and slope for each participant, and functional severity at 18 months included as a fixed effect.

**Competing interests**
The authors declare that they have no competing interests.
Authors’ contributions:

PSWD, RNB, KLB, ST, KW and RDS contributed to the study design, study protocol and grant writing. KLB modified the grant for publication with input from all coauthors. All authors read and approved the final manuscript.

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Figure 1: Conceptual model illustrating the hypothesized interactions of the principle factors to be investigated in the prospective, longitudinal study of growth, nutrition and physical activity in young children with cerebral palsy.
**Figure 2:** Flow chart of study timeline & measures from baseline (left), to completion (right).

**FUTURE STUDIES**
- Anthropometry at 9 and 12 yrs.
- Body composition at 9 and 12 yrs.
- Physical activity at 12 years.
- Bone age at 12 years.
- GMFCS at 12 yrs.
- QOL: child report at 9 and 12 yrs.

**Key:** GMFCS = the Gross Motor Function classification System; FMS = Functional Mobility Scale; TBW = Total Body Water; PEDI = The Paediatric Evaluation of Disability Inventory; CAPE = the Children’s Assessment of Participation and Enjoyment; CP-QOL-child = the Cerebral Palsy Quality of Life measure (child version); Dx = Confirmed diagnosis