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Early lifestyle determinants of adiposity trajectories from childhood into late adolescence

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Ce mémoire intitulé

Early lifestyle determinants of adiposity trajectories from childhood into late adolescence

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Résumé

Contexte: L'obésité infantile est un facteur de risque majeur de mortalité et de morbidité, car les enfants avec obésité ont tendance à maintenir leur obésité à l'âge adulte. Parmi les enfants canadiens, 27% ont un surpoids ou une obésité, ce qui pose un grave problème de santé publique, vu les conséquences en termes de morbidité et mortalité de l'obésité à l'âge adulte.

Objectifs: Les principaux objectifs de ma recherche sont les suivants: (1) examiner le lien entre l'activité physique durant la pré-puberté et les trajectoires d'adiposité de l'enfance à l'adolescence; (2) examiner le lien entre les comportements sédentaires dans la pré-puberté et les trajectoires d'adiposité de l'enfance à l'adolescence; et (3) examiner les associations entre les apports alimentaires dans la pré-puberté et les trajectoires d'adiposité de l'enfance à l'adolescence. Mon hypothèse est que moins d'activité physique, plus de temps sédentaire et une alimentation moins saine (ex. moins de fruits et légumes, plus de boissons sucrées) pendant l'enfance seront associés à des trajectoires défavorables d'obésité de l'enfance à l'adolescence.

Méthodes: Cette recherche porte sur les données de l'étude QUALITY (QUebec Adipose and Lifestyle Investigation in Youth). Cette cohorte comprend 630 enfants caucasiens âgés de 8 à 10 ans, recrutés au départ sur la base d'antécédent d'obésité chez leurs parents. De ce nombre, 377 ont été suivis à 10-12 ans et à 15-17 ans. Les comportements sédentaires et l'activité physique ont été mesurés par accélérométrie sur une période de 7 jours, le temps d'écran a été mesuré par questionnaire et l'apport alimentaire avec trois rappels alimentaires de 24 heures. Le poids et la taille ont été mesurés à chaque période et transformés en scores z de l'indice de masse corporelle (IMC-z) selon les normes de l'OMS (Organisation Mondiale de la Santé). La modélisation des trajectoires basée sur les groupes a été utilisée pour identifier les trajectoires longitudinales de l'IMC-z. Des régressions logistiques multinomiales ont ensuite été utilisées pour examiner les associations entre les habitudes de vie durant l'enfance et les trajectoires d'adiposité, en ajustant l'âge, le sexe, les stades du développement pubertaire de Tanner et l'éducation parentale.

Résultats principaux: Six trajectoires distinctes d'IMC-z ont été identifiées: Poids-Faible-à-Normal-Stable (5,7%), deux groupes de Poids-Normal-Stable qui ont ensuite été combinés (33,0% et 24,8%), Surpoids-Stable (19,8%), Obèse-Stable (8,8%) et Surpoids-Décroissants (7,9%). Pour chaque portion supplémentaire de fruits et légumes à 8-10 ans, la probabilité de faire partie du groupe en Surpoids-Décroissants est

augmentée de 26% (OR 1,26, IC 95% 1,06-1,49) par rapport à ceux du groupe Poids-Normal-Stable. Pour chaque heure supplémentaire de comportement sédentaire mesurée par l'accéléromètre à 8-10 ans, la probabilité d'appartenir au groupe Surpoids-Décroissants est augmentée de 51% (OR 1,51, IC à 95% 1,03-2,22) par rapport au groupe Poids-Normal-Stable. En termes d'activité physique, toutes les 10 minutes supplémentaires d'activité physique modérée à vigoureuse (APMV) au départ étaient associées à une probabilité plus faible d'appartenir au groupe Obèse-Stable (OR 0,75, IC à 95% 0,61-0,91) et Groupe Surpoids-Décroissants (OR 0,78, IC 95% 0,62-0,98) par rapport au groupe Poids-Normal-Stable.

Importance: Cette étude a permis d'identifier différents groupes de trajectoires de développement du score IMC-z qui restent stables de l'enfance à la fin de l'adolescence ainsi qu'un groupe d'enfants qui sont passés d'un surpoids à un poids normal. Ces derniers avaient un apport alimentaire plus favorable en fruits et légumes à 8-10 ans. Cependant, ils avaient également une APMV inférieure et un comportement plus sédentaire comparativement au groupe de Poids-Normal-Stable.

Mots-clés : adiposité; obésité; habitudes de vie; analyse de trajectoire; pédiatrie; indice de masse corporelle; enfants/ adolescents

Abstract

Background: Childhood obesity is a major risk factor for mortality and morbidity as children with obesity tend to remain obese into adulthood. Among Canadian children, 27 % have overweight or obesity, which is a serious public health concern.

Objectives: The main objectives of my research are to (1) examine the associations between physical activity in pre-puberty or early puberty and obesity trajectories across childhood and adolescence; (2) examine the associations between sedentary behaviors in pre-puberty or early puberty and obesity trajectories across childhood and adolescence; and (3) to examine associations between dietary intake in pre-puberty or early puberty and obesity trajectories across childhood and adolescence. My hypothesis is that lower physical activity, more time spent in sedentary behaviours and unhealthy diets (e.g., higher sugar-sweetened beverage consumption, lower fruit and vegetable intake) in childhood (pre to early puberty) will be associated with adverse patterns of obesity into adolescence.

Methods: This study uses data from the Quebec Adipose and Lifestyle Investigation in Youth (QUALITY) study. This cohort includes 630 Caucasian children aged 8-10 years, recruited at baseline based on a parental history of obesity. Of these, 377 were re-assessed at 10-12 years and at 15-17 years. Sedentary behavior and physical activity using 7-day accelerometry, self-reported screen time and dietary intake with three 24-hr diet recalls were measured. Weight and height were measured at each time period and transformed to body mass index (BMI) z-scores using WHO (World Health Organization) Standards. Group based trajectory modeling was used to identify longitudinal trajectories of z-BMI. Multinomial logistic regressions were used to examine associations between lifestyle behaviors at 8-10 years and distinct obesity trajectory groups, while adjusting for age, sex, tanner stage and parental education.

Results: Six distinct z-BMI trajectory groups were identified: Stable-Low-Normal-Weight (5.7%), two Stable-Normal-Weight groups that were subsequently combined (33.0% and 24.8%), Stable-Overweight (19.8%), Stable-Obese (8.8%) and Overweight-Decreasers (7.9%). For every additional vegetable and fruit serving at baseline, the likelihood of being in the Overweight–Decreasers group increased by 26% (OR 1.26, 95% CI: 1.06, 1.49) compared to those in the Stable-Normal-Weight group. For every additional hour of sedentary behavior at baseline, the likelihood of belonging to the Overweight-Decreasers group increased by 51% (OR 1.51, 95% CI: 1.03, 2.22) as compared to Stable-Normal-Weight group. In terms of physical activity, every additional 10 mins of Moderate to Vigorous Physical Activity (MVPA) at baseline was associated with a lower likelihood of belonging to the Stable-Obese group (OR 0.75, 95% CI: 0.61,

0.91) and to the Overweight-Decreasers group (OR=0.78, 95% CI: 0.62, 0.98) compared to the Stable-Normal-Weight group.

Conclusion: Stable trajectories of z-BMI from childhood to late adolescence were found, with the exception of one decreasing trajectory from overweight in childhood to normal weight in adolescence. The latter had more favourable dietary intake of fruits and vegetables at baseline, however, they also had lower MVPA and more sedentary behavior.

Keywords: Adiposity; obesity; lifestyle behaviors; trajectory analysis; paediatrics; body mass index; children/adolescents

Table of contents

List of tables

List of figures

List of abbreviations

BMI: Body Mass Index

WHO: World Health Organization

ANOVA: ANalysis Of VAriances

PA: Physical Activity

MVPA: Moderate to Vigorous Physical Activity

MET: Metabolic Equivalent

QUALITY: QUebec Adipose and Lifestyle Investigation in Youth

95% CI: 95% Confidence Interval

SES: Socio-economic status

I would like to dedicate this thesis to my parents and my brother for their unconditional love and support.

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Chapter 1

1. Literature review

1.1 Public health burden of childhood obesity

1.1.1 Epidemiology of overweight and obesity in children

Obesity is a problem that arises from a complex system of individual, genetic, socio-cultural and environmental factors that influence individual behaviors such as food consumption and nutritional choices (energy intake), physical activity and sedentary behaviors [1, 2]. Obesity is the result of an energy imbalance between calories consumed and calories expended, creating an energy surplus and a state of positive energy balance resulting in excess body weight [3]. Obesity is a major public health challenge and a key global health priority is to monitor, prevent and manage obesity [4].

Obesity and overweight have been on the rise over the past three decades in children and adolescents, with marked variations in prevalence across countries [5]. In 1975, less than 1% of children and adolescents aged 5-19 years had obesity, while in 2016, this figure increased to more than 124 million (6% of girls and 8% of boys) worldwide [4].

The prevalence of pediatric obesity in Canada tripled over the past three decades [6]. However, recent patterns indicate a stabilization in the prevalence of overweight at approximately 18% and a reduced prevalence of obesity from 14.3% to 10.4% [7, 8]. Although the prevalence of overweight and obesity appears to be stabilizing, it remains high [5]. Moreover, it continues to have significant impacts on morbidity, and thus remains an important public health issue [9, 10].

1.2 Impact of overweight and obesity

1.2.1 Impact of overweight and obesity on body systems

Obesity affects almost every organ system, namely the metabolic, cardiovascular, orthopedic, neurological, hepatic, pulmonary and renal systems [10, 11]. It is associated with social-emotional (e.g., negative image of health, depression) [12] and long-term health consequences (e.g., cardiovascular

disease and type 2 diabetes) [12-14]. Moreover, the burden of obesity in children is responsible for premature deaths, loss of productivity and social stigmatization [15].

Childhood and adolescence are considered to be important time periods where obesogenic behaviors (namely physical inactivity, sedentary behaviors, unhealthy dietary intake) are shaped [16]. Studies suggest that these behaviors may track into adulthood [16, 17]. Obesity in children predicts adolescent obesity [18] and subsequent adult obesity [19, 20]. As demonstrated by high quality prospective studies, the net impact of overweight and obesity during childhood is increased morbidity and mortality in adulthood [21, 22]. It is mainly from cardiovascular diseases and diabetes, but also from cancer and other acute and chronic diseases like liver and kidney diseases, sleep apnea and depression [23, 24]. Evidence suggests that children aged 5 years or older who are overweight have an approximately 10-fold increased risk of becoming obese as adolescents whereas there is only a 3 to nearly 5-fold increased risk in children aged 5 years or less [18]. Approximately 70% of adolescents who are obese will grow up to be obese adults [25]. The risk of mortality is higher in individuals who were obese before the age of 50 years compared with non-obese individuals of the same age group [21, 26].

1.2.2 Impact of overweight and obesity on healthcare system

The negative health consequences of obesity place a substantial economic burden on the healthcare system and society. In 2014, the economic impact of obesity globally was nearly $2.0 trillion (USD) which represents 2.8% of the global gross domestic product [27]. In Canada, the proportion of total healthcare costs attributable to overweight and obesity has been estimated to be as high as 12% [28]. In particular, a study on the burden of childhood obesity in Canada estimated the total direct healthcare costs over a 3-year period to be 21% higher among obese 5th grade children compared to normal weight children [29]. Obesity is responsible for directly impacting healthcare system costs (hospital care, pharmaceuticals) and indirectly the cost of productivity (premature death and reduced longevity) [3, 28].

1.3 Measuring overweight and obesity in children

1.3.1 Definition and classification of obesity in children

Overweight and obesity are defined as an abnormal or excessive body fat accumulation that may impair health [4]. Adiposity and body composition measurements are often used as measures of obesity.

An ideal measure would be accurate, simple, cost-effective, comparable to the published reference values and acceptable to the participants [30]. Nevertheless, no existing measure fulfills all the criteria. The gold standard for measuring adiposity is under water weighing [31]. This method measures body composition, however, it is complicated and difficult to perform accurately [32]. Several alternate methods have been validated against under water weighing, in particular DXA (Dual-energy X-ray absorptiometry).

Body Mass Index (BMI), calculated as weight in kilograms divided by height in meters squared (kg/m^2), is a clinical measure used to classify healthy and unhealthy weight statuses [33].

$$BMI = \frac{kg}{m^2}$$

BMI *z*-scores, also called BMI standard deviation (S.D.) scores, are measures of relative BMI adjusted for a child's age and sex using a reference population [34]. The age and sex adjusted WHO (World Health Organization) growth reference charts are widely used to classify overweight (BMI z-score: ≥1), obesity (BMI z-score: ≥2) and severe obesity (BMI z-score: ≥3) among children aged 5- to 19-years old [35]. BMI z-scores between -2 and 1 are considered "healthy weight" and are associated with more favourable health outcomes [3]. Table 1.1 describes the BMI z-scores and corresponding percentile cut-offs for underweight, healthy weight, overweight, obesity and severe obesity from children aged 5 to 19 years according to WHO reference norms.

Table 1.1- Classification of weight status in children aged 5-19 years according to WHO cut-offs for age and sex adjusted BMI

Weight Status Category	Percentile	Z score
Underweight	<3	<-2
Normal or healthy weight	3-85	-2 to 1
Overweight	≥85	≥1
Obesity	≥97	≥2
Severe obesity	≥99.9	≥3

The simplest measure of obesity is weight; however, on its own this provides little useful information, as confounding variables such as a person's height and body composition are not taken into consideration [36]. Other simple measures of obesity are BMI, waist circumference, Waist-to-Height ratio and body fat percentage calculated from skin folds or bio-electrical impedance [37]. In clinical research, BMI is the most commonly used measure given the feasibility [34, 38, 39].

Using z-BMI as a measure of adiposity in children has advantages and disadvantages. One disadvantage is that z-BMI cannot distinguish fat mass (adipose mass) and lean mass (skeletal and muscle mass) [40]. On the other hand, BMI is easy to measure using simple equipment or self-reported measures of height and weight [41]. It is a good public health surveillance tool as it is inexpensive and easy to use in large study samples [34]. Z-BMI is a strong predictor of total fat mass in normal weight children aged 9 to 18 years, however it overestimates percent fat mass in similarly aged overweight and obese children [42]. In clinical research, BMI is used as a screening tool for obesity and related diseases on the assumption that a high BMI is reflective of higher levels of adiposity [43].

The direct measures to calculate body fat are DXA, hydrometry, magnetic resonance imaging, air displacement plethysmography, computed tomography, and underwater weighing [32]. DXA measures bone mineral mass using a differential absorption of X-rays of different energies and calculated as bone mineral content divided by bone area [44]. It also calculates relative fat mass and lean mass [45]. DXA is considered to be robust against the BMI [42]. However, trunk composition by DXA is based on prediction rather than measurement and estimation of soft tissue is less accurate in limbs [32]. Due to cost and limited resources, DXA is difficult to use in larger populations [46]. These direct technically complex and expensive measures provide the most accurate measurements; however, these measures are not appropriate for large epidemiological studies [32, 40, 41].

Despite various limitations of BMI, it continues to be good measurement of obesity as it is the most clinically applicable and widely used.

1.4 Important periods for the development of obesity

The period of adiposity rebound, and adolescence (biological maturation) appear to represent critical periods for the development of obesity that persists into adulthood [47].

1.4.1 Adiposity rebound

The adiposity rebound refers to the age after infancy when a child's BMI is at its minimum [48]. Specifically, z-BMI increases throughout the first year of life after which it declines to a nadir around the age of 6 years, marking the beginning of the adiposity rebound period [43]. Early adiposity rebound is strongly associated with increased z-BMI and fatness in adolescence [49]. Early adiposity rebound in children with obesity suggests unhealthy lifestyle behaviors particularly related to food intake and physical activity operated early in life [48]. A recent study found that z-BMI at the age of adiposity rebound partially mediated the relationship between adiposity in infancy and adiposity in adolescence [50].

1.4.2 Adolescence and puberty

The onset of the period of puberty is vital and a normal process for human growth and development. Tables 1.2 and 1.3 describe the normal physiologic changes and secondary sex characteristics of boys and girls that define the stages of pubertal development. Tanner stages are used to define the development of external primary and secondary sex characteristics across puberty, such as development of breasts in girls, genital size in boys and development of pubic hair in both sexes [51, 52]. Studies have revealed that early onset of puberty is associated with negative health outcomes in adolescence and adulthood [53]. Excess adiposity in early childhood has an influence on the process of both growth and puberty [54, 55].

Adolescence corresponds to 10-24 yrs of age stretching between childhood and adulthood [56]. During the transition between childhood and adolescence, there is an increase in body adiposity in both sexes due to change in the distribution of body fat due to sex hormones [47, 50]. The increase in central adiposity during this transition points to the importance of monitoring body adiposity and to the importance of investigating preventive strategies, such as lifestyle factors in this critical period, for later obesity [50].In addition to the biological increase in adiposity in the transition from childhood to adolescence, children and adolescents are prone to adopt obesogenic behaviors as they become more

autonomous with their choices of food and physical activities [16]. Studies suggested that behaviors related to dietary intake, physical activity and sedentary behaviors may track to adulthood [57].

Table 1.2- Pubertal changes in girls

Stages	*Breast stages*	*Pubic hair stages*
1	Pre-adolescent	No hair
2	Breast budding stage	Hair around the labia only
3	Palpable breast tissue, no areolar development	Hair filling the junction of pubis
4	Elevation of areola above the level of the breast	Pubic hairs adult in type but smaller area
5	Mature stage	Adult type

Adapted from pubertal changes in girls by Marshall and Tanner [52]

Table 1.3- Pubertal changes in boys

Stages	*Stages of genitalia*	*Pubic hair stages*
1	Pre-adolescent. Same size of testes, scrotum and penis as in early childhood	No pubic hair
2	Enlargement of scrotum	Downy hair
3	Increase in length and breadth of penis	Hair filling the junction of pubes
4	Further enlargement of penis, testes and scrotum	Adult type but smaller area
5	Adult size genitalia	Adult type

Adapted from pubertal changes in boys by Marshall and Tanner [51]

The next section will focus on the definition of adiposity trajectories, highlighting the importance of tracking BMI overtime to understand the associations between adiposity and lifestyle behaviors.

1.5 Defining Adiposity Trajectories

A trajectory is defined as established sequences of transitions from one state or phenotype to another, describing its evolution over time [58]. A typical BMI trajectory in childhood is defined as one that increases gradually until 1 year of life, then gradually declines to a minimum at about 4-6 years of age (adiposity rebound) [49], then increases again throughout childhood [50]. BMI trajectories help to identify groups of individuals following similar patterns of adiposity over time in order to discover different pathways of overweight onset and development during childhood and increase our understanding of the mechanisms underlying increasing trends in overweight prevalence [59].

Different approaches to exploring trajectories exist like Group-based trajectory modelling (GBTM), latent growth curve models (LGC), hierarchical linear models (HLM) [60]. GBTM is an analytical method to estimate longitudinal trajectories and is used in clinical research to approximate unknown trajectories across population groups [60]. It is a type of growth mixture model which allows for the classifications of individuals into a finite number of sub-groups, or classes, that follow similar patterns over time, for example in z-BMI [60, 61]. In contrast, LGC and HLM methods are based on the continuous distribution of a study population and do not establish distinct classes of trajectories [59, 61]. The group-based approach segments data into groups of participants who share similar longitudinal patterns of a given construct (e.g. BMI), which in turn helps to summarize large amounts of data in a comprehensible manner [61]. Group-based trajectory modelling involves multinomial models instead of multivariate continuous distributions used by both the LGC and HLM models [62].

1.6 Putative lifestyle determinants of adiposity in children

Obesity in children is a consequence of complex interactions of genetic, environmental, and lifestyle factors. Lifestyle behaviors such as physical activity, sedentary behavior and dietary intake are modifiable factors that are associated with health and obesity among children and adolescents [63]. Changes in z-BMI in children are associated with different types of lifestyle behaviors, for example, time

spent in intense physical activity and sedentary behaviors, television viewing time, fruit and vegetable intake, and snacking in front of the television [64]. Individual physical activity, sedentary behaviors, and screen time behaviors during childhood are independently associated with weight changes in adulthood [65]. Combining them with diet, these behaviors have synergistic and likely cumulative effects on the individual's ability to maintain a healthy body weight [3, 66].

Sedentary behavior

Sedentary behaviour has been defined as low energy sitting (or reclining) during waking hours, thus excluding sleep or seated exercise [67], and is characterized by an energy expenditure <1.5 Metabolic Equivalents (METs) [68]. A MET is defined as the resting metabolic rate, that is, the amount of oxygen consumption at rest (approximately 3.5 ml O_2/kg/min) [69]. Sedentary behavior includes time spent engaging in screen-based activities like watching TV, video/computer game use [70]. The presence of excessive sedentary behaviours has been linked to unfavorable adiposity indicators [70, 71]. In addition to being linked to increased adiposity, sedentary behaviors have been associated with increased risk of cardiometabolic disease [72] all-cause mortality, and poor mental health [70]. Additional prospective studies are needed to better understand the impact of sedentary behaviours over time on adiposity-related outcomes among children and adolescents [73].

Screen time

Higher levels of sedentary time have been found to be associated with an increase in z-BMI between ages 9 and 15 years, independent of physical activity [74]. In particular, studies have shown that higher screen time adversely affects adiposity in youth [70, 75, 76]. One possible causal explanation is that increased screen time in children can disrupt sleep, leading to short sleep duration [77], which is well known to be associated with later obesity [78]. Screen time is one form of sedentary behaviour [79]. Alternately, associations between screen time and dietary intake may be at play. Indeed, accessibility to televisions and computers in the home has been found to be linked to more screen-based sedentary behaviour among children [76] which in turn has consistently been associated with lower fruit and vegetable consumption and higher consumption of energy-dense snacks and drinks, total energy intake, and fast foods in children [80]. Current recommendations state that children aged 5-18 years should engage in <2h/day of recreational screen time daily [68]. The Canadian Health Measures Survey revealed

that 51% of 5-17 years old are spending more screen time than is recommended by Canadian 24-Hour Movement Guidelines [6, 70].

Physical activity

Current recommendations state that children aged 5-18 years should engage in at least 60 minutes of moderate to vigorous physical activity (MVPA) daily [68]. Moderate to vigorous physical activity and TV viewing are independently associated with adiposity in children [81]. Higher intensity physical activity, mainly MVPA, has positive effects on the health status of adolescents [16, 21, 73]. Higher levels of MVPA, along with less sedentary time, are associated with increased health-related quality of life among children and adolescents in the general population [82].

Dietary intake

The stability of body adiposity indicators can also be influenced by mechanisms involving dietary behaviors over time [50]. Early childhood stands out as an important time period to focus both on individual preventive initiatives and targeting those at high risk of obesity [20]. Unhealthy dietary habits result in unfavorable adiposity indicators [50, 71]. The prevalence of childhood obesity has increased concurrently with an increase in fast food consumption among children and adolescents [83-85]. Some studies have found convincing evidence of association of obesity in children with both total and saturated fat intake [86, 87], revealing that saturated fat intake is associated with a metabolically unhealthy profile in adolescents [88]. There is no clear consensus on the role of dietary fat in pediatric obesity, as previous evidence has also suggested that there is no association between dietary fat intake and obesity in children [87]. A systematic review and meta-analysis of observational studies revealed a direct association of higher fat intakes with adiposity risk in children and adolescents [89].

Children and adolescents tend to increase their consumption of sugar-sweetened beverages from childhood into late adolescence which is associated with adiposity risk later in life [59, 90, 91]. A systematic review by Keller et al., revealed discrepant results regarding the association of sugar-sweetened beverage intake and obesity in children and adolescents [90]. However, a systematic review of prospective cohort studies by Luger et al. revealed independent positive associations of sugar-sweetened beverages and body weight gain in children.

Low fruit and vegetable consumption is also related to the advent of obesity during childhood and adolescence [92]. Pearson et al., have found that screen time was inversely associated with fruit and vegetable servings and positively associated with fast food consumption [80] and, BMI *z*-score change is related to increased fruit and vegetable servings [93]. Consequently, it is important to examine associations between dietary indicators such as fast-food consumption, sugar-sweetened beverages, servings of vegetables and fruits, percent saturated fat intake and percent fat intake and adiposity trajectories.

A study conducted in Spain identified a number of concurrent obesogenic behaviours associated with an increased risk of overweight and obesity in children and adolescents, including low physical activity, high screen time, skipping breakfast, and low meal frequency [66]. Specific unhealthy lifestyle behavior combinations like physical inactivity/sedentary time and unhealthy diet (e.g., low fibre intake) may be more harmful for later obesity in adolescents [17].

While unhealthy lifestyle behaviors are responsible for higher prevalence of total body and abdominal obesity among adolescents [17, 94], the role of early lifestyle habits in shaping adiposity trajectories from childhood to adolescence remains uncertain. Research on the association between behavioral determinants and adiposity over time, from early childhood into late adolescence is limited. Indeed, few studies have examined sedentary behaviors, dietary intake and MVPA across childhood and adolescence and their possible associations with adiposity. Understanding the relationships between multiple unhealthy lifestyle behaviors is important to prevent obesity in adolescence.

1.7 Potential confounders in associations between lifestyle factors and obesity

A confounding variable is defined as a variable that is correlated with the exposure variable as well as with the outcome variable [95]. Literature from observational studies examining associations between lifestyle factors and obesity have identified several potential confounders that, if not accounted for, would

bias the association between adiposity and lifestyle behaviors [96]. The current project considered the most important of these confounders.

Firstly, parental education, a proxy of socio-economic status, is strongly associated with childhood weight [97]. Previous studies reveal that children growing up with more educated parents are less exposed to unhealthy lifestyle behaviors [98]. Parental education can affect nutritional choices of the child and his/her family, as well as engagement in physical and cognitive activities and is an important confounder in the association between adiposity and lifestyle behaviors in children [99].

Secondly, there is evidence supporting an association between early puberty and increased adiposity in children and adolescents[54, 100] as well as adults [53]. Puberty as a proxy of age also strongly linked to the adoption of patterns of lifestyle habits that track into adulthood, namely unhealthy diet, [101], lower physical activity [102] and higher sedentary behaviors [100, 103]. As discussed above, puberty is an important confounder in the association between early lifestyle habits and adiposity, given its established impact on adiposity and body composition, as well as the developmental impacts of puberty on lifestyle habits.

Moreover, age and sex are equally potential confounders in the association between lifestyle habits and obesity. Lifestyle habits change during transition from childhood into late adolescence [70] and are also differential across boys and girls [104]. Indeed, boys are more likely to be obese or overweight in adolescent period as compared to girls, and the reasons for this are likely multifactorial [104], however may relate to differences in lifestyle habits.

The next section will address knowledge gaps and rationale of this study.

1.8 Knowledge gaps and study rationale

Current knowledge of the relationship between lifestyle factors and obesity from childhood to late adolescence is limited, yet research on lifestyle exposures and their impact on adiposity outcomes over time is important [96]. Knowing which lifestyle behaviors in childhood are associated with unfavourable trajectories of weight gain into late adolescence will inform preventive strategies.

Many epidemiological studies examining associations between obesity and dietary and sedentary/physical activity behaviors have focused on assessing BMI at one point in time as a measure of obesity, ignoring the dynamic changes of BMI over time and the diversity in patterns that may emerge during the natural development in children [59]. Yet, it is recognised that it is important to track children's BMI over time in order to better understand the dynamics of adiposity [105].

There are several limitations in the previous longitudinal studies that have explored associations between lifestyle behaviours in childhood and adiposity over time. For example, retrospective studies examining adiposity trajectories using weight and height data from medical records are limited in terms of the quality of the data used [50, 59, 106]. Moreover, several studies relied on self-reported data to calculate z-BMI (i.e., parental report of height and weight data during early childhood), which also substantially increases the possibility of introducing measurement error [107]. Additionally, most studies typically include short follow-up durations (2-3 years) [105, 108] which may not allow for sufficient time to detect smaller but cumulative behavioral effects on adiposity. Lastly, several studies have missed one or more critical periods of development such as early childhood or the transition from childhood into adolescence. To address these limitations, this thesis is based on the QUALITY cohort study for which strengths include well phenotyped participants with detailed assessments of children followed over 7 years, objective measurements of physical activity and sedentary time, and use of valid and reliable methods to measure dietary intake.

The etiology of obesity is multifaceted and recent trends in the prevalence of obesity suggest the importance of tracking adiposity from childhood into late adolescence. Obesity in children is associated with short- and long-term health consequences as well as economic burden. It is preventable through modifiable behavioral lifestyle risk factors, for example physical activity, dietary intake and sedentary

behaviors. Although many studies have established associations between these lifestyle behaviours and obesity, fewer methodologically rigorous studies have examined associations with adiposity over time from childhood to late adolescence. The QUALITY study's comprehensive and state-of-the art assessment of exposures and outcomes of interest will help to examine how lifestyle habits in childhood influence adiposity over time into adolescence. This study will focus on the critical periods of biological maturation from pre-puberty to post-puberty to understand associations of lifestyle behaviors with adiposity.

1.9 Research objectives

The overarching objective of this thesis is to examine the associations between lifestyle behaviors in pre-puberty or early puberty and obesity trajectories across childhood and adolescence. The lifestyle behaviours of interest in this study are physical activity, sedentary behaviors and dietary intake. These were selected a priori given the availability of data and their relevance as potentially modifiable factors.

Hypothesis:

1. It is hypothesized that spending more time in physical activity during childhood will be associated with more favorable adiposity trajectory profiles into adolescence.
2. It is hypothesized that spending more time in sedentary behaviours during childhood will be associated with adverse patterns of obesity into adolescence.
3. It is hypothesized that unhealthy diets (e.g., higher sugar-sweetened beverage consumption, lower fruit and vegetable intake) in childhood will be associated with adverse patterns of obesity into adolescence.

1.10 Statement of Contribution

Data used in this research study were collected by the QUALITY cohort research team from 2005-2008, 2008-2011 and 2012-2015. The data relevant to this research were extracted from the main database and given to me in SAS format dataset. From this dataset, I created new variables which were required to answer my research objectives. Trajectory analyses were already computed by Gabrielle Simoneau. However, I labelled all trajectories described herein and developed the statistical analysis plan with advice from my thesis supervisors and other members and students of their research teams. I conducted all statistical analysis and the interpretation of the results presented is my own interpretation after discussion with my supervisors.

Chapter 2

2. Methodology

2.1 Study design and study population

This research study is based on data from the QUebec Adipose and Lifestyle Investigation in Youth (QUALITY) Cohort study, an ongoing cohort study designed to increase the understanding of the natural history of excessive weight and its consequences in youth [109]. This is secondary data analysis of a prospective cohort study.

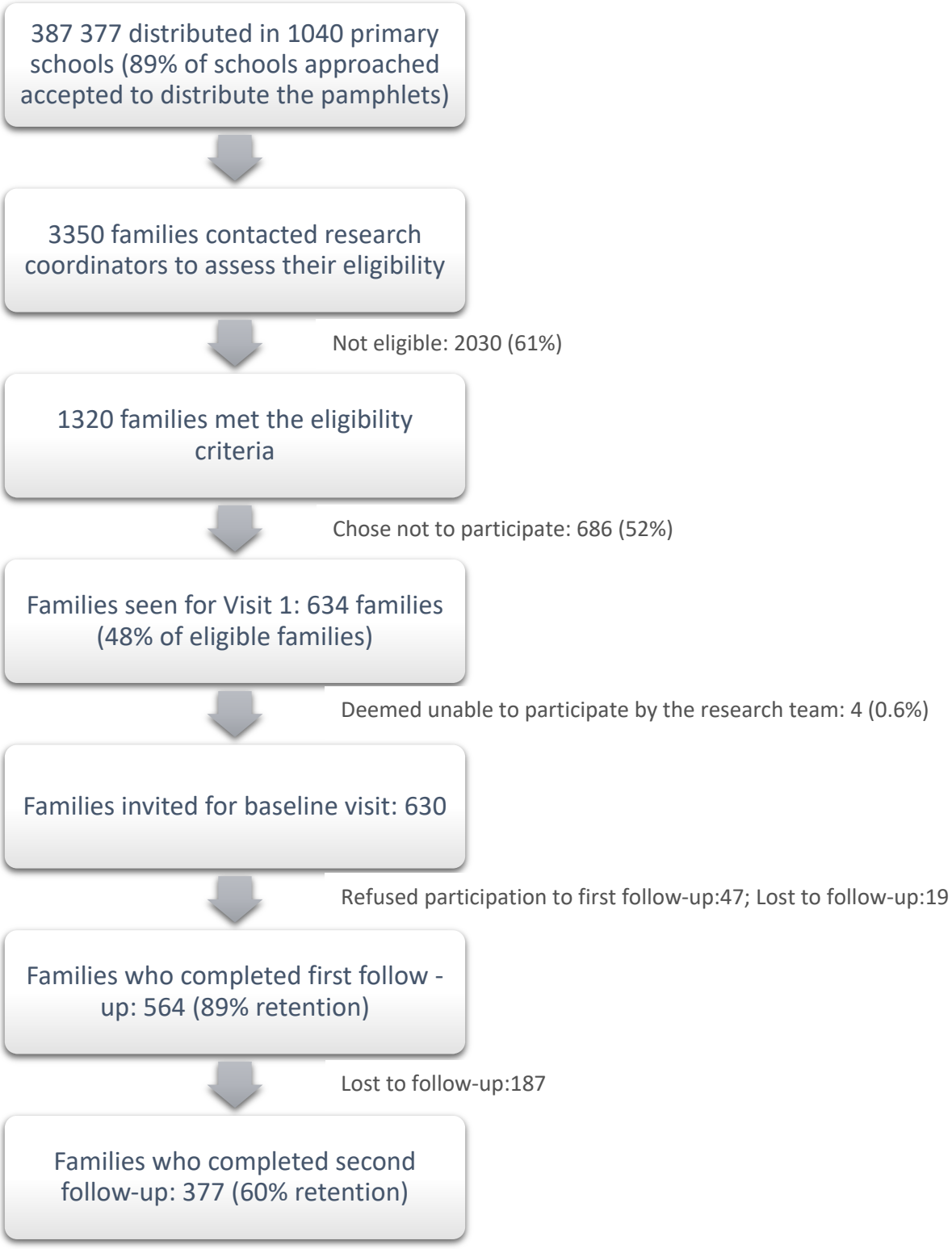
2.1.1 Inclusion and exclusion criteria

Children of Caucasian origin of Western European ancestry with parental obesity (i.e., body mass index $\geq$ 30 kg/m^2 or waist circumference >102 cm in men and >88 cm in women based on self-reported height, weight and waist circumference) [110] were included in the study. Children at high risk of obesity were chosen as the population of interest given the primary study's aim of understanding the natural history of development of obesity in children. Additionally, the QUALITY cohort was restricted to Caucasian children to reduce genetic mixture. The study of obesity and its consequences is not only of interest in Caucasian children, however including other ethnic groups would have required a substantially larger sample size to permit examination of differential effects across multiple ethic groups. Participants were recruited through a school-based sampling strategy. School boards within a 75 km radius of Montreal, Sherbrooke and Quebec City, in the province of Quebec, Canada, were approached to participate. Information pamphlets were distributed to all 2-5th grade students among schools that agreed to participate.

Families planning to move to out of the province of Quebec and those with a pregnant or breastfeeding mother at baseline were excluded. Children diagnosed with type 1 or type 2 diabetes, a serious illness, any cognitive disorder or being treated with anti-hypertensive medication or steroids or with a very restricted diet of less than 600 kcal/day were also excluded. A total of 630 children completed the baseline assessment (2005-2008). Subsequently, a first follow up (2008-2011) and second follow up (2012-2015) were done at ages 10-12 years (n=564) and 15-17 years (n=377), respectively. Families were followed up at the CHU Sainte-Justine in Montreal and the Quebec Heart and Lung Institute.

The current analysis is restricted to 377 participants who completed the baseline, first follow-up and second follow-up, of which 8 participants missed the first follow-up.

Figure 2.1- Recruitment of participants and data available in QUALITY cohort



2.2 Ethics

The Ethics Review Boards of the CHU Sainte Justine and the Quebec Heart and Lung Institute gave approval for this study. Parental consent and child assent were obtained at baseline and at each subsequent research visit.

2.3 Measurements

2.3.1 Exposures

The main exposure measures were moderate-to-vigorous physical activity (MVPA), screen time, sedentary behaviors, fruit and vegetable servings, percent fat, percent saturated fat and sugar-sweetened beverage intake at baseline. In sensitivity analyses, I also used MVPA, screen time and sedentary behaviors measured at the first and second follow-ups, as well as dietary intake from the second follow-up (diet was not assessed at the first follow-up). Methods to measure lifestyle behaviors were the same across all visits.

An accelerometer (Actigraph LS 7164 activity monitor) worn at the waist over a 7-day period was used to measure physical activity [111]. Children were instructed to remove the accelerometer before going to sleep and to put it on again upon getting up. At the second follow-up visit, a newer accelerometer model (GT3X+, ActiGraph, LLC, Pensacola, Floride, USA) was used to measure physical activity. Instructions were given to wear the accelerometer 24 hours per day for 7 consecutive days. At least 4 days with a minimum of 10 hours of accelerometer wear time were needed for data to be considered valid.

Moderate-to-vigorous physical activity (MVPA) was calculated by taking the average total minutes spent daily in moderate (>2296 and < 4012 counts per minute) and in vigorous physical activity (>4012 counts per minute) divided by the total number of valid days of wear [112, 113]. The counts are defined as accelerometer's raw output. Initial signals for accelerometer data after filtration and amplification are converted to analog voltage signals which are called raw counts [114]. The filtration signal is then digitized and the magnitude is estimated over a user-specified time period as epoch [115]. The activity count is retained as memory at the end of each epoch [114, 115].

Accelerometry was also used to estimate sedentary time as the average number of minutes with activity counts of < 100 counts per minute, divided by the total number of valid days of wear [116].

Screen time was calculated by averaging the total number of hours watching television as well as leisure computer and video game use over the week using a child reported questionnaire. The average daily hours of screen time were then calculated. Self-reported questionnaires are the most frequent method used to assess screen time and these are valid and reliable method of measurement in children [117].

Dietary intake was assessed with three 24h dietary recalls on non-consecutive days [118] at baseline and the second follow-up. A disposable kit of food portion models (i.e., bowl, plate and glass with measurements), along with a ruler to estimate portion sizes and instructions about use were given to the participants at the clinic visits. A trained registered dietician gathered 24-hour dietary recall data from the child and the parent who prepared the meals for 2 weekdays and one weekend day over the 4-6-week duration following the visit. Dietary intake reported by the participants during the recalls were entered into the CANDAT (Godin and Associates, London, Ontario, Canada) software to technically convert them to macronutrients using the 2010 version of the Canadian Nutrient File (CNF) at baseline and second follow-up. CNF is a computerized database to calculate food composition as average values of nutrients in Canadian foods. The average intake of 3 days was used to decrease intra-individual variations in dietary intake [119]. Specific dietary intake variables in this study include sugar-sweetened beverage consumption, vegetable and fruit servings, percent saturated fat intake and percent fat intake. These diet intake variables were selected given the evidence for their association with obesity in children [2, 82, 90, 94, 120]. Percent fat and saturated fat intake were calculated by converting grams into percent fat and saturated fat intake respectively. Daily servings of fruits and vegetables were based on 2010 Canada's Food Guide. Sugar-sweetened beverage intake was measured as daily consumption (in mL) of high sugar drinks (e.g., soft drinks) excluding fruit juice.

2.3.2 Outcomes

The main outcome was a variable describing six z-BMI trajectories based on z-BMI values from the three research visits. Z-BMIs were calculated from height and weight. Height was measured in meters using a stadiometer and weight was measured in kilograms using an electronic scale [109]. WHO (World Health Organization) reference norms were used to derive BMI z-scores at each time period from measured weight and height (Canadian Pediatric Endocrine Group, 2010). As previously described in Table 1.1, WHO growth reference cut-offs for children aged 5-19 years are widely used to classify weight status categories- normal weight (BMI z-score: -2 to 1), overweight (BMI z-score: $\geq$1), obesity (BMI z-score: $\geq$2) and severe obesity (BMI z-score: $\geq$3) [35].

QUALITY cohort children who completed the three waves of evaluation were classified into latent classes of z-BMI trajectories; there were 8 missing participants at first follow-up. Longitudinal trajectories of adiposity (i.e., using BMI z-scores measured at 3 clinical visits) were estimated using Group-based trajectory modeling (GBTM). Using GBTM, specific groups of children with similar patterns of z-BMI from early childhood to late adolescence were identified A six-group solution was used as best fitting model to the data based on the Bayesian Information Criterion values using quadratic equation (Figure 2.2). The PROC TRAJ procedure in SAS was used. Participants were assigned a probability of belonging to a specific trajectory based on their growth pattern. An average class membership probability >70 is considered good. BIC is a relative measure of model fit where an increase in Bayes factor of an alternative model (j) relative to the null model (i) is suggestive of a better fit (Table 2.1).

Table 2.1- Model fit criteria and interpretation

Bayes factor (Bij)	Interpretation
Bij < 1/10	Strong evidence for model j
1/10 < Bij < 1/3	Moderate evidence for model j
1/3 < Bij < 1	Weak evidence for model j
1 < Bij < 3	Weak evidence for model i
3 < Bij < 10	Moderate evidence for model i
Bij > 10	Strong evidence for model i

BIC is a relative measure of model fit, whereas Bayes factor (Bij) of an alternative model (j) is estimated as relative to the null model (i). Bayes factor compares the information (BIC) of two nested models and discovers whether the bigger model (e.g., more classes or same number of classes with quadratic terms) is associated with an important gain in information.

Figure 2.2- Trajectories of z-BMI across 3 waves of data in the QUALITY Cohort

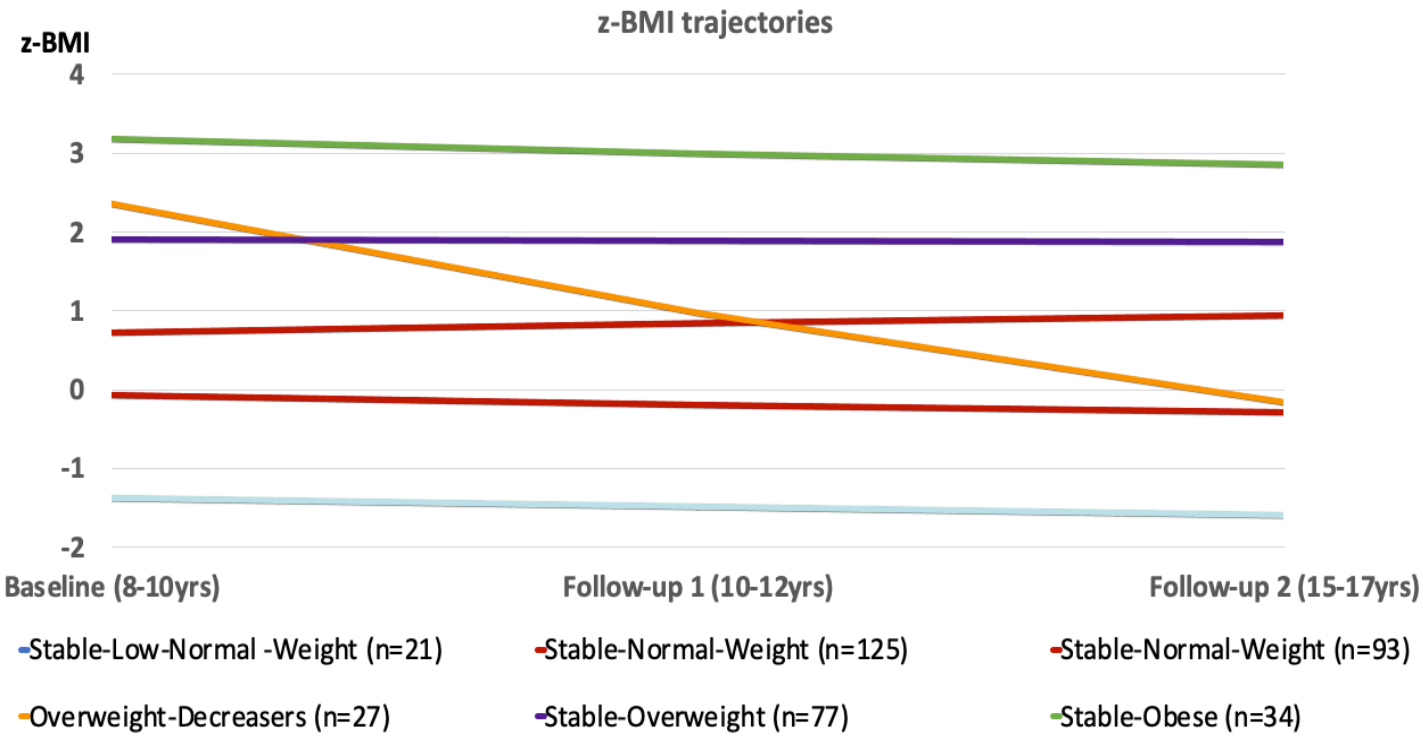


Table 2.2- Trajectory groups

Trajectory groups	N (%)	Intercept (p-value)	Slope (p-value)
Stable-Low-Normal-Weight	21 (5.7%)	-1.37 (<0.01)	-0.02 (0.46)
Stable-Normal-Weight 1	125 (33%)	-0.07 (0.13)	-0.02 (0.02)
Stable-Normal-Weight 2	93 (25%)	0.72 (<0.01)	0.02 (0.03)
Stable-Overweight	77 (19.8%)	2.36 (<0.01)	-0.23 (<0.01)
Overweight-Decreasers	27 (7.9%)	1.91 (<0.01)	-0.002 (0.82)
Stable-Obese	34 (8.8%)	3.18 (<0.01)	-0.03 (0.12)

2.3.3 Covariates

Socio-demographic characteristics including children's age in years (at each visit) and parental education (at baseline only) were determined using parent self-reported questionnaires (children's age as continuous and parental education as a categorical variable).

Parental education was based on completing high school, technical, vocational/trade school or university degree. In the analyses, it was categorized as a binomial variable: at least one parent with university-level education vs less.

Pubertal development was assessed at each cycle by trained nurses using the Tanner stages [51, 52]. For girls, stages were defined based on changes in breast and pubic hair. For boys, stages were defined based on changes in pubic hair. Testicular volume was not measured. The participants were classified as pre-pubertal (Stage-1) vs pubertal (Stages 2-5).

Total daily caloric intake was included in our models as a proxy of energy requirements for dietary variables.

2.4 Analyses

Descriptive statistics including means, medians and proportions were used to examine the distribution of variables. For categorical variables, frequency distributions were performed. Distinct trajectories available in the QUALITY cohort were labelled as *Low-Stable-Normal-Weight*, *Stable-Normal-Weight-1*, *Stable-Normal-Weight-2*, *Stable-Overweight*, *Stable-Obese* and *Overweight-Decreasers*. For subsequent multinomial regression analyses, *Stable-Normal-Weight-1* and *Stable-Normal-Weight-2* were merged as a single trajectory group, *Stable-Normal-Weight.* Potential collinearity was assessed using Pearson correlations between chosen lifestyle determinants at baseline and z-BMI at three points of evaluation. One-way analysis of variance was used to test the differences among means of different lifestyle variables across z-BMI trajectory groups. The false discovery rate method was used to reduce the likelihood of identifying false associations due to Type 1 error as a result of multiple testing [121]. This method is preferred over Bonferroni given that Bonferroni is a conservative approach to adjust for multiple testing and we found discrepant significant p values without any significant differences among groups. The false discovery rate method allowed us to identify statistically significant differences in baseline lifestyle behaviors between adiposity trajectory groups while maintaining a low false positive rate (type 1 error). The α level was set at 0.05.

Using multinomial logistic regressions with the combined Stable-Normal-Weight trajectory as the reference group, associations between lifestyle determinants at baseline and different adiposity trajectories were examined. Model 1 estimated crude associations between each baseline lifestyle behavior and z-BMI trajectory groups while Model 2 adjusted for covariates (i.e., sex, age, pubertal development, and parental education at baseline). Models with dietary intake variables (fruit and vegetable portions, sugar-sweetened beverages) were additionally adjusted for total daily kilocalorie intake (energy-adjusted).

Findings relating to the Overweight-Decreasers group were intriguing, and it was deemed relevant to explore further the changes in lifestyle habits across childhood and adolescence in this group, compared to those who remained overweight or obese across the three time points. Sensitivity analyses were thus conducted in order to better understand the difference among lifestyle behaviors at all three waves of evaluation for: 1) Overweight-Decreasers, and 2) the combined Stable-Overweight and Stable-Obese groups. T-tests or Wilcoxon tests were used to test statistical significance based on variable distributions. All analyses were conducted using SAS version 9.4 (SAS Institute's Inc, Cary, North Carolina). I conducted all the analyses presented herein, except for the creation of the z-BMI trajectory groups.

Chapter 3

3. Manuscript

Early lifestyle determinants of adiposity trajectories from childhood into late adolescence

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Count: Abstract 393, Manuscript 3630, References 45, Figures 2, Tables 4, Supplemental Table 1

ABSTRACT

Background: Childhood obesity is known to track into adolescence and later into adulthood. A better understanding of which childhood lifestyle factors are associated with specific adiposity patterns across the early lifespan is needed to inform early prevention based on modifiable lifestyle behaviors.

Objectives: This study aims to examine associations between physical activity, sedentary behavior and dietary intake in childhood with adiposity trajectories from childhood to adolescence.

Methods: Data stem from the Quebec Adipose and Lifestyle Investigation in Youth (QUALITY, n=630) study, including the 377 Caucasian children with data at each of the following time points: baseline (8-10 years), 10-12 years and 15-17 years. Children were recruited based on a parental history of obesity. Physical activity and sedentary behavior (7-day accelerometry), screen time (self-reported) and dietary intake (three 24-hr diet recalls) were measured. Weight and height were measured at each time point and transformed to age and sex adjusted Body Mass Index z-scores (z-BMI) using WHO Standards. Group based trajectory modeling was used to identify longitudinal trajectories of z-BMI. Multinomial logistic regressions were used to examine associations between baseline lifestyle behaviors and distinct z-BMI trajectory groups while adjusting for age, sex, tanner stage and parental education.

Results: Six distinct z-BMI trajectory groups were identified: Stable-Low-Normal-Weight (5.7%), two Stable-Normal-Weight groups that were subsequently combined (33.0% and 24.8%), Stable-Overweight (19.8%), Stable-Obese (8.8%) and Overweight-Decreasers (7.9%). For every additional serving of vegetable and fruit at baseline, the likelihood of being in the Overweight–Decreasers group increased by 26% (OR 1.26, 95% CI: 1.06, 1.49) compared to those in the Stable-Normal-Weight group. For every additional hour of sedentary behavior at baseline, the likelihood of belonging to the Overweight-Decreasers group increased by 51% (OR 1.51, 95% CI: 1.03, 2.22) as compared to Stable-Normal-Weight group. In terms of physical activity, every additional 10 mins of Moderate to Vigorous Physical Activiy (MVPA) at baseline was associated with a lower likelihood of belonging to the Stable-Obese group (OR 0.75, 95% CI: 0.61, 0.91) and to the Overweight-Decreasers group (OR=0.78, 95% CI: 0.62, 0.98) compared to the Stable-Normal-Weight group.

Conclusion: Trajectories of z-BMI from childhood to late adolescence were generally stable over time, except for one group that decreased from overweight in childhood to normal weight in adolescence. The

latter had more favourable dietary intake of fruits and vegetables at baseline. Paradoxically, they were also more sedentary and engaged in less physical activity.

Keywords: Adiposity, obesity, lifestyle behaviors, trajectory analysis, paediatrics, body mass index, children/adolescents

Abbreviations: BMI, Body Mass Index; MVPA, Moderate-to-vigorous physical activity; QUALITY, Quebec Adipose and Lifestyle InvesTigation in Youth: 95% CI, 95% confidence interval

INTRODUCTION

The prevalence of overweight and obesity in children and adolescents increased worldwide between 1975 and 2016 [1]. In Canada, the prevalence of obesity among children aged 5 to 17 years tripled over the past three decades [2,3], with recent trends (2009-2017) suggesting a stabilization in the prevalence of overweight (approximately 18%) and decrease in prevalence of obesity from 14.3% to 10.6% [4].

Obesity is known to track from early to later childhood [5] and into adulthood [6]. The prevalence of overweight and obesity is higher among Canadian adolescents aged 12-17 years (32%) compared to children aged 5-11 years (19%) [7]. Being overweight at the age of 5 years is associated with an approximately 10-fold increased risk of being obese during adolescence [5, 8]. The examination of longitudinal adiposity trajectories allows for the identification of groups of individuals following similar patterns of adiposity over time [9]. Several potentially modifiable lifestyle habits have been associated with the advent of obesity, including physical activity [10], sedentary behaviors [11] and diet [12, 13]. However, the etiology of changes in weight patterns from childhood into late adolescence remains unclear [14]. The identification of such determinants may serve to target children at greater risk of displaying unfavourable adiposity trajectories who may benefit from early prevention. We therefore set out to determine whether specific childhood lifestyle behaviors, namely physical activity, sedentary behaviour, screen time and dietary intake (sugar-sweetened beverages, servings of vegetables and fruits, percent fat and saturated fat intake) are associated with particular patterns of body weight status from childhood to adolescence.

METHODS

Study design and population

The Quebec Adipose and Lifestyle Investigation in Youth (QUALITY) Cohort Study is an ongoing study of the natural history and determinants of obesity [15]. A total of 630 children aged 8-10 years were recruited at baseline, using a school-based recruitment strategy targeting children in grades 2-5 from three major urban centers in the province of Quebec, Canada.

Caucasian children with at least one obese biological parent (i.e., body mass index ≥ 30 kg/m^2 or waist circumference >102 cm in men and >88 cm in women based on parental self-reported height, weight and

waist circumference) were eligible. Families were excluded if the mother was pregnant or breastfeeding at the baseline visit or if the family had plans to move out-of-province. Children with a previous diagnosis of type 1 and type 2 diabetes, a serious illness, any cognitive disorder or undergoing treatment with anti-hypertensive medication or steroids or following a very restricted diet of less than 600 kcal/day were also excluded. A total of 630 children completed the baseline assessment (2005-2008; Time 1). Subsequently, a first follow up (2008-2011; Time 2) and second follow up (2013-2017; Time 3) were conducted at ages 10-12 years (n=564) and 15-17 years (n=377) respectively. The current analysis is restricted to the 377 participants who completed the 3 waves of data collection, of which 8 participants completed the baseline and second follow-up visit only.

The Ethics Review Boards of the CHU Sainte Justine and the Quebec Heart and Lung Institute approved the study. Parental consent and child assent were obtained at baseline and at each subsequent research visit.

Measurements

Lifestyle behaviors

Lifestyle behaviors including physical activity, sedentary behavior, screen time and dietary intake were measured at baseline. Follow up measures of these lifestyle behaviours at 10-12 years (diet not included) and 15-17 years were also examined in sensitivity analyses. Physical activity was measured by accelerometry using an Actigraph LS 7164 activity monitor over a 7-day period shortly after the baseline and first follow up visits [16]. Instructions were given to remove the accelerometer before going to bed and to put it on again upon awakening. At the second follow-up, a newer model of accelerometer was used to measure physical activity (GT3X+, ActiGraph, LLC, Pensacola, Florida, USA) and adolescents were instructed to wear the accelerometer 24 hours per day for 7 consecutive days. Four or more days with a minimum of 10 hours of wear time were considered sufficient for data analysis. Moderate-to-vigorous physical activity (MVPA) was calculated by averaging the total minutes spent daily in moderate (>2296 and < 4012 counts per minute) and in vigorous physical activity (>4012 counts per minute) per number of valid days of wear [17, 18].

Sedentary behavior was estimated using accelerometry data as the average number of minutes (excluding non-wear and sleep) with activity counts of less than 100 counts per minute per number of valid days of

wear [19]. Using a questionnaire, duration of screen time was estimated as the daily hours of television viewing and leisure computer and video game use on a typical weekday and weekend day. A weighted average of daily hours of screen time was calculated.

Dietary intake was assessed at baseline and at the second follow-up only using three 24h dietary recalls on non-consecutive days, including a weekend day [20]. A disposable kit of food portion models, along with information on how to use them, was provided to families at the clinic visits. Dietitians conducted telephone interviews for the dietary recalls with the child and the parent who prepared the meals over a 4-6-week period following the clinic. Foods reported on the recalls were entered into the CANDAT (Godin and Associates, London, Ontario, Canada) nutrient analysis program for conversion to macronutrients using the 2010 version of the Canadian Nutrient File for the baseline and second follow-up visits respectively. The average intake of three days was used to decrease intra-individual variations in dietary intake [20]. Dietary intake of total fats (%) and saturated fat (%) and of specific food group variables, namely sugar-sweetened beverages and daily servings of vegetables and fruits were used in this study. These were selected a priori given previously described associations with obesity in children [2, 21-25]. Fat intake and saturated fat intake were calculated by converting mean total fat from grams to calories and further into percent fat and saturated fat intake respectively. Vegetable and fruit servings were estimated using the 2010 Canadian Food Guide (including vegetable and fruit juices). Sugar sweetened beverage intake was measured in mean mL per day of high sugar drinks such as soft drinks.

Outcomes

Weight (in kilograms) and height (in meters) were measured at each time period using standard procedures [15] and transformed into BMI z-scores, which were derived according to WHO (World Health Organization) reference norms (Canadian Pediatric Endocrine Group, 2010). The WHO growth reference charts are widely used to classify underweight (BMI z-score: <-2), normal or healthy weight (BMI z-score: -2 to 1), overweight (BMI z-score: $\geq$1), obesity (BMI z-score: $\geq$2) and severe obesity (BMI z-score: $\geq$3) among children aged 5 to 19 years-old [26].

GBTM (Group-based trajectory modeling) allows for the identification of specific groups of children with similar patterns of z-BMI from childhood to late adolescence. In order to determine the optimum number

of groups for our data, we first fitted a one-group model and successively added additional groups until reaching the point where the model fit was not improved with a higher number of groups based on the Bayesian Information Criterion values. Using quadratic equation, a six-group solution was used as best fit for Bayesian Information Criterion values (Figure 3.1).

Covariates

Children's age in years at each visit was assessed as a continuous variable. Pubertal development was assessed at each visit by trained nurses using Tanner stages [27, 28]. Participants were classified as pre-pubertal (Stage-1) vs pubertal (Stages 2-5). Parental education was determined at baseline using parent self-reported questionnaires (defined as at least one parent with university-level education vs less).

Analyses

Means (standard deviations), medians (interquartile ranges) and proportions were used to examine the distribution of variables. Pearson's correlations were used to assess potential collinearity among chosen lifestyle determinants at baseline and z-BMI score at all three visits. GBTM was used to identify longitudinal trajectories of z-BMI measured at 3 time points. Different trajectory groups were labelled as Low-Stable-Normal-Weight, Stable-Normal-Weight-1, Stable-Normal-Weight-2, Stable-Overweight, Stable-Obese and Overweight-Decreasers.

One-way analysis of variance (ANOVA) with the false discovery method was used to test statistically significant differences in lifestyle behavior means at each visit across different adiposity groups using an α level of 0.05. Associations (odds ratios and 95% confidence intervals) between baseline lifestyle behaviors and membership to the distinct adiposity trajectory groups were examined using multinomial logistic regressions, using the merged Stable-Normal-Weight-1 and Stable-Normal-Weight-2 as reference category. Distinct models were estimated for each lifestyle determinant while adjusting for baseline covariates (i.e., sex, age, pubertal development, and parental education). For models examining associations with vegetable and fruit servings and with sugar sweetened beverages, models were additionally adjusted for total kilocalorie intake. Last, sensitivity analyses were conducted to compare Overweight-Decreasers to the combined Stable-Overweight and Stable-Obese groups over the first 2 waves using t-tests or Wilcoxon tests based on variable distributions. All statistical analyses were done with SAS, version 9.4 (SAS Institute's Inc, Cary, North Carolina).

RESULTS

Participants' characteristics are described in Table 3.1. The final sample included 204 boys and 173 girls. At each visit, more than half of the children were normal weight, approximately 23% were overweight, 16% to 20% were obese and 5% had severe obesity.

Using Pearson correlations (Table 3.2), we found positive correlation between sedentary behavior and age across all three time points. In terms of MVPA and z-BMI scores, there was mild negative correlation at baseline and first follow-up. In addition, fruit and vegetable servings were also negatively correlated with percent fat, percent saturated fat and sugar and sweetened beverage consumption. Using one-way analyses of variances, we compared means for lifestyle behaviors measured at baseline across adiposity trajectory groups (Table 3.3). At 8-10 years, children belonging to the Stable-Obese group spent nearly twice as much time engaging in screen time compared to children in the Low-Normal-Weight group [p=0.02]. Similarly, statistically significant differences in mean vegetable and fruit servings at baseline were found among three groups (Overweight-Decreasers vs Stable-Normal-Weight, Overweight-Decreasers vs Stable-Overweight, Overweight-Decreasers vs Stable-Obese) [p=0.01]. Children belonging to the Overweight-Decreasers group reported the highest servings of vegetables and fruits at baseline as compared to other groups. In contrast to the baseline visit, we found no significant differences in lifestyle habits across adiposity groups at first and second follow up (Table 3.5).

Adjusted associations between baseline lifestyle behaviors and z-BMI trajectories from multinomial logistic regressions are presented in Figure 3.2. Children were less likely to belong to the Stable-Low-Normal-Weight group (vs Stable-Normal-Weight group) with each additional hour of screen time per day (OR 0.69, 95% CI: 0.44, 1.00). For every additional hour of sedentary behavior measured by accelerometer at baseline, the likelihood of belonging to the Overweight-Decreasers group increased by 51% (OR 1.51, 95% CI: 1.03, 2.22) as compared to Stable-Normal-Weight group. In terms of physical activity, every additional 10 mins of MVPA at baseline was associated with a lower likelihood of belonging to the Stable-Obese group (OR 0.75, 95% CI: 0.61, 0.91) and to the Overweight-Decreasers group (OR=0.78, 95% CI: 0.62, 0.98) compared to the Stable-Normal-Weight group. Last, for dietary intake, associations were only found for fruit and vegetable servings and membership to the Overweight-Decreasers group, wherein a higher

number of servings per day at baseline was associated with a higher likelihood of belonging to the Overweight-Decreasers group compared to the reference group (OR 1.31 95% CI: 1.08, 1.58).

We conducted sensitivity analyses to examine whether changes in lifestyle behaviours from baseline to the second follow-up could explain the favorable weight trajectory of the Overweight-Decreasers group as compared to the merged Stable-Obese and Stable-Overweight groups (Table 3.4). Overweight-Decreasers had higher servings of fruits and vegetables at baseline compared with the combined Stable-Obese and Stable-Overweight ($p<0.001$). Similarly, while the Overweight-Decreasers intake of sugar-sweetened beverages consumption relatively remained unchanged from baseline to second follow-up, while the combined Stable-Obese and Stable-Overweight group increased their consumption considerably in this time period, although this difference was not statistically significant but clinically meaningful.

DISCUSSION

Using data from three evaluation periods of a prospective longitudinal study, with group-based trajectory modelling, distinct stable trajectories of z-BMI (Stable-Low-Normal-Weight, Stable-Normal-Weight, Stable-Overweight, Stable-Obese) were observed from early childhood to late adolescence in addition to one unique decreasing trajectory (Overweight-Decreasers). At baseline, children spending higher MVPA were associated with the lower odds of belonging to the Stable-Obese group whereas children spending lower time in screen-based activities were associated with belonging to the Stable-Low-Normal Weight group as compared to the Stable-Normal-Weight group. Overall, compared to the Stable-Normal-Weight group, membership to the Overweight-Decreasers group was associated with lower MVPA, higher sedentary behavior and higher fruit and vegetable servings at baseline.

In adjusted models, we found associations between Overweight-Decreasers and the Stable-Normal-Weight group in terms of fruit and vegetable intake, with the Overweight-Decreasers group having higher servings of fruits and vegetables at baseline compared to the Stable-Normal-Weight group. This is consistent with findings from some studies reporting that higher fruit and vegetable servings in childhood is associated with a reduction in BMI in adolescence [30, 31], however, findings in the literature are mixed on this subject [32-34]. It is unclear whether servings of fruit and vegetable alone or whether multiple small positive behavior changes lead to a decrease in adiposity across adolescence [35]. Our sensitivity

analyses comparing children who were overweight at baseline but returned to normal weight during follow up to those children who remained obese/overweight across follow up suggest that differences in fruit and vegetable intake, and possibly sugar-sweetened beverages consumption, may explain membership to the Overweight-Decreasers group compared to those children who remained overweight or obese throughout follow up.

There is growing evidence for the role of sugar-sweetened beverages in childhood and adolescent obesity [12, 36]. Consumption of sugar-sweetened beverages is known to increase as children transition into adolescence [33]. We did not find an association between baseline sugar-sweetened beverage intake and z-BMI trajectories across adolescence. While not reaching statistical significance, we did observe that the combined Stable-Obese and Stable-Overweight groups tended to increase their sugar-sweetened beverage consumption, while Overweight-Decreasers their sugar-sweetened beverages consumption remained unchanged from early childhood into late adolescence. In our study, there was important variability across subjects in sugar-sweetened beverage intake with a highly skewed distribution that could explain non statistically significant differences in sugar-sweetened beverage intake between Overweight-Decreases vs combined Stable-Obese and Stable-Overweight groups. Nevertheless, these findings are potentially clinically relevant.

Our results are in line with our hypothesis that engaging in more MVPA at baseline is associated with more favourable weight profiles. Indeed, MVPA was inversely associated with the likelihood of belonging to the Stable-Obese (vs. Stable-Normal-Weight) group, which is consistent with other studies showing that MVPA is associated with lower adiposity and important for preventing excess weight gain in childhood [37, 38]. However, baseline MVPA was also inversely associated with belonging to the more favourable Overweight-Decreasers group. We found a similar counterintuitive association between sedentary behaviour and membership to the Overweight-Decreasers group [39, 40]. These counterintuitive findings suggest that z-BMI trajectories cannot be predicted solely by lifestyle behaviours at one point in time, nor are they likely predicted by any one lifestyle behaviour but rather by a combination of lifestyle behaviours. Our sensitivity analyses do suggest that among children with overweight, subtle favorable dietary trends over time, taken together, may be associated with a return to normal weight status by adolescence.

Lifestyle behaviours such as physical activity can change significantly from childhood to adolescence and young adulthood and therefore, it is possible that baseline activity pattern might be very unstable during this period of interest. Several reasons may explain the fact that few lifestyle habits in childhood actually were predictive of adiposity trajectories into adolescence. Firstly, it may be that lifestyle habits at a given moment in childhood are less predictive of z-BMI trajectories than patterns in lifestyle behaviors over time [41]. For instance, we only found higher fruit and vegetable servings at baseline to be associated with the unique Overweight-Decreasers group. Alternatively, it may not be a single lifestyle habit pattern that predicts adiposity, but rather that adiposity trajectories are determined by the cumulative effects of small changes in multiple behavioral lifestyle factors from early childhood to late adolescence [42, 43]. This underscores the complexity of factors determining patterns in adiposity from early childhood to late adolescence. It may also be that lifestyle habits influence adiposity trajectories at an earlier age (i.e., before 8-10 years) [44, 45]. This would suggest that interventions to prevent obesity must occur much earlier in development. Further research is needed to examine these associations concurrently along with the consideration of other potential risk factors such as sleep, genetics, environmental and social factors.

The strengths of our study include its prospective design, with objective, valid and reliable measurements of physical activity, sedentary behavior, diet and adiposity. Several limitations should be considered. First, generalizability of findings to other ethnic groups needs to be demonstrated as only Caucasian children with a history of parental obesity were studied. Nonetheless, this represents an important proportion of the Canadian population. Second, the sample size in some trajectory groups was small, which limited our power (e.g., sample size for Stable-Low-Normal-Weight was only n= 21); this may have prevented us from detecting small effects of baseline lifestyle on weight status trajectories that span 7 years. Also, selective loss to follow-up of children with obesity at the 2nd follow-up may have led to selection bias. Third, dietary intake was only measured at baseline and at the second follow-up, thus differences in diet between groups at the first follow up could not be examined in sensitivity analyses. In addition, potential confounders are taken into consideration namely sex, age, parental education and pubertal development, however residual confounding cannot be excluded. Last, although we used validated and reliable methods to measure lifestyle behaviors, measurement error may have led to non-differential misclassification and an attenuation of measured associations.

CONCLUSION

In a sample of children with a history of parental obesity, we found different trajectory groups of z-BMI development that remain stable from early childhood to late adolescence and one that decreased from overweight to normal weight over 7 years of follow up. Our study highlights that few childhood lifestyle habits predicted these z-BMI trajectories, with higher dietary intake of fruits and vegetables, higher MVPA, and lower sedentary behavior at baseline showing beneficial impacts on trajectories. Future studies with larger sample sizes that enable the inclusion of multiple factors that influence growth (namely behavioural, environmental, genetic, epigenetic and social factors), and their changes overtime, should be done to explore the complex etiology of obesity in children and adolescents.

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Declarations of interest: None.

Table 3.1- Characteristics of QUALITY participants at baseline, first and second follow-up

	Baseline (T1) (n=377)	First follow-up (T2) (n=369)	Second follow-up (T3) (n=377)
Age, years, mean (SD)	9.5 (0.9)	11.6 (0.9)	16.8 (0.9)
Tanner stage, %			
Pre-pubertal	77.0	34.3	0.3
Pubertal	23.0	65.7	99.7
BMI z score, mean (SD)	0.9 (1.2)	0.8 (1.2)	0.7 (1.3)
BMI category, n (%)	-	4 (1.1)	5 (1.3)
Underweight	215 (57.0)	199 (53.9)	222 (58.9)
Normal	89 (23.6)	93 (25.2)	86 (22.8)
Overweight	54 (14.3)	58 (15.7)	44 (11.7)
Obese	19 (5.0)	15 (4.1)	20 (5.3)
Severe obese			
Screen time (hrs/day) median (IQR)	2.0 (1.2, 3.3)	2.9 (1.8, 4.3)	4.0 (2.6, 5.7)
Sedentary behavior (min/day), mean (SD)	364.1 (68.3)	425.9 (75.1)	635.4 (119.3)
MVPA (min/day), median (IQR)	48.1 (30.5, 66.3)	39.0 (24.9, 56.1)	22.4 (13.1, 36.7)
% Fat intake, mean (SD)	31.9 (4.9)	-	32.8 (6.1)
% Saturated fat intake, mean (SD)	11.4 (2.6)	-	11.6 (2.9)
Fruit and vegetable servings, mean (SD)	4.5 (2.1)	-	4.6 (2.6)
Sugar and sweetened beverages intake(mL) median (IQR)	83.8 (0, 207.9)	-	116.2 (0, 249.5)

BMI- Body Mass Index; MVPA- Moderate to vigorous physical activity; SD-Standard deviation; IQR-Interquartile range

Table 3.2- Correlation Matrix

Variables	Age at T1	Age at T2	Age at T3	z-BMI at T1	z-BMI at T2	z-BMI at T3	Screen time at T1	Sedentary behavior at T1	MVPA at T1	% Fat at T1	% Saturated fat at T1	Fruit-veg servings at T1	SSB at T1
Age at T1	1												
Age at T2	0.99**	1											
Age at T3	0.98**	0.97**	1										
z-BMI at T1	0	0	0	1									
z-BMI at T2	-0.03	-0.04	-0.03	0.91**	1								
z-BMI at T3	-0.01	-0.02	0	0.75**	0.82**	1							
Screen time at T1	0.09	0.11*	0.09	0.12*	0.13*	0.14	1						
Sedentary behavior at T1	0.30**	0.28**	0.26**	0.12*	0.11*	0.05	0.11	1					
MVPA at T1	-0.12*	-0.09	-0.10	-0.16*	-0.13*	-0.08	0.01	-0.43**	1				
% Fat at T1	-0.01	-0.02	-0.02	-0.01	0	0.01	0.02	0	-0.04	1			
% Saturated fat at T1	-0.08	-0.09	-0.06	-0.06	-0.03	-0.03	0.04	0.06	-0.07	-0.75**	1		
Fruit-veg servings at T1	-0.01	-0.01	-0.03	-0.02	-0.01	-0.03	-0.04	0.02	0.16*	-0.21**	-0.18*	1	
SSB at v1	0.08	0.10*	0.09	0.03	0.04	0.01	0.05	0.04	0.08	-0.04	-0.09	-0.10*	1

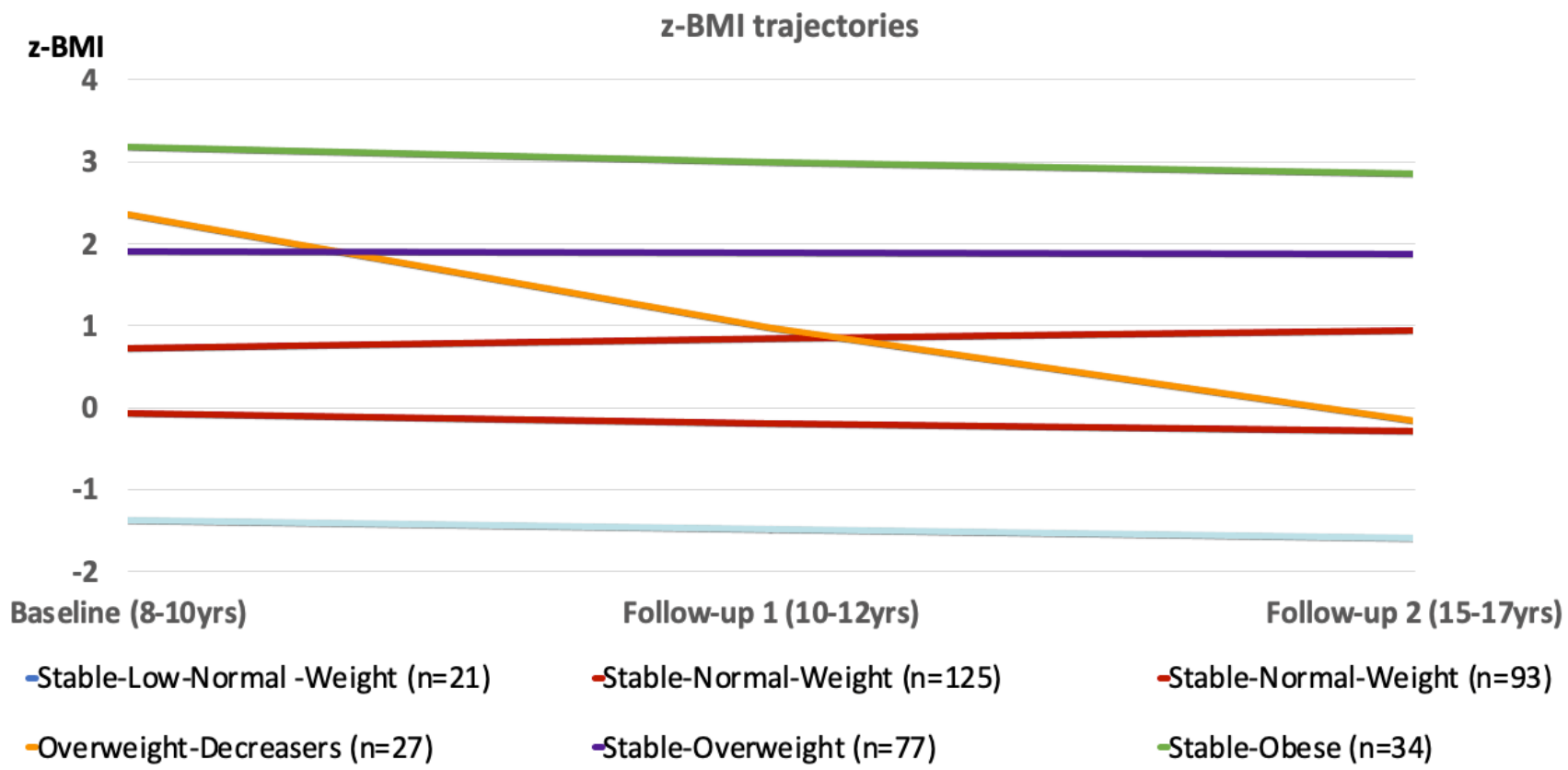
MVPA=moderate to vigorous physical activity; Z-BMI=body mass index standard deviation scores; SSB=sugar sweetened beverages; *p-value=<.05; **p-value=<.0001

Table 3.3- Comparison of means of values of lifestyle habits at baseline across BMI trajectory groups using ANOVA

	Stable-Low-Normal-Weight (n=21)	Stable-Normal-Weight (n=218)	Overweight-Decreasers (n=27)	Stable-Overweight (n=77)	Stable-Obese (n=34)	*p-value*
Screen Time (hrs/day)	1.8 (1.5)	2.5 (2.1)	2.5 (1.9)	2.7 (1.8)	3.5 (2.1)	**0.02**
Sedentary behavior(min/day)	336.3 (47.6)	361.9 (69.4)	395.4 (64.8)	361.2 (67.1)	377.7 (69.9)	0.05
MVPA (min/day)	52.5 (24.2)	53.9 (25.5)	41.3 (16.4)	48.3 (22.2)	41.4 (19.1)	0.11
% Fat intake	32.9 (6.7)	31.9 (4.8)	31.5 (4.3)	32.2 (4.5)	32.1 (5.5)	0.80
% Saturated fat intake	12.1 (2.9)	11.5(2.6)	10.8(2)	11.7(2.8)	11.2 (2.9)	0.42
Fruit and vegetable servings	4.5 (2.6)	4.5 (2.0)	5.8 (2.5)	4.1 (1.7)	4.1 (2.3)	**0.01**
SSB (mL)	103.1 (127.2)	137.2 (156.0)	141.0 (155.1)	128.1 (125.2)	147.0 (138.1)	0.82

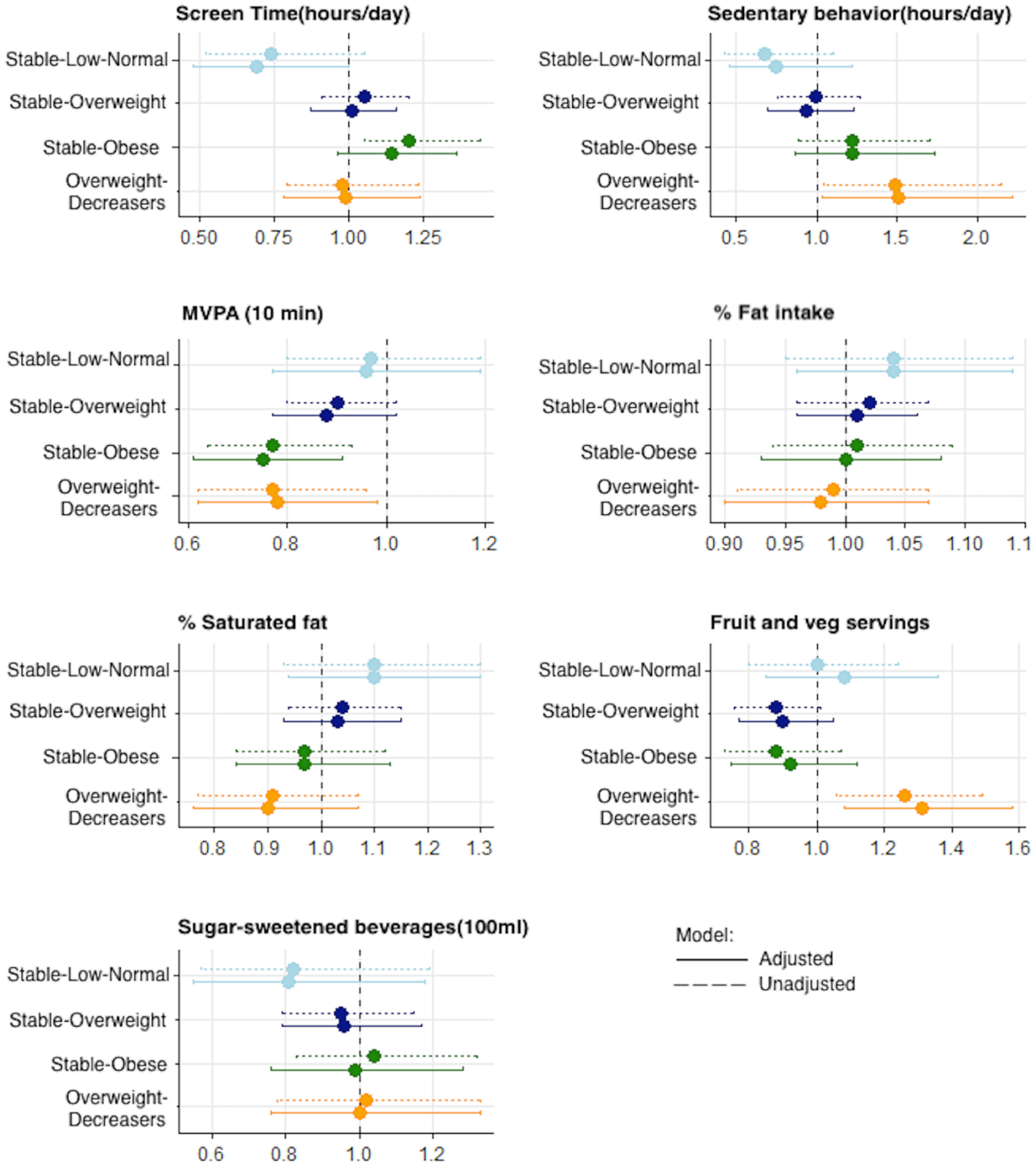
Means (SD) are calculated for all lifestyle behaviors across all BMI trajectory groups; MVPA- Moderate to vigorous physical activity; SSB- Sugar-sweetened beverage; bold figures represent statistically significant differences ($p < 0.05$); false discovery rate method used to assess false positive associations due to Type 1 error. Children belonging to the Stable-Obese group at baseline spent nearly twice as much time engaging in screen time compared to children in the Low-Normal-Weight group (p=0.02). Similarly, statistically significant differences in mean vegetable and fruit servings at baseline were found among three groups (Overweight-Decreasers vs Stable-Normal-Weight, Overweight-Decreasers vs Stable-Overweight, Overweight-Decreasers vs Stable-Obese).

Figure 3.1- Trajectories of z-BMI across 3 waves of data in the QUALITY Cohort



z-BMI: Body Mass Index z score

Figure 3.2- Odds ratios and 95% confidence intervals from Multinomial Logistic Regressions for associations between lifestyle behaviours at baseline and z-BMI Trajectories



Models adjusted for baseline age, sex, Tanner stage and Parental education; MVPA: Moderate to vigorous physical activity. Reference group is the Stable-Normal-Weight Group. Interpretation of MVPA: every additional 10-min increment of MVPA at baseline is associated with a lower likelihood of belonging to the Stable-Obese group (OR 0.75, 95% CI: 0.61, 0.91) compared to the Stable-Normal-Weight Group.

Table 3.4- Comparison of descriptive statistics of Stable-Obese and Stable-Overweight vs Overweight-Decreasers at all three time points

	Baseline(T1)		First follow-up(T2)		Second follow-up(T3)	
	Combined Stable-Overweight and Obese	Overweight-Decreasers	Combined Stable-Overweight and Obese	Overweight-Decreasers	Combined Stable-Overweight and Obese	Overweight-Decreasers
BMI category, n (%)						
Underweight	-	-	-	-	-	-
Normal	1 (0.9)	-	1 (0.9)	3 (11.5)	-	25 (92.6)
Overweight	45 (40.5)	19 (70.4)	38 (35.2)	19 (73.1)	50 (45.0)	2 (7.4)
Obese	46 (41.4)	8 (29.6)	54 (59.0)	4 (15.4)	41 (36.9)	-
Severe obese	19 (17.1)	-	15 (13.9)	-	20 (18.0)	-
Screen time (hrs/day) median (IQR)	2.4 (1.5,4.1)	2.0 (1.3,2.8)	3.4 (1.4, 4.6)	3.1 (1.9, 4.6)	4.6 (3.1,6.6)	4.1 (2.6,6.1)
Sedentary behavior (hrs/day), median (IQR)	6.4 (5.6,7.2)	6.4 (5.9,7.6)	7.9 (6.0,8.6)	7.2 (6.7,7.8)	10.4 (9.0,11.6)	11.1 (9.4,11.6)
MVPA (min/day), median (IQR)	40.4 (30.5,50.3)	39.4 (29.8,55.0)	32.0 (22.0,44.3)	31.6 (19.5,42.2)	20.9 (11.4,33.0)	29.4 (14.1,34.8)
% Fat intake, mean (SD)	32.1 (4.8)	31 .6(4.3)	-	-	32.9 (6.2)	31.1 (5.8)
% Saturated fat intake mean (SD)	11.5* (2.8)	11.1* (2.0)	-	-	11.7* (3.3)	10.7* (2.5)
Vegetable- fruit servings, median (IQR)	3.8** (3.8,4.9)	5.5** (4.1,6.7)	-	-	3.6 (2.5,5.4)	5.0 (3.5,6.8)
SSB (ml), median (IQR)	93.2 (20.9,208.6)	82.9 (0,207.6)	-	-	120.9 (0,246.7)	83.8 (0,277.5)

BMI- Body Mass Index; MVPA- Moderate to vigorous physical activity; Reference group: merged Stable-Overweight and Stable-Obese; SD-Standard deviation; IQR- Interquartile range, data presented as mean (SD) and median (IQR). Comparisons are done between Stable-Obese and Stable-Overweight vs Overweight- Decreasers at a given time points using independent sample t test and Wilcoxon signed rank test. *p<0.01**p<0.001. E.g., significant difference of fruit and veg servings among Stable-Obese and Stable-Overweight (3.8) vs Overweight-Decreasers (5.5) at baseline (<0.001).

Supplementary Table 3.5 - Comparison of means of values of lifestyle behaviors across BMI trajectory groups using ANOVA at all three time points

	Stable Low-Normal Weight	Stable Normal-Weight	Overweight-Decreasers	Stable-Overweight	Stable-Obese	*p-value*
Screen Time (hrs/day)						
Time 1	1.8 (1.5)	2.5 (2.1)	2.5 (1.9)	2.7 (1.8)	3.5 (2.1)	**0.02**
Time 2	3.4 (2.6)	3.1 (2.0)	3.5 (2.5)	3.7 (2.5)	3.7 (1.8)	0.55
Time 3	3.9 (2.0)	4.2 (2.7)	4.5 (2.1)	4.8 (2.4)	5.6 (3.0)	0.05
Sedentary behavior (min/day)						
Time 1	336.3 (47.6)	361.9 (69.4)	395.4 (64.8)	361.2 (67.1)	377.7 (69.9)	0.05
Time 2	434.9 (98.9)	418.1 (69.7)	432.1 (51.9)	437.6 (76.6)	444.3 (97.9)	0.25
Time 3	644.4 (83.2)	634.1 (127.3)	631.3 (97.8)	635.4 (95.9)	641.4 (152.1)	0.99
MVPA (min/day)						
Time 1	52.5 (24.2)	53.9 (25.5)	41.3 (16.4)	48.3 (22.2)	41.4 (19.1)	0.11
Time 2	41.6 (20.6)	46.1 (24.3)	34.7 (19.4)	39.8 (19.0)	37.3 (18.2)	0.05
Time 3	30.8 (21)	27.4 (19.0)	26.8 (16.4)	26.1 (17.1)	24.1 (15.7)	0.89
% Fat intake						
Time 1	32.9 (6.7)	31.9 (4.8)	31.5 (4.3)	32.2 (4.5)	32.1 (5.5)	0.80
Time 3	34.4 (5.4)	32.6 (6.2)	31.1 (5.8)	32.6 (5.9)	33.8 (6.9)	0.44
% Saturated fat intake						
Time 1	12.1 (2.9)	11.5 (2.6)	10.8 (2.0)	11.7 (2.8)	11.2 (2.9)	0.42
Time 3	11.9 (2.6)	11.7 (3.1)	10.7 (2.5)	11.7 (2.9)	11.7 (4.1)	0.71
Vegetable and fruit servings						
Time 1	4.5 (2.6)	4.5 (2.0)	5.8 (2.5)	4.1 (1.7)	4.1 (2.3)	**0.01**
Time 3	4.9 (2.9)	4.8 (2.6)	4.9 (2.6)	4.3 (2.4)	4.0 (3.1)	0.40
SSB (mL)						
Time 1	103.1 (127.2)	137.2 (156.0)	141.0 (155.1)	128.1 (125.2)	147.0 (138.1)	0.82
Time 3	216.3 (214.1)	166.2 (203.1)	168.0 (213.4)	142.2 (162.1)	212.1 (256.2)	0.40

Means (SD) are calculated for all lifestyle behaviors across all BMI trajectory groups; MVPA- Moderate to vigorous physical activity; SSB- Sugar-sweetened beverage; bold figures represent statistically significant differences ($p < 0.05$); false discovery rate method used to determine p-values.

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Chapter 4

4. Discussion

4.1 Key findings

In this study, z-BMI trajectories from 8-10 years to 15-17 years were modeled using data from a sample of 377 Caucasian children with a history of parental obesity. In this 7-year follow-up of the QUALITY cohort, we found distinct stable trajectories of z-BMI (Stable-Low-Normal-Weight (5.7%), Stable-Normal-Weight (57.8%), Stable-Overweight (19.8%) and Stable-Obese (8.8%)), and one unique decreasing trajectory (Overweight-Decreasers (7.9%)) from childhood to late adolescence using Group-based trajectory modelling. Overall, we found few statistically significant associations between baseline behavioral determinants and membership to trajectory groups. Compared to the Stable-Normal-Weight group, lower MVPA at baseline was associated with belonging to the Stable-Obese while lower screen time was associated with belonging to the Stable-Low-Normal Weight group. Moreover, lower MVPA, higher sedentary behavior and higher servings of fruits and vegetables at baseline were associated with higher odds of belonging to the Overweight-Decreasers group as compared to the Stable-Normal-Weight group.

The Overweight-Decreasers trajectory merits discussion. A unique characteristic of this group includes the consumption of a higher number of servings of fruits and vegetables at baseline (8-10 years) compared to all other groups. This is in keeping with prior studies that found a higher intake of fruits and vegetables in childhood to be associated with a decrease in z-BMI in adolescence [92, 93, 122]. Studies also support a favorable impact of fruit and vegetable servings on z-BMI in other age groups, namely preschool-aged children [123, 124]. Nonetheless, some studies did not find a protective effect of fruit and vegetable servings alone against obesity [123]. It is possible that while fruit and vegetable servings may be a marker of healthier diets overall, many other lifestyle habits could also contribute to the beneficial trajectory of the Overweight-Decreasers [105, 125, 126]. It is therefore possible that the combined effects of multiple lifestyle behaviours are involved in children who shifted from overweight at baseline to healthy weight status during second follow-up. We set out to better understand the factors that differentiated the children in the QUALITY cohort who remained obese throughout follow-up from those who did not by way of sensitivity analyses that compared the Stable-Obese and Stable-Overweight groups with Overweight-

Decreasers in terms of all lifestyle habits of interest. We found subtle differences among these lifestyle determinants. Notably, the children belonging to the combined Stable-Obese and Stable-Overweight groups had a lower intake of fruit and vegetable servings as compared to the Overweight-Decreasers both in childhood and in adolescence. Moreover, there is robust evidence from previous studies for a positive association between sugar-sweetened beverage intake and z-BMI among children and adolescents [83, 90, 127] and its intake tends to increase as children reach adolescence [66]. We did not find any associations between the consumption of sugar-sweetened beverages at baseline and membership to adiposity trajectories. Nonetheless, in our sensitivity analyses, while not reaching statistical significance, sugar-sweetened beverage intake increased considerably among the combined Stable-Overweight/Stable-Obese groups but remained relatively unchanged in the Overweight-Decreasers group over the span of 7 years. The significant variation in sugar-sweetened beverage intake across subjects, with a highly skewed distribution, may explain why these differences were not statistically significant. Lastly, in terms of saturated fat, although intake was slightly decreased in the Overweight-Decreasers group as compared to the combined Stable-Overweight/Stable-Obese group, the difference was not clinically significant.

Overall, our results are in line with our hypothesis that engaging in more MVPA at baseline is associated with more favourable weight profiles. Others have found associations between school-aged children's MVPA and adiposity [128, 129]. Consistent with these results, we found that a higher duration of MVPA was linked to lower odds of belonging to the Stable-Obese (vs. Stable-Normal-Weight) group. However, we also found that a higher MVPA at baseline was associated with a lower odd of belonging to the Overweight-Decreasers group. Paradoxically, we found similar counter-intuitive results in terms of sedentary behavior and membership to the Overweight-Decreasers trajectory group, with higher sedentary behavior at baseline being associated with a higher odd of belonging to the Overweight-Decreasers group (vs. Stable-Normal-Weight). These findings suggest that it is difficult to predict adiposity trajectories based on lifestyle behaviors at one point in development (i.e., childhood) or by a single behavioral determinant, and that it may be a combination of multiple lifestyle behaviors over time that are involved in determining membership to a given adiposity trajectory. Our sensitivity analyses support this notion, suggesting that a combination of subtle favorable dietary habits (e.g., Stable SSB consumption, higher fruit and vegetable servings, lower saturated fat intake), taken together, may be associated with a progression to lower adiposity across adolescence among children who were previously overweight.

4.2 Methodological challenges

Several studies have explored BMI trajectories in children and adolescents [57, 94, 130, 131]. The most commonly used approach to identify trajectory groups is GBTM which is helpful for the identification of distinct groups that share similar z-BMI patterns over time, as well as for the description of changes over time and the comparison across different groups [57, 61]. The method is based on an estimation of the probability of each individual's group membership and assigns them to a group based on the highest membership probability [61]. However, limitations of the GBTM approach cannot be ignored. GBTM modelling does not take into consideration the individual variability within each group [61]. It could result in misinterpretation of results as GBTM models are based on the assumption of a discrete probability distribution, and model misspecification bias can also occur [60, 61]. Despite these limitations, GBTM was used as it is considered the best approach to gather statistically similar trajectories of children into meaningful subgroups.

Despite the demonstration of distinct BMI trajectories in childhood, few studies have examined early lifestyle determinants of patterns of weight across the early lifespan (i.e., from childhood to late adolescence). BMI trajectory patterns identified in our study are slightly different to the trajectory patterns of previous studies. Most of the previous studies that modeled z-BMI trajectories in childhood have missed one or more important periods of development such as early childhood [132] or the transition to adolescence [133]. Moreover, previous studies generally considered short time spans e.g., from infancy to childhood [130, 134] or conversely very long-time spans (from infancy or childhood to adulthood) [106, 135]. No previous study focused on the critical development period that is puberty, and its impact on adiposity trajectories. The present study spanning seven years, was focused specifically on this period from childhood into late adolescence in order to understand the subtle patterns across early development and into adolescence. Our study also extends the results from other studies which have typically identified fewer (e.g., two, three or four) adiposity trajectories from childhood into late adolescence using GBTM [130, 135, 136], whereas we found 6 distinct trajectory groups with data from a well-phenotype cohort study.

4.3 Etiological challenges

Our results revealed that few childhood behaviors are predictive of z-BMI trajectories into adolescence. We have several possible explanations for this. Lifestyle habits such as physical activity can change significantly from early childhood to adolescence and young adulthood and therefore, baseline activity patterns may not reflect later patterns during this time period. It may be that it is not lifestyle behaviours *at a given point in time* that predict adiposity trajectories, but rather *patterns* of behavioral determinants over time (specifically here from early childhood into late adolescence) that contribute to adiposity trajectories. Another possible explanation may be that lifestyle determinants *earlier* on in life (i.e., before the age of 8 years) have long term impacts on weight status trajectories across adolescence. Further, a single lifestyle habit pattern may not predict adiposity patterns, but rather it may be that adiposity trajectories depend on the additive (or cumulative) effects of small changes in different lifestyle behaviors that are responsible for obesity from early childhood to late adolescence [27]. Finally, it is possible that genetic, epigenetic, social and environmental factors not examined in this study contribute to specific adiposity trajectories and should be included in future research to examine these associations.

4.4 Strength and Limitations of this study

4.4.1 Strengths of this study

The main strength of the study is its prospective longitudinal design and the validity and reliability of lifestyle behaviors and adiposity measurements used. All anthropometric measurements are taken according to standardized protocols with detailed and extensive quality assurance, reducing measurement error. Measures of physical activity (using accelerometer) and dietary intake (using 24-hour recalls) were done using rigorous and arguably the best objective methods available. In most of the previous studies, subjective measures are used in the form of self-reports by children and their parents to calculate z-BMI which are subject to measurement error that can lead to biased associations, including those due to social desirability bias.

Moreover, this study covers an important lifespan of seven years from childhood into late adolescence. The time span between the three waves of evaluation is relatively small, which makes trajectories more sensitive to z-BMI changes from childhood into late adolescence.

4.4.2 Limitations of the study

Despite these strengths, this study has limitations. These relate to precision, selection bias, measurement error, residual confounding and generalizability.

4.4.2.1 Precision:

The loss to follow-up at the first and second follow-up visits is one of the important limitations in the QUALITY cohort. The total number of participants at Time 1 was 630 which subsequently reduced to 564 at Time 2 and further to 377 at Time 3, which consisted of the sample for the analysis of this study. In some of the identified trajectory groups, small sample sizes may have restricted statistical power to observe subtle associations between baseline behavioral determinants with membership to adiposity trajectories (for example, the Stable-Low-Normal-Weight group included 21 participants). This study would have been better powered to detect associations with greater precision without the loss to follow-up and resulting smaller sample size.

While not considered measurement error, it is noteworthy to mention that dietary intake was not measured during first follow-up (10-12 years). This consequently hindered our sensitivity analyses examining differences in diet among BMI trajectory groups at first follow-up.

4.4.2.2 Selection bias:

Selection bias can result in a biased estimate of an association due to the selection of participants in a study sample when participation is associated with both the study exposure and outcome [137]. Previous studies using QUALITY cohort data have described baseline characteristics of participants lost to follow-up and found that these children were more likely to present unfavorable health profiles (e.g., higher adiposity, more insulin resistant, unhealthier diets) [138, 139]. Associations estimated in the current study may be biased due to the exclusion of these participants.

4.4.2.3 Measurement error:

Despite using reliable methods to measure lifestyle behaviours, including objective measures, measurement error remains possible. For example, it is difficult to understand the complexities surrounding dietary behavior along with errors related to recalling dietary intake [40]. Dietary intake measurement with 24-hour recall is arguably the most reliable tool especially when conducted for 3 or more non-consecutive days. However, it can result in measurement error as it depends on one's memory. Moreover, the possibility of social desirability bias is also difficult to exclude. Random error can also result from intra-individual variation in intake on a daily basis, but interviews were repeated and averaged across 3 days to reduce this source of error as much as possible.

Although several lifestyle behaviors previously associated with obesity were examined, we did not examine whether sleep duration in childhood is associated with z-BMI trajectories due to the poor quality of the sleep measure available at the baseline assessment. Evidence suggest that short sleep duration is associated with adiposity and is a risk factor for overweight and obesity in children [78]. In the QUALITY cohort, sleep duration was estimated from the time children took off their accelerometer at bedtime to the time they put it back on upon awakening. Sleep duration is likely overestimated due to the inclusion of the time when the accelerometer was removed prior to bedtime and the inclusion of time from awakening until the accelerometer was but back on. During the follow-up visits, sleep duration was estimated using self-report questionnaires. Given the different methods for measuring sleep across the study follow-up visits, as well as concerns with validity of the baseline measure of sleep, we decided not to include it in this research study.

Lastly, another source of measurement error, self-report bias, cannot be excluded namely for screen time which was obtained using self-reported questionnaires. However, this method of measurement is one of the most commonly used methods to assess screen time in children and adolescence [117].

4.4.2.4 Residual confounding:

Another limitation from the current observational study is the potential for residual confounding. Despite the adjustment of potential covariates, namely parental education, sex, age and puberty, confounding may not be fully accounted for. For example, we used parental education as a proxy for socio-

economic status. We decided not to add an additional variable (like annual income) because we had small sample sizes in some trajectory groups, limiting the number of covariates that could be considered.

For multinomial logistic regression models estimating dietary intake, we additionally adjusted for kilocalorie intake. Residual confounding is possible because kcal is used as a proxy for energy requirements. There is evidence that children who carry out a lot of physical activity have a higher metabolic rate, which means they will have greater energy requirements [140], hence the importance of adjusting for energy requirements. An alternative approach to adjusting models for kilocalorie intake would be to express our dietary outcome variables per specified kilocaloric intake (e.g., 100 kcal). However, the interpretation of beta coefficients when using this approach may be less intuitive for clinicians, which is why we opted for the approach of adjusting for total kcal intake.

4.4.2.5 Generalizability:

The QUALITY Cohort study only included Caucasian children by design in order to reduce the occurrence of genetic admixture in other cohort analyses examining genetic factors. Generalizability of the current study's findings to other ethnic groups needs to be determined. Another limitation to generalizability is the inclusion criteria to participate in the QUALITY Cohort that required children to have at least one parent with obesity. This gives a certain attribute to the whole study sample. However, the focus of this cohort is children who are more vulnerable to obesity and its cardiometabolic consequences. Moreover, the high prevalence of obesity in adulthood in the general population suggests that the population of children with an obese parent is a relevant group to study [5]. Thus, despite these limitations, the group studied accounts for an important segment of the Canadian population

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Chapter 5

5. Public Health Significance

Obesity in children is a major contributing factor to preventable disease and acute/chronic disease conditions in the world. It is associated with both short-term and long-term complications, including heart disease, diabetes, depression and other chronic diseases. Moreover, obesity in children predicts obesity in adolescence and later in adulthood [141]. Obesity also represents a significant economic burden on the Canadian healthcare system and economy. It is an unprecedented task to address it at a public health level, clinical level, family level and individual level. Risk factors responsible for obesity are complex and require a deep understanding of their interrelation so that effective measures can be adopted to combat this problem [142].

This research study focused on children with a history of at least one parent with obesity which is a strong risk factor for obesity in childhood. Indeed, there is ample evidence demonstrating that children born to parents with obesity are more likely to develop obesity [143-145]. This heighted risk of obesity, combined with the high prevalence of obesity in adults worldwide, make the findings of the current study relevant for public health and it represents an initial step in developing preventive strategies targeted to subpopulation of high-risk children.

This project contributes to our understanding of the associations of z-BMI trajectories with modifiable lifestyle behaviors in childhood. This is relevant to both etiology and prevention of overweight and obesity in children: this project helps clinicians and public health officials alike identify high-risk behaviors for the development of adverse adiposity trajectories early in life. It also provides potential targets for the development of tailored interventions for these high-risk children. Use of group-based trajectory modelling is helpful to inform public health strategies targeting populations with higher risk of negative health outcomes. Previous studies revealed that children who are overweight and obese are likely to be overweight and obese as adolescents [20, 21]. Our findings also demonstrated that from childhood into late adolescence, most of the trajectories were stable which suggests the need for preventive strategies to be implemented at an earlier age (before 8 years). It also confirms that children outgrowing

their excess weight in adolescence is a misconception. Previous studies have revealed that early-life preventive approaches could be useful to prevent later cardiometabolic risk in young adulthood [146, 147]. Our findings reinforce that fact, suggesting that the ideal timing would be earlier than in children 8-10 years. It may be that the ideal timing for interventions is prior to adiposity rebound [49, 142], however our findings could not confirm this.

The fact that fruit and vegetable servings are associated with a more favourable BMI trajectory, and that less physical activity and more sedentary behavior are associated with deleterious BMI trajectories suggests the importance of public health and clinical interventions to encourage healthy lifestyle behaviours among children and adolescents. In addition, our study looked into the combination of moderate and vigorous physical activity in analyses. Future studies could explore separate associations of vigorous physical activity and moderate physical activity with adiposity, as well as consider bouts of physical activity [148] and light physical activity [149] as potential targets for intervention. Physical activity is multifaceted, and a granular approach to understanding what facets are most important to a healthy body weight will be helpful to shape future interventions in early childhood. In addition, WHO also adopted a more comprehensive approach on Physical Activity and Sedentary behavior guidelines across the whole age spectrum [150, 151]. A recent update from the 2020 guidelines for MVPA supports changing from 'at least 60 min of MVPA' to 'an average of 60 min of MVPA' daily to measure MVPA more accurately for children and adolescents [150].

A multilevel approach to focus on screen time, sedentary behavior, dietary intake, and physical activity involving parents could be a goal for future obesity-prevention interventions. Early prevention strategies could prove one of the promising efforts in reducing obesity in future. Early interventions focused on promoting healthy eating and physical activity could be implemented during regular medical visits in the toddler and early childhood years by supporting the parents, integrating interventions in daycares and schools [142]. Sensitizing parents to the importance of physical activity, healthy diets and limiting screen time should be done during pregnancy. Policies should be made to reduce barriers to physical activity (notably in terms of active transport and increased space for recreational activities) and increase access and affordability of healthy foods, including fruits and vegetables. Strategies could be tailored to focus on multiple lifestyle behaviors such as physical activity, dietary intake, and sedentary behaviors, in order for obesity prevention efforts to be successful. School based interventions could focus

on reducing the density of fast-food consumption and marketing of unhealthy foods and drinks. At the school and family level, leisure activities could be offered to the children and adolescents like sports activities and creative activities. Rewarding new healthy dietary habits and active participation in physical training to achieve a goal of prospected weight loss. Concerted action is required from government to provide leadership, develop and implement policies and community-based actions that create healthy food and activity environments.

5.1 Directions for future research

We found that BMI trajectories from childhood to late adolescence were generally stable over time, except for one group that decreased from overweight in childhood to normal weight in adolescence. Our results underscore the importance of focusing on the effect of cumulative changes in multiple lifestyle behaviors to decrease adiposity from childhood into late adolescence. Our findings provide policy makers, as well as healthcare providers with some directions for solutions to optimise adiposity trajectories in children and adolescents. Future studies should broaden the scope of this work, using larger samples, to examine multiple factors across behavioural, environmental, genetic, epigenetic and social factors, and their changes overtime, to develop an understanding of the complex etiology of obesity patterns in children and adolescents.

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