At what age do normal weight Canadian children become overweight adults? Differences according to sex and metric

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Background: The prevalence of overweight and obesity doubles between adolescence and young adulthood. However, the exact age, and appropriate metric to use, to identify when overweight develops is still debated. Aim: To examine the age of onset of overweight by sex and four metrics: body mass index (BMI), fat mass (%FM), waist circumference (WC) and waist-to-height ratio (WHtR). Methods: Between 1991 and 2017, serial measures of body composition, were taken on 237 (108 males) individuals (aged 8 to 40 years of age). Hierarchical random effects models were used to develop growth curves. Curves were compared to BMI, %FM and WC overweight age and sex-specific cut-points. Results: In males the BMI growth curve crossed the cut-point at 22.0 years compared to 23.5 and 26.5 years for WHtR and %FM respectively; WC cut-off were not reached until 36 years. In females the BMI growth curve, crossed the overweight cut-point at 21.5 years compared to 14.2 years for %FM and at 21.9 and 27.5 years for WC and WHtR respectively. Conclusions: Overweight onset occurs during young adulthood with the exception of WC in males. BMI in males and %FM in females were the metric identifying overweight the earliest.

Introduction

Canadian rates of overweight and obesity have more than doubled in adults over the past 40 years(Tremblay, Katzmarzyk and Willms, 2002; Roberts *et al.*, 2012; Statistics Canada, 2017). Being overweight, in both adults and children, correlates with several chronic conditions including coronary heart disease and type II diabetes, as well as to risk factors for these diseases such as hypertension, dyslipidaemia, and insulin resistance(Staiano, Gupta and Katzmarzyk, 2014). As such, excess adiposity remains a major Canadian public health concern. The most recent estimates from Statistics Canada (2015) suggest that 34% of 12-17 year old Canadians are overweight and obese(Statistics Canada, 2017). This number increases to 37% in 20-24 year olds and to 50% in 25-34 year olds(Statistics Canada, 2017). Of interest, therefore, is the age when normal weight children become overweight adults.

Being overweight is defined by the World Health Organization (WHO) as a condition of excess body fat to the point that health is compromised(World Health Organization, 2000)The most common measure used to identify being overweight is body mass index (BMI; kg/m^2)(Popkin and Slining, 2013); however, this metric operates on the assumption that a higher BMI will be associated with a higher fat mass. Yet at a given BMI, percentage total body fat mass (%FM), fat distribution (waist circumference [WC] and waist-to-height ratio [WHtR]) and associated health risk can vary substantially(Romero-Corral *et al.*, 2010; Griffiths *et al.*, 2012; Katzmarzyk *et al.*, 2012; Wildman *et al.*, 2013; Shen *et al.*, 2017). The relationship between BMI, adiposity and fat distribution is, among other factors, a function of sex, degree of fatness, maturation, and chronological age(Freedman and Sherry, 2009). The variability in the measures of BMI and %FM between individuals and between sexes becomes more pronounced from the onset of adolescence into emerging adulthood (18-25 years), as pubertal hormones and individual genotypes influence the relative amounts of lean and fat mass being accrued(Malina, Bouchard and Bar-Or, 2004; Flegal *et al.*, 2009; Freedman and Sherry, 2009). During this period of growth, fat mass accrual comprises a greater proportion of weight gain in females, whereas lean mass comprises a greater proportion of weight gain in males(Malina, Bouchard and Bar-Or, 2004). The adolescent/emerging adulthood period is also typified by the cessation of growth, however a continued fat mass accrual beyond this period has been reported(Racette *et al.*, 2005; Gropper *et al.*, 2012; Erin Barbour-Tuck *et al.*, 2018).

Although it is known that normal weight youth become overweight adults during emerging adulthood(Wisemandle *et al.*, 2000) the exact timing during emerging adulthood has not been identified and neither have sex differences by overweight status metrics(Wisemandle *et al.*, 2000; E. Barbour-Tuck, Erlandson, Muhajarine, Foulds and A. D. G. Baxter-Jones, 2018). Using different metrics and cut-points for overweight, especially during periods of body composition changes, may have led to spurious conclusions about the age at onset of overweight status. For example, De Lorenzo et al. (2013) found that 17% of 19-80 year olds defined as being overweight by %FM were found to be normal weight by BMI(De Lorenzo *et al.*, 2013). The agreement of BMI and %TBF categories was significantly higher in 19-34 year olds than in 64-79 year olds (0.5; 95%CI: 0.39, 0.58)(De Lorenzo *et al.*, 2013).

Discovering the metric that provides the best identification of being overweight is justified by the cumulative nature of health risk imposed by prolonged exposure to being overweight. The purpose of this study was to identify if there were sex or metric specific differences in the age of onset of overweight status in a cohort of normal weight Canadian children.

Methods

Study Design and Participants**.** Participants for this study were drawn from the Pediatric Bone Mineral Accrual Study (PBMAS). The PBMAS has been described in detail elsewhere(Bailey *et al.*, 1999). In brief, this mixed longitudinal study was initiated in 1991 with the recruitment of 220 (107 males) children (Table 1); an additional 31 children were added in 1992/93. These 251 children were aged between 8 and 15 years at study entry and between 32 to 40 years at the last collection occasion (Table 1). From 1991 to 1998 annual measures were taken, these were repeated between 2003-2005 and 2007-2011. In 2016-17 participants returned for one further measure (Table 1). The median number of serial measures between 1991 and 2017 was 10, ranging from 1 to 15 occasions. The sample was 95% Caucasian (of the 94% who identified race). Inclusion criteria of participant data for the present study was that they were identified as normal weight at study entry and had a minimum of two measure between 1991 and 2017. There were 237 (108 males) participants who met these criteria and who were measured on a median of 10 occasions (range 2 to 15).

Chronological Age**:** Chronological age (CA) was determined by subtracting the date of birth from the decimal date of measurement.

Anthropometry**:** Height , weight and waist circumference were measured according to standards set out by Ross and Marfell-Jones (1991)(Ross and Warfell-Jones, 1991). BMI was calculated as weight (kg)/height (m) and WHtR as waist circumference (cm) / height (cm)

Body Composition and Overweight Classification**:** Total body fat mass (TBFM), bone mineral content (TBBMC) and total lean mass (TBLM) were assessed using total body dual energy x-ray absorptiometry (DXA) scans (Hologic QDR -2000, Hologic, Waltham, MA). The coefficient of variation (%) for short-term precision in vivo for TBFM was 2.95%(Bailey *et al.*, 1999). Percentage fat mass (%FM) was calculated as: ((TBFM/[TBFM+TBBMC+TBLM]) *100). The following age and sex specific cut-points for overweight for ages 18 years and under were used: BMI cut-points developed by Cole et al. (2012)(Cole *et al.*, 2000); %FM cut-points developed by McCarthy et al. (2006)(McCarthy *et al.*, 2006); WC cut-points corresponding to Adult Treatment Panel cut-points developed by Cook et al. (2009) (Cook, Auinger and Huang, no date) to identify cardio-metabolic risk and childhood centiles by Katzmarzyk (2004)(Katzmarzyk, 2004). WHtR boundary value of 0.500 are recommended in a public health context for assessing increased health risk in children and adults(McCarthy and Ashwell, 2006). Adult overweight cut-points used were as follows: BMI cut-points from WHO (Overweight= 25kg/m^2)[6]); %FM cut-point developed by Gallagher et al. (2000) using prediction equations developed using WHO BMI limits (20-39 years Overweight≥20% in males; ≥33% in females)(Gallagher *et al.*, 2000); WC cut-points based on a World Health Organization (2011) expert consultation (94 cm for males; 80 cm for females)(Genest *et al.*, 2009).

Statistical Analysis: Growth curves for BMI, %FM and WC were developed using hierarchical (multilevel) linear modelling (MLwiN version 3.02, Centre for Multilevel Modelling, University of Bristol, Bristol, UK). This procedure has been described in detail previously(Baxter-Jones and Mirwald, 2004). In brief, parameters (BMI, %FM, WC and WHtR) were measured repeatedly in individuals (level 1 of the hierarchy) and between individuals (level 2 of the hierarchy). Models that contain linked variables (in this case age centered) measured at various levels of a hierarchy are known as multilevel random effect regression models. Specifically, the following additive random effects multilevel regression models were adopted to describe the developmental changes in fat parameters with age.

Fixed effects:

$$y_{ij} = \beta_{0ij}\text{Constant} + \beta_{1j}\text{AgeC}_{ij} + \beta_2\text{AgeC}^2_{ij}$$

$$\beta_{0ij} = \beta_0 + \mu_{0j} + \varepsilon_{0ij}$$

$$\beta_{1j} = \beta_1 + \mu_{1j}$$

Random effects:

$$\text{Level 2} \quad \begin{vmatrix} \mu_{0j} \\ \\ \mu_{1j} \end{vmatrix} \sim N(0, \Omega_\mu) : \Omega_\mu = \begin{vmatrix} \delta^2_{\mu 0} & \delta_{\mu 01} \\ \\ \delta_{\mu 01} & \delta^2_{\mu 1} \end{vmatrix}$$

$$\text{Level 1} \quad [\varepsilon_{0ij}] \sim N(0, \Omega_\varepsilon) : \Omega_\varepsilon = [\delta^2_{\varepsilon 0}]$$

Where, in the fixed effects, y is the fat parameter (e.g. BMI, %FM, WC or WHtR) on measurement occasion *i* in the *j*-th individual; β_{0ij} is a constant (constant = 1); β_{1j} is the slope of the fat parameter over time (age centered around 18 years [AgeC]) for the *j*-th individual; β_2 is the coefficients of a time dependent explanatory variables ($AgeC^2$) at assessment occasion *i* in the *j*-the individual. μ_{0j} μ_{1j} , and ε_{0ij} are random effects, whose means are equal to zero. They are assumed to be uncorrelated and follow a normal distribution and thus their variances can be estimated. Age (time) varies at level one giving a flexible residual variance. Random effects at level two gives a constant covariance thus the underlying correlation is actually changing and this implies a heterogeneous compound symmetry correlation.

Models were built in a stepwise procedure, i.e. predictor variables (β-fixed effects) were added one at a time, and the log likelihood ratio statistics was used to judge the effects of including further variables on the fit of the model. Level 1 variance ε_{0ij} indicated variance within individuals over time ($\delta^2_{\varepsilon 0}$). Age center ($\beta_j AgeC_{ij}$) was added as both a random (level 2) and a fixed variable. This permits individuals to have independent intercepts ($\delta^2_{\mu 0}$) and slopes ($\delta^2_{\mu 1}$) and a calculation of the intercept-slope covariance relationship ($\delta_{\mu 01}$). The power functions $AgeC^2$ was introduced into the linear models to allow for the non-linearity of growth and were retained whether or not they were significant so as to shape the fat developmental curves. The β coefficients in the final models (Table 2) were used to develop average growth curves for BMI, %FM, WC and WHtR with accompanying level 2 variance (level 2 variance = [(Constant*Constant*$\delta^2_{\mu 0}$) + (AgeC*AgeC*+ $\delta^2_{\mu 1}$) + (2*Constant*AgeC* $\delta_{\mu 01}$)]). A total of eight independent multilevel (hierarchical) random effects models were constructed; one for each fat metric by sex. Sex and age specific overweight cut-points were used to identify the age at which growth curves of BMI, %FM, WC and WHtR crossed over their metric specific cut-points (Figure 1).

Results

A total of 2,157 (982 males) measures were available from 237 (108 males) measured on a median of 10 occasions between the ages of 8 and 40 years of age (Table 1). Tables 2 summarizes the results from the six multilevel models for BMI, %FM, WC and WHtR development by sex. For all models, within individual's fat metric increased with increasing age ($p<0.05$) and between individuals there were differences in individuals intercepts and slopes of the curves ($p<0.05$). In the fixed effects it was shown that, in general, age centered and age centered^2 were significant independent predictors of fat metric development (BMI, %FM, WC and WHtR) ($p<0.05$).

Growth curves (mean and SD) were created for each sex and metrics from the models in Table 2 (Figure 1). Overweight age cut-points were added to the graphs and the age at which the growth curve crossed the cut-off lines was identified. The age at onset of overweight in females by BMI was found to be 21.5 years compared to 22.0 years in males. The age of onset of overweight in females by %FM was 14.5 years compared to 26.5 years in males. The age at onset of overweight by WC was 21.9 years in females and 36.0 years in males. The cut point for WHtR was set at 0.5 and was crossed at 27.5 years in females and 23.5 years in males.

Discussion

This study investigated the age of onset of overweight status in a cohort of children who were categorized by BMI as normal weight at study initialization (8 to 15 years). Previously it had been shown that at peak height velocity (females 11.9 years and males 13.5 years) 91% of males and 86% of females from the entire PBMAS cohort were normal weight by BMI, but by 25 years of age this had dropped to 50% of participants being normal weight by BMI[19]. In the present study, it was found that the average age of transition from normal weight to overweight status depended on age and metric used. BMI curves predicted an earlier onset in males in contrast percentage fat mass (%FM) predicted an earlier onset in females. Waist circumference (WC) curves crossed-cut off in females at a similar age to BMI, however in males WC cut points were not crossed until 36 years of age. Waist-to-height ratio cut points occurred earlier in males compared to females. In males, waist-to-height cut points were crossed after BMI but before percentage fat mass. The implication of the results is that emerging adulthood (18-25 years) appears to be a critical period for fat gain and overweight onset in normal weight youth and that the ability of metrics used to identify overweight status are not equal.

There are large individual and sex differences in body composition and as such having a BMI cut-point does not necessarily match up with the WHO definition of overweight status which specifies it as a condition of excess body fat[6]. From the age of 8 to 18 years, lean mass accrual demonstrates a linear relationship with BMI; while the relationship of BMI with %TBF and WC, and of %TBF and WC with age are not linear(Demerath *et al.*, 2006; Freedman and Sherry, 2009; Weber *et al.*, 2013; Sharma *et al.*, 2015). An increase in a unit BMI likely corresponds to an increase in lean mass (kg) up to and during the adolescent period; however, as sexual dimorphism arises and differences in health behavior and underlying genetics manifest, the relationship between BMI, body composition and age becomes less consistent(Demerath *et al.*, 2006; Freedman and Sherry, 2009; Weber *et al.*, 2013; Sharma *et* *al.*, 2015). During adolescences the increased lean mass accrual seen in boys compared to the observed increase in fat mass seen in girls, highlights the inability of BMI to distinguish between these two tissue types. Differences in the observed prevalence of overweight status BMI and %FM has been previously demonstrated in this cohort with %FM identifying a greater proportion of overweight than BMI in young adult females, and a lesser proportion of overweight in young adult males(E. Barbour-Tuck, Erlandson, Muhajarine, Foulds and A. D. G. Baxter-Jones, 2018). These findings were based on cross-sectional analyses and are now confirmed by the present longitudinal analysis.

In 2017 Statistics Canada released national estimates of overweight and obesity based on self-report data, indicating that 22% of 18-19 year old's and 50% of 25-34 year old's were overweight(Statistics Canada, 2017). This suggests that normal weight youth become overweight during the years of emerging adulthood (18 to 25 years of age). Previously published observational data from the current cohort identifies a prevalence of overweight similar to self-reported national estimates of BMI from 12-17 years (23.1%)(Statistics Canada, 2015, 2017). We have shown previously in this cohort, that the period from 22-30 years is identified as the period when many become overweight(E. Barbour-Tuck, Erlandson, Muhajarine, Foulds and A. Baxter-Jones, 2018). During this same period, overweight prevalence changed from 30-50% (BMI) and 50-60% (%FM) in females, and 50%-70% (BMI) and 30-50% (%FM) in males(E. Barbour-Tuck, Erlandson, Muhajarine, Foulds and A. D. G. Baxter-Jones, 2018). National data are similar[8], suggesting that rates of overweight almost double between adolescence (approximately 25%) to young adulthood (approximately 50%)(Rao *et al.*, 2016; Statistics Canada, 2017). There are no current national estimates of the prevalence of overweight by percentage fat mass or waist circumference (WC) but it can be assumed that the estimates would not be identical to each other or to BMI, as discrepancies between measures have been documented. For example, data from the United States suggests that there has been an increase in BMI and waist circumference, but BMI can only account for 75% of WC changes in males and 50% (Freedman *et al.*, 2015). Longitudinal data from our lab has demonstrated previously that BMI did not increase in youth aged 8-16 between 1963 and 1998 but skinfolds (an estimate of subcutaneous fat) did(Thompson *et al.*, 2002). Looking specifically at the association between DXA derived adiposity and BMI, Sun et al. (2010) found that the correlation between measures of BMI and whole-body fat mass in 20-39 year old's was significant with r= 0.79 in males and r= 0.84 in females(Sun *et al.*, 2010). These findings taken together suggest that BMI is correlated with adiposity but may not represent the entire picture of the prevalence of excess adiposity and may be overlooking consequential body composition such as high WC.

Findings from a large cross-sectional NHANES study(Flegal *et al.*, 2009) agreed with Sun et al. (2010) (Sun *et al.*, 2010) and concluded that BMI (and WC) perform well as proxies for adiposity. Results from the NHANES study indicated that both BMI and WC metrics are highly correlated with %TBF in adults > 20 years of age, such that 46% of men and 49% of woman had exact agreement between %TBF and BMI categories, and 93% of men and 94% of women had agreement within one category. WC had similar correlations with %TBF, with 51% males and 42% females having exact agreement, and 97% males and 91% of females being within one category(Flegal *et al.*, 2009). The agreement was highest in those 25-30 years of age. While these correlations seem high, it also indicates that BMI and WC failed to identify over 40% of participants with high adiposity. In the 20-39-year age group, BMI under-classified almost 30% of participants, and 25% of participants with a %TBF above overweight cut-offs. WC performed slightly better than BMI in males, but slightly worse in females. The authors concluded that BMI and WC worked well as indicators of %BF(Flegal *et al.*, 2009). The current findings in males disagree and suggest that WC does not identify excess adiposity or the onset of overweight at the same time as %FM, WHtR or BMI. Better agreement was found between

BMI, WC and WHtR in females with %FM identifying overweight onset occurring much earlier during adolescence rather than in emerging adulthood. Results from the current study suggest that BMI may be an appropriate proxy for adiposity during emerging adulthood in males but perhaps not in females. Furthermore, our results question the ability of the female %FM cut-offs(Gallagher *et al.*, 2000; McCarthy *et al.*, 2006) to distinguish between normal fat mass development during adolescence and being overweight in emerging adulthood. Our results, with respect to waist-to-height ratio in males, but to a lesser extent in females, are in agreement with Ashwell and Gibson (2014)(Ashwell and Gibson, 2014) that a WHtR of 0.5 during emerging adulthood makes a perfectly acceptable cut-point for detecting overweigh status and lends itself to the simple message 'Keep your waist to less than half your height'.

Beyond accurately representing the prevalence of excessive adiposity, using an accurate metric is important for identifying those who are at potential risk of health consequences(Freedman *et al.*, 2015). The associations between %FM and WC with cardiometabolic health have been shown to be stronger than, and independent of, the association between BMI(Freedman *et al.*, 2015) and cardiometabolic health, suggesting that not all measures are equal in terms of risk assessment(Romero-Corral *et al.*, 2010). Indeed, the study by Tomiyama et al. (2016) found that in a sample of over 40,000 American adults, having a BMI over 25kg/m^2 did not confer the same cardiometabolic for everyone(Tomiyama *et al.*, 2016). One third of those classified as overweight were metabolically healthy while 1/3 classified as overweight were cardio metabolically unhealthy. This is concerning as exposure to cardiometabolic risks (i.e. high blood triglycerides or hypertension) are known to be cumulative in their contribution to chronic disease risk such as cardiovascular disease and diabetes(Magnussen, Smith and Juonala, 2013). In a study of Chinese men Shen et al. (2017) found that cardiovascular health was correlated negatively with WC and WHtR, with a stronger correlation existing between cardiovascular health and WHtR than WC(Shen *et al.*, 2017). With that said there is evidence that BMI is a simple method for identifying metabolic risk with associations to biomarkers of cardiometabolic risk similar to those of DXA, and WC as indicated in findings by Sun et al. (2010)(Sun *et al.*, 2010). It is important to keep in mind that these association may be different in younger individuals as the analysis by Sun et al. (2010) used data from adults over 20 years with a mean age of 41. In children, when the composition of BMI is more similar between individuals there may also be a greater sensitivity of BMI to identify adiposity and cardiometabolic risk; for example in the study by Sardinha et al. (2016) BMI and WC and WHtR had similar sensitivity in identifying clustered cardiometabolic risk factors in children and adolescents(Sardinha *et al.*, 2016). Yet, the study by Laurson et al (2014)(Laurson, Welk and Eisenmann, 2014) found that almost 5% of children identified as normal weight by BMI had WC values over Cook's (2009) cut-points(Laurson, Welk and Eisenmann, 2014). Perhaps the optimal solution is to combine metrics such that those both BMI and WC or WHtR be considered when identifying children with elevated risk.

Limitations.

It must be noted that differences between ages and metrics in this study may have arisen due to the method of analysis and the overlapping cohort design. Longitudinal data was used but not all participants were included in every measure, although the models did adjust for such missing data. With that said, the direction of the differences, by both sex and metric, have been demonstrated previously and a similar age at onset of overweight status identified(Wisemandle *et al.*, 2000; E. Barbour-Tuck, Erlandson, Muhajarine, Foulds and A. D. G. Baxter-Jones, 2018). In their Wisemandle et al. (2000)(Wisemandle *et al.*, 2000) cohort, the most common age at onset of overweight status was the period of 20-25 years; ages similar to the current finings. It is has also been argued that percentage body fat is not a great measure of adiposity(Cole, Fewtrell and Prentice, 2008); however, cut-points for overweight by total body fat mass are not available. It is also noted that the %FM cut-offs were derived from data collected using bioelectrical impedance analysis rather than DXA as used in the present study. Although a number of studies have shown that the two methods are comparable in their accuracy of measuring fat, discrepancies in percent body fat measurements among lean and obese participants, whereby percent body fat is respectively over- and under-estimated, have been shown(Sun *et al.*, 2010). It is possible this influenced the cut-points observed.

Conclusions

There are few longitudinal studies that follow normal weight children into young adulthood that can identify the onset of overweight status by various metrics. Our findings suggest that BMI classifications and waist-to-height ratios could be used concurrently as screening tool for overweight status and that identifying onset with current adult WC cut-offs, particularly in males, may not be applicable in emerging adulthood. WC cut-offs that align with childhood values of WC are warranted if they are to be used in younger populations for early CMR identification. %FM cut-offs may erroneously detect overweight in adolescent females who are laying down fat mass as a result of pubertal changes.

The advantage of using the appropriate tool is that individuals at risk of health consequences, owing to high fat mass distribution, can be identified earlier, monitored more closely and have intervention programs begun earlier. Despite evidence that BMI can operate as a diagnostic of excess adiposity, its value beyond other measures such as %FM at identifying health-related information is still unclear, particularly during adolescence when body composition development is sex specific and related to, in males, lean rather than fat mass accrual. In this cohort of Saskatchewan Canadian children, we have found that in the 1990's the clear majority were normal weight in childhood and adolescence; however, on entering emerging adulthood (18 to 25 years) the majority became overweight. This suggest that further studies are required to determine the long-term health implications of becoming overweight during this critical period of transition from adolescence to adulthood. Given that females accrue more fat and less lean mass in adolescence further work is required in discerning whether the same metrics to identify overweight status should be used when making sex comparisons.

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