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**Total and regional body fat status among children and young people with cerebral palsy: a scoping review**

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**Abstract**

The purpose of our scoping review was to determine if children and young people with cerebral palsy (CP) have elevated total or regional body fat compared to children and young people without CP.

Databases (Ovid MEDLINE, Embase Ovid, CINHALL, and Scopus) were systematically searched from 01/01/1993-12/07/2018 to identify articles that compared weight status, total body fat, or regional body fat (e.g., abdominal) between children and young people (0-21 years) with and without CP. Extracted data included country, subject characteristics, group sample sizes and matching strategies, methods/measures for weight status/fat depot, fat depot(s) assessed, and key findings.

Twenty-two studies were included. 19 studies examined total body fat; the most common method was use of anthropometrics and the more common measures were body mass index and skinfold thickness. 12 studies examined at least one regional fat depot; the most common method was use of anthropometrics and the most common measure was skinfold thickness. Findings were inconsistent across studies. Further, among 10 studies that examined total and regional body fat depots, 8 found differences across fat depots within the same children and young people (e.g., no difference in total body fat but higher abdominal fat).

This review provides a summary of inconsistent findings from published studies on body fat comparisons between children and young people with vs. without CP, highlights limitations for evaluating body fat for children with CP, and discusses future research directions.

## Introduction

Cerebral palsy (CP) is a clinical neurological syndrome<sup>1</sup> that results from damage to or malformation of the developing brain. CP is the most common pediatric physical disability affecting approximately 3.1 per 1,000 children in the U.S.<sup>2</sup> Although the severity and resulting health and functional sequelae of CP varies, the condition is associated with a disruption in the development of neuro-motor pathways<sup>3</sup> leading to a wide range of fine and gross motor function impairments. Many secondary complications that arise during childhood include problems with neuromuscular,<sup>4</sup> musculoskeletal,<sup>5,6</sup> and psychological<sup>7</sup> systems. In addition, children with CP tend to have lower societal integration and social enjoyment,<sup>8-10</sup> which can amplify the already present complications, and lead to new problems throughout development. Furthermore, there is a decline in mobility as children with CP transition into and throughout their adult years.<sup>11</sup> When taken together, these factors may increase the risk for developing excess body fat throughout the lifespan; however, accurately assessing body fat in children and young people with CP is challenging.

Commonly used methods (i.e., processes to obtain measures, such as anthropometrics and *in vivo* imaging) and measures (e.g., % body fat, body mass index [BMI]) to estimate or evaluate body fat can lead to erroneous interpretation for children and young people with CP. This is because growth is often stunted<sup>12</sup> and accompanied by an underdeveloped fat-free mass,<sup>5, 13-16</sup> which are both exacerbated by the severity of their CP condition.<sup>12, 16</sup> For example, Day et al.<sup>17</sup> reported that height and weight centiles for children and adolescents with CP lagged behind age-

and sex-based norms from the general population, but differences were more substantial among children with more severe forms of CP. Furthermore, while the stunted growth trajectories were also present for height, they were in general not as pronounced as the stunted growth trajectories for weight centiles. Therefore, interpretation of body fat using BMI is particularly affected by low weight predominantly due to low fat-free mass rather than fat mass. Moreover, interpretation of body fat using % fat is also affected by low fat-free mass given the interdependency of fat and fat-free mass to estimate % fat.

Studies in children without CP have shown that excess total and regional body fat is associated with cardiometabolic disease risk factors,<sup>18, 19</sup> and cardiometabolic morbidity and mortality in adulthood.<sup>20, 21</sup> Indeed, adults with CP have a markedly higher prevalence of several obesity-related health problems compared to adults without CP, including musculoskeletal diseases,<sup>22-25</sup> cardiometabolic diseases,<sup>22, 24, 26, 27</sup> mental health disorders,<sup>28, 29</sup> and cardiovascular-related death.<sup>30, 31</sup> Therefore, accurate assessment of body fat among individuals with CP during growth and development is clinically important, as it may inform preventive and rehabilitative strategies to maximize health and function as they age throughout their lifespan. Accordingly, the aim of this scoping review was to determine if children and young people with CP have elevated total or regional body fat compared to children and young people without CP. In doing so, we provide a critical assessment of the state of the literature regarding commonly-used approaches to assess body fat among children and young people with CP, and discuss the advantages or limitations of these approaches for use in this pediatric population.

## Method

We followed the Joanna Briggs Institute Reviewer's Manual for guidance in conducting the present systematic scoping review.<sup>32</sup> Scoping reviews, which are beneficial for clarifying conceptual boundaries of a topic or field,<sup>33</sup> are particularly useful when the body of literature for a specific topic has not been comprehensively reviewed, or when findings are heterogeneous or equivocal in nature.<sup>32</sup> Scoping reviews can be conducted to summarize findings from the literature in order to identify gaps or make recommendations for future research.<sup>34</sup> In the case of the present review, we use the summarized findings to provide a framework for informing clinical evaluation of body fat in children and young people with CP, and provide direction for future research in this area.

### *Search strategy*

We systematically searched for published studies from Ovid MEDLINE, Embase Ovid, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Scopus from January 01, 1993 to December, 7 2018 (period of 24 years and 11.2 months). The full search strategy for each database is presented in the **Supplementary Material**. Briefly, search terms relating to CP, body tissue composition or morphology (e.g., fat, adipose), and body composition assessment (e.g., skinfold thickness, dual-energy x-ray absorptiometry, BMI) were included in the search strategy. To be included in the present scoping review, the study had to: (1) be a full original

research article published in an English peer-reviewed journal; (2) include individuals with CP (exclusively) and a reference group for comparison that were between 0 and 21 years of age for both groups; (3) collect data on the reference group using the same methods, by the same investigators, and the same time period as the data collected from children and young people with CP (e.g., excluded studies with comparisons using previously published data or normative values); and (4) have at least one of the study's objectives focused on comparing total body fat or regional body fat (e.g., abdominal, intramuscular, bone marrow) between children and young people with CP and the reference group. We chose to exclude studies using reference data because comparisons using different methods, devices/software, staff, techniques, and time periods can bias outcomes,<sup>35</sup> especially for smaller sample sizes, which is typically the case for research studies focused on pediatric CP populations.

#### *Search decision process*

**Figure 1** is a flowchart of the search decision process, which was independently performed by DGW and PGR. The initial search yielded 3,578 records. Following deduplication, titles and abstracts of 2,381 records were screened for eligibility. Forty-two records seemed to meet the inclusion criteria, in which case, the full-text articles were retrieved. After reviewing the full-text articles, 22 met full inclusion criteria and were agreed upon by DGW and PGR. The reasons for exclusion from the 42 records are presented in **Figure 1**. Data were extracted on country of origin; CP characteristics; sample size for CP group and reference group, and if any

matching strategies were used for the reference group; measures for weight status or fat depot; fat depot(s) assessed; and key findings. Information for CP characteristics were basic and were not primary criteria to stratify results. This was done because of the inconsistent reporting of common classification systems (e.g., gross motor function classification system [GMFCS], eating and drinking ability classification system, manual ability classification system, communication function classification system) to identify severity measures of CP throughout the decades, leading to an inability to reliably stratify results. However, if mentioned in the article, we noted GMFCS or whether the children were nonambulatory (i.e., “wheelchair users”) to examine body fat status by severity of motor impairment (i.e. GMFCS I/II or non-wheelchair users [ambulatory] vs. GMFCS III-V or wheelchair users [nonambulatory]).

## Results

**Table 1** provides a description of the 22 articles that met inclusion criteria for this scoping review.<sup>5, 6, 14, 36-54</sup> Studies were conducted in Asia (n=8), North America (n=7), Australia (n=4), Europe (n=2), and Africa (n=1). All studies were cross-sectional. The sample size for the CP group included in each study ranged from 12 to 110, and the sample size for the reference group included in each study ranged from 10 to 111. Most studies included children that were younger than 13 years (n=13). While 7 studies included individuals between 13 and 18 years in the CP group, none of these studies exclusively examined teenagers with CP. Two studies did not indicate an age range for their inclusion criteria for study participation.<sup>44, 50</sup> Of the 22 articles



included, 19 had a total body fat outcome<sup>5, 6, 14, 36-39, 41, 43-53</sup> and 12 had at least one regional body fat outcome.<sup>5, 6, 40-44, 47, 48, 50, 51, 53, 54</sup>

### *Total body fat*

The methods used to assess weight status or total body fat were anthropometrics (e.g., to assess BMI) (n=17), isotope dilution (n=5), bioelectrical impedance (n=3), and/or dual-energy x-ray absorptiometry (n=2). The measure used to assess weight status was BMI (n=13) and the measures used to assess total body fat were % fat (n=11), fat mass (n=8), skinfold thickness (n=6), and/or fat mass index (fat mass [kg] / height [m]<sup>2</sup>; n=3).

Assessing weight status using BMI and compared to the reference group, 3 studies found that children and young people with CP had lower BMI,<sup>44, 45, 50</sup> 9 studies found no statistical difference between groups for BMI,<sup>5, 6, 43, 47, 48, 51-53</sup> and 1 study found higher BMI.<sup>39</sup>

Assessing total body fat using skinfold thickness and compared to the reference group, 4 studies found that children and young people with CP had lower fat mass,<sup>36, 38, 44</sup> % fat,<sup>38, 44, 49</sup> and/or fat mass index,<sup>44</sup> 1 study found no statistical difference between groups for % fat,<sup>37</sup> and 1 study found higher % fat.<sup>39</sup>

Assessing total body fat using isotope dilution methods and compared to the reference group, 1 study found that children and young people with CP had lower body fat mass,<sup>36</sup> 3 studies found no statistical difference between groups for body fat mass or % fat,<sup>14, 38, 46</sup> and 1 study found higher % fat.<sup>39</sup>

Assessing total body fat using bioelectrical impedance and compared to the reference group, 1 study found that children and young people with CP had lower body fat mass and % fat,<sup>47</sup> 1 study found no statistical difference between groups for % fat,<sup>45</sup> and 1 study found lower body fat mass, but no statistical difference between groups for % fat.<sup>50</sup>

Assessing total body fat using dual-energy x-ray absorptiometry and compared to the reference group, 1 study found no statistical difference between groups for body fat mass or fat mass index<sup>53</sup> and 1 study found that children with CP had higher body fat mass, % fat, and fat mass index.<sup>52</sup>

### *Regional body fat*

The regional body fat depots examined were upper extremities (n=6), abdominal (n=4), and/or lower extremities (n=4). The methods used to assess regional body fat were anthropometrics (n=8), magnetic resonance imaging (n=3), dual-energy x-ray absorptiometry (n=2), and/or bioelectrical impedance (n=1). The measures used to assess regional body fat were skinfold thickness (n=6), fat mass, area, or volume (n=6), waist/hip ratio (n=3), % fat (n=2), fat mass or area index (n=2), and/or musculoskeletal fat concentration (n=1).

For assessment of upper extremity fat and compared to the reference group, 3 studies found that children and young people with CP had lower skinfold thickness,<sup>40, 43, 47</sup> 2 studies found no statistical difference between groups for skinfold thickness,<sup>41, 48</sup> and 1 study found higher skinfold thickness for boys, but not girls.<sup>42</sup>

For assessment of abdominal fat and compared to the reference group, 1 study found that children and young people with CP had lower waist/hip ratio and visceral fat area, but no statistical difference between groups for visceral fat area index using bioelectrical impedance,<sup>50</sup> 2 studies found no statistical difference between groups using waist/hip ratio,<sup>44, 47</sup> and 1 study found higher trunk, abdominal, and visceral fat mass index, but no statistical difference between groups for trunk, abdominal, visceral, or subcutaneous fat mass, or for subcutaneous fat mass index using dual-energy x-ray absorptiometry.<sup>53</sup>

For assessment of lower extremity fat and compared to the reference group, 1 study found higher skinfold thickness for boys and girls<sup>42</sup> and 1 study found higher % fat and intermuscular fat area of the thigh, but no statistical difference between groups for total, subcutaneous, or subfascial fat area of the thigh using magnetic resonance imaging.<sup>6</sup> Further, 1 study found higher intermuscular fat volume, subfascial fat volume, intramuscular fat concentration, and bone marrow fat concentration of the leg, but no statistical difference between groups for total or subcutaneous fat volume of the leg using magnetic resonance imaging.<sup>5</sup> Finally, 1 study found no statistical difference between groups for leg subcutaneous fat volume when absolute or normalized to body mass.<sup>54</sup>

#### *Multiple body fat regions*

There was a total of 10 studies that examined more than 1 body fat region. Only 2 of these studies found a similar direction of weight status or body fat across the body fat regions

examined when compared to the reference group. Specifically, Unay et al.<sup>41</sup> and Chen et al.<sup>48</sup> reported no statistical difference between groups for BMI or upper extremity skinfold thickness. The other 8 studies found discrepancies across body fat regions. Kong et al.<sup>42</sup> found that boys had higher skinfold thickness of the arm, thigh and calf, but girls had higher skinfold thickness of the thigh and no statistical difference between groups for the arm or calf. Yakut et al.<sup>43</sup> found lower upper extremity skinfold thickness, but no difference for BMI. Grammatikopoulou et al.<sup>44</sup> found lower BMI, total body fat mass, total body % fat, and total body fat mass index, but no difference for waist/hip ratio. Johnson et al.<sup>6</sup> found higher thigh % fat and intermuscular fat area, but no difference for BMI or thigh total, subcutaneous, or subfascial fat area. Tomoum et al.<sup>47</sup> found lower arm skinfold thickness, total body fat mass, and total body % fat, but no difference for BMI or waist/hip ratio. Sung et al.<sup>50</sup> found lower BMI, waist/hip ratio, total body fat mass, and visceral fat area, but no difference for total body % fat or visceral fat area index. Whitney et al.<sup>5</sup> found higher leg intermuscular fat volume, subfascial fat volume, intramuscular fat concentration, and bone marrow fat concentration, but no difference for BMI or leg total and subcutaneous fat volume. Whitney et al.<sup>53</sup> found higher trunk, abdominal, and visceral fat mass index, but no difference for BMI, total body fat mass, total body fat mass index, abdominal fat mass, visceral fat mass, subcutaneous fat mass, or subcutaneous fat mass index.

*Total and regional body fat by ambulatory and nonambulatory status*

There were a total of 8 studies that examined total body fat that had all ambulatory (n=4) or nonambulatory (n=4) children and young people with CP. For ambulatory children and young people with CP, all 4 studies found no statistical difference between groups for fat mass,<sup>46, 53</sup> % fat,<sup>46</sup> fat mass index,<sup>53</sup> or BMI.<sup>5, 48, 53</sup> For nonambulatory children and young people with CP, 1 study found lower % fat,<sup>49</sup> 2 studies found no statistical difference between groups for % fat<sup>37</sup> or BMI,<sup>6</sup> and 1 study found lower fat mass and % fat derived from skinfold thickness but no group difference in fat mass or % fat derived from isotope dilution.<sup>38</sup>

There were a total of 6 studies that examined regional body fat depots that had all ambulatory (n=4) or nonambulatory (n=2) children and young people with CP. For ambulatory children and young people with CP, 2 studies found no statistical difference between groups for arm skinfold thickness<sup>48</sup> or leg subcutaneous fat,<sup>54</sup> 1 study found higher intermuscular fat volume, subfascial fat volume, intramuscular fat concentration, and bone marrow fat concentration of the leg, but no statistical difference between groups for total or subcutaneous fat volume of the leg,<sup>5</sup> and 1 study found higher trunk, abdominal, and visceral fat mass index, but no statistical difference between groups for trunk, abdominal, visceral, or subcutaneous fat mass, or for subcutaneous fat mass index.<sup>53</sup> For nonambulatory children and young people with CP, 1 study found higher thigh skinfold thickness<sup>42</sup> and 1 study found higher % fat and intermuscular fat area of the thigh, but no statistical difference between groups for total, subcutaneous, or subfascial fat area of the thigh.<sup>6</sup>

## Discussion

In summary, there were inconsistent findings across methods and measures regarding whether children and young people with CP had greater total or regional body fat as compared to children and young people without CP. In general, the majority of studies that examined weight status or total body fat indicate that children and young people with CP have no difference in weight status using BMI, have lower body fat using skinfold thickness, and have no difference in total body fat using isotope dilution compared to children and young people without CP. Three studies that used bioelectrical impedance found lower or no group difference, while 2 studies that used dual-energy x-ray absorptiometry found no group difference or higher total body fat between children and young people with and without CP. When regional body fat depots were examined, in general, the majority of studies suggested either no group difference or greater abdominal fat, lower fat in the upper extremities, and higher fat in the lower extremities among children and young people with CP compared to children and young people without CP. Within studies that examined two or more body fat regions, findings suggest that some fat depots may be higher or lower while others are not different in the same children and young adults (e.g., no difference in total body fat but higher abdominal fat); however, no clear patterns emerged across studies. When examining the studies that had all ambulatory children and young people with CP, findings were consistent across studies for no difference in total body fat, but inconsistent across studies for regional fat depots. Similar inconsistencies were found for the studies that contained

all nonambulatory children and young people with CP. Finally, findings were also inconsistent across and within countries (not presented in the results).

The reasons for these heterogeneous findings may be due to CP-related characteristics examined across studies (e.g., severity, comorbidities), as well as the method and measure selected to evaluate body fat. For example, the study by Stallings et al.<sup>38</sup> found that when assessing total body fat using skinfold thickness, children and young people with CP had higher fat mass and % fat compared to children and young people without CP. However, in the same children and young people, there were no differences in fat mass or % fat when assessed using isotope dilution. In light of the heterogeneous status of the literature, we briefly discuss the limitations of commonly-used approaches (i.e., methods and measures) to evaluate body fat status among children and young people with CP, and highlight opportunities for future research directions.

*Limitations of commonly-used approaches to assess body fat among children and young people with CP*

*Body mass index.* Body mass index is commonly used to assess weight status and is associated with fat mass in typically developing children.<sup>55</sup> The equation for BMI is:  $\text{BMI} = \text{body mass [kg]} / \text{height [m]}^2$ . Because BMI is not able to distinguish between the fat and fat-free components that make up the numerator (i.e., body mass), BMI only serves as a proxy for total body fat.

Children and young people with CP have an underdeveloped fat-free mass.<sup>5, 13-16</sup> Fat-free mass accounts for approximately 70-90% of body mass for boys and girls.<sup>56</sup> Therefore, for a given amount of body fat, BMI may underestimate total body fat for children and young people with CP. Moreover, a relative unit change in fat-free mass would have a more profound impact on BMI interpretation of total body fat than a relative unit change in fat mass. This limits the utility of BMI for longitudinal follow up for children and young people with CP since fat-free mass may be accruing slower compared to typically developing children. Moreover, given that many children and adolescents with CP have spinal curvature, scoliosis, or cannot stand up straight, height measurement or estimation can be flawed,<sup>57</sup> making BMI calculations prone to bias.

*Skinfold thickness.* Skinfold measurement is done to evaluate the thickness of subcutaneous fat at various regions of the body. Evidence from a single study suggests that children with CP may have higher visceral fat, but not subcutaneous fat, within the abdomen compared to typically developing children.<sup>58</sup> Evidence from a single study also suggests that children with CP may have higher intermuscular, intramuscular, and bone marrow fat of the lower extremities, but not subcutaneous fat at the lower extremities, compared to typically developing children.<sup>5, 6</sup>

Therefore, for a given amount of body fat, skinfold thickness may underestimate total and regional body fat for children and young people with CP.



*Waist circumference and waist/hip ratio.* Children and young people with CP are smaller than their typically developing peers. Therefore, for a given amount of total body fat, waist circumference as an absolute measure may underestimate abdominal fat for children and young people with CP. The use of waist/hip ratio to estimate abdominal fat is less clear. Indeed, children with CP may have higher visceral fat, but not subcutaneous fat, compared to typically developing children.<sup>58</sup> There is a greater proportion of visceral fat mass than subcutaneous fat mass in the abdomen for the general population. However, visceral fat is housed within the abdominal cavity and surrounded by muscle tissue, and it is unknown how excess visceral fat affects abdominal circumference for this pediatric population. Conversely, children and young people with CP have smaller hips due to an underdeveloped musculoskeletal system.<sup>5, 6, 59</sup> In this case, for a given amount of body fat, waist/hip ratio would overestimate abdominal fat. How these scenarios play out among children and young people with CP, and if the interplay is associated with different severity levels of CP or other CP-related factors requires further attention. Nevertheless, interpretations with waist/hip ratio should be performed with caution, or at least until future efforts to allow for CP-specific cutoffs can be established.

*Fat mass.* Children and young people with CP are generally smaller and have less overall body mass than their typically developing peers. Absolute quantities of mass, area, or volume will always be lower for a similar relative tissue distribution. Therefore, for a given amount of body

fat, using absolute fat mass may underestimate body fat for children and young people with CP relative to their stunted growth.

*Percent fat.* Percent body fat is interdependent on fat and fat-free tissue. This is a major problem for children and young people with CP because they are known to have low fat-free mass.<sup>5, 13-16</sup> Therefore, for a given amount of body fat, % fat may overestimate total or regional body fat depots for children and young people with CP. This is an important consideration, because in light of the limitations assessing body fat using common methods, researchers have developed CP-specific equations<sup>60</sup> or identified new cut-off thresholds<sup>61</sup> to better identify the status of body fat. However, these studies<sup>60, 61</sup> used total body % fat from which to make their equations/cut-off points. While the risk of misinterpretation may be less for higher functioning children and young people with CP (e.g., GMFCS I), this risk may be amplified with greater levels of CP severity. Further, the use of % fat for longitudinal follow up is not advised for children and young people with CP. Interventions, surgeries, or other medical procedures may influence muscle, bone, or fat independent of one another, thus affecting the % fat measure that may not have resulted in actual changes to fat mass.

*Fat mass index.* Fat mass index may be a preferred method to evaluate body fat among children and young people with CP, because it accounts for height and is independent of fat-free tissue. However, methods to obtain fat mass index are usually expensive, time-consuming, and may

pose risk of ionizing radiation. In terms of research, because of the disproportionate growth of height, fat, and fat-free tissue throughout childhood, fat mass index is sensitive to age and pubertal growth, which may pose a challenge for group comparisons that may have slightly different ages. Nevertheless, for a given amount of body fat, fat mass index may be a better measure of body fat compared to absolute fat mass or % fat.

#### *Future research directions*

Clinical research is needed to identify CP-specific growth trajectories throughout development for fat mass, BMI, and other commonly used clinical approaches to assess body habitus. Establishing CP-specific fat mass growth charts may aid clinical assessment of body composition that is unique to the CP population. This is important for non-CP specific clinicians. For example, a high functioning child with CP that falls on the 30<sup>th</sup> percentile for age- and sex-based BMI may, although underweight according to normative reference standards for children and young people without CP, actually have adequate body fat stores. However, pediatric dieticians not familiar with the altered body composition among children and young people with CP may suggest weight gain strategies, which will likely result in greater fat mass than fat-free mass gain.

Clinical research is also needed to develop algorithms that predict adverse medical outcomes (e.g., noncommunicable diseases, fracture) or biomarkers of disease risk (e.g., lipids, glucose metabolism) from commonly used clinical approaches to assess body fat. These

algorithms should be specific to children and young people with CP and account for CP-related characteristics (e.g., GMFCS, comorbidities). Although many methods and measures have limitations for assessing or estimating body fat for children and young people with CP, the limitations of certain approaches may be scaled to the severity of CP and other important CP-related characteristics (e.g., developmental comorbidities). For example, Modlesky and colleagues<sup>52</sup> developed statistical models to estimate fat mass index from easily obtained characteristics. The study found that BMI, age, sex, and a dichotomous variable for ambulatory status (as GMFCS I/II vs. III-V) explained 86% of the variance for FMI. However, this study was cross-sectional and did not assess associations with disease risk factors. Proper understanding of risk factors and development of best practices for screening protocols will require studies of large, heterogeneous samples of individuals with CP across multiple sites. Large, multi-site registry projects, such as the Cerebral Palsy Research Network, the Canadian Cerebral Palsy Registry, and the Australian Cerebral Palsy Register, among others, can provide the infrastructure to answer these questions. Some European countries have national databases that track body composition, CP, and many other factors and can make population-based studies possible.<sup>62</sup>

Basic and translational research is needed to determine inflammatory and other biologically important characteristics of various fat depots (e.g., adipocyte function, adipokine secretory profiles) among children and young people with CP. While excess body fat in childhood leads to

cardiometabolic morbidity and mortality in adulthood,<sup>20, 21</sup> abdominal fat may have a unique influence on cardiovascular and glucose disease processes.<sup>18, 19</sup> Within the abdominal cavity, visceral fat may be more related to cardiometabolic disease risk factors,<sup>19</sup> and may have a stronger role in the pathogenesis of pre-diabetes and type 2 diabetes<sup>63</sup> than subcutaneous fat. This may be due to differences in adipocyte characteristics<sup>64</sup> and inflammatory profiles<sup>65</sup> between these abdominal fat depots. Moreover, excess musculoskeletal fat has been implicated in the pathogenesis of central and peripheral insulin resistance and inflammation.<sup>66-68</sup> Identifying how these fat depots differ in terms of biological function, and how they interact with local tissue and systemic energy metabolism could provide needed insight into how different fat depots in children and young people with CP are behaving for pharmaceutical development.

## Conclusion

Children and young people with CP have stunted growth<sup>12</sup> and an underdeveloped fat-free mass,<sup>5, 13-16</sup> which are both more pronounced among those with more severe forms of CP.<sup>12, 16</sup> More recent evidence suggests that fat partitioning is favoring abdominal and musculoskeletal depots among children and young adults with CP,<sup>5, 6, 58, 69</sup> but not subcutaneous fat depots,<sup>5, 6, 58</sup> as compared to individuals without CP. This becomes important because examining body fat status using common clinical methods and measures (e.g., BMI, skinfold thickness) is not sufficiently capturing the true extent of the overall fat accumulation,<sup>5, 52, 53</sup> that may pose a greater risk for cardiometabolic disease processes.<sup>18, 66</sup>

The unique growth and body composition properties of children and young people with CP present barriers to accurately evaluate body fat status using many common, and clinically feasible, approaches, thus potentially misleading clinical practice. Evidence suggests that the prevalence of obesity-related noncommunicable diseases and mortality are higher for adults with CP than the general population.<sup>22, 28, 30</sup> Since many chronic disease processes initiate in childhood, this systematic scoping review highlights the need for further clinical and translational research regarding body fat assessment and biology, because of its potential impact on growth, function, and health among children and young people with CP.

When body fat assessment is conducted for children and young people with CP, we recommend that interpretations should be made cautiously, and selection of approaches to assess and/or monitor body fat should be tailored to the individual and the overall goals for the child (e.g., function, health, body fat loss, musculoskeletal mass gain). Accurate information about body composition will lead to better choices regarding nutrition and physical activity for children and young people with CP, with improved health outcomes across the lifespan.

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**Table 1:** Summary of studies.

Author (year); Country of origin	CP characteristics	Age	Sample size (CP; reference group)	Methods	Fat depot(s)	Key findings
<b>WEIGHT STATUS OR TOTAL BODY FAT</b>						
Stallings et al. (1995); United States	All had spastic quadriplegia; 90% wheelchair users; 45% had oral motor difficulty; Girls (53.7% for n=108; 39.3% for n=28)	2-12 years	108 or 28; 39	Skinfold thickness (triceps, biceps, suprailiac, subscapular) for fat mass, n=108; D <sub>2</sub> O dilution for fat mass, n=28	Total body	CP had lower fat mass compared to the reference group for both methods: skinfold thickness, mean 1.6 ± 1.0kg vs. 3.4 ± 1.2kg; D <sub>2</sub> O dilution, mean 2.9 ± 2.0kg vs. 4.6 ± 1.8kg; both p<0.01.
Azcue et al. (1996); Canada	All had spastic quadriplegia; Nonambulatory; Girls (38%)	2-16 years	13; 21	Skinfold thickness (triceps, biceps, suprailiac, subscapular) for % body fat	Total body	No statistical difference between CP and reference group for % body fat: mean 20.4 ± 6.1% vs. 27.0 ± 13.0%; p>0.05.
Stallings et al. (1996); United States	All had spastic quadriplegia; All were wheelchair users; 66% had severe feeding problems; Girls (51%)	2-18 years	61; 37 matched to CP for sex, body weight, and distribution of fat-free body mass	Skinfold thickness (triceps and suprailiac) for fat mass and % body fat; Isotope dilution for fat mass and % body fat	Total body	CP had lower fat mass and % body fat compared to the reference group for skinfold thickness method: mean 2.3 ± 2.4kg vs. 3.4 ± 1.3kg; mean 11.2 ± 5.8% vs. 15.3 ± 3.6%; both p<0.05. No statistical difference between CP and reference group for fat mass or % body fat using isotope dilution: mean 4.4 ± 3.8kg vs. 4.7 ± 1.8kg; mean 20.4 ± 10.9% vs. 21.2 ± 6.8%; both p>0.05.
van den Berg-Emons et al. (1998); Netherlands	All had spastic diplegia or tetraplegia; Half were ambulatory and half were nonambulatory; Girls (50%)	7-13 years	22; 10	BMI; D <sub>2</sub> O dilution for % body fat; Skinfold thickness (triceps, biceps, suprailiac, subscapular) for % body fat	Total body	CP had higher BMI and % body fat measured by D <sub>2</sub> O dilution and skinfold thickness: mean 18.3 ± 2.9kg/m <sup>2</sup> vs. 15.8 ± 1.1kg/m <sup>2</sup> ; mean 28.6 ± 8.0% vs. 15.9 ± 5.1%; mean 39.8 ± 13.0% vs. 25.3 ± 7.4%; all p<0.01.
Unay et al. (2003); Turkey	55% were nonambulatory; Girls (62.5%)	2-14 years	40; 40	BMI	Total body	No statistical difference between CP and reference group for BMI: mean 14.7 ± 1.1kg/m <sup>2</sup> vs. 15.5 ± 1.1kg/m <sup>2</sup> ; p>0.05

Yakut et al. (2006); Turkey	Spastic (90%) and mixed type (10%); Quadriplegic (70%), hemiplegic (12.5%), diplegic (7.5%); 72.5% were nonambulatory; Girls (42.5%)	3-17 years	40; 18 matched to CP for age	BMI	Total body	No statistical difference between CP and reference group for BMI (data not shown).
Grammatikopoulou et al. (2009); Greece	Spastic (56.3%), hypotonic (31.3%), mixed type (12.5%); Quadriplegic (75%) and diplegic (25%); 56.3% were nonambulatory; Girls (31.2%)	Not given	16; 16 that was a sibling of the CP participant; CP, 11 boys, mean age 10.1 ± 2.9 years; Reference, 8 boys, mean age 9.4 ± 3.9 years	BMI; Skinfold thickness (triceps, subscapular, calf) for fat mass, % body fat, and fat mass index (fat mass [kg] / height [m] <sup>2</sup> )	Total body	CP had lower BMI, fat mass, % body fat, and fat mass index compared to their sibling without CP: mean 14.0 ± 3.4kg/m <sup>2</sup> vs. 17.9 ± 3.1kg/m <sup>2</sup> ; mean 3.7 ± 2.5kg vs. 8.3 ± 5.9kg; mean 14.9 ± 5.7% vs. 21.9 ± 6.7; mean 2.2 ± 1.1kg/m <sup>2</sup> vs. 4.0 ± 1.7kg/m <sup>2</sup> ; all p<0.05.
Johnson et al. (2009); United States	All were GMFCS III-V and had quadriplegia; Girls (66.7%)	5-12 years	12; 12 matched to CP for age, pubertal development, race, and sex	BMI	Total body	No statistical difference between CP and reference group for BMI: mean 17.0 ± 4.7kg/m <sup>2</sup> vs. 17.6 ± 2.0kg/m <sup>2</sup> ; p>0.05.
Sert et al. (2009); Turkey	All had spasticity; Girls (not given)	5-12 years	41; 56	BMI; Bioelectrical impedance for % body fat	Total body	CP had lower BMI compared to the reference group: mean 14.46 ± 2.72kg/m <sup>2</sup> vs. 15.11 ± 1.84kg/m <sup>2</sup> ; p<0.05. No statistical difference between CP and reference group for % body fat: mean 12.83 ± 8.21% vs. 11.18 ± 5.49%; p>0.05.
Bell et al. (2010); Australia	All were GMFCS I or II; Diplegic (56.3%) and hemiplegic (43.7%); Girls (43.8)	5-12 years	16; 16	D <sub>2</sub> O dilution for fat mass and % body fat	Total body	No statistical difference between CP and reference group for fat mass or % body fat: mean 7.8 ± 3.6kg vs. 7.6 ± 4.8kg; mean 28.0 ± 7.9% vs. 25.6 ± 6.7%; both p>0.05.

Tomoum et al. (2010); Egypt	GMFCS I (20%), II (17.5%), III (20%), IV (10%), V (32.5%); Girls (47.5%)	2-8 years	40; 40 matched to CP for age and sex	BMI; Bioelectrical impedance for fat mass and % body fat	Total body	CP had lower fat mass and % body fat compared to the reference group: mean $2.86 \pm 1.66\text{kg}$ vs. $4.27 \pm 1.75\text{kg}$ ; mean $21.03 \pm 9.21\%$ vs. $24.89 \pm 6.89\%$ ; all $p < 0.05$ . No statistical difference between CP and reference group for BMI (data not shown).
Chen et al. (2011); China	GMFCS I (50%), II (50%); Quadriplegic (8.8%), diplegic (38.2%), hemiplegic (53%); Girls (35.3%)	4-12 years	34; 33 matched to CP for age and sex	BMI	Total body	No statistical difference between CP GMFCS I or II with the reference group for BMI: mean GMFCS I $19.6 \pm 4.4\text{kg/m}^2$ , GMFCS II $16.4 \pm 2.3\text{kg/m}^2$ , reference $17.7 \pm 3.3\text{kg/m}^2$ ; $p > 0.05$ .
Arrowsmith et al. (2012); Australia	All were GMFCS V; 58.9% were tube-fed; Girls (35.7%)	3-18 years	56; 111	Skinfold thickness (triceps, biceps, suprailiac, subscapular) for % body fat	Total body	CP had lower % body fat compared to the reference group: mean $14.8 \pm 7.4\%$ vs. $19.4 \pm 6.4\%$ ; $p < 0.001$
Walker et al. (2015); Australia	GMFCS I/II (61.2%), III (15.3%), IV/V (23.5%); Spasticity (84.7%), dystonia (2.4%), athetosis (3.5%), hypotonia (9.4%); Girls (32%)	1.4-5.1 years	85; 16	Isotope dilution for fat mass and % body fat	Total body	No statistical difference between CP and reference group for fat mass or % body fat: mean $2.8 \pm 1.5\text{kg}$ vs. $3.9 \pm 0.7\text{kg}$ ; mean $20.1 \pm 8.1\%$ vs. $23.0 \pm 3.6\%$ ; both $p > 0.05$ .
Sung et al. (2017); South Korea	GMFCS I (20%), II (13%), III (24%), IV (23%), V (20%); 46% were diplegic; Girls (36%)	Not given	100; 46	BMI; Bioelectrical impedance for fat mass and % body fat	Total body	CP had lower BMI and fat mass compared to the reference group: mean $17.5 \pm 4.5\text{kg/m}^2$ vs. $19.5 \pm 3.9\text{kg/m}^2$ ; mean $6.9 \pm 6.4\text{kg}$ vs. $11.3 \pm 7.2\text{kg}$ ; both $p < 0.05$ . No statistical difference between CP and reference group for % body fat: mean $18.8 \pm 12.9\%$ vs. $23.2 \pm 10.1\%$ ; $p > 0.05$ .
Whitney et al. (2017); United States	GMFCS I (66.7%), II (33.3%); All had spasticity; Girls (33.3%)	4-11 years	12; 12 matched to CP for age, sex, and race	BMI	Total body	No statistical difference between CP and reference group for BMI: mean $17.0 \pm 3.4\text{kg/m}^2$ vs. $17.0 \pm 2.6\text{kg/m}^2$ ; $p = 0.97$ .

Kim et al. (2018); South Korea	Quadriplegic (31.3%), diplegic (43.7%), hemiplegic (25%); Girls (23.1%)	4-12 years	16; 16	BMI	Total body	No statistical difference between CP and reference group for BMI: mean $16.13 \pm 3.88\text{kg/m}^2$ vs. $17.07 \pm 2.09\text{kg/m}^2$ ; $p>0.05$ .
Whitney et al. (2018); United States	GMFCS I/II (42.9%), III-V (57.1%); Girls (40.5%)	4-12 years	42; 42 matched to CP for age, sex, and race	BMI; Dual-energy x-ray absorptiometry for fat mass, % body fat, and fat mass index (fat mass [kg] / height [m] <sup>2</sup> )	Total body	CP had higher fat mass, % body fat, and fat mass index compared to the reference group (ANCOVA using BMI as a covariate): unadjusted mean $8.3 \pm 5.9\text{kg}$ vs. $6.6 \pm 2.7\text{kg}$ ; unadjusted mean $31.5 \pm 10.7\%$ vs. $24.4 \pm 6.3\%$ ; unadjusted mean $4.9 \pm 3.0\text{kg/m}^2$ vs. $3.6 \pm 1.3\text{kg/m}^2$ ; all $p<0.05$ . No statistical difference between CP and reference group for BMI: mean $17.1 \pm 3.9\text{kg/m}^2$ vs. $16.8 \pm 2.1\text{kg/m}^2$ ; $p=0.77$ .
Whitney et al. (2018); United States	GMFCS I (38.9%), II (61.1%); All had spasticity; Girls (27.8%)	4-12 years	18; 18 matched to CP for age, sex, and race	BMI; Dual-energy x-ray absorptiometry for fat mass and fat mass index (fat mass [kg] / height [m] <sup>2</sup> )	Total body	No statistical difference between CP and reference group for BMI, total body fat mass, or total body fat mass index: mean $17.9 \pm 4.4\text{kg/m}^2$ vs. $16.6 \pm 2.2\text{kg/m}^2$ ; mean $8.3 \pm 5.2\text{kg}$ vs. $7.2 \pm 3.1\text{kg}$ ; mean $5.2 \pm 2.7\text{kg/m}^2$ vs. $4.1 \pm 1.7\text{kg/m}^2$ ; all $p>0.05$ .
<b>REGIONAL BODY FAT</b>						
Zainah et al. (2001); Malaysia	Spastic quadriplegic (54.5%), hemiplegic (12.9%), diplegic (11.9%), dyskinetic (19.8%), ataxic (1%); 87.1% were "severely disabled"; 69.3% had absent or minimal feeding problems; Girls (40.6%)	2-12 years	101; 101 matched to CP for age, sex, and race	Skinfold thickness (triceps)	Arm subcutaneous fat	CP had lower triceps skinfold thickness compared to the reference group: mean $7.1 \pm 3.6\text{cm}$ vs. $9.5 \pm 3.7\text{cm}$ ; $p<0.001$ .
Unay et al. (2003); Turkey	55% were nonambulatory; Girls (62.5%)	2-14 years	40; 40	Skinfold thickness (triceps)	Arm subcutaneous fat	No statistical difference between CP and reference group for skinfold thickness: mean $8.4 \pm 0.9\text{cm}$ vs. $9.2 \pm 1.0\text{cm}$ ; $p>0.05$

Kong et al. (2005); China	Dyskinetic (8.2%), spastic/mixed type (91.8%); 43.6% were tube-fed, 56.4 were orally fed; All were nonambulatory; Girls (49.1%)	2-18 years	110; 62	Skinfold thickness (mid-upper arm, mid-thigh, calf) for fat area	Arm, thigh, and calf subcutaneous fat	ANCOVA for skinfold thickness using height as a covariate, tube-fed CP boys had higher skinfold thickness at all locations compared to orally fed CP boys and boys without CP. Orally fed CP boys had higher thigh skinfold thickness compared to boys without CP. Tube-fed CP girls had higher thigh skinfold thickness compared to orally fed CP girls and girls without CP, and higher arm skinfold thickness compared to orally fed CP girls. Similar patterns were observed when fat area was the outcome.
Yakut et al. (2006); Turkey	Spastic (90%) and mixed type (10%); Quadriplegic (70%), hemiplegic (12.5%), diplegic (7.5%); 72.5% were nonambulatory; Girls (42.5%)	3-17 years	40; 18 matched to CP for age	Skinfold thickness (triceps)	Arm subcutaneous fat	CP had lower skinfold thickness compared to the reference group: mean $7.47 \pm 0.43\text{mm}$ vs. $9.28 \pm 0.43\text{mm}$ ; $p < 0.01$ .
Grammatikopoulou et al. (2009); Greece	Spastic (56.3%), hypotonic (31.3%), mixed type (12.5%); Quadriplegic (75%) and diplegic (25%); 56.3% were nonambulatory; Girls (31.2%)	Not given	16; 16 that was a sibling of the CP participant; CP, 11 boys, mean age $10.1 \pm 2.9$ years; Reference, 8 boys, mean age $9.4 \pm 3.9$ years	Waist/hip ratio	Abdominal fat	No statistical difference between CP and their sibling without CP for waist/hip ratio: mean $0.98 \pm 0.05$ vs. $0.95 \pm 0.05$ ; $p = 0.12$ .
Johnson et al. (2009); United States	All were GMFCS III-V and had quadriplegia; Girls (66.7%)	5-12 years	12; 12 matched to CP for age, pubertal development, race, and sex	Magnetic resonance imaging at the middle-third thigh for fat area and % fat	Thigh total, subcutaneous, intermuscular, and subfascial fat	CP had higher % fat and intermuscular fat of the thigh: mean $57.8 \pm 11.5\%$ vs. $40.6 \pm 8.4\%$ ; mean $3.5 \pm 2.4\text{cm}^2$ vs. $1.5 \pm 0.5\text{cm}^2$ ; both $p < 0.05$ . No statistical difference between CP and reference group for total, subcutaneous, or subfascial fat area of the thigh: mean $53.8 \pm$

							29.1cm <sup>2</sup> vs. 50.2 ± 15.8; mean 45.5 ± 24.6cm <sup>2</sup> vs. 45.9 ± 14.8cm <sup>2</sup> ; mean 4.8 ± 3.4cm <sup>2</sup> vs. 2.8 ± 0.8cm <sup>2</sup> ; both p>0.05.
Tomoum et al. (2010); Egypt	GMFCS I (20%), II (17.5%), III (20%), IV (10%), V (32.5%); Girls (47.5%)	2-8 years	40; 40 matched to CP for age and sex	Skinfold thickness (triceps); Waist/hip ratio	Arm subcutaneous fat; Abdominal fat		CP had lower skinfold thickness compared to the reference group: mean 8.31 ± 2.60cm vs. 9.23 ± 1.93cm; p<0.05. No statistical difference between CP and reference group for waist/hip ratio (data not shown).
Chen et al. (2011); China	GMFCS I (50%), II (50%); Quadriplegic (8.8%), diplegic (38.2%), hemiplegic (53%); Girls (35.3%)	4-12 years	34; 33 matched to CP for age and sex	Skinfold thickness (triceps)	Arm subcutaneous fat		No statistical difference between CP GMFCS I or II with the reference group for skinfold thickness: GMFCS I 18.1 ± 11.5, GMFCS II 11.4 ± 7.5, reference 14.0 ± 10.1; p>0.05.
Sung et al. (2017); South Korea	GMFCS I (20%), II (13%), III (24%), IV (23%), V (20%); 46% were diplegic; Girls (36%)	Not given	100; 46	Bioelectrical impedance for visceral fat area and visceral fat area index (visceral fat area [cm <sup>2</sup> ] / height [m] <sup>2</sup> ) Waist/hip ratio	Abdominal fat		CP had lower waist/hip ratio and visceral fat area compared to the reference group: mean 0.8 ± 0.1 vs 0.8 ± 0.1; mean 28.7 ± 24.0cm <sup>2</sup> vs. 46.3 ± 29.2cm <sup>2</sup> ; both p<0.05. No statistical difference between CP and reference group for visceral fat area index: mean 15.5 ± 11.2cm <sup>2</sup> /m <sup>2</sup> vs. 19.7 ± 10.2cm <sup>2</sup> /m <sup>2</sup> ; all p>0.05.
Whitney et al. (2017); United States	GMFCS I (66.7%), II (33.3%); All had spasticity; Girls (33.3%)	4-11 years	12; 12 matched to CP for age, sex, and race	Magnetic resonance imaging at the middle-third leg for fat volume, concentration, and % fat	Leg total, subcutaneous, intermuscular, and subfascial fat volume; Leg intramuscular and bone marrow fat concentration		CP had higher intermuscular and subfascial fat volume, and intramuscular and bone marrow fat concentration of the leg compared to the reference group: mean 5.1 ± 7.0cm <sup>3</sup> vs. 1.4 ± 1.1cm <sup>3</sup> ; mean 4.2 ± 5.4cm <sup>3</sup> vs. 1.3 ± 0.7cm <sup>3</sup> ; mean 25.0 ± 8.0% vs. 16.1 ± 3.3%; mean 82.1 ± 1.8% vs. 80.5 ± 1.9%; all p<0.05. No statistical difference between CP and reference group for total or subcutaneous fat volume of

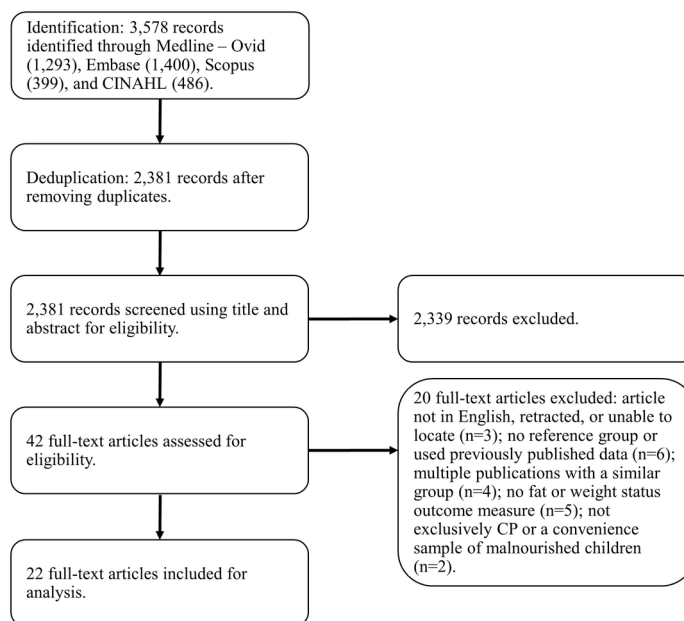
						the leg: mean $128.8 \pm 66.2\text{cm}^3$ vs. $143.3 \pm 44.7\text{cm}^3$ ; mean $119.5 \pm 58.3\text{cm}^3$ vs. $140.6 \pm 43.3\text{cm}^3$ ; $p > 0.05$ .
Whitney et al. (2018)	GMFCS I (38.9%), II (61.1%); All had spasticity; Girls (27.8%)	4-12 years	18; 18 matched to CP for age, sex, and race	Dual-energy x-ray absorptiometry for fat mass and fat mass index (fat mass [kg] / height [m] <sup>2</sup> )	Trunk; Abdominal, visceral and subcutaneous	CP had higher trunk fat mass index, abdominal fat mass index, and visceral fat mass index compared to the reference group: mean $2.2 \pm 1.3\text{kg/m}^2$ vs. $1.7 \pm 0.8\text{kg/m}^2$ ; data represented in figure for abdominal fat mass index and visceral fat mass index; all $p < 0.05$ . No statistical difference between CP and reference group for trunk fat mass, abdominal fat mass, visceral fat mass, subcutaneous fat mass, or subcutaneous fat mass index: mean $3.5 \pm 2.4\text{kg}$ vs. $2.9 \pm 1.4\text{kg}$ ; data represented in figure for abdominal, visceral, and subcutaneous fat mass and for subcutaneous fat mass index; all $p > 0.05$ .
Pitcher et al. (2018)	GMFCS I (58.9%), II (41.1%); All had spasticity Girls (41.2%)	5-12 years	17; 19 matched to CP for age and BMI	Magnetic resonance imaging of entire leg for subcutaneous fat volume	Leg subcutaneous fat volume	No statistical difference between CP and reference group for leg absolute subcutaneous fat volume, or when normalized by body mass: mean GMFCS I $249.6\text{cm}^3$ , GMFCS II $328\text{cm}^3$ , reference $306.2\text{cm}^3$ ; mean GMFCS I $10.84\text{cm}^3/\text{kg}$ , GMFCS II $12.93\text{cm}^3/\text{kg}$ , reference $11.34\text{cm}^3/\text{kg}$ ; all $p > 0.05$ .

**Table and figure legends.**

**Table 1:** Summary of studies.

**Figure 1:** Flowchart of search decision process.





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**Total and regional body fat status among children and young people with cerebral palsy: a scoping review**

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**Key words:** cerebral palsy; obesity assessment; scoping review

**Running title:** body fat, cerebral palsy, scoping review

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