Temporal trends of severe obesity prevalence in children and youth from primary care electronic medical records in Ontario, Canada

Sarah Carsley[1] PhD, Eliza Pope[2] BSc, Laura N. Anderson[3] PhD, Mark S. Tremblay[4] PhD, Karen Tu[5,6] MD, MSc, and Catherine S. Birken[7,8] MD, MSc. on behalf of Team ABC[3]

Affiliations:

1. Department of Health Promotion, Chronic Disease and Injury Prevention, Public Health Ontario, 480 University Avenue, Suite 300, Toronto, ON, M5G1V2
2. Faculty of Medicine, University of Toronto, 1 King's College Circle, Medical Sciences Building, Toronto, ON, M5S 1A8
3. Department of Health Research Methods, Evidence, and Impact, McMaster University, 1280 Main Street West, Hamilton, ON, L8S 4K1
4. Healthy Active Living and Obesity Research, CHEO Research Institute, 401 Smyth Road, Ottawa, ON, K1H 8L1
5. Department of Family and Community Medicine, University of Toronto, 500 University Avenue, Toronto, ON, M5G 1V7
6. Toronto Western Hospital Family Health Team, University Health Network, 399 Bathurst Street, Toronto, ON, M5T 2S8
7. Peter Gilgan Centre for Research and Learning, Child Health Evaluative Sciences, the Hospital for Sick Children; Pediatric Outcomes Research Team (PORT), Division of Paediatric Medicine, the Hospital for Sick Children, 686 Bay Street, Toronto, ON, M5G 0A4
8. Department of Pediatric Medicine, University of Toronto, 1 King's College Circle, Medical Sciences Building, Toronto, ON, M5S 1A8

Corresponding Author:
Catherine S. Birken
Division of Paediatric Medicine, Department of Paediatrics, The Hospital for Sick Children,
Room 109801, 10th Floor - Peter Gilgan Centre for Research and Learning
686 Bay Street, Toronto, ON M5G 0A4 Canada,
Phone: 416-813-7654 ext 304930
E-mail: catherine.birken@sickkids.ca

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Abstract

Background: The objective of this study was to determine the prevalence of severe obesity in children 0-18 years in Ontario, Canada, and to determine if the prevalence of severe obesity changed over time from 2004 to 2015.

Methods: This was a repeated cross-sectional study using heights/lengths and weights of children 0-18 years from the Electronic Medical Record Administrative data Linked Database (EMRALD), a database of primary care electronic medical records in Ontario. Body mass index (for-age and sex) z-scores (zBMI) were calculated. Multivariable linear regression generalized estimating equations were used to estimate the association of calendar year and mean zBMI.

Results: In 2014-2015, the prevalence of zBMI>3 in children <5 years was 0.9% (95% CI 0.8-1.1). The prevalence of severe obesity (zBMI>3) in children 5-9 years was 2.9% (95% CI 2.5-3.3), 10-14 years was 3.0% (95% CI 2.5-3.4) and 15-18 years was 3.8% (95% CI 3.2-4.5). Males 5-9 years had a significantly higher prevalence of severe obesity than females 5-9 years. From 2004 to 2015, in children 0-18 years, the mean zBMI decreased by 0.02 (95% CI -0.02 to -0.01) units per year, with the overall prevalence of severe obesity in all ages highest at 3% in 2005 and decreased to 2% in 2015.

Interpretation: In Ontario, the prevalence of severe obesity is consistent with other reported prevalence estimates from similar countries. There is a trend toward decreasing mean zBMI over time. Further understanding of the impact of prevention efforts on these estimates is an important next step.

Introduction

The prevalence of childhood obesity has increased around the world since 1980, with rates doubling in 73 countries.(1) In 2015, 107.7 million children were classified as obese, reaching a worldwide prevalence of 5%.(1) Since 2000, prevalence rates have started to plateau in some developed countries.(2) However, national studies in the United States have shown conflicting trends; one study of low-income children 2 to 5 years reported a decrease in severe obesity,(3) while another study using National Health and Nutrition Examination Survey (NHANES) data showed an increase in the prevalence of severe obesity in children 2 to 5 years.(4) In Canada, using data from the Canadian Health Measures Survey (CHMS), the prevalence of overweight or obesity in children 3 to 18 years was found to be declining, from 30.7% in 2004 to 27.0% in 2013.(5) Unfortunately, it was not possible to estimate the proportion of children with severe obesity because data from this nationally representative sample was small, with less than 500 children 3 to 5 years of age, and no data on children under 3. Therefore, less is known about severe obesity rates in Canadian children, as well as overweight and obesity in children under 6 years.

Obesity and severe obesity in childhood has been associated with increased cardiovascular risk,(6, 7) obstructive sleep apnea,(8) nonalcoholic fatty liver disease,(9) impaired glucose tolerance,(10) and increased exposure to bullying.(11) Furthermore, severity of childhood obesity has been linked to severity of these negative outcomes.(6, 12) Although Canadian national and provincial governments, have prioritized childhood obesity prevention and management,(13) headway on improvements in healthy weights of our population remains unclear. The absence of data on severe obesity in Canadian children constitutes a significant gap in our understanding of the topic. Continued population surveillance of prevalence and trends is

essential to assess any impact of overarching public health policies as well as evaluating investments in clinical programs and interventions. The primary objective of this study was to calculate the prevalence of severe obesity and to describe the trends of severe obesity in children and adolescents in Ontario from 2004 to 2015. The secondary objectives were to estimate the prevalence of all weight status categories and trends over time.

Methods

Setting and study design

This was a repeated cross-sectional study that included children 0 to 18 years of age over multiple years from January 1, 2004 to December 31, 2015. To determine the period prevalence of severe obesity (primary objective) we used two years of data from 2014-2015. To describe weight status trends over time from 2004 to 2015 (secondary objective) we used all time periods. This study was approved by the Research Ethics Boards at Sunnybrook Health Sciences and the Hospital for Sick Children.

Study Population

Children were identified through the Electronic Medical Records Administrative data Linked Database (EMRALD), a database of family practices across Ontario, Canada. As of 2015, the database comprised of 339 active family physicians, at 41 primary care practices spread across the province. Children were included if they met the following criteria: physicians had to be using an EMR for a minimum of two years, patients had to be registered to an active EMRALD physician, have a valid identification number to link with the administrative databases at the Institute for Clinical Evaluative Sciences (ICES), and have a valid height/length and weight measurement to calculate body mass index z-score (zBMI). Patients had to be <19 years

at the end of each year. For example, a patient who was 18 years as of December 31, 2004 would only contribute data to that year.

Measurement

zBMIs were calculated by dividing weight (kg) by height squared (m^2) and standardizing values by age and sex to the WHO Growth Standards and Reference charts that are recommended for growth monitoring in Canada.(14) Height and weight data were cleaned using a standard set of data cleaning rules (15) and zBMI values outside -5 and +6 were excluded. The lower limit was based on WHO recommendations for biologically implausible values(16) and the upper limit was increased from +5 to +6 to captured those at the higher end of the distribution.(17) For the calculation of 2014-15 prevalence the most recent valid zBMI measurement from a well-child visit was used. If no measurements were recorded during a well-child visit in the prevalence period, measurements performed during any type of visit on the same date were used. Weight status was categorized by WHO definitions; for children ≥5 years, zBMI <-2 was defined as underweight, zBMI≥ -2 to ≤1 as healthy weight, zBMI>1 to ≤2 as overweight, zBMI>2 to ≤3 as obese, and zBMI>3 as severely obese. For children <5 years of age the same cutoffs have different labels for the upper weight categories (as defined by WHO), zBMI <-2 was defined as underweight, zBMI≥ -2 to ≤1 as healthy weight, zBMI >1 to ≤2 as *at-risk-for-overweight*, zBMI ≥2 to <3 as *overweight* and zBMI >3 as *obesity*. For children <5 years of age the zBMI category of >3 is defined as obesity not severe obesity according to WHO.(14) However, for the purpose of this manuscript and for consistency between age groups we have applied the older age group cutoff labels to all ages.(18) zBMI cutoffs of 1, 2, and 3 correspond approximately to the 85th, 97th and 99.9th BMI percentiles, respectively.(19)

To control for changes in distribution of potential confounding variables by year, several variables were included in the multivariate analyses between year and zBMI. These were identified *a priori* based on previously established predictors of obesity and the available datasets at ICES and included: age, sex, rural or urban residence, neighbourhood income quintile, the Ontario Marginalization Index, immigration status, and ethnicity.(20-22) Age and sex were retrieved from the patient's EMR. Rural or urban residence and income quintile were based on the patient's postal code and retrieved through the Ontario Registered Persons Database (RPDB), a database linked to the 2006 Canadian Census data. Similarly, the Ontario Marginalization Index is a census-based, geographically-based index using postal code as a proxy for individual-level socio-demographics.(23) Immigration status of the child was determined using the Immigration, Refugees and Citizenship Canada database (IRCC). Ethnicity was categorized as general population, Chinese, or South Asian using a database that assigns ethnicity based on surname using a validated algorithm, used previously by others.(24)

Statistical Analysis

Descriptive statistics were performed on all variables to determine distributions and frequencies of baseline characteristics. To evaluate the potential generalizability of the findings to the entire province, baseline characteristics of the children included in the prevalence period (January 1, 2014 to December 31, 2015) were compared with all Ontario children during the same time period. We used the RPDB to identify children in Ontario, 0 to 18 years, as of January 1st, 2015, the halfway point in the time window. We excluded those with non-Ontario postal codes and those not eligible for the Ontario Health Insurance Plan (OHIP). To assess objective 1, prevalence and 95% confidence intervals (CI) were estimated for each zBMI category for each age group and by sex.

A multivariable generalized estimating equation (GEE) specified for linear regression was performed to account for the influence of calendar time (year) on BMI z-score as a continuous outcome. The GEE was used to adjust for the non-independence of patients contributing BMI measurements to multiple years. The model also adjusted for potential confounding variables that may have changed the demographics of the patient population contributing data to each year, as previously described.

Results

Study population

A total of 73,443 patients 0 to 18 years from 2004 to 2015 were identified from the EMRALD database. Twenty-four percent of patients were ineligible due to missing zBMI and 0.8% due to implausible zBMI (Figure 1). Overall, 31,312 patients were included in the period prevalence estimate of severe obesity (2014-2015) and 55,292 patients contributed 130,098 zBMI measurements to the time trends analysis (2004-2015). Socio-demographic characteristics of the EMRALD prevalence sample compared to the Ontario population are presented in Table 1. The EMRALD sample are generally younger, have a slightly higher proportion in the upper income quintiles, higher rural residence, a lower proportion of immigrants, and lower proportion of children with Chinese and South Asian ethnicities.

Period prevalence of severe obesity

Between 2014 and 2015, the prevalence of severe obesity (zBMI>3) in children and adolescents 5 to 18 years was 3.1% (95% CI 2.8-3.4%). The prevalence of each zBMI category is presented by age and sex in Table 2. Overall, the prevalence of severe obesity (zBMI>3) increases with age; 0.9% in infants and toddlers (0 to 4 years), 2.9% of children 5 to 9 years,

3.0% of children 10 to 14, and 3.8% of adolescents (15 to 18 years). The prevalence of severe obesity in males at 5 to 9 years was significantly higher compared to females.

Trends over time

From 2004 to 2015 there was a reduction in mean zBMI of 0.02 units per year adjusting for child age, sex, rural residence, neighbourhood income quintile, Ontario Marginalization Index, immigration status, and ethnicity (Table 3). Figure 2 shows the prevalence of overweight, obesity and severe obesity from 2004 to 2015. Temporal trends of weight status prevalence by sex are presented in Supplemental Figure 1. There is a noticeable decline in overweight status, and slight decreases in the prevalence of obesity and severe obesity. The model controlled for potential changes in the demographics of the sample over the 12 year period. Children living in rural areas or in low-income neighbourhoods had significantly higher zBMIs compared to children living in urban areas or higher income neighbourhoods. These statistically significant associations were in the expected direction. Similarly, children with Chinese or South Asian ethnicity, or were immigrants, had lower zBMI compared to the general population. The Ontario Marginalization Index was in the opposite direction as expected; lower marginalization was associated with higher zBMI, however the upper confidence interval was zero, therefore clinical significance is questionable.

Interpretation

The prevalence of severe obesity in children and adolescents, 5-18 years, was 3.1%. The prevalence of severe obesity in males in middle childhood (5-9 years 3.8%) was significantly higher than girls in this age group (2.0%). Rodd and Sharma reported 16.3% of males were overweight or obese in 2012-2013 compared to only 10.4% of females; and when adjusting for potential confounders females were 19% less likely to have obesity compared to males.(5) This

sex difference was not seen in reported prevalence of obesity and severe obesity from the NHANES data in the US.(25) Our results for the trends over the past decade show that the mean BMI z-score of children decreased from 2004 to 2015 by 0.02 units per year. Prevalence estimates of overweight, obesity, and severe obesity from 2004 to 2015 also decreased.

These are the first estimates of severe obesity in Ontario children and in Canada. To compare to other jurisdictions it is important to note the differences in definitions of severe obesity in children. There are several different classifications for weight status, which vary by age, country, and growth reference. In the United States, class II obesity is defined as a BMI >120% of the 95th percentile or a BMI $\geq$ 35 kg/m^2, whichever is lower, and class III is defined as a BMI >140% of the 95th percentile or a BMI $\geq$ 40 kg/m^2, whichever is lower.(26) Other developed countries use the International Obesity Task Force (IOTF) definition for morbid obesity which is equivalent to age and sex adjusted BMI >35 kg/m^2 at 18 years.(27) Due to the paucity of other provincial or Canadian estimates for severe obesity prevalence, our only comparative estimates are to other developed countries. These comparisons should be made with caution because of the differences of international definitions of severe obesity and the use of different growth reference charts. The U.S. has the highest estimate of severe obesity (class II and class III) of about 8% in children 2 to 17 years.(28) Unlike our study, they have shown an increasing trend in the proportion of children in the class II and class III obesity categories.(4) National survey data from Australia reported a prevalence of 2.0% using the U.S. definition, or 1.8% using the IOTF definition for morbid obesity.(29) The authors also reported a significant increase in the prevalence of morbid obesity from 1985 to 2012. In the UK, prevalence of severe obesity (defined as $\geq$ 99.87th percentile of the UK 1990 growth charts) was 1.5% for both boys and girls 4-5 years and 1.1% for girls and 1.2% for boys 10-11 years.(30) New Zealand reported

an estimate of 2.5% for children aged 13 to 17 years in 2013 (based on the IOTF definition).(11) Taking into consideration the multiple limitations for comparison to these international estimates, our overall estimate of 3.1% for children aged 5 to 18 years and 0.9% for 0-4 years appear relatively consistent.

The decreasing trend in mean BMI z-score corroborates the most recent trends data from the Canadian Health Measures Survey, comparing the 2004/05 cycle to the 2012/13 cycle.(5) In their study, the temporal change in mean BMI z-score over the 10-year period was -0.12 (-0.2 to -0.05) for children 3 to 17 years. Our study results show a higher magnitude decrease of 0.24, if extrapolated over a 12-year period. Unlike the U.S. and Australia, who have shown increasing trends in the proportion of children with higher levels of obesity (class I, class II, or class III), our data shows no significant increase, rather a decrease in the prevalence over time.

The use of routinely collected data from electronic medical records in primary care has many advantages (31) including a relatively accessible source of valid measurement of BMI from health providers.(32) A limitation of this study may be the lack of generalizability to children who do not access primary care. It is also possible that complex severe obesity patients are not seen by primary care physicians routinely, but rather specialists or subspecialists. As such, the true prevalence may be underestimated. The population characteristics describing those in EMRALD to the overall Ontario population differed mainly on variables that are related to routine use of primary care such as age. The CHMS sampling method (5) has the advantage of a representative national survey. However the CHMS does not presently include children <3 and there are few children of other age groups (only 363 children between 3 and <5 years in 2012-13 and 2097 children 5 to 19 years). Therefore the number with obesity is small limiting the ability to examine important subgroups such as those children with severe obesity. Given the large

sample size and longitudinal data in our study, we were able to provide estimates in all age groups and examine the trends over multiple years. Concerns about the completeness and accuracy of child height and weight measurements in EMRs have been examined in this database previously, and shown to be of high quality.(33)

The prevalence estimates of severe obesity in children and youth in Ontario are similar to other international estimates from developed countries, excluding the United States. Our results suggest a decrease in overall mean zBMI consistent with previous national Canadian data.(5, 34) However, we are unable to attribute this decrease to any specific intervention or policy change. Efforts to evaluate current childhood obesity initiatives should be encouraged to determine their effectiveness and applicability to subgroups that are at increased risk. In this study, about 25-30% of children and youth were still above a healthy weight, and 2-3% were severely obese. In recent years there has been increasing evidence that demonstrates children as young as two years with extreme zBMI are at much higher risk of obesity-related co-morbidities.(6) A sustained clinical and public health focus on childhood obesity is still required to further reduce obesity. Continued monitoring and information about the prevalence and longitudinal trends of severe obesity will help to characterize the burden in childhood as well as inform potential therapeutic targets for this population.

Figure 1: Selection of study sample from EMRALD cohort

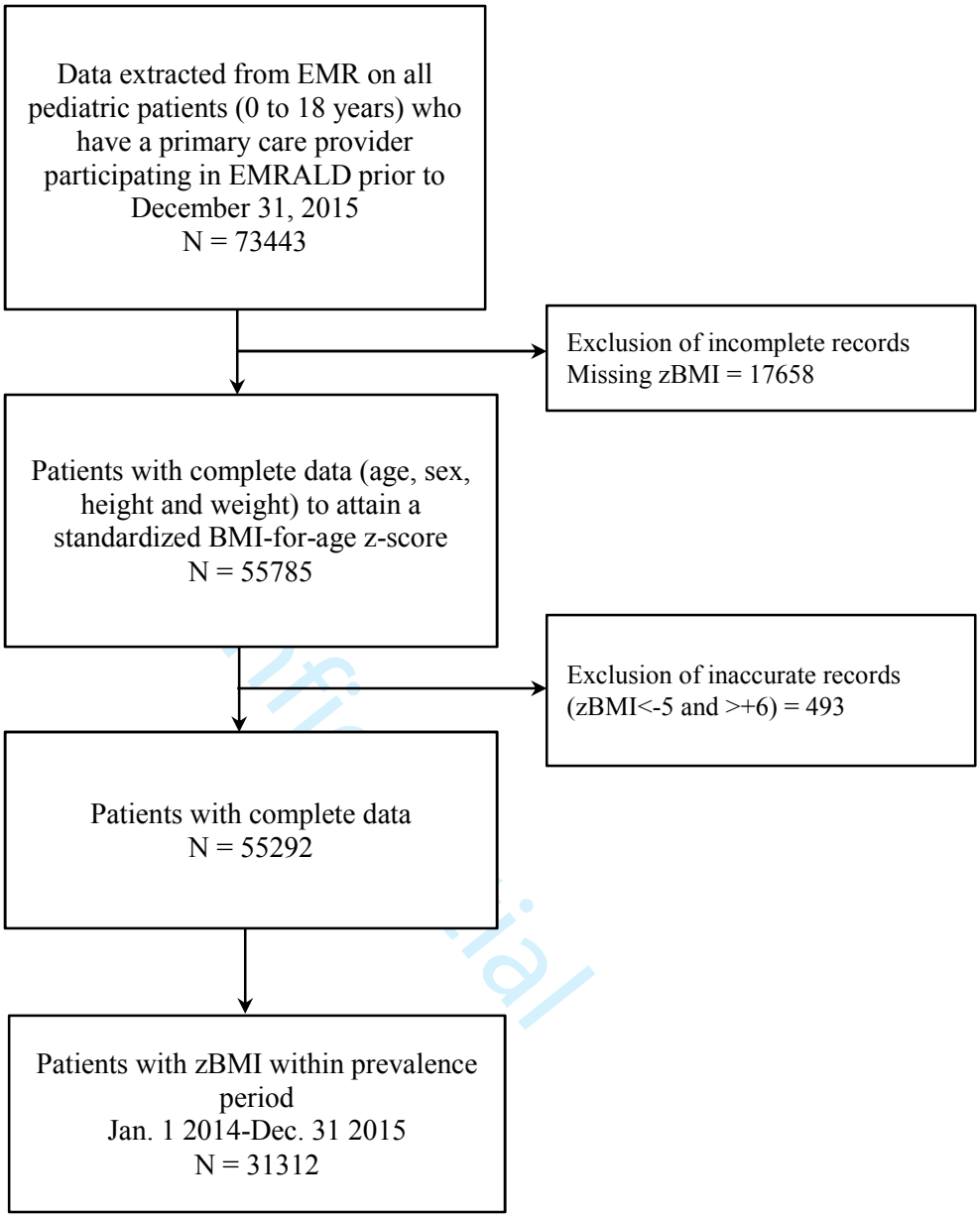

Table 1: Baseline characteristics of patients in the EMRALD Cohort and the Ontario Population

Baseline characteristics	**EMRALD® Cohort**		**Ontario Population**	
	N	%	N	%
N	31312		2746896	
Sex				100
Female	15491	49.5	1337763	48.7
Male	15821	50.5	1409133	51.3
Age group				
0-4	15097	48.2	362514	13.2
5-9	6926	22.1	771702	28.1
10-14	5623	18.0	782697	28.5
15-19	3666	11.7	829983	30.2
Income quintile				
1- Lowest	4264	13.6	523297	19.1
2	5990	19.1	498942	18.2
3	6827	21.8	548594	20.0
4	7053	22.5	609048	22.2
5- Highest	7021	22.4	555924	20.2
Rural Residence				
Yes	5085	16.2	292412	10.6
Immigration				
Child is an immigrant	523	1.7	170551	6.2
Mother is immigrant	3366	10.7	509445	18.5
Ethnicity				
General population	30015	95.9	2499719	91.0
Chinese	848	2.7	132024	4.8
South Asian	442	1.4	115153	4.2
Chronic conditions				
Asthma	3716	11.9	484892	17.7
Diabetes	76	0.2	8953	0.3
Complex chronic conditions	1543	4.9	140384	5.1

Table 2: Prevalence estimates of weight status in children and adolescents by age and sex 2014-2015

		BMI z-score categories									
Age group, years	**No. of children**	**<-2**		**≥-2 to ≤ 1**		**>1 to ≤ 2**		**>2 to ≤ 3**		**>3**	
All children		%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
0-4	15097	4.8	(4.5 to 5.1)	75.5	(74.8 to 76.1)	14.7	(14.1 to 15.2)	4.2	(3.9 to 4.5)	0.9	(0.8 to 1.1)
5-9	6926	2.3	(1.9 to 2.7)	72.7	(71.7 to 73.8)	15.1	(14.3 to 15.9)	7.0	(10.6 to 12.1)	2.9	(2.5 to 3.3)
10-14	5623	2.2	(1.8 to 2.6)	62.9	(61.6 to 64.2)	21.1	(20.0 to 22.2)	10.8	(10.0 to 11.6)	3.0	(2.5 to 3.4)
15-19	3666	1.9	(1.4 to 2.3)	67.1	(65.6 to 68.6)	18.1	(16.9 to 19.4)	9.1	(8.2 to 10.1)	3.8	(3.2 to 4.5)
Total	31312	3.4	(3.2 to 3.6)	71.6	(71.1 to 72.1)	16.3	(15.9 to 16.7)	6.6	(6.3 to 6.8)	2.1	(1.9 to 2.2)
Males											
0-4	7690	5.0	(4.5 to 5.5)	73.7	(72.7 to 74.7)	15.3	(14.5 to 16.1)	4.8	(4.3 to 5.3)	1.2	(1.0 to 1.5)
5-9	3563	2.2	(1.8 to 2.8)	71.3	(69.7 to 72.7)	15.3	(14.2 to 16.5)	7.4	(6.5 to 8.3)	3.8	(3.2 to 4.5)
10-14	2828	2.4	(1.9 to 3.1)	61.5	(59.7 to 63.3)	20.5	(19.0 to 22.0)	12.2	(11.0 to 13.4)	3.4	(2.8 to 4.2)
15-19	1740	2.8	(2.0 to 3.6)	64.1	(61.8 to 66.4)	19.2	(17.4 to 21.1)	10.2	(8.9 to 11.8)	3.7	(2.8 to 4.7)
Total	15821	3.7	(3.4 to 4.0)	69.9	(69.2 to 70.6)	16.6	(16.1 to 17.2)	7.3	(6.9 to 7.7)	2.5	(2.3 to 2.7)
Females											
0-4	7407	4.5	(4.1 to 5.0)	77.3	(76.3 to 78.3)	14.0	(13.2 to 14.8)	3.5	(3.1 to 4.0)	0.6	(0.4 to 0.8)
5-9	3363	2.3	(1.8 to 2.9)	74.2	(72.7 to 75.7)	14.8	(13.7 to 16.1)	6.6	(5.8 to 7.5)	2.0	(1.5 to 2.5)
10-14	2795	2.0	(1.5 to 2.6)	64.4	(62.6 to 66.1)	21.8	(20.2 to 23.3)	9.4	(8.4 to 10.6)	2.5	(2.0 to 3.2)
15-19	1926	1.0	(0.6 to 1.6)	69.8	(67.7 to 71.8)	17.2	(15.5 to 18.9)	8.0	(6.9 to 9.4)	3.9	(3.1 to 4.9)
Total	15491	3.2	(2.9 to 3.4)	73.4	(72.7 to 74.1)	16.0	(15.4 to 16.6)	5.8	(5.5 to 6.2)	1.7	(1.5 to 1.9)

Table 3: Adjusted linear regression model of the association of year on zBMI from 2004-2015

Variable	Estimate (95% CI)	p-value
Year	-0.02 (-0.02 to -0.01)	<0.01
Age (years)	0.05 (0.05 to 0.05)	<0.01
Sex (ref=Female)	-0.07 (-0.09 to -0.05)	<0.01
Rural residence (ref=No)	0.09 (0.07 to 0.12)	<0.01
Income quintile (ref=1, lowest)		
2	0.15 (0.11 to 0.19)	<0.01
3	0.12 (0.09 to 0.16)	<0.01
4	0.10 (0.07 to 0.13)	<0.01
5	0.07 (0.04 to 0.09)	<0.01
Ontario Marginalization Index	-0.02 (-0.03 to -0.00)	0.01
Ethnicity (ref=General population)		
Chinese	-0.22 (-0.28 to -0.15)	<0.01
South Asian	-0.40 (-0.49 to -0.31)	<0.01
Child immigrant (ref=No)	-0.08 (-0.15 to -0.00)	0.05

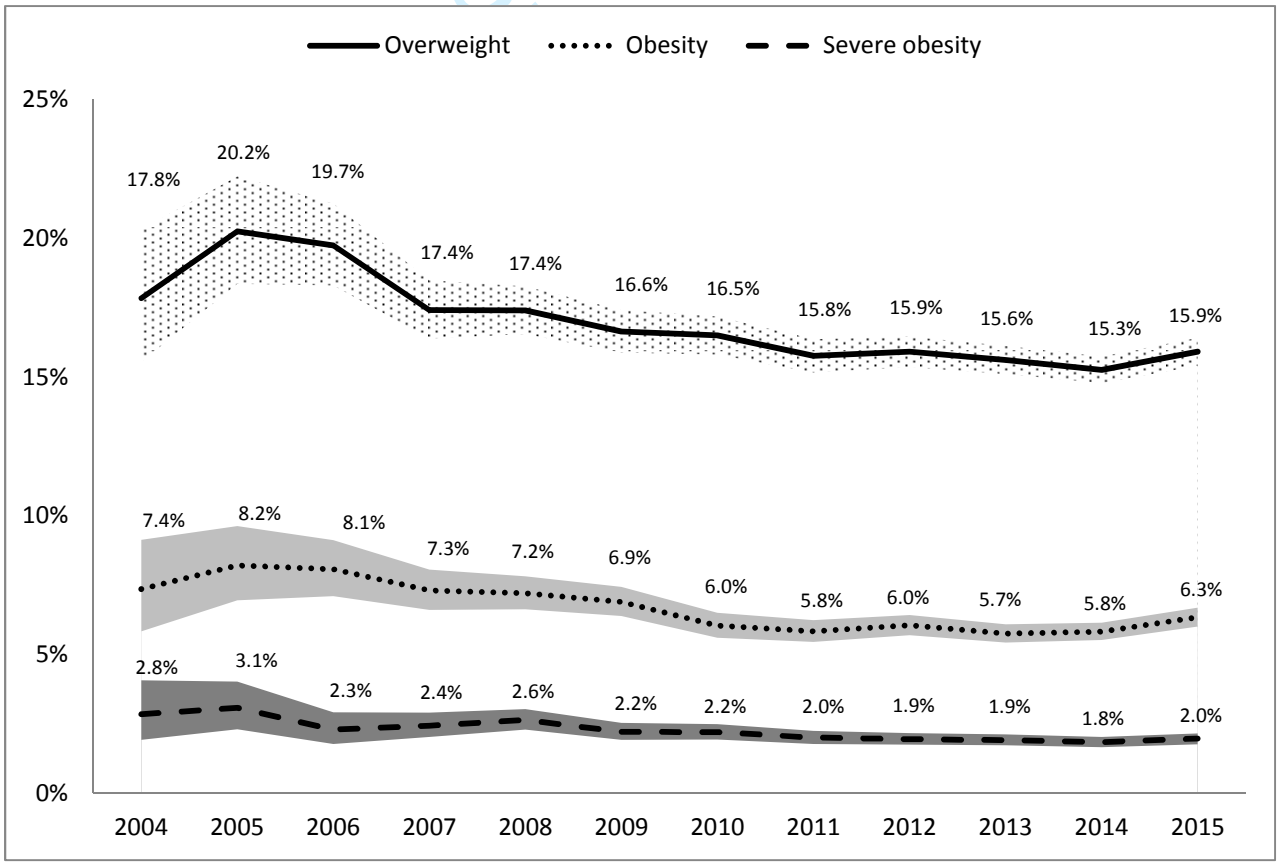

Figure 2: Prevalence of overweight, obesity and severe obesity of children 0 to 18 years from 2004 to 2015

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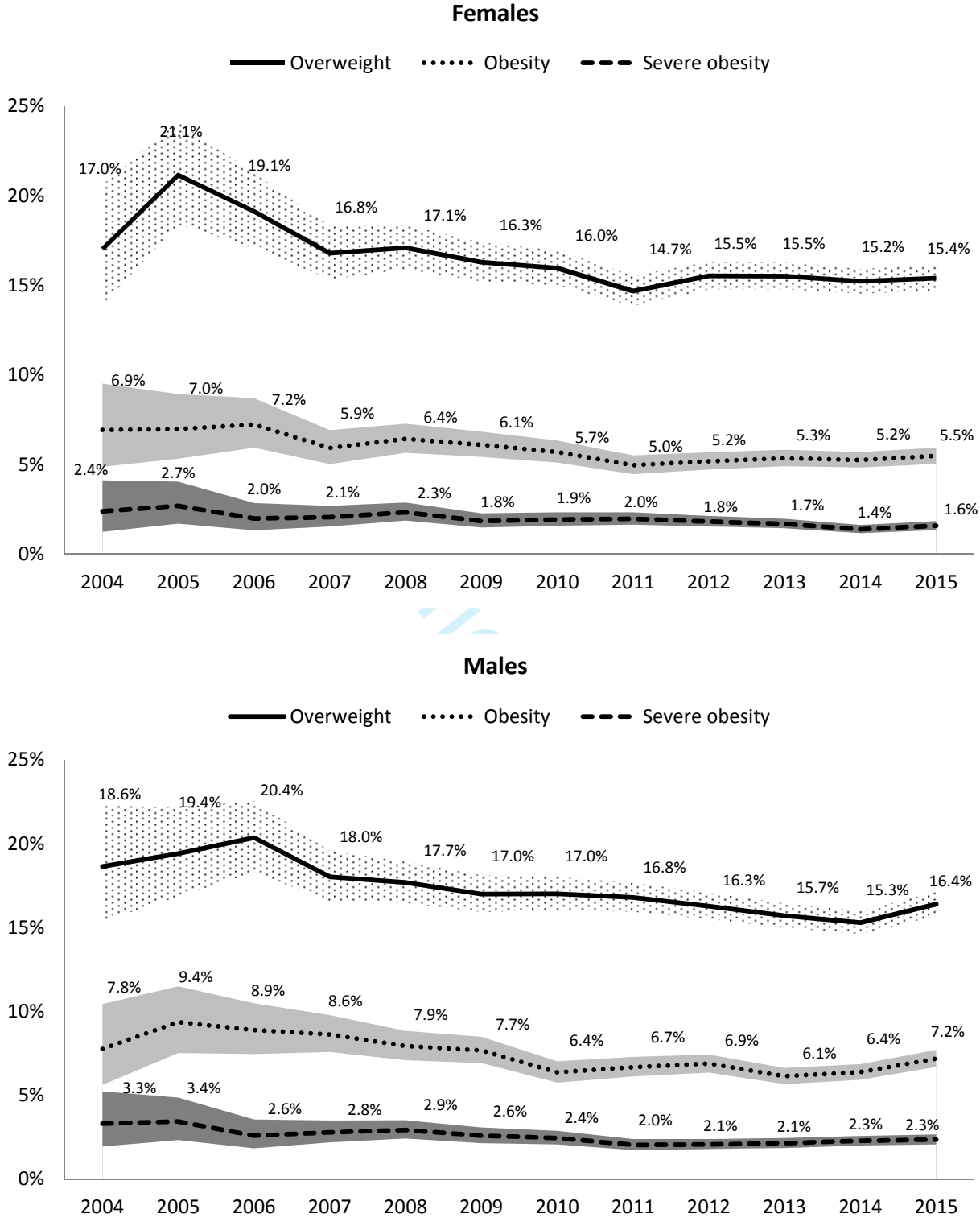

Supplemental Figure 1: Prevalence of overweight, obesity and severe obesity of children 0 to 18 years by sex from 2004 to 2015

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Study design is in the abstract	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Type of data (EMR) and database is specified in the title and abstract. P. 2 line 7-8 Geographic region is mentioned in methods of abstract. P. 2 line 4
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Included in introduction		P. 3, line 21-23
Objectives	3	State specific objectives, including any prespecified hypotheses	Included in introduction		P. 4 line 2-4
Methods					

Study Design	4	Present key elements of study design early in the paper	Methods section, first paragraph		p. 4 line 8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	All included in methods		p. 4 lines 8-11, 13-24
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	Described in methods section on study design and population. As well in figure 1. Study inclusion criteria are described on page 4 lines 13-24.	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	No algorithms were used to select the population of interest. None were used to selection population. A flow chart of study selection was provided (Figure 1 on page 12)

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	A reference to the algorithm to determine child ethnicity is provided in the methods. Page. 5, lines 12-13
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	These are described in the section "Measurement" in the methods		Page 5 lines 4-22
Bias	9	Describe any efforts to address potential sources of bias			
Study size	10	Explain how the study size was arrived at	All eligible children in the EMRALD cohort and described in Figure 1.		Page 12
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Described in the methods section.		Page 5 lines 4-22
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions	Described in methods section. No subgroup analysis performed.		Page 6 lines 14-23 Continues on page 7 lines 1-6

		(c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	Complete case analysis.		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	EMRALD database access described in Methods: study population. P. 4 lines 8-14 Data cleaning methods are described in the definition of exposure and reference previously published papers. Page 5 lines 6-9
Linkage		..		RECORD 12.3: State whether the	Data linkage is

				study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	described in the section on study population in methods. Page 4 lines 8-14
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	There is a description of the study population in the first paragraph of the methods and a follow chart to describe exclusions (figure 1). Page 12
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	Table 1 includes this information. All missing data on covariates was below 5%.		Page 7 and 13
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time	Table 2 presents prevalence estimates by age		Page 7 and 14

		Case-control study - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	and sex.		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 3 shows the adjusted models with 95% confidence intervals and p-values. Temporal trends are presented in Figure 2. As well by sex in supplemental figures.		Page 8 and table on page 14-15
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	N/A		
Discussion					
Key results	18	Summarise key results with reference to study objectives	First paragraph of discussion		Page 8-9 lines 19-24, 1-4
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both	A summary and discussion of the limitations are presented in the 3rd	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s).	We discuss our attempts to mitigate specific limitations and

		direction and magnitude of any potential bias	paragraph.	Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	are presented in the paragraph on limitations. Page 10 lines13-23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Interpretation in given in the conclusion of the paper.		Page 11, lines 4-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussed in limitations paragraph.		Page 10 lines13-23
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Provided on title page of the manuscript		Page 1
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	All relevant information is kept at the Institute of Clinical Evaluative Sciences.

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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