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RESOURCES

# Severe obesity and global developmental delay in preschool children

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## Severe obesity

Approximately one in three Canadian children meets the criteria for overweight or obesity.[1] In the United States, some data suggest that the total proportion of children with obesity has plateaued,[2,3] but over the past 15 years, the prevalence of severe obesity in preschool children has continued to increase.[4] Severe obesity (SO) is defined by the World Health Organization as an age- and sex-specific body mass index (BMI) $\geq 99.9^{th}$ percentile.[5] Currently, approximately 1–2% of preschool children in the United States have SO, a level expected to increase by ~130% by 2030.[6] Unfortunately, there are currently no national estimates of SO in Canadian children.[7]

The causes and consequences of SO are complex, influenced by a host of genetic, environmental, family, social, and societal factors. Risk factors for obesity include a positive family history of obesity, higher than expected maternal weight gain during pregnancy, and exposure to diabetes *in utero* through maternal gestational diabetes mellitus or pre-gestational type 1 or type 2 diabetes.[8] Several reports have identified health risks associated with SO in children, with many focusing on risk factors for type 2 diabetes and cardiovascular disease.[9,10] Other studies have linked SO in children with physical and cognitive disabilities,[1] poor psychosocial and mental health,[11,12] and detrimental health behaviours.[13] There is also a high risk that obesity in childhood will persist into adulthood.[14] Monitoring changes in weight status can provide useful insight for clinicians and families regarding the development and progression of unhealthy weight gain, especially in the first five years of life (preschoolers). First-line treatment recommendations

to prevent or limit unhealthy weight gain include limiting sugar-sweetened beverages, reducing screen time, increasing fruit and vegetable intake, and increasing physical activity.[14] For those with SO, referring preschoolers and their families to a dietitian or a multidisciplinary paediatric weight management clinic may be of value, if available locally.[15]

## Global developmental delay

Global developmental delay (GDD) represents a significant delay (i.e., performing ≥2 standard deviations below the mean on developmental screening/assessment tests[16]) in ≥2 developmental domains, including gross motor, fine motor, speech/language, cognitive, social/personal, or delay in activities of daily living.[16] The extent of a child's delay can be classified as *mild*, *moderate*, or *severe* if functional age is <33, 33-66, or >66% of chronological age, respectively.[17] GDD is a neurodevelopmental condition in children less than 5 years of age, however when it persists beyond 5 years, the terminology changes to intellectual disability (defined as deficits in cognitive functioning [IQ<70] and adaptive skills) to indicate a more permanent state. Children with a sustained developmental delay are at risk of experiencing learning difficulties, behavioural problems, and functional impairments later in life.[18,19] Many factors are associated with increased risk of developmental delay, including poor maternal health during pregnancy, birth complications, infections, genetics, exposure to toxins, trauma, and low socioeconomic status.[20,21] The broad category of causes for GDD include prenatal intrinsic (e.g., genetic/metabolic), prenatal extrinsic (e.g., teratogens/toxins), perinatal (e.g., prematurity, asphyxia), and postnatal (e.g., infections, trauma). Genetic etiologies are the most frequent causes, which are found in >50% of patients and inborn errors of metabolism represent the largest category of genetic conditions for which therapy is available. In the United States, GDD is present in 1–2% of children.[16] In Canada, 7,600–11,500 children are born with GDD annually.[22]

Developmental delay is among the most common problems encountered in community paediatrics, so it is important to investigate to identify causation, assist with management, and provide information about prognosis, recurrence risks, and strategies to optimize growth and development. The Canadian Task Force on Preventive Health Care does not recommend screening for developmental delay in 1–4 year olds who have no apparent signs of developmental delay and whose parents and clinicians have no concerns about development.[23] Others have called for additional research to develop and evaluate appropriate and effective screening interventions.[24,25] The Canadian Paediatric Society position statement on the enhanced well-baby visit provides some guidance on facilitating a conversation between clinicians and parents about early child development.[26] For children suspected of having GDD, a history and examination are of potential value, which may provide insight into etiology. Current guidelines recommend chromosome microarray as a first-line investigation in all children with unexplained GDD,[18] which will identify individuals with common copy-number variations (e.g., 22q11). In lieu of chromosome microarray, karyotype analysis is recommended for children with clinically-suspected aneuploidy or a known positive family history of chromosomal rearrangements.[27] For children without a diagnosis who are suspected to have a syndrome, whole-exome or genome sequencing can be useful. The management of GDD depends on the specific needs of the child, but a combination of therapies (e.g., speech and language therapy for communication skills; physiotherapy and occupational therapy for gross and fine motor skills; behaviour and music therapy for social and emotional functioning) can be beneficial. Canadian guidelines for evaluating a child with GDD are forthcoming. [28]

## SO and GDD

Some evidence suggests obesity and GDD may be related. For instance, a large birth cohort study in the United Kingdom demonstrated that, by 3 years of age, children with developmental delay were more likely to have obesity than their typically developing peers (odds ratio [OR] 1.30, 95% confidence interval [CI]: 1.01–1.67), with odds increasing to 1.80 (95% CI: 1.23–2.54) by 5 years of age.[29] Similarly, an Australian study reported a greater risk of obesity in children with GDD (15%) compared to national data (6%).[29] Health care providers often distinguish between "syndromic obesity" (obesity with other features such as intellectual disability or structural birth defects) and "non-syndromic obesity" (obesity without other medical features),[30] although these characterizations may become more challenging as genetic diagnostic abilities increase. A number of rare genetic syndromes feature both SO and GDD. For example, SO and GDD will occur concurrently due to polygenic or multifactorial reasons, epigenetic or environmental reasons, or identifiable syndromes for which paediatricians may initiate etiological investigations.[30,31] Data from large epidemiologic studies of SO in children have suggested that 5–8% of SO in children has a genetic cause,[31] although detailed analyses of children with both SO and GDD have yet to be published.[32]

There is limited research regarding the risk factors related to SO and GDD.[33] A recent US-based study found that SO in women during the pre-pregnancy period was associated with developmental delay in children at 2 years of age.[34] These data led to more questions than answers, including: Are there shared risk factors for SO and GDD? What diagnostic tests are needed in this population? What interventions meet the needs of families?

Screening and treatment programs for children with SO or GDD are resource-intensive and may not address the unique needs of children who present with both conditions. Gaining a better understanding of the incidence, risk factors, and health care needs of preschoolers with SO and GDD is needed to inform the development of health services and policies that allow clinicians, and paediatricians in particular, to tailor their care to meet the needs of their young patients and families.

## Conclusion

As paediatricians are among the only group of physicians who see and care for children with SO and GDD in their day-to-day practices, it is critically important to gain a better understanding of the incidence and risk factors of SO and GDD in Canada. In turn, these data can be used to guide investigations, interventions, and policies for appropriate health services and care that optimize the health and well-being of children with SO and GDD.

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## Quiz

**1. The clinical definition of SO in preschool-aged children includes:**

a) Body fat percentage of >30%
b) A BMI between 25 and 29.9 kg/m$^2$
c) Age- and sex-specific BMI ≥99.9%, according to the World Health Organization
d) All of the above

**2. The clinical definition of GDD includes:**

a) A significant delay (2 standard deviations or more below age-expected developmental norms)
b) Concerns regarding gross motor, fine motor, speech/language, cognitive, social/personal, or delay in activities of daily living
c) Delay in two or more developmental domains
d) All of the above

3. **Current guidelines recommend chromosome microarray as a first genetic test for children with:**
   a) Unexplained GDD
   b) Common copy-number variations
   c) Any identifiable risk factors for excessive environmental lead exposure
   d) A & B
   e) B & C

4. **A 2-year-old child is referred for severe obesity with a BMI ≥99.9$^{th}$ percentile. There is delay in the acquisition of both motor and speech skills. There are no dysmorphic facial features. Which investigation should be conducted first:**
   a) Ophthalmology assessment
   b) Chromosomal microarray analysis
   c) Renal ultrasound
   d) Next-generation sequencing panel
   e) All of the above

**Answers: 1-C, 2-D, 3-D, 4-B. However, if it's negative, the remaining tests should be conducted.**