DETERMINANTS OF BODY COMPOSITION IN UNDERGRADUATE STUDENTS

IDENTIFYING DETERMINANTS OF BODY COMPOSITION IN UNDERGRADUATE STUDENTS: A SYSTEMATIC REVIEW AND PROTOCOL FOR A PROSPECTIVE OBSERVATIONAL STUDY

By: RITA E. MORASSUT, B.Sc.H.

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Author: Rita E. Morassut, B.Sc.H. (Queen's University)

Supervisor: Dr. David Meyre

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Abstract

Young adulthood is an important period in the development of obesity. Undergraduate students are particularly at-risk since they gain more weight than those not attending university. As students transition from high school to university, they often adopt unhealthy lifestyle behaviours which are thought to lead to weight gain. On average, students gain three to five pounds (1.4-2.3 kg) during their first year of undergraduate education. However, less is known about how body composition changes throughout the four-year course of undergraduate education and what causes these changes. We thus conducted a systematic review to synthesize a comprehensive list of factors associated with obesity traits (e.g. body mass index, body fat percentage, muscle mass) in undergraduate students. Two hundred thirty-eight studies were included (175 cross-sectional, 49 cohort, 11 interventional, 3 qualitative). We identified age, sex, ethnicity, socioeconomic status, religion, diet, eating habits, physical activity, sedentary activity, sleep, stress, university campus life, alcohol use, smoking, psychiatric disorders, body image, eating attitude, eating regulation, personality, and social/cultural influences as factors which are associated with obesity traits. These factors guided the design of the Genetic and EnviroNmental Effects on weight in University Students (GENEiUS) study, a prospective observational study which investigates the genetic and environmental determinants of body composition in undergraduate students over four years. The GENEiUS study will recruit 2500 multiethnic first-year undergraduates aged 17–25 years and will follow them every six months for four years. Primary outcomes are body mass index, waist circumference, waist-to-hip ratio, body fat mass and body fat percentage. This study will help design obesity prevention programs in universities.

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Table of contents

Abstract iii

Acknowledgements iv

Table of contents v

Glossary of abbreviations ix

Glossary of anthropometric terms xvi

Declaration of academic achievement xvii

Preface xviii

Chapter 1: Introduction 1

1.1 Measurement of obesity 1

1.2 Genetic epidemiology of obesity 2

1.3 Environmental determinants of obesity 4

1.4 Why the undergraduate population is important 4

1.5 Rationale for further study 5

1.6 References 7

Chapter 2: Factors associated with obesity traits in undergraduate students: a systematic review 10

2.1 Summary 11

2.2 Introduction 11

2.3 Methods 13

2.3.1 Literature search 13

2.3.2 Article review 14

2.3.3 Data extraction and analysis 15

2.4 Results 15

2.4.1 Literature flow 15

2.4.2 Overview of studies 16

2.4.3 Factors associated with BMI level 17

2.4.4 Factors associated with BMI change 19

2.4.5 Factors associated with weight 19

2.4.6 Factors associated with adiposity measures 21

2.4.7 Factors associated with lean/muscle mass measures 22

2.4.8 Factors associated with other obesity traits 22

2.5 Discussion 23
2.5.1 Strengths and limitations 25
2.5.2 Implications 26

2.6 Figures and tables 27
Figure 1. PRISMA literature flow diagram of eligible studies 27
Table 1. Factors associated with body mass index change 28
Table S1. Full search queries 29
Table S2. Factors associated with body mass index level 32
Table S3. Factors associated with weight 41
Table S4. Factors associated with weight change 42
Table S5. Factors associated with body adiposity index 45
Table S6. Factors associated with body fat mass 46
Table S7. Factors associated with body fat percentage level 46
Table S8. Factors associated with body fat percentage change 48
Table S9. Factors associated with fat mass index 48
Table S10. Factors associated with skinfold thickness 48
Table S11. Factors associated with visceral fat 49
Table S12. Factors associated with conicity index 49
Table S13. Factors associated with muscle mass 49
Table S14. Factors associated with muscle mass percentage 49
Table S15. Factors associated with fat-free mass 49
Table S16. Factors associated with fat-free mass index 50
Table S17. Factors associated with fat-free mass percentage 50
Table S18. Factors associated with waist circumference 50
Table S19. Factors associated with hip circumference 52
Table S20. Factors associated with waist-to-hip ratio 52
Table S21. Factors associated with corpulence index 52
Table S22. Factors associated with body surface area 52

2.7 References 53

Chapter 3: Rationale and design of GENEiUS: a prospective observational study on the genetic and environmental determinants of body mass index evolution in Canadian undergraduate students **73**

3.1 Abstract 74

3.2 Strengths and limitations of this study 75

3.3 Introduction 75
3.3.1 Obesity in young adulthood 75
3.3.2 Predictors of undergraduate weight change 77
3.3.3 Study objectives 80

3.4 Methods and study design 80
3.4.1 Participant selection and recruitment 80
3.4.2 Data collection 81
3.4.3 Outcomes 82
3.4.4 Predictor variables 83
3.4.4.1 DNA extraction, whole-genome genotyping and whole-exome sequencing 83
3.4.4.2 Energy intake 84
3.4.4.3 Alcohol consumption 84
3.4.4.4 Physical activity 85
3.4.4.5 Exercise motivation 85
3.4.4.6 Sleep 85
3.4.4.7 Stress 86
3.4.4.8 History of abuse 86
3.4.4.9 Impulsivity 86
3.4.4.10 Eating disorders 87
3.4.4.11 Body dissatisfaction 87
3.4.4.12 Self-esteem 88
3.4.4.13 Depression 88
3.4.4.14 Anxiety 88
3.4.4.15 Religiosity 89
3.4.5 Sample size calculation 89
3.4.6 Statistical methods 90
3.4.6.1 Analysis of environmental risk factors 90
3.4.6.2 Analysis of genetic risk factors 91
3.4.6.3 Prediction models of weight change 93

3.5 Discussion 93
3.5.1 Ethics and dissemination 96

3.6 Figures and tables 98
Table 1. Study timeline, outcomes risk factor variables, and measurements 98
Table 2. Sample size estimates for BMI level 100
Table 3. Sample size estimates for BMI change 100
Table S1. Sample size estimates for BMI level by GWAS 101
Table S2. Sample size estimates for BMI level by exome-wide association study 102
Table S3. Sample size estimates for environmental traits with BMI level 102
Table S4. Sample size estimates for BMI change by GWAS 103
Table S5. Sample size estimates for BMI change by exome-wide association study 104
Table S6. Sample size estimates for environmental traits with BMI change 105

3.7 References 106

Chapter 4: Conclusion **114**

4.1 Summary of conclusions and methodological limitations 114

4.2 Sources of bias 115

4.2.1 Factors associated with obesity traits in undergraduate students: a systematic review 115

4.2.2 Rationale and design of GENEiUS: a prospective observational study on the genetic and environmental determinants of body mass index evolution in Canadian undergraduate students 116

4.3 Feasibility of the GENEiUS study and practical considerations 117

4.4 Ethical considerations with the GENEiUS study 118

4.5 Future directions 120

4.6 References 121

Glossary of abbreviations

ACSS	Acceptance of Cosmetic Surgery Scale
ADHD	Attention Deficit Hyperactivity Disorder
AES	Anger Expression Scale
ASA24	Automated Self-Administered 24-hour Recall
ASCS	Adolescent Self-Concept Scale
ASI-R	Appearance Schemas Inventory-Revised
AUDIT	Alcohol Use Disorders Identification Test
BAS	Body Appreciation Scale
BCQ	Body Checking Questionnaire
BCS	Body Cathexis Scale
BES	Binge Eating Scale
BFM	Body fat mass
BIA	Bioelectric impedance analysis
BI-AAQ	Body-Image Acceptance and Action Questionnaire
BIS	Barratt Impulsiveness Scale
BISS	Body Image State Scale
BITE	Bulimic Inventory Test, Edinburgh
BMI	Body mass index
BSQ	Body Shape Questionnaire
BSRQ	Body-Self Relations Questionnaire

BUILT-R	Bulimia Test-Revised
CAS	Celebrity Attitude Scale
CBPAQ	Cognitive Behavioral Physical Activity Scale
CDC	Centers for Disease Control and Prevention
CDRS	Contour Draw Rating Scale
CES-D	Centre for Epidemiological Studies Depression Scale
CESD-R	Centre for Epidemiological Studies Depression Scale- Revised
CIA	Clinical Impairment Assessment Questionnaire
CTQ	Childhood Trauma Questionnaire
DA+	Diet Analysis Plus version 10
DASS	Depression Anxiety Stress Scales
DDQ	Daily Drinking Questionnaire
DDT	Delayed discounting task
DEBQ	Dutch Eating Behaviour Questionnaire
DHQ	Diet History Questionnaire
DIS	Dietary Intent Scale
DNA	Deoxyribonucleic acid
DRES	Dutch Restrained Eating Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DUREL	Duke University Religion Index
EADES	Eating and Appraisal Due to Emotions and Stress Questionnaire

EAH-C	Eating in the Absence of Hunger questionnaire- Child and adolescents
EAMS	Exercise Avoidance Motivation Scale
EAS	Emotionality, Activity, and Sociability
EAT	Eating Attitudes Test
EAUQ	Eating and Alcohol Use Questionnaire
EBS	Eating Behavior Scale
EDDS	Eating Disorder Diagnostic Scale
EDE-Q	Eating Disorder Examination
EDI	Eating Disorder Inventory
ED_{50}	Effective delay 50%
EEI	Eating Expectancy Inventory
EEICA	Escala de Evaluación de la Insatisfacción Corporal para Adolescentes
EES	Emotional Eating Scale
EPQ	Eating Patterns Questionnaire
FCQ	Food Craving Questionnaire
FFQ	Food Frequency Questionnaire
FHQ	Food Healthfulness Questionnaire
FRS	Figure Rating Scale
FTO	Fat mass and obesity-associated
GAD	Generalized Anxiety Disorder Scale
GENEiUS	Genetic and EnviroNmental Effects on weight in University Students

GHQ	General Health Questionnaire
GPAQ	Global Physical Activity Questionnaire
GSLTPAQ	Godin-Shepard Leisure-Time Physical Activity Questionnaire
GWAS	Genome-wide association study
HC	Hip circumference
HEIFA	Healthy Eating Index for Australian Adults
HSC-D	Hopkins Symptom Check List- Depression
IAT	Internet Addiction Test
IES	Intuitive Eating Scale
IPAQ	International Physical Activity Questionnaire
MBAS	Male Body Attitudes Scale
MBSRQ	Multidimensional Body-Self Relations Questionnaire
MCI	Mainz Coping Inventory
MEQ	Mindful Eating Questionnaire
MOCI	Maudsley Obsessive-Compulsive Inventory
MPAM-R	Motives for Physical Activity Measure-Revised
MSPSS	Multidimensional Scale of Perceived Social Support
NCHRBS	National College Health Risk Behavior Survey
NCI	National Cancer Institute
NEQ	Night Eating Questionnaire
NLSCY	National Longitudinal Survey of Children and Youth

NQoL	Nutrition Quality of Life
NSPS	Negative Self-Portrayal Scale
OS	Opener Scale
PANAS	Positive and Negative Affect Schedule
PEMS	Palatable Eating Motives Scale
PFS	Power of Food Scale
POMC	Proopiomelanocortin
PRS	Perceived Racism Scale
PSPS	Perceived Sociocultural Pressures Scale
PSQI	Pittsburg Sleep Quality Index
PSRS	Perceived Stress Reactivity Scale
PSRSDS	Perceived Self-Regulatory Success in Dieting Scale
PSS	Perceived Stress Scale
PTSD	Post-traumatic Stress Disorder
QEWP-R	Questionnaire of Eating and Weight Patterns- Revised
RAPI	Rutgers Alcohol Problems Index
REBS	Regulation of Eating Behavior Scale
REI	Reasons for Exercise Inventory
rMEQ	reduced Morningness–Eveningness Questionnaire
RSES	Rosenberg Self-Esteem Scale
SAAS	Social Appearance Anxiety Scale

SAT	Scholastic Assessment Test
SATAQ	Sociocultural Attitudes Towards Appearance Questionnaire
SCL-90-D	Symptom Check List
SCS	Self-Compassion Scale
SD	Standard deviation
SDS	Self-Determination Scale
SECI	Satter Eating Competence Inventory
SHS	Subjective Happiness Scale
SIT	Specific Interpersonal Trust Scale
SNP	Single nucleotide polymorphism
SPAQ	Sexual and Physical Abuse Questionnaire
SPS	Social Provisions Scale
SPSRQ	Sensitivity to Punishment and Sensitivity to Reward Questionnaire
SSES	State Self-Esteem Scale
STPI	State-Trait Personality Inventory
SWED	Stanford-Washington Eating Disorder Screen
SWLS	Satisfaction with Life Scale
TFEQ	Three Factor Eating Questionnaire
TIPI	Ten-Item Personality Inventory
TPS	Transition Perspective Scale
TSRQ	Treatment Self-Regulation Questionnaire

UCLA	University of California, Los Angeles
USQ	Undergraduate Stress Questionnaire
VCOPAS	Verbal Commentary on Physical Appearance Scale
WC	Waist circumference
WCS	Weight Concerns Scale
WES	Whole exome sequencing
WHO	World Health Organization
WHR	Waist-to-hip ratio
YFAS	Yale Food Addiction Scale
YRBSS	Youth Risk Behavior Surveillance System
%BF	Body fat percentage

Glossary of anthropometric terms

Body adiposity index $$Body\ adiposity\ index = \frac{100 \times hip\ circumference}{height \times \sqrt{height}} - 18$$

where height and hip circumference are in meters

BFM — Body fat mass; the total amount of bodily adipose tissue

BMI — Body mass index; weight divided by squared height (kg/m^2)

Corpulence index — Total body mass divided by cubed height (kg/m^3)

Conicity index $$conicity\ index = \frac{waist\ circumference}{0.109} \times \sqrt{\frac{height}{weight}}$$

where height and waist circumference are in m and weight is in kg

Fat-free mass — Total body mass subtracted by body fat mass

Fat-free mass index — Fat-free mass divided by squared height (kg/m^2)

Fat-free mass percentage — Fat-free mass divided by total body mass

Fat mass index — Body fat mass divided by squared height (kg/m^2)

Muscle mass — The total amount of bodily muscle tissue

Muscle mass percentage — Muscle mass divided by total body mass

Skinfold thickness — A measure of subcutaneous fat

Subcutaneous fat — Fat underlying the skin

Visceral fat — Intra-abdominal fat lying around bodily organs

WHR — Waist-to-hip ratio; waist circumference divided by hip circumference

%BF — Body fat percentage; body fat mass divided by total body mas

Declaration of academic achievement

Chapter 1: My own work.

Chapter 2: I designed the protocol for this systematic review with Dr. David Meyre and Chenchen Tian. I was the first reviewer and was responsible for data extraction, data synthesis, and writing of the manuscript. Chenchen Tian was a co-reviewer for screening titles/abstracts and critically reviewed the manuscript for intellectual content.

Chapter 3: I was responsible for the design, implementation, and coordination of this prospective observational study. The initial concept is credited to Dr. David Meyre and Christine Langlois who designed a preliminary form of this study. I expanded on this original concept and selected variables to investigate as well as their measurement tools. Dr. David Meyre, Dr. Marie Pigeyre, Dr. James MacKillop, Dr. Hudson Reddon, and Alexandra Mayhew helped in the selection of these tools. Dr. Hudson Reddon performed the sample size calculations. Akram Alyass helped design the data analytic plan. Adeola Ishola and Fereshteh Yadzi helped in the implementation of the preliminary study protocol. I wrote the manuscript for this study, obtained ethical approval, and contributed to the grant application for CIHR funding. All authors approved the final version of the manuscript.

Chapter 4: My own work.

Preface

This master's thesis is a "sandwich" thesis consisting of an introductory Chapter 1, two core Chapters 2 and 3, and a conclusion Chapter 4. The introductory chapter provides background and rationale for the core chapters of my thesis. Chapter 2 is the manuscript of a systematic review to be submitted shortly for publication. I was the first reviewer and contributed to the design, data collection, and writing of the manuscript for this review. Chapter 3 is a protocol for a prospective observational study for which I contributed to the design, implementation, data collection, coordination, and writing of the manuscript. This paper was published in the British Medical Journal Open. For both these papers, I am the first author. Chapter 4 is a conclusion chapter in which I summarize the findings of the core thesis papers and discuss bias, feasibility, ethical issues, and future directions.

Chapter 1: Introduction

1.1 Measurement of obesity

According to the World Health Organization, obesity is defined as "abnormal or excessive fat accumulation that may impair health" (1). More precisely, obesity is often characterized by having a body mass index (BMI) of 30 kg/m^2 or greater. BMI can be categorized into underweight (<18.5 kg/m^2), normal weight (18.5 to <25 kg/m^2), overweight (25 to <30 kg/m^2), class I obese (30 to <35 kg/m^2), class II obese (35 to <40 kg/m^2), and class III obese (≥40 kg/m^2). While BMI is the most commonly used parameter to measure body weight status in individuals, it lacks information regarding body composition. This is because BMI looks at total body mass as a function of height and fails to discriminate between body fat, lean mass, and bone. As a result, this could make someone who has high muscle mass and relatively low fat mass appear to be overweight. More precise measures of body composition can be attained through dual-energy X-ray absorptiometry (DXA) which is considered to be the gold standard (2). However, this method is costly and has limited accessibility, rendering it an unfeasible option for many studies. Other methods such as bioelectric impedance analysis (BIA) and skinfold thickness are therefore often employed to estimate adiposity. Skinfold thickness may be measured through the use of calipers at multiple body sites (usually biceps, triceps, subscapular, and suprailiac) and equations are then used to estimate various adiposity outcomes like body fat percentage (%BF) (3). In BIA, electrodes are placed on an individual and a current is transmitted through the body at the time of measurement. These signals are then read by a computer which calculates adiposity outcomes based on a given equation. Both are generally good estimates of adiposity (2, 4). However, they may under- or over- estimate adiposity at extremes, equations may not be generalizable to all populations, and BIA is sensitive to changes in hydration (5, 6).

1.2 Genetic epidemiology of obesity

Obesity is a global epidemic which has risen dramatically over the last four decades with over 671 million adults living with obesity (7). This is a major public health concern since obesity is associated with depression, sleep apnea, chronic back pain, osteoarthritis, gallbladder disease, type 2 diabetes, fatty liver, hypertension, cardiovascular disease, and some cancers (8, 9). Causes of obesity are diverse and stem from a combination of genetic and environmental factors (10). It is estimated that 40-75% of the variation in BMI can be attributed to genetics, according to twin and family studies (11). There are 79 genetic syndromes with obesity, 11 non-syndromic monogenic obesity genes, and genome-wide association studies (GWAS) have identified over 850 loci associated with obesity (12-16). These genes predispose individuals to developing obesity through underlying mechanisms in the central nervous system, digestive system, musculoskeletal system, and adipose tissue (16).

Obesity is a complex disease which can have monogenic or polygenic origins. Monogenic obesity arises from a single mutation in one gene and follows a Mendelian pattern of inheritance (17). Monogenic obesity can be further classified as syndromic or non-syndromic. Syndromic monogenic obesity is rare and characterized by obesity, cognitive deficits, behavioural abnormalities, and tissue-specific malformations (18). The most common form is Prader-Willi syndrome which is often caused by paternally inherited chromosome 15q11.2-q13 deletions (18).

Non-syndromic monogenic obesity is highly penetrant and usually involves genetic mutations in the leptin-melanocortin pathway which plays a role in appetite regulation and energy balance (16). However, total loss-of-function of these genes are rare and oligogenic (heterozygous, non-fully penetrant) obesity is more common (19).

Obesity is predominately polygenic in nature such that genetic variations in multiple genes each contribute risk toward obesity, with modest effect sizes (11, 16). Genes associated with polygenic obesity can be discovered through linkage analysis, candidate gene study, or GWAS (16). Linkage analysis identifies genetic markers for a disease by looking for co-segregation between these markers and affected individuals in a pedigree (17). Candidate gene studies are hypothesis-driven and involve the selection of strong candidate genes based on previous knowledge (17). These studies are advantageous in that the burden from multiple testing is reduced, compared to hypothesis-free genome-wide approaches (17). GWAS is one such hypothesis-free approach which can be used to rapidly identify single nucleotide polymorphisms (SNPs) associated with either monogenic or polygenic obesity (17). In particular, common variants, those with a SNP frequency >5%, are best captured through GWAS (16, 20). To capture low-frequency variants or rare mutations, either whole-exome sequencing (of protein-coding genes) or whole-genome sequencing (of both protein coding and non-coding genes) can be employed (17). Currently, whole-exome sequencing is preferred over whole-genome sequencing due to its cost-effectiveness (17).

After the identification of genetic variants, the clinically utility of these markers should be assessed. Receiver operating characteristic curves can assess clinical utility of genetic variants by examining how well they predict the risk of having a Mendelian disease (21). There has been less success in utilizing receiver operating characteristic curves to assess clinical utility for common polygenic diseases, due in part to the modest effect sizes of the genetic variants and a potentially incomplete knowledge of disease-associated SNPs (21). Genome-wide consortium studies with large sample sizes and new mathematical modelling techniques may help improve the prediction of polygenic diseases in the future (21). Ultimately, this knowledge will facilitate the ability to personalize medical treatment for patients according to their individual genetic profiles (21).

1.3 Environmental determinants of obesity

Environmental factors are also involved in the development of obesity. General demographic factors, like ethnicity, are related to weight status with Asian individuals having lower and other ethnic minorities having higher BMI values when compared to Europeans (22). Those of low socioeconomic status, especially women, are also more likely to be obese (7, 22, 23). In terms of lifestyle factors, it is widely considered that diet and physical activity play a major role in the development of obesity. The consumption of dietary sweeteners, refined carbohydrates, fast foods, and Western diets are thought to lead to increased body fat (24). Physical inactivity during adolescence is also associated with increased risk of obesity in young adulthood (25). Another well-described lifestyle contributor is sleep quantity which has a U-shaped relationship with BMI, such that greater or fewer than 8 hours of sleep is associated with increased BMI (26).

1.4 Why the undergraduate population is important

Young adulthood is a period where individuals develop personal lifestyle habits. Undergraduate students, transitioning from high school to university life, go through many lifestyle changes as some move away from their family home and have greater freedom to make their own choices regarding their diet, exercise, and sleep habits, among others. The transition from high school to university is marked by poorer eating habits, increased alcohol consumption, decreased physical activity, increased sedentary behaviour, decreased sleep quantity, and decreased sleep quality (27-31). These lifestyle changes may contribute to the weight gain students face during their first year of undergraduate education (32). On average, first-year undergraduates gain 3-5 lbs (1.4-2.3 kg) over the course of their first academic year (33-35). This period is important in the development of obesity as elevated BMI during adolescence and young adulthood is associated with an increased risk of obesity later in life as well as increased morbidity and mortality (36-41). Undergraduate students are especially at risk since they are more likely to gain weight or have obesity that those not attending university (42, 43).

1.5 Rationale for further study

Given the importance of the young adulthood period in adopting healthy lifestyle habits and developing obesity later in life, it is critical that obesity-prevention programs target this population. To design effective obesity-prevention programs, a good understanding of the determinants of weight gain are needed. While several reviews have described weight changes in undergraduates, less is known about what causes this change (33-35). The aim of the systematic review in Chapter 2 was to address this gap in knowledge by synthesizing a thorough list of factors associated with obesity traits (e.g. BMI, %BF) in undergraduate students. This systematic review also provided insight when designing the Genetic and EnviroNmental Effects on weight in University Students (GENEiUS) study, a prospective observational study, described in Chapter 3 by identifying under-investigating variables warranting further research. This prospective observational study was needed, not only to attain a better understanding of the factors which cause weight change, but also to explore what body composition changes occur after first year. At present, most studies only investigated weight changes over first year using BMI as the primary outcome and failed to observe changes in adiposity (e.g. %BF) over the entire four years of undergraduate education (33). The study described in Chapter 3 therefore aims to fill these gaps in knowledge. The GENEiUS study currently has 250 participants enrolled and is actively recruiting. Together this systematic review and prospective observational study will provide evidence to design better obesity-prevention programs in universities.

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Chapter 2: Factors associated with obesity traits in undergraduate students: a systematic review

Rita E. Morassut[1], Chenchen Tian[1], David Meyre[1,2]

Affiliations

[1]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada

[2]Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

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Correspondence to:

Dr D Meyre, McMaster University, 1280 Main St West, Michael DeGroote Centre for Learning & Discovery, Room 3205, Hamilton, ON L8S 4K1, Canada

E-mail: meyred@mcmaster.ca

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2.1 Summary

Young adulthood is a critical period for the development of lifestyle habits and weight change. Undergraduate students are susceptible to weight change and gain 3-5 lbs (1.4-2.3 kg) during their first year of postsecondary education. The determinants of these weight changes remain elusive. This systematic review aimed to identify factors associated with obesity traits including body mass index, weight, and body fat percentage in undergraduate students. CINAHL, EMBASE, MEDLINE, and PsycINFO were searched from inception to June 11, 2017. Observational, experimental, and qualitative studies of undergraduate students in which an obesity trait was associated with an environmental factor were eligible. Two hundred forty-four articles were included comprising of 238 studies: 175 cross-sectional, 49 cohort, 11 interventional, and 3 qualitative. We identified a broad variety of factors associated with obesity-traits including age, sex, ethnicity, socioeconomic status, religion, diet, eating habits, physical activity, sedentary activity, sleep, stress, university campus life, alcohol use, smoking, psychiatric disorders, body image, eating attitude, eating regulation, personality, social/cultural influences and genetics. No meta-analysis or risk of bias assessment was conducted which limits any inferences to be drawn regarding the strength of relationships or the strength of evidence. This review will help researchers and decision-makers identify gaps in literature, generate novel hypotheses, further knowledge and design obesity-prevention programs in universities.

2.2 Introduction

The global prevalence of obesity has increased seven-fold over the last four decades, from 111 million children and adults in 1975 to 795 million in 2016 (1) . The health risks associated with obesity include depression, sleep apnea, chronic back pain, osteoarthritis, gallbladder disease, type 2 diabetes, fatty liver, hypertension, cardiovascular disease, and some cancers (2, 3). Adolescence and young adulthood may be critical periods for the development of obesity as elevated body mass index (BMI) during this time is associated with chronic obesity later in adulthood, and higher morbidity and mortality (4-9). In North America, young adults tend to have the greatest increase in the prevalence of overweight or obesity over time, compared to other adult age groups (10, 11). While education status is negatively correlated with BMI in the general population from high-income countries, young adults with higher education gain more weight and are more likely to be obese than those without university education in the United States (12-14).

The "Freshman 15" is a popular notion which suggests that undergraduate students gain 15 pounds (6.8 kg) during their first year of university education. Previous studies have found this to be an exaggeration, estimating an average weight gain of 3 to 5 lbs (1.4 to 2.3 kg) (15-17). These observed weight changes may reflect underlying modifications in lifestyle habits and other health-related behaviours during the transition from secondary school to university (18). These include decreased quality of overall diet, decreased physical activity, increased sedentary behaviour from internet usage, increased alcohol use, and decreased sleep quantity and quality (19-23). Other important considerations include anxiety, depression, and eating disorders, each with a high prevalence of 21%, 17%, and over 3% in undergraduate students, respectively (24).

However, the determinants of weight change in undergraduate students remain elusive. A better understanding is needed to identify at-risk individuals and to design strategies to combat the obesity epidemic in university students.

Reviews and meta-analyses of the “Freshman 15” phenomenon have primarily focused on the evaluation of mean weight gain rather than on the predictors of such weight change (15-17). In addition, an assessment of the existing literature is critical to evaluate the quality of past studies and identify areas for improvement to provide direction for future research. This paper aims to systematically review literature examining predictors of weight gain in undergraduate students to better understand factors influencing freshman weight change. The primary objective of the study was to examine factors associated with body mass index (BMI) level and BMI change in undergraduate university students. Secondary objectives aim to investigate factors associated with additional obesity trait level and change (i.e. body adiposity index, conicity index, corpulence index, fat mass, fat mass index, fat mass percentage, muscle mass, muscle mass percentage, fat-free mass, fat-free mass index, fat-free mass percentage, hip circumference, waist circumference, waist-to-hip ratio, and weight).

2.3 Methods

A protocol for the present systematic review was registered on PROSPERO (2017 #CRD42017068742). Criteria for search methods, article eligibility, factors associated with obesity traits (e.g. diet) and obesity trait outcomes (e.g. BMI) were determined *a priori*. The PRISMA statement was used to guide reporting of this systematic review (25).

2.3.1 Literature search

In collaboration with an information specialist (LEB), we developed search strategies tailored to each database and conducted a systematic search of CINAHL, EMBASE, MEDLINE, and PsycINFO to identify studies investigating obesity trait level and change in undergraduate students. We used search terms such as "undergraduate", "college", "university", "bachelor", "higher education", "student", "body mass index", "weight loss", "weight gain", "weight change", "lean", "overweight", "obesity", "body fat", "waist to hip ratio", "waist circumference", "skinfold thickness", "adiposity", "body composition", and "freshman fifteen" with Boolean operators to identify studies investigating undergraduate weight/body composition change (see Table S1 for the full search strategy). The search was conducted from the inception of each database to June 11, 2017.

2.3.2 Article review

Title and abstract screening was conducted in duplicate by REM and CT to identify studies for full-text review. Observational, interventional, or qualitative studies on samples of undergraduate university students, excluding medical students, were included for full-text review. Since BMI is the most commonly reported measure of body composition among "Freshman 15" studies, BMI level and change were the primary outcomes of this study (15). Data for other obesity traits including body adiposity index, conicity index, corpulence index, fat mass, fat mass index, fat mass percentage, muscle mass, muscle mass percentage, fat-free mass, fat-free mass index, fat-free mass percentage, hip circumference, triceps skinfold thickness, waist circumference, waist-to-hip ratio, visceral fat, and weight were also collected as secondary outcomes. Articles were excluded if they had a sample size less than 30 (for the whole set or relevant subgroup); or had obesity traits only associated with pregnancy or physical medical conditions (e.g. polycystic ovarian syndrome, bone fractures), cardiovascular/metabolic/biochemical factors (e.g. serum blood glucose, hypertension), or other anthropometric measurements (e.g. height, neck circumference). Only English full-text, original research journal articles were eligible for inclusion (e.g. we excluded reviews, commentaries, editorials). A sample of 100 abstracts were screened in a training exercise by REM, CT, and a subject matter expert (DM). Disagreements at the screening stage were reconciled through discussion by REM and CT. After full-text review, papers which contained original research showing an association between an obesity trait and a factor in undergraduate students were included. Full-text articles were assessed for eligibility by REM and a subject matter expert (DM). Additional references were identified from previous reviews on the "Freshman 15" or through references of included papers.

2.3.3 Data extraction and analysis

Study characteristics, participant demographics, type of factor and its method of measurement, obesity trait and its method of measurement were extracted by REM. A descriptive analysis is presented for this systematic review. Data are summarized first by obesity trait and then by its associated factor.

2.4 Results

2.4.1 Literature flow

Our search yielded 14,119 titles and abstracts to be screened, after the removal of 5900 duplicates (Figure 1). One additional article identified by a "freshman 15" review paper not captured in the initial search was also added (26, 27). After completion of title and abstract screening, 791 records proceeded to full-text review. Five hundred forty-seven articles were excluded for the following: 339 non-undergraduate student sample, 117 non-full text original research journal articles, 37 for having no factors associated with an obesity trait, 25 non-English, 14 for not having an obesity trait as an outcome, 10 for having a sample size less than 30 in the whole set or relevant subgroup, 3 duplicates, and 2 which had an inappropriate comparator group of non-undergraduate students. Two hundred forty-four articles met eligibility criteria.

2.4.2 Overview of studies

The 244 included papers comprised of 238 studies: 175 cross-sectional, 48 prospective cohort, 1 retrospective cohort, 11 interventional, and 3 qualitative studies. Papers from 1953 to 2017 were included, with a median publication date of 2012. Sixty percent of studies were conducted in North America followed by 15% in Europe, 10% in Asia, 6% in the Middle East, 3% in South America, 2% in Oceania, 2% in Africa, and 2% international. Only 50% of studies reported an ethnicity. In total, 22 studies (9% of all studies) were comprised predominately of one ethnic group (≥90%). Among studies, the median sample size was 235 individuals and ranged from 30 to 24,613. The median proportion of males in studies was 35%, with studies ranging from 0% to 100% male. The median BMI of participants in studies was 23.0 kg/m^2 (range from 19.9 to 29.2 kg/m^2). Of the prospective studies, the median follow-up time was 8 months, reflecting the first year of undergraduate education. Follow-up times ranged from 2 months to 3 years, the latter reflecting time to fourth-year undergraduate education.

2.4.3 Factors associated with BMI level

We identified associations between BMI level and factors related to demographic characteristics including ethnicity, religion, and calendar year (i.e. year of data collection); diet/nutrition; eating habits; eating attitudes; eating regulation; physical activity; sedentary activity; healthy lifestyle; sleep; stress; university campus life; substance use; medical history; body image; personality/emotions; social/cultural influences; and psychiatric illness/disorders (Table S2) from cross-sectional, prospective, and interventional studies. Specifically, the following traits were positively associated with BMI: age, darker skin color, African/Hispanic/Native American/other minority ethnicity (vs. European), number of children, single (vs. dating), married (vs. single), religiosity, calendar year, fat intake, protein intake, meat and egg consumption, junk food consumption, coffee/tea/energy drink consumption, Western diet (vs. Chinese diet), comfort eating, junk food cravings, high appetite, plate-clearing behavior, skipping meals, being an athlete, exercising for appearance/weight control, electronic screen time, stress, being in greater than first-year undergraduate studies, alcohol use, prescription medication use, smoking, family history of overweight/obesity, anxiety, depression/suicide attempts, post-traumatic stress disorder, binge eating disorder/bingeing, bulimia, risk or being treated for an eating disorder, psychosocial impairment from eating disorders, body dissatisfaction, desire to lose weight, body image/shape/weight concern, clothing for assurance or camouflage, ideal body size, perceived body size, weight fluctuations, emotional eating, eating concern, dieting, eating restraint, eating beyond satiety, poor oral control, food preoccupation, fasting, changing eating behaviors, amotivation, autonomous eating regulation, willing to change eating pattern, agreeableness, anger, attention/concentration, emotional stability, extraversion, loneliness, impulsivity, abuse during childhood, directive support, encouragement to diet, negative comments about weight, racism, and romantic relationship satisfaction. Conversely, BMI was negatively associated with number of family members, socioeconomic status, Asian ethnicity (vs. European), Muslim (vs. Christian), avoiding high carbohydrate meals, fiber intake, dairy consumption, fruit/vegetable intake, rice and grains consumption, calcium supplement use, diet quality/guideline adherence, eating while bored, night eating, snacking, choosing healthy foods, exercise motivation, physical activity, healthy lifestyle, sleep quantity, being a nutrition major or sorority member, living on-campus, the walkability or bikeability of university campus, problems with alcohol use, flu immunization in the past year, obsessive compulsive disorder, body affect, ability to tolerate negative thoughts about weight, acceptance of cosmetic surgery, weight overestimation, eating until full, hunger, intuitive eating, coping via cognitive avoidance, self-compassion, illness orientation (being self-aware of illnesses), psychologically secure, satisfaction with life, self-concept, self-determination, social withdrawal, emotional reactivity or fearful temperament, being told to gain weight, intense-personal or entertainment-social attitudes toward celebrities, social support, and sociocultural influences/pressures. Factors which were associated but showed an uncertain direction in effect (i.e. 50% of studies showed positive associations and 50% showed negative associations) include male sex, energy intake, legume consumption, physical fitness, sleep quality, and controlled eating regulation. Other associated factors with no specified direction included type of exercise, university institution, external eating, and laxative use.

2.4.4 Factors associated with BMI change

Similar factors were identified with positive BMI change, including the addition of genetic factors and weight loss interventions (Table 1). In general, male sex, being heterozygous AT (vs. TT) for the *FTO* single nucleotide polymorphism rs9939609, fatty food preference, eating quickly, skipping meals, eating after consuming alcohol, eating at a friend's house, electronic screen time, going to sleep late, living on-campus, accessibility of dining halls, proximity to gyms, smoking, desire to lose weight, emotional eating, eating restraint, and controlled eating regulation were positively associated with BMI change. Conversely, age, Native American (vs. European) ethnicity, fruit and vegetable intake, physical activity, behavioral/educational weight loss interventions, stress, summer months, proximity to grocery stores, number of vending machines in dorms, choosing healthy foods, perceived success in dieting, autonomous eating regulation, and autonomous support were negatively associated with BMI change. Associations were also identified for alcohol consumption and frequent weighing behaviour, however the direction of these effects are uncertain.

2.4.5 Factors associated with weight

Several factors were found to influence weight and weight change (Tables S3-S4). Specifically, age, male sex, African ethnicity (vs. European), calendar year, junk food consumption, physical activity, playing volleyball (vs. doing ballet), living in a dorm with an on-site dining hall, alcohol consumption, bulimia, disordered eating, body dissatisfaction, shape concern, perceived body size, dieting, positive affect, weight loss-related comments by friends and family were positively associated with weight. Factors negatively associated with weight included being a nutrition major, self-esteem, and pressure to eat more.

Factors positively associated with positive weight change included male sex; foreign nationality; being heterozygous AT (vs. TT) for *FTO* single nucleotide polymorphism rs9939609; high calories foods; energy intake; dairy intake; consumption of satiating foods; unhealthy eating habits; alcohol-related food consumption; eating while bored, studying, or socializing; snacking; physical activity; sedentary activity; being in first year undergraduate studies; being a member of a student group; living on-campus, without parents, or undergoing a change in housing; dining hall accessibility; having buffet-style meals; frequency of meal plan use; alcohol consumption; smoking; depression; bulimia; body dissatisfaction (change and at follow-up); perceived unattractive appearance; disordered eating (change and at baseline, follow-up); greater freedom in making food choices; confidence in academic ability; impulsivity; negative well-being in females; self-esteem in males; relationship with parents in females; and roommate's weight. On the other hand, food and vegetable consumption, having autonomous support to lose weight, academic performance, access to vending machines, summer months, having more free time, attending a rural mid-size university, body image, frequent weighing behavior, carefully making food choices, autonomous eating regulation, happiness, negative well-being in males, negative feelings about transitioning to university, self-esteem in females, autonomy support from others, body image comments from friends/family, perceived success in finding a romantic partner, relationship with parents in males were negatively associated with weight change. Stress exemplified a more complex relationship whereby high stress was associated with both weight gain and weight loss. Associations for sleep quantity, body dissatisfaction (at baseline), dieting, eating restraint were also identified, however the direction of these effects is uncertain. Consumption of healthy or junk foods, eating at restaurants or pay-cash facilities, number of meals in the evening or weekend, dormitory location, negative affect, and concern about interpersonal relationships were also related to positive weight change although no direction was reported.

2.4.6 Factors associated with adiposity measures

Associations were also found for obesity traits measuring adiposity (i.e. body adiposity index, body fat mass, body fat percentage, fat mass index, triceps skinfold thickness, visceral fat, conicity index) (Tables S5-12). Age, African ethnicity or other ethnic minority (vs. European), calendar year, energy intake, exercising for appearance, stress, being in fourth-year undergraduate studies, smoking, body dissatisfaction, ideal body size, perceived body size, putting effort into physical appearance, eating restraint, autonomous eating regulation, controlled eating regulation, achievement self-esteem in appearance, having a history of abuse during childhood were positively associated with adiposity measures. In contrast, male sex, socioeconomic status, Muslim religion (vs. Christian), dairy intake, fiber intake, eating a healthy diet, exercising for competence (i.e. desire to improve at a physical activity), physical activity, body satisfaction, and self-acceptance / self-esteem in performance were negatively associated with adiposity measures.

For positive changes in adiposity measures, male sex, being in first year for undergraduate studies, living on-campus, summer months, amotivation in eating regulation, and disinhibition in eating were positively associated. Conversely, physical activity, being in second-year undergraduate studies (vs. first or third year), reading and studying, putting effort into physical appearance, and autonomous eating regulation were negatively associated with changes in adiposity measures.

2.4.7 Factors associated with lean/muscle mass measures

We also found associations for lean/muscle mass measures (i.e. muscle mass, muscle mass percentage, fat-free mass, fat-free mass index, fat-free mass percentage) (Tables S13-17). Male sex, physical activity, responsiveness to food environments, being in second-year undergraduate studies (vs. third year), and being in a nutritional course were positively related to positive changes in lean/muscle mass. Male sex, physical activity, body building (vs. playing soccer), and playing volleyball (vs. doing ballet) were positively associated with lean/muscle mass measures while calendar year and summer months were negatively associated.

2.4.8 Factors associated with other obesity traits

Waist circumference was positively associated with age, male sex, being married, socioeconomic status, energy intake, avoiding fatty foods, following a Western diet (vs. Chinese diet), hunger and overeating, inconsistent meal times, skipping meals, preference for sweets, sleep quality, academic performance, family history of obesity, body dissatisfaction, disordered eating, and binge eating (Table S18). Conversely, African ethnicity, fiber intake, diet quality, physical activity, physical fitness, following a healthy lifestyle, sleep quantity, considering changing eating habits, attention deficit hyperactivity disorder, and being psychologically secure were negatively associated with waist circumference. Male sex and meal plan use were positively associated with positive waist circumference change.

Positive associations were identified for age and disordered eating with hip circumference. Physical activity and body dissatisfaction were negatively associated with hip circumference. Positive hip circumference change was negatively associated with male sex (Table S19).

Waist-to-hip ratio was positively associated with age and disordered eating and negatively associated with African ethnicity (Table S20).

Being in fourth-year undergraduate studies (vs. other years) was positively associated with corpulence index (Table S21). Male sex was positively associated with body surface area (Table S22).

2.5 Discussion

We identified a broad range of factors associated with obesity traits including demographics, calendar year, diet/nutrition, eating habits, physical activity, sedentary activity, weight loss interventions, lifestyle, sleep, stress, university campus life, substance use, medical history, psychiatric illness/disorders, body image, eating attitude, eating regulation, personality/emotions, social/cultural influences, and genetics. The most commonly reported obesity outcomes in the included studies were BMI and weight. In general, the factors we identified had similar directions of effect between these two outcomes (e.g. body dissatisfaction was positively associated with both weight and BMI level). The direction of effects also agreed with previous studies in the general population such that age and female sex are positively associated with %BF; Asians have lower BMI while other ethnic minorities have higher BMI when compared to Europeans; diets high in refined carbohydrates, fast foods, and low in fruits and vegetables are related to increased adiposity; physical inactivity leads to increased BMI; body dissatisfaction is associated with increased BMI; bulimia and binge-eating disorder are positively associated with BMI; anxiety and depression are associated with higher obesity risk; high alcohol consumption is associated with excess weight and weight gain; and stress is related to weight gain and weight loss (3, 28-35). However, most of the analyses were linear and failed to look at more complex associations such as with sleep, which shows a U-shaped relationship with BMI (36). Moreover, when comparing cross-sectional and longitudinal studies of BMI (i.e. BMI level vs. BMI change), the direction of associations differed in some cases. One illustration is Native American ethnicity being positively associated with BMI level but negatively associated with BMI change, as compared to Europeans. Since Native Americans have a higher baseline BMI, it is possible they gain less weight during undergraduate studies than other students. Additionally, BMI and weight do not consider the composition of fat or muscle mass. This is an important point to consider. For instance, this review found living closer to gyms was positively associated with BMI change which seemingly contrasts the finding that physical activity is negatively associated with BMI change. However, this BMI change may have reflected an increase in muscle mass instead of adiposity. Effects may also differ by sex as evidenced by self-esteem, negative well-being, and one's relationship with their parents on weight change. In addition, some studies investigated differences in obesity traits (i.e. BMI, weight, and waist circumference) between individuals of different nationalities. Providing a direction of effect was challenging given the diversity of nationalities and comparators among these studies. While variation in body composition may exist within ethnic groups, the results of these studies should be interpreted with caution as more comprehensive international multi-centre studies are needed to gain a better understanding of these differences.

2.5.1 Strengths and limitations

This study finds strength in using broad search criteria to increase the likelihood of finding relevant papers. We also considered qualitative studies in addition to observational and interventional studies to obtain a more holistic understanding of factors affecting weight changes in undergraduates. These qualitative findings generally agreed with the findings from the quantitative studies, but also provided some unique information that quantitative studies do not usually capture (e.g. feelings about buffet-style meals, having greater freedom to make food choices). One limitation of this review is that no meta-analysis was conducted, meaning the strength of the identified associations cannot be determined. Given the small number of papers investigating each specific factor and the great diversity of measurement tools used in the included studies, scarcity of data and heterogeneity would have posed major problems. Nor can the quality of evidence be inferred as no risk of bias assessment was conducted. Most studies (94%) however were observational in nature, lending to low quality of evidence (37). The validity of findings may be questionable as many studies did not use validated questionnaires to measure some factors nor did they describe the methods used. Finally, the majority of associations were from cross-sectional studies and are therefore correlational in nature. Any inference of causality is therefore limited and results should be interpreted with caution as unmeasured confounders could affect significance, magnitude, and direction of associations.

2.5.2 Implications

This is the first systematic review to synthesize the factors associated with obesity traits in undergraduate students. This systematic review will help guide the design of high quality longitudinal studies investigating undergraduate weight change by helping investigators select variables which are under-investigated and require further study, like the GENEiUS study (38). For example, few studies investigated the effect of adverse life experiences on body composition. This is a critical area of interest given the high prevalence (about 14-44%) of students ever experiencing sexual assault during their undergraduate education (39). Our review also highlights the need to investigate changes in both fat and muscle mass, as these reflect important changes that BMI alone cannot capture. In addition, it revealed some factors which had complex relationships with body composition, suggesting future studies conduct sex-specific or non-linear analyses. Finally, these findings will help universities understand potential factors which influence body composition change and design more effective obesity prevention programs.

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Author Contributions: All authors designed the study protocol; REM, CT, and DM conducted the research; REM and DM wrote the manuscript; CT critically reviewed the manuscript; DM had primary responsibility for final content. All authors read and approved the final manuscript.

2.6 Figures and tables

Figure 1. PRISMA literature flow diagram of eligible studies

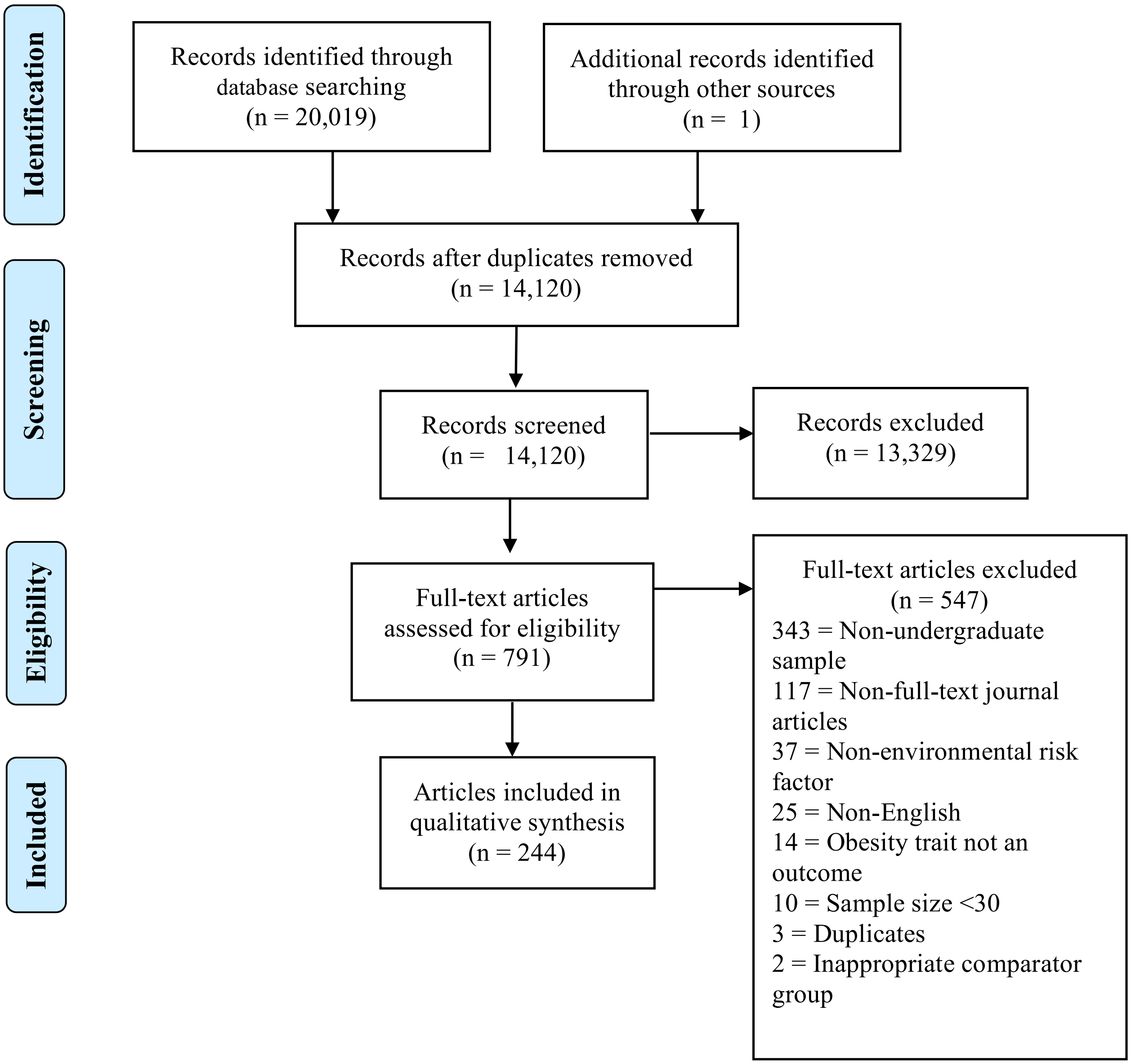

Table 1. Factors associated with body mass index change

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Negative (100%)	Prospective	(40)
	Sex (male)	—	Positive (80%)	Prospective	(41-47)
			Negative (100%)	Interventional	(48, 49)
Ethnicity (vs. European)	Native American	—	Negative (100%)	Prospective	(50)
Genetics	*FTO* SNP rs9939609 risk allele A (vs. T)	Genotyping	Positive (100%)	Prospective	(40)
Diet/nutrition	Fatty food preference	Self-reported items	Positive (100%)	Prospective	(51)
	Fruit and vegetable intake	Self-reported	Negative (100%)	Prospective	(52)
Eating habits	Eating quickly	—	Positive (100%)	Prospective	(47)
	Skipping meals	—	Positive (100%)	Prospective	(51)
	Alcohol-related food consumption	EAUQ	Positive (100%)	Prospective	(53)
	Eating at a friend's house	—	Positive (100%)	Prospective	(41)
Physical activity	Physical activity	Adaptations of NLSCY and YRBSS; self-reported items	Negative (100%)	Prospective	(27, 51)
Sedentary activity	Electronic screen time	—	Positive (100%)	Prospective	(41)
Weight loss intervention	Autonomous support to lose weight	—	Negative (100%)	Interventional	(54)
	Behavioral healthy weight intervention		Negative (100%)	Interventional	(55, 56)
	Nutrition education		Negative (100%)	Interventional	(57)
Sleep	Evening chronotype	rMEQ	Positive (100%)	Prospective	(58)
Stress	Stress	DASS	Negative (100%)	Prospective	(59)
University campus life	Living on-campus	—	Positive (100%)	Prospective	(52)
	Bicycle sharing program	—	Negative (100%)	Prospective	(60)
	Summer	—	Negative (100%)	Prospective	(61)
	Meal plan use	Number of meal card swipes	Positive (100%)	Prospective	(62)
	Accessibility of dining halls	—	Positive (100%)	Interventional	(48)
	Dorm proximity to grocery store	—	Negative (100%)	Interventional	(48)
	Number of vending machines in dorm	—	Negative (100%)	Interventional	(48)
	Dorm proximity to gym	—	Positive (100%)	Interventional	(48)
Substance use	Alcohol	AUDIT	Positive (100%)	Prospective	(53)
		—	Negative (100%)	Retrospective	(51)
	Smoking	Items adapted from (63)	Positive (100%)	Prospective	(50)

Body image	Frequent weighing	Wi-Fi scale and weight feedback; self-logging	Uncertain (50%)	Interventional	(64, 65)
	Desire to lose weight	—	Positive (100%)	Prospective	(66)
Eating attitude	Eating to cope and emotional eating	Emotional Stroop tests (color identification)	Positive (100%)	Prospective	(59)
	Eating restraint	Revised Restraint scale	Positive (100%)	Prospective	(52)
		Restraint scale	Positive (100%)	Interventional	(65)
	Tendency to choose healthy foods	Reaction time test	Negative (100%)	Prospective	(59)
	Perceived success in dieting	PSRSDS	Negative (100%)	Prospective	(67)
Eating regulation	Autonomous eating regulation	REBS (intrinsic motivation, integrated regulation, identified regulation subscales)	Negative (100%)	Prospective	(68)
	Controlled eating regulation	REBS (introjected regulation subscale)	Positive (100%)	Prospective	(68)
Social influences and pressures	Autonomy support	Items adapted from (69)	Negative (100%)	Interventional	(54)

<u>Abbreviations:</u> AUDIT, Alcohol Use Disorders Identification Test; DASS, Depression Anxiety Stress Scales; EAUQ, Eating and Alcohol Use Questionnaire; NLSCY, National Longitudinal Survey of Children and Youth; PSRSDS, Perceived Self-Regulatory Success in Dieting Scale; REBS, Regulation of Eating Behavior Scale; rMEQ, reduced Morningness–Eveningness Questionnaire; SNP, single nucleotide polymorphism; YRBSS, Youth Risk Behavior Surveillance System

* Percentage calculated per study; direction of majority (>50%) is shown

Table S1. Full search queries

Database	Search Period	Search
EMBASE	Through June 9, 2017	1. (undergrad* or college* or universit* or bachelor* or "higher education").ti,ab,kw. 2. (student* or freshman or freshmen or frosh or fresher* or "young adult*").ti,ab,kw. 3. ("body mass ind*" or BMI or (weigh* adj2 (los* or change* or gain*)) or lean or obese or obesity or overweight or "over weight" or "over-weight" or "fat mass" or "body fat" or "waist circumference" or "waist-hip ratio" or "waist hip ratio" or "waist to hip ratio" or "waist-to-hip ratio" or WHR or "skinfold thickness" or "skin fold thickness" or "skin-fold thickness" or adipos* or "body fat distribution" or "body composition" or "body adiposity ind*" or BAI).ti,ab,kw. 4. ("freshman 15" or "freshman fifteen" or "frosh 15" or "frosh fifteen").ti,ab,kw. 5. undergraduates.ti,ab,kw.

		6. university/ or college/ 7. student/ or young adult/ 8. college student/ 9. body mass/ or anthropometric parameters/ or "weight, mass and size"/ or body weight/ or "physical constitution and health"/ or ideal body weight/ or lean body weight/ or weight change/ or weight control/ or weight fluctuation/ or weight gain/ or weight reduction/ or weight variation/ or obesity/ or body distribution/ or body fat/ or adipose tissue/ or body composition/ or body fat caliper/ or body fat distribution/ or body fat meter/ or waist circumference/ or skinfold thickness/ 10. 1 or 6 11. 2 or 7 12. 10 and 11 13. 5 or 8 or 12 14. 3 or 9 15. 13 and 14 16. 4 or 15 17. remove duplicates from 16
CINHAL	Through June 11, 2017	S1. (MH "Colleges and Universities") S2. undergrad* OR college* OR universit* OR bachelor* OR "higher education" S3. (MH "Students") OR (MH "Young Adult") S4. student* OR freshman OR freshmen OR frosh OR fresher* OR "young adult*" S5. (MH "Students, Undergraduate") OR (MH "Students, College") S6. undergrad* S7. (MH "Body Weight Changes+") OR (MH "Body Weights and Measures+") OR (MH "Body Composition+") OR (MH "Adipose Tissue") S8. "body mass ind*" OR BMI OR (weigh* N2 los* OR change* OR gain*) OR lean OR obesity OR obese OR overweight OR "over weight" OR "over-weight" OR "fat mass" OR "body fat" OR "waist circumference" OR "waist-hip ratio" OR "waist hip ratio" OR "waist to hip ratio" OR "waist- to-hip ratio" OR WHR OR "skinfold thickness" OR "skin fold thickness" OR "skin-fold thickness" OR adipos* OR "body fat distribution" OR "body composition" OR "body adiposity ind*" OR BAI S9. "freshman 15" OR "freshman fifteen" OR "frosh 15" OR "frosh fifteen" S10. S1 OR S2

		S11. S3ORS4 S12. S10 AND S11 S13. S5 OR S6 OR S12 S14. S7 OR S8 S15. S13 AND S14 S16. S9 OR S15 S17. S16
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)	Through June 11, 2017	1. (undergrad* or college* or universit* or bachelor* or "higher education").ti,ab,kf. 2. Universities/ 3. (student* or freshman or freshmen or frosh or fresher* or "young adult*").ti,ab,kf. 4. Students/ or Young adult/ 5. undergraduates.ti,ab,kf. 6. ("body mass ind*" or BMI or (weigh* adj2 (los* or change* or gain*)) or lean or obese or obesity or overweight or "over weight" or "over-weight" or "fat mass" or "body fat" or "waist circumference" or "waist-hip ratio" or "waist hip ratio" or "waist to hip ratio" or "waist-to-hip ratio" or WHR or "skinfold thickness" or "skin fold thickness" or "skin-fold thickness" or adipos* or "body fat distribution" or "body composition" or "body adiposity ind*" or BAI).ti,ab,kf. 7. exp "Body Weights and Measures"/ or body weight/ or exp overweight/ or Adipose Tissue/ or exp Body Composition/ 8. ("freshman 15" or "freshman fifteen" or "frosh 15" or "frosh fifteen").ti,ab,kf. 9. 1 or 2 10. 3 or 4 11. 9 and 10 12. 5 or 11 13. 6 or 7 14. 12 and 13 15. 8 or 14 16. remove duplicates from 15
PsycINFO	Through June Week 1 2017	1. colleges/ or college environment/ or higher education/ 2. (undergrad* or college* or universit* or bachelor* or "higher education").ti,ab. 3. (student* or freshman or freshmen or frosh or fresher* or "young adult*").ti,ab. 4. students/ or emerging adulthood/ 5. exp College Students/

		6. undergraduates.ti,ab. 7. exp body mass index/ or exp body size/ or exp body weight/ or exp obesity/ or exp overweight/ or exp body fat/ or exp anthropometry/ 8. ("body mass ind*" or BMI or (weigh* adj2 (los* or change* or gain*)) or lean or obese or obesity or overweight or "over weight" or "over-weight" or "fat mass" or "body fat" or "waist circumference" or "waist-hip ratio" or "waist hip ratio" or "waist to hip ratio" or "waist-to-hip ratio" or WHR or "skinfold thickness" or "skin fold thickness" or "skin-fold thickness" or adipos* or "body fat distribution" or "body composition" or "body adiposity ind*" or BAI).ti,ab. 9. ("freshman 15" or "freshman fifteen" or "frosh 15" or "frosh fifteen").ti,ab. 10. 1 or 2 11. 3 or 4 12. 10 and 11 13. 5 or 6 or 12 14. 7 or 8 15. 13 and 14 16. 9 or 15 17. remove duplicates from 16

Table S2. Factors associated with body mass index level

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Positive (100%)	Cross-sectional	(70-90)
				Prospective	(40, 91)
				Interventional	(49)
	Sex (male)	—	Positive (95%)	Cross-sectional	(71-74, 78, 85, 92-126)
			Positive (100%)	Prospective	(40, 58, 127-130)
			Positive (100%)	Interventional	(48, 49)
	Nationality	—	—	Cross-sectional	(78, 131-133)
	Darker skin color	Color matching	Positive (100%)	Cross-sectional	(134)
	Number of children	—	Positive (100%)	Cross-sectional	(77)
	Number of family members	—	Negative (100%)	Cross-sectional	(135, 136)
	Single (vs. dating)	—	Positive (100%)	Cross-sectional	(137)

	Married (vs. single)	—	Positive (100%)	Cross-sectional	(72, 135, 136)
	Socioeconomic status	Income; parent's education status	Negative (71%)	Cross-sectional	(73, 74, 106, 108, 115, 136, 138)
		Income	Negative (100%)	Prospective	(139)
Ethnicity (vs. European)	African	—	Positive (100%)	Cross-sectional	(83, 106, 109, 138, 140-144)
			Positive (100%)	Prospective	(91, 127)
	Asian	—	Negative (100%)	Cross-sectional	(82, 84, 106, 140, 145)
	Hispanic	—	Positive (100%)	Cross-sectional	(82, 96, 106)
	Native American	—	Positive (100%)	Cross-sectional	(106)
	Other ethnic minority	—	Positive (100%)	Cross-sectional	(92, 113, 140)
Religion	Muslim (vs. Christian)	—	Negative (100%)	Cross-sectional	(146)
	Religiosity	DUREL (organizational activity subscale)	Positive (100%)	Cross-sectional	(73)
Calendar year	Year	—	Positive (100%)	Cross-sectional	(106, 147)
Diet/Nutrition	Energy intake	3-day food record; self-reported items	Negative (100%)	Cross-sectional	(148)
		2-day food recall	Positive (100%)	Interventional	(149)
	Fat intake	5-day food record; self-reported items	Positive (100%)	Cross-sectional	(73, 78, 150, 151)
		2-day food recall	Positive (100%)	Interventional	(149)
	Protein intake	DA+; self-reported items	Positive (100%)	Cross-sectional	(95, 97)
		2-day food recall	Positive (100%)	Interventional	(149)
	Avoiding high carbohydrate meals	Self-reported items	Negative (100%)	Cross-sectional	(126)
	Fiber intake	3-day food record; 7-day food record; DHQ	Negative (100%)	Cross-sectional	(107, 148, 152)
	Dairy consumption	3-day food record; FFQ; self-reported items	Negative (67%)	Cross-sectional	(93, 95, 148, 153)
	Fruit and vegetable consumption	Brazil Ministry of Health food questionnaire; DA+; FFQ; self-reported items	Negative (83%)	Cross-sectional	(75, 93, 95, 97, 125, 154)
	Fruit, vegetables, and whole grains consumption	FFQ	Negative (100%)	Prospective	(155)

	Rice and grains consumption	5-day food record; 7-day food record; self-reported items	Negative (100%)	Cross-sectional	(93, 107, 150)
	Meat and egg consumption	5-day food record; self-reported items	Positive (67%)	Cross-sectional	(93, 99, 150)
	Legume consumption	3-day food record; self-reported items	Uncertain (50%)	Cross-sectional	(93, 148)
	Junk food consumption	FFQ; self-reported items	Positive (83%)	Cross-sectional	(99, 108, 125, 135, 136, 153)
		Gray-Donald EPQ	Positive (100%)	Prospective	(58)
	Coffee, tea, and energy drink consumption	Self-reported items	Positive (100%)	Cross-sectional	(99, 156)
	Calcium supplement use	—	Negative (100%)	Cross-sectional	(108)
	Western diet (vs. Chinese diet)	FFQ	Positive (100%)	Cross-sectional	(157)
	Diet quality and guideline adherence	FFQ; 5-day food record with analysis by HEIFA-2013; Malay version of the NQoL	Negative (100%)	Cross-sectional	(99, 158, 159)
Eating habits	Junk food cravings, high appetite, and plate-clearing	—	Positive (100%)	Cross-sectional	(47, 70, 151, 160)
	Eating while bored	EAH-C (boredom subscale)	Negative (100%)	Cross-sectional	(161)
	Night eating	Modified NEQ	Negative (100%)	Cross-sectional	(144)
	Snacking and meal frequency	5-day food record; self-reported items	Negative (100%)	Cross-sectional	(99, 108, 150, 162)
	Skipping meals	—	Positive (100%)	Cross-sectional	(78, 108, 125, 126, 162)
	Tendency to choose healthy foods	Food choice task; self-reported items	Negative (100%)	Cross-sectional	(154, 163)
Physical activity	Athlete	—	Positive (100%)	Cross-sectional	(95)
	Exercising for appearance and weight control	REI (weight control and physical attractiveness subscales); self-reported items	Positive (100%)	Cross-sectional	(126, 164)
	Exercise motivation	Bandura self-efficacy scale; self-reported items	Negative (100%)	Cross-sectional	(81, 165)
	Physical activity	Arab Teens Lifestyle Questionnaire; CBPAQ (personal barriers subscale);	Negative (75%)	Cross-sectional	(73, 74, 100, 106, 108, 111, 119,

		EAMS; GSLTPAQ; IPAQ; pedometer; self-reported items			136, 151, 166-172)
		YRBSS; adaptations of NLSCY and YRBSS	Negative (100%)	Prospective	(27, 128)
	Physical fitness	Cardiovascular fitness test; sit and reach test; 1600 m run test	Uncertain (50%)	Cross-sectional	(173, 174)
	Type of exercise	—	—	Cross-sectional	(123)
Sedentary activity	Electronic screen time	IAT; self-reported items	Positive (100%)	Cross-sectional	(106, 110, 166, 175-178)
Lifestyle	Healthy lifestyle (vs. high risk)	Cluster analysis based on composite of GHQ-12, IPAQ, NCI fruit and vegetable screener, TFEQ, and SECI	Negative (100%)	Cross-sectional	(98)
	Healthy lifestyle	—	Negative (100%)	Prospective	(45)
Sleep	Sleep quality	PSQI; self-reported items	Uncertain (50%)	Cross-sectional	(133, 173)
	Sleep quantity	PSQI; self-reported items	Negative (67%)	Cross-sectional	(74, 133, 173)
Stress	Stress	PSS; PSRS (prolonged, social conflict, social evaluation subscales)	Positive (75%)	Cross-sectional	(123, 134, 179, 180)
University campus life	Greater than first-year undergraduate studies	—	Positive (100%)	Cross-sectional	(70, 78, 106, 168, 181, 182)
	Nutrition majors	—	Negative (100%)	Cross-sectional	(183)
	Sorority members	—	Negative (100%)	Cross-sectional	(168)
	Living on-campus	—	Negative (67%)	Cross-sectional	(74, 93-95)
	Walkability or bikeability	CDC and Prevention's Healthier Worksite Initiative Walkability Audit	Negative (100%)	Cross-sectional	(60)
	Institution	—	—	Cross-sectional	(140)
Substance use	Alcohol	DDQ; self-reported items	Positive (100%)	Cross-sectional	(99, 184, 185)
		—	Positive (100%)	Prospective	(186)
	Problems with alcohol use	RAPI	Negative (100%)	Cross-sectional	(184)
	Prescription medication use	—	Positive (100%)	Cross-sectional	(99)

	Smoking	—	Positive (67%)	Cross-sectional	(73, 82, 93, 94, 99, 108)
		Items adapted from (63)	Positive (100%)	Prospective	(50)
Medical history	Family history of overweight/obesity	—	Positive (100%)	Cross-sectional	(70, 83, 108, 119, 135, 136, 181)
			Positive (100%)	Prospective	(45)
	Flu immunization within the past year	—	Negative (100%)	Cross-sectional	(95)
Psychiatric illnesses or disorders	Depression and suicide attempts	CESD; CESD-10; self-reported items	Positive (75%)	Cross-sectional	(71, 74, 187, 188)
	Obsessive compulsive disorder	MOCI	Negative (100%)	Cross-sectional	(116)
	Post-traumatic stress disorder	Breslau's 7-item PTSD screener	Positive (100%)	Cross-sectional	(73)
	Binge eating disorder and bingeing	BES; Turkish BITE; EAT-26 items; EDDS; SWED	Positive (100%)	Cross-sectional	(79, 121, 126, 140, 168, 180, 189, 190)
	Bulimia	BITE; BUILT-R; EAT-26; EDI (bulimia subscale);	Positive (100%)	Cross-sectional	(114, 116, 191-193)
	Risk or treated for eating disorder	EAT-26; EAT-40; EBS; EDE-Q 6.0; EDI; SWED; composite of QEWP-R and NEQ	Positive (93%)	Cross-sectional	(84, 116, 131, 140, 143, 168, 179, 183, 194-199)
	Psychosocial impairment from eating disorders	CIA	Positive (100%)	Cross-sectional	(140)
Body image	Body dissatisfaction, body preoccupation, and desire to lose weight	BCQ; BSQ; Contour drawing scale; EDI (body dissatisfaction, drive for thinness subscales); EEICA; FRS; self-reported items	Positive (100%)	Cross-sectional	(74, 80, 88, 114, 126, 131, 150, 164, 165, 179, 194, 200-207)
		EDI (body dissatisfaction subscale); self-reported items	Positive (100%)	Interventional	(49, 208)
	Body affect/satisfaction, weight satisfaction, ability to tolerate negative thoughts on body image	BAS; BI-AAQ; BISS; BSRQ (body areas satisfaction subscale); EDE-Q 6.0 items; MBAS; self-reported items	Negative (71%)	Cross-sectional	(86, 118, 164, 195, 197, 209, 210)
		Self-reported items	Negative (100%)	Prospective	(45)

	Body image, shape, and weight concern	BSRQ (overweight preoccupation subscale); EDE-Q (weight concern subscale); EDE-Q 6.0 (weight and shape concern subscales); WCS; or self-reported items	Positive (100%)	Cross-sectional	(112, 140, 164, 180, 195, 211, 212)
		WCS	Positive (100%)	Interventional	(208)
	Clothing for assurance or camouflage	Adapted items from (213)	Positive (100%)	Cross-sectional	(214)
	Acceptance of cosmetic surgery	ACSS (consider and intrapersonal subscales)	Negative (100%)	Cross-sectional	(86, 87)
	Ideal body size or shape	FRS	Positive (100%)	Cross-sectional	(204, 215)
	Perceived BMI/weight, body image/shape, or weight	BSRQ (self-classified weight subscale); modified CDRS; FRS; self-reported items	Positive (100%)	Cross-sectional	(80, 96, 102, 104, 114, 120, 132, 162, 164, 194, 204, 215, 216)
	Weight overestimation	Self-reported items	Negative (100%)	Cross-sectional	(118, 204)
	Weight fluctuations	Restraint scale (weight fluctuations subscale)	Positive (100%)	Cross-sectional	(217)
Eating attitude	Eating to cope and emotional eating	DEBQ (emotional eating subscale); EADES-40 Spanish version (emotional eating subscale); EADES-49 (emotion/stress-related eating and appraisal of outside stressors subscales); EEI; EES (anxiety, depression, and anger/frustration subscales); PEMS (total, coping, and reward enhancement subscales); TFEQ-R18 (emotional eating subscale); self-reported items	Positive (90%)	Cross-sectional	(70, 71, 79, 89, 121, 144, 180, 218-222)

		PEMS (coping subscale)	Positive (100%)	Prospective	(91)
	Eating concern	EDE-Q 6.0 (eating concern subscale)	Positive (100%)	Cross-sectional	(180, 195)
	Dieting	EAT-26 (dieting subscale); adapted items from (223)	Positive (100%)	Cross-sectional	(95, 96, 114, 118, 124, 132, 143, 164, 168, 191, 194, 199)
	Eating restraint	DEBQ (restraint subscale); composite of DEBQ (restraint subscale) and DIS; Revised Restraint Scale; TFEQ-R18 (cognitive restraint subscale);	Positive (90%)	Cross-sectional	(122, 142, 143, 163, 202, 219, 221, 222, 224-226)
	External eating	DEBQ (external eating subscale)	Uncertain (50%)	Cross-sectional	(163, 219)
	Eating beyond satiety, poor oral control, food preoccupation, and food cravings	EAT-26 items; FCQ-Trait; adapted TFEQ (disinhibition subscale); YFAS; items from (227)	Positive (100%)	Cross-sectional	(144, 168, 183, 191, 228)
	Eating until full	—	Negative (100%)	Cross-sectional	(151)
	Fasting	SWED	Positive (100%)	Cross-sectional	(140)
	Hunger	Modified TFEQ (hunger subscale); items from (227)	Negative (100%)	Cross-sectional	(144)
	Laxative use	—	—	Cross-sectional	(126)
	Intuitive eating	IES; MEQ	Negative (100%)	Cross-sectional	(90, 199, 229)
	Changing eating behaviors	—	Positive (100%)	Cross-sectional	(75, 230)
Eating regulation	Amotivation	REBS (amotivation subscale)	Positive (100%)	Cross-sectional	(92)
	Autonomous eating regulation	REBS (intrinsic motivation, integrated regulation, identified regulation subscales)	Positive (100%)	Cross-sectional	(92)
		Modified TSRQ	Positive (100%)	Interventional	(54)
	Controlled eating regulation	REBS (introjected regulation, external regulation subscales)	Negative (100%)	Cross-sectional	(92)
	Willing to change eating pattern	—	Positive (100%)	Prospective	(231)
Personality/ emotions	Agreeableness	TIPI (agreeableness subscale)	Positive (100%)	Cross-sectional	(88)

	Anger	AES; STPI (anger subscale)	Positive (100%)	Cross-sectional	(101)
	Anxiety	STPI (trait anxiety subscale); composite of SAAS and NSPS (physical appearance subscale)	Positive (100%)	Cross-sectional	(101, 232)
	Attention and concentration	Running memory continuous performance task; Standard continuous performance task	Positive (100%)	Cross-sectional	(233)
	Coping via cognitive avoidance and self-compassion	MCI; SCS short form-12	Negative (100%)	Cross-sectional	(101, 199)
	Emotional stability	TIPI (emotional stability subscale)	Positive (100%)	Cross-sectional	(88)
	Extraversion	TIPI (extraversion subscale)	Positive (100%)	Cross-sectional	(88)
	Loneliness	Revised UCLA Loneliness Scale	Positive (100%)	Cross-sectional	(234)
	Illness orientation	BSRQ (illness orientation subscale)	Negative (100%)	Cross-sectional	(164)
	Impulsivity	Go-no-go task (reaction time); BIS; SPSRQ (sensitivity to reward subscale)	Positive (100%)	Cross-sectional	(163, 228, 233, 235)
	Psychologically secure (vs. healthy lifestyle habits and high risk)	Cluster analysis based on composite of GHQ-12, IPAQ, NCI fruit and vegetable screener, TFEQ, and SECI	Negative (100%)	Cross-sectional	(98)
	Satisfaction with life	SWLS	Negative (100%)	Cross-sectional	(81)
	Self-concept and self-esteem	ASCS; MBSRQ; RSES (original and modified versions); SSES; Worth Index (total, appearance and performance subscales)	Negative (82%)	Cross-sectional	(112, 114, 164, 194, 195, 236-238)
	Self-determination	SDS	Negative (100%)	Cross-sectional	(200)
	Social withdrawal	OS; SIT	Negative (100%)	Cross-sectional	(234)
	Temperament	EAS Temperament Scale (activity, emotional distress, and fear subscales)	Negative (100%)	Cross-sectional	(191)

Social/cultural influences	Told to gain weight	—	Negative (100%)	Cross-sectional	(137)
	Abuse during childhood	CTQ; adapted items from (239, 240); self-reported items	Positive (100%)	Cross-sectional	(73, 113, 138, 196)
	Attitudes toward celebrities	CAS (intense-personal and entertainment-social subscales)	Negative (100%)	Cross-sectional	(87, 88)
	Directive support	—	Positive (100%)	Interventional	(54)
	Encouragement to diet and negative comments about weight	PSPS; VCOPAS (negative weight and shape subscale); social control scale from (241)	Positive (100%)	Cross-sectional	(114, 164, 179, 242)
	Racism	Modified PRS	Positive (100%)	Cross-sectional	(134)
	Romantic relationship satisfaction	—	Positive (100%)	Cross-sectional	(137)
	Social support	MSPSS	Negative (100%)	Prospective	(243)
	Sociocultural influences and pressures	SATAQ 1995(internalization subscale); SATAQ-3 (internalization-general, athlete subscales)	Negative (67%)	Cross-sectional	(86, 88, 131)

Abbreviations: ACSS, Acceptance of Cosmetic Surgery Scale; AES, Anger Expression Scale; ASCS, Adolescent Self-Concept Scale; BAS, Body Appreciation Scale; BCQ, Body Checking Questionnaire; BES, Binge Eating Scale; BI-AAQ, Body-Image Acceptance and Action Questionnaire; BIS, Barratt Impulsiveness Scale; BISS, Body Image State Scale; BITE, Bulimic Inventory Test, Edinburgh; BSQ, Body Shape Questionnaire; BSRQ, Body-Self Relations Questionnaire; BUILT-R, Bulimia Test-Revised; CAS, Celebrity Attitude Scale; CBPAQ, Cognitive Behavioral Physical Activity Scale; CDC, Centers for Disease Control and Prevention; CDRS, Contour Draw Rating Scale; CESD, Center for Epidemiological Studies-Depression; CIA, Clinical Impairment Assessment Questionnaire; CTQ, Childhood Trauma Questionnaire; DA+, Diet Analysis Plus version 10; DDQ, Daily Drinking Questionnaire; DEBQ, Dutch Eating Behaviour Questionnaire; DHQ, Diet History Questionnaire; DIS, Dietary Intent Scale; DUREL, Duke University Religion Index; EADES, Eating and Appraisal Due to Emotions and Stress Questionnaire; EAH-C, Eating in the Absence of Hunger questionnaire- Child and adolescents; EAT, Eating Attitudes Test; EAMS, Exercise Avoidance Motivation Scale; EAS, Emotionality, Activity, and Sociability; EBS, Eating Behavior Scale; EDDS, Eating Disorder Diagnostic Scale; EDE-Q, Eating Disorder Examination; EDI, Eating Disorder Inventory; EEI, Eating Expectancy Inventory; EEICA, Escala de Evaluación de la Insatisfacción Corporal para Adolescentes; EES, Emotional Eating Scale; EPQ, Eating Patterns Questionnaire; FCQ, Food Craving Questionnaire; FFQ, Food Frequency Questionnaire; FRS, Figure Rating Scale; GHQ, General Health Questionnaire; GSLTPAQ, Godin-Shepard Leisure-Time Physical Activity Questionnaire; HEIFA, Healthy Eating Index for Australian Adults; IAT, Internet Addiction Test; IES, Intuitive Eating Scale; IPAQ, International Physical Activity Questionnaire; MBAS, Male Body Attitudes Scale; MBSRQ, Multidimensional Body-Self Relations Questionnaire; MCI, Mainz Coping Inventory; MEQ, Mindful Eating Questionnaire; MOCI, Maudsley Obsessive-Compulsive Inventory; MSPSS, Multidimensional Scale of Perceived Social Support; NCI, National Cancer Institute; NEQ, Night Eating Questionnaire; NLSCY, National Longitudinal Survey of Children and Youth; NQoL, Nutrition Quality of Life; NSPS, Negative Self-Portrayal Scale; OS, Opener Scale; PEMS, Palatable Eating Motives Scale; PRS, Perceived Racism Scale; PSPS, Perceived Sociocultural Pressures Scale; PSQI, Pittsburg Sleep Quality Index; PSRS, Perceived Stress Reactivity Scale; PSS,

Perceived Stress Scale; PTSD, Post-traumatic Stress Disorder; QEWP-R, Questionnaire of Eating and Weight Patterns- Revised; RAPI, Rutgers Alcohol Problems Index; REBS, Regulation of Eating Behavior Scale; REI, Reasons for Exercise Inventory; RSES, Rosenberg Self-Esteem Scale; SAAS, Social Appearance Anxiety Scale; SATAQ, Sociocultural Attitudes Towards Appearance Questionnaire; SCS, Self-Compassion Scale; SDS, Self-Determination Scale; SECI, Satter Eating Competence Inventory; SIT, Specific Interpersonal Trust Scale; SPSRQ, Sensitivity to Punishment and Sensitivity to Reward Questionnaire; SSES, State Self-Esteem Scale; STPI, State-Trait Personality Inventory; SWED, Stanford-Washington Eating Disorder Screen; SWLS, Satisfaction with Life Scale; TFEQ, Three Factor Eating Questionnaire; TIPI, Ten-Item Personality Inventory; TSRQ, Treatment Self-Regulation Questionnaire; UCLA, University of California, Los Angeles; VCOPAS, Verbal Commentary on Physical Appearance Scale; WCS, Weight Concerns Scale; YFAS, Yale Food Addiction Scale; YRBSS, Youth Risk Behavior Surveillance System
* Percentage calculated per study; direction of majority (>50%) is shown

Table S3. Factors associated with weight

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Positive (100%)	Cross-sectional	(76, 77, 244)
	Sex (male)	—	Positive (100%)	Cross-sectional	(80, 92, 103, 111, 114, 116, 117, 120, 148, 198, 245-247)
				Prospective	(58, 127, 129, 248)
				Interventional	(48, 149)
	Nationality	—		Cross-sectional	(78, 131)
Ethnicity	African (vs. European and Hispanic)	—	Positive (100%)	Prospective	(127)
Calendar year	Year	—	Positive (100%)	Cross-sectional	(147, 249)
Diet/nutrition	Junk food consumption	Gray-Donaldson EPQ	Positive (100%)	Cross-sectional	(58)
Physical activity	Physical activity	—	Positive (100%)	Cross-sectional	(111)
	Volleyball (vs. ballet)	—	Positive (100%)	Cross-sectional	(111)
University campus life	Dorm with on-site dining hall	—	Positive (100%)	Prospective	(250)
	Nutrition major	—	Negative (100%)	Cross-sectional	(183)
Substance use	Alcohol	Drinking Habits Questionnaire (total and wine subscale)	Positive (100%)	Cross-sectional	(246)
Psychiatric illnesses or disorder	Bulimia	EDI (bulimia subscale)	Positive (100%)	Cross-sectional	(114)
Body image	Body dissatisfaction	EDI (body dissatisfaction and drive for thinness subscales); Color-A-Person Test	Positive (67%)	Cross-sectional	(114, 251)

	Shape concern	BSQ	Positive (100%)	Cross-sectional	(205)
	Perceived body size	Computer body size manipulation task; self-reported items	Positive (67%)	Cross-sectional	(114, 118, 251)
Eating attitude	Dieting	Items from (223)	Positive (100%)	Cross-sectional	(114)
	Disordered eating	EAT-26	Positive (100%)	Cross-sectional	(198)
Personality/ Emotions	Positive affect	PANAS (positive subscale)	Positive (100%)	Prospective	(58)
	Self-esteem	SSES	Negative (100%)	Cross-sectional	(114)
Social influences and pressures	Weight loss-related comments by friends and family	Items adapted from (241)	Positive (100%)	Cross-sectional	(114)
	Pressure to eat more	EAT-40	Negative (100%)	Cross-sectional	(103)

Abbreviations: BSQ, Body Shape Questionnaire; Drinking Habits Questionnaire; EAT, Eating Attitudes Questionnaire; EPQ, Eating Patterns Questionnaire; PANAS, Positive and Negative Affect Schedule; SSES, State Self-Esteem Scale

* Percentage calculated per study; direction of majority (>50%) is shown

Table S4. Factors associated with weight change

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex	—	Positive (100%)	Prospective	(42-44, 62, 252, 253)
	Foreign nationality (vs. American)	—	Positive (100%)	Prospective	(62)
Genetics	*FTO* SNP rs9939609 risk allele A (vs. T)	Genotyping	Positive (100%)	Prospective	(40)
Diet/nutrition	High calorie foods	FHQ	Positive (100%)	Cross-sectional	(254)
	Energy intake	5-day food record	Positive (100%)	Prospective	(255)
	Fat intake	FHQ	Positive (100%)	Cross-sectional	(254)
		—	—	Prospective	(256)
	Dairy intake	—	Positive (100%)	Prospective	(257)
	Fruit and vegetable consumption	—	Negative (100%)	Prospective	(258)
	Junk food consumption	—	—	Prospective	(256)
	Healthy food consumption	—	—	Prospective	(259)
	Satiating foods	FHQ	Negative (100%)	Cross-sectional	(254)
Eating habits	Unhealthy eating habits	—	—	Prospective	(259)
		—	Positive (100%)	Qualitative	(260)
	Alcohol-related food consumption	—	Positive (100%)	Qualitative	(261)

	Eating at restaurants/pay cash facilities	—	—	Prospective	(256)
	Eating while bored, studying or socializing	—	Positive (100%)	Qualitative	(261)
	Number of meals in the evening or weekend	—	—	Prospective	(256)
	Snacking	—	Positive (100%)	Prospective	(262)
Physical activity	Physical activity	GPAQ; GSLTPAQ; IPAQ; self-reported items	Positive (100%)	Prospective	(62, 259, 263, 264)
Sedentary activity	Sedentary activity	—	Positive (100%)	Qualitative	(260)
Weight loss intervention	Autonomous support to lose weight	—	Negative (100%)	Interventional	(54)
Sleep	Sleep quantity	—	Uncertain (50%)	Prospective	(45, 256, 265)
Stress	Stress	USQ	Complex (100%)	Prospective	(262)
University campus life	Academic performance	SAT scores	Negative (100%)	Prospective	(127)
	First year students (vs. upper years)	—	Positive (100%)	Interventional	(266)
	Membership to a student group	—	Positive (100%)	Prospective	(231)
	Living on-campus, without parents, or change in housing situation	—	Positive (100%)	Prospective	(130, 231, 267)
	Dormitory location	—	—	Interventional	(250)
	Dining hall accessibility	Hours and days per week open	Positive (100%)	Interventional	(48)
	Buffet-style meals	—	Positive (100%)	Qualitative	(261)
	Vending machines	—	—	Prospective	(256)
		—	Negative (100%)	Interventional	(48)
	Meal-plan use	Number of meal card swipes	Positive (100%)	Prospective	(62)
	Summer	—	Negative (100%)	Prospective	(61)
	Free time	—	Negative (100%)	Prospective	(258)
		—	Negative (100%)	Qualitative	(260)
	Rural mid-size university (vs. large urban university)	—	Positive (100%)	Prospective	(130)
Substance use	Alcohol	—	Positive (100%)	Prospective	(231, 258, 259, 263)

				Qualitative	(260, 261, 268)
	Smoking	—	Positive (100%)	Prospective	(259)
Psychiatric illnesses or disorder	Depression	Combination of CES-D, HSC-D, and SCL-90 (depression subscale)	Positive (100%)	Cross-sectional	(269)
	Bulimia	EDI (bulimia subscale)	Positive (100%)	Prospective	(270)
Body image	Body dissatisfaction (baseline)	EDI (body dissatisfaction subscale); EDI (drive for thinness subscale)	Uncertain**	Prospective	(130, 251, 270)
	Body dissatisfaction (at follow-up)	EDI (body dissatisfaction subscale)	Positive (100%)	Prospective	(270)
	Body dissatisfaction (change)	EDI (body dissatisfaction subscale)	Positive (100%)	Prospective	(130, 270)
	Body image	Modified BCS; self-reported items	Negative (100%)	Prospective	(259, 271)
		—		Qualitative	(236)
	Frequent weighing	Wi-Fi scale and weight feedback	Negative (100%)	Interventional	(64)
	Unattractive appearance	—	Positive (100%)	Qualitative	(236)
Eating attitude	Careful about food choices	—	Negative (100%)	Qualitative	(236)
	Dieting	Items from (272); self-reported-items	Positive (100%)	Prospective	(256, 273)
		—	Negative (100%)	Interventional	(54)
	Eating restraint	DRES; Restraint Scale (revised and regular)	Uncertain**	Prospective	(130, 274, 275)
	Disordered eating (baseline)	EDI; EDI + Revised Restraint Scale	Positive (67%)	Prospective	(130, 259, 270)
	Disordered eating (at follow-up)	EDI	Positive (100%)	Prospective	(270)
	Disordered eating (change)	EDI	Positive (100%)	Prospective	(130, 270)
Eating regulation	Autonomous eating regulation	REBS (intrinsic motivation, integrated regulation, identified regulation subscales)	Negative (100%)	Prospective	(68)
	Greater freedom in making food choices	—	Positive (100%)	Qualitative	(268)
Personality and emotions	Happiness	SHS	Negative (100%)	Prospective	(263)
	Confidence in academic ability	—	Positive (100%)	Prospective	(258)

	Impulsivity	BIS-15; Stop signal task	Positive (100%)	Prospective	(276, 277)
	Negative affect	—	—	Prospective	(259)
	Negative-well being (male)	Sum of CES-D, SPS, PSS	Negative (100%)	Prospective	(130)
	Negative-well being (female)	Sum of CES-D, SPS, PSS	Positive (100%)	Prospective	(130)
	Negative feelings about transitioning to university	TPS	Negative (100%)	Prospective	(130)
	Self-esteem (male)	RSES	Positive (100%)	Prospective	(130)
	Self-esteem (female)	RSES	Negative (100%)	Prospective	(130)
Social influences and pressures	Autonomy support	Items adapted from (69)	Negative (100%)	Interventional	(54)
	Body image comments from family/friends	—	Negative (100%)	Qualitative	(268)
	Concern about interpersonal relationships	—	—	Prospective	(259)
	Perceived success in finding a romantic partner	—	Negative (100%)	Qualitative	(236, 268)
	Relationship with parents (male)	—	Negative (100%)	Prospective	(259)
	Relationship with parents (female)	—	Positive (100%)	Prospective	(259)
	Roommate's weight	—	Positive (100%)	Prospective	(278)

Abbreviations: BCS, Body Cathexis Scale; BIS, Barratt Impulsiveness Scale; CES-D, Center for Epidemiologic Studies-Depression Scale; DRES, Dutch Restrained Eating Scale; EDI, Eating Disorder Inventory; FHQ, Food Healthfulness Questionnaire; GPAQ, Global Physical Activity Questionnaire, GSLTPAQ, Godin-Shepard Leisure-Time Physical Activity Questionnaire; HSC-D, Hopkins Symptom Check List- Depression Scale; IPAQ, International Physical Activity Questionnaire; PSS, Perceived Stress Scale; RSES, Rosenberg Self-Esteem Scale; SAT, Scholastic Assessment Test; SCL-90, Symptom Check List; SHS, Subjective Happiness Scale; SNP, single nucleotide polymorphism; SPS, Social Provisions Scale; TPS, Transition Perspective Scale; USQ, Undergraduate Stress Questionnaire
* Percentage calculated per study; direction of majority (>50%) is shown
** Positive, negative and U-shaped distributions from the included studies

Table S5. Factors associated with body adiposity index

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Negative (100%)	Cross-sectional	(245)
	Socioeconomic status	Composite of parent education, household income	Negative (100%)	Cross-sectional	(138)

Ethnicity (vs. European)	African	—	Positive (100%)	Cross-sectional	(138)
Interpersonal pressures and influences	Abuse during childhood	Adapted items from (239, 240)	Positive (100%)	Cross-sectional	(138)
* Percentage calculated per study; direction of majority (>50%) is shown					

Table S6. Factors associated with body fat mass

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Positive (100%)	Cross-sectional	(152)
	Sex (male)	—	Negative (100%)	Cross-sectional	(111, 198, 245)
			Positive (100%)	Prospective†	(43, 44, 279)
Calendar year	Year	—	Positive (100%)	Cross-sectional	(249)
Diet/nutrition	Energy intake	DHQ	Positive (100%)	Cross-sectional	(152)
	Fiber intake	DHQ	Negative (100%)	Cross-sectional	(152)
Physical activity	Physical activity	—	Negative (100%)	Cross-sectional	(111)
University	First year undergraduate studies (vs. second year)	—	Positive (100%)	Prospective†	(43)
Substance use	Smoking	—	Positive (100%)	Cross-sectional	(152)
Abbreviations: DHQ, Diet History Questionnaire * Percentage calculated per study; direction of majority (>50%) is shown † Association for change in body fat mass					

Table S7. Factors associated with body fat percentage level

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Negative (100%)	Cross-sectional	(92, 111, 117, 148, 198, 245, 280-282)
				Prospective	(283, 284)
				Interventional	(149)
Ethnicity (vs. European)	African	—	Positive (100%)	Cross-sectional	(285)
	Other minority	—	Positive (100%)	Cross-sectional	(92)
Calendar year	Year	—	Positive (100%)	Cross-sectional	(249)
Diet/nutrition	Energy intake	DHQ	Positive (100%)	Cross-sectional	(152)
	Dairy intake	3-day food record	Negative (100%)	Cross-sectional	(148)
	Fiber intake	DHQ	Negative (100%)	Cross-sectional	(152)
	Healthy diet (whole foods, healthy fats)	FFQ	Negative (100%)	Prospective	(155)
Physical activity	Exercising for appearance	MPAM-R (appearance subscale)	Positive (100%)	Cross-sectional	(286)

	Exercising for competence	MPAM-R (competence subscale)	Negative (100%)	Cross-sectional	(286)
	Introjected regulation to exercise	BREQ-2 (introjected regulation subscale)	Positive (100%)	Cross-sectional	(286)
	Physical activity	IPAQ; pedometer; self-reported items	Negative (100%)	Cross-sectional	(111, 166, 170)
Stress	Stress	PSS	Positive (100%)	Cross-sectional	(92)
University campus life	Fourth year undergraduate studies (vs. second, third year)	—	Positive (100%)	Cross-sectional	(182)
Substance use	Smoking	—	Positive (100%)	Cross-sectional	(152)
Body image	Body dissatisfaction	FRS	Positive (100%)	Cross-sectional	(287, 288)
	Body satisfaction	MBSRQ (body areas satisfaction subscale)	Negative (100%)	Prospective	(284)
	Ideal body size	FRS	Positive (100%)	Cross-sectional	(288)
	Perceived body size	FRS	Positive (100%)	Cross-sectional	(288)
	Motivational salience (effort put into appearance)	ASI-R (motivational salience subscale)	Positive (100%)	Prospective	(284)
Eating attitude	Eating restraint	Modified DEBQ	Positive (100%)	Cross-sectional	(224)
Eating regulation	Autonomous eating regulation	REBS (intrinsic motivation, integrated regulation, identified regulation subscales)	Positive (100%)	Prospective	(92, 284)
	Controlled eating regulation	REBS (introjected and external regulation)	Positive (100%)	Cross-sectional	(92)
Personality/ emotions	Achievement self-esteem in appearance	Worth Index (appearance subscale)	Positive (100%)	Cross-sectional	(237)
	Self-acceptance self-esteem in performance	Worth Index (performance subscale)	Negative (100%)	Cross-sectional	(237)

Abbreviations: ASI-R, Appearance Schemas Inventory-Revised; DEBQ, Dutch Eating Behavior Questionnaire; DHQ, Diet History Questionnaire; FFQ, Food Frequency Questionnaire; FRS, Figure Rating Scale; IPAQ, International Physical Activity Questionnaire; MPAM-R, Motives for Physical Activity Measure-Revised; PSS, Perceived Stress Scale; REBS, Regulation of Eating Behavior Scale

* Percentage calculated per study; direction of majority (>50%) is shown

Table S8. Factors associated with body fat percentage change

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Prospective	(43, 44, 279)
Physical activity	Physical activity	NCHRBS	Negative (100%)	Prospective	(283)
	Second year undergraduate studies (vs. first and third year)	—	Negative (100%)	Prospective	(43)
Sedentary activity	Reading and studying	—	Negative (100%)	Prospective	(41)
University campus life	Living on-campus	—	Positive (100%)	Prospective	(41)
	Summer	—	Positive (100%)	Prospective	(61)
Body image	Motivational salience (effort put into appearance)	ASI-R (motivational salience subscale)	Negative (100%)	Prospective	(284)
Eating regulation	Amotivation	REBS (amotivation subscale)	Positive (100%)	Prospective	(68)
	Autonomous eating regulation	REBS (intrinsic motivation, integrated regulation, identified regulation subscales)	Negative (100%)	Prospective	(68, 284)

Abbreviations: MBSRQ, Multidimensional Body-Self Relations Questionnaire; NCHRBS, National College Health Risk Behavior Survey; REBS, Regulation of Eating Behavior Scale
* Percentage calculated per study; direction of majority (>50%) is shown

Table S9. Factors associated with fat mass index

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Negative (100%)	Cross-sectional	(245)
Calendar year	Year	—	Positive (100%)	Cross-sectional	(249)
Eating attitude	Disinhibition	—	Positive (100%)	Prospective†	(289)

Abbreviations: DHQ, Diet History Questionnaire
* Percentage calculated per study; direction of majority (>50%) is shown
† Association for change in body fat mass

Table S10. Factors associated with skinfold thickness

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Body image	Body dissatisfaction	EDI (body dissatisfaction subscale)	Positive (100%)	Cross-sectional	(202)

Abbreviations: EDI, Eating Disorder Inventory
* Percentage calculated per study; direction of majority (>50%) is shown

Table S11. Factors associated with visceral fat

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Religion	Muslim (vs. Christian)	—	Negative (100%)	Cross-sectional	(146)

Abbreviations: EDI, Eating Disorder Inventory
* Percentage calculated per study; direction of majority (>50%) is shown

Table S12. Factors associated with conicity index

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Negative (100%)	Cross-sectional	(245)

* Percentage calculated per study; direction of majority (>50%) is shown

Table S13. Factors associated with muscle mass

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Cross-sectional	(198, 281)
			Positive (100%)	Interventional	(149)
Diet/nutrition	Nutrition course	—	Positive (100%)	Interventional†	(149)

* Percentage calculated per study; direction of majority (>50%) is shown
† Association for change in muscle mass

Table S14. Factors associated with muscle mass percentage

Table S14. Factors associated with muscle mass percentage

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Cross-sectional	(148, 198)

* Percentage calculated per study; direction of majority (>50%) is shown

Table S15. Factors associated with fat-free mass

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Cross-sectional	(111, 198, 245)
			Positive (100%)	Prospective†	(42, 44)
Physical activity	Physical activity	—	Positive (100%)	Cross-sectional	(111)
	Bodybuilding (vs. playing soccer)	—	Positive (100%)	Cross-sectional	(111)
	Volleyball (vs. ballet)	—	Positive (100%)	Cross-sectional	(111)
University campus life	Second year undergraduate studies (vs. third year)	—	Positive (100%)	Prospective†	(43)
	Summer	—	Negative (100%)	Prospective	(61)

* Percentage calculated per study; direction of majority (>50%) is shown
† Association for change in fat-free mass

Table S16. Factors associated with fat-free mass index

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Prospective†	(289)
Calendar year	Year	—	Negative (100%)	Cross-sectional	(249)
Physical activity	Physical activity	IPAQ	Positive (100%)	Prospective†	(289)
Eating attitude	Responsiveness to food environment	PFS	Positive (100%)	Prospective†	(289)

Abbreviations: IPAQ, International Physical Activity Questionnaire; PFS, Power of Food Scale
* Percentage calculated per study; direction of majority (>50%) is shown
† Association for change in fat-free mass index

Table S17. Factors associated with fat-free mass percentage

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Cross-sectional	(198)

* Percentage calculated per study; direction of majority (>50%) is shown

Table S18. Factors associated with waist circumference

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Positive (100%)	Cross-sectional	(72, 75, 77, 78, 290)
	Sex (male)	—	Positive (67%)	Cross-sectional	(72, 78, 105, 111, 198, 290)
			Positive (100%)	Prospective†	(42, 62)
	Married	—	Positive (100%)	Cross-sectional	(72)
	Nationality	—	—	Cross-sectional	(78, 133)
	Socioeconomic status	Self-reported net income	Positive (100%)	Cross-sectional	(78)
Ethnicity (vs. European)	African	—	Negative (100%)	Cross-sectional	(285)
Diet/nutrition	Energy intake	DHQ	Positive (100%)	Cross-sectional	(152)
	Fiber intake	DHQ	Negative (100%)	Cross-sectional	(152)
	Avoiding fatty foods	—	Positive (100%)	Cross-sectional	(78)
	Diet quality	HEIFA-2013 from a 5-day food record	Negative (100%)	Cross-sectional	(158)
	Western diet (vs. Chinese)	FFQ	Positive (100%)	Cross-sectional	(157)

Eating habits	Hunger, overeating	—	Positive (100%)	Cross-sectional	(290)
	Inconsistent mealtime, skipping meals	—	Positive (100%)	Cross-sectional	(78, 290)
	Preference for sweets	—	Positive (100%)	Cross-sectional	(290)
Physical activity	Physical activity	Pedometer; self-reported items	Negative (100%)	Cross-sectional	(111, 170)
	Physical fitness	Cardiovascular fitness test	Negative (100%)	Cross-sectional	(174)
Lifestyle	Healthy lifestyle (vs. high risk)	Cluster analysis based on composite of GHQ-12, IPAQ, NCI fruit and vegetable screener, TFEQ, and SECI	Negative (100%)	Cross-sectional	(98)
Sleep	Sleep quality	—	Positive (100%)	Cross-sectional	(133)
	Sleep quantity	—	Negative (100%)	Cross-sectional	(133)
University campus life	Academic performance	Matric score	Positive (100%)	Cross-sectional	(77)
	Meal plan use	Number meal card swipes	Positive (100%)	Prospective†	(62)
Medical history	Family history of obesity	—	Positive (100%)	Cross-sectional	(290)
Body image	Body dissatisfaction	EDI (body dissatisfaction subscale); FRS	Positive (100%)	Cross-sectional	(287)
Eating attitude	Considering changing eating habits	Items from a Brazilian Ministry of Health questionnaire (291)	Negative (100%)	Cross-sectional	(75)
	Disordered eating	EAT-26	Positive (100%)	Cross-sectional	(198)
Psychiatric illness or disorders	ADHD	Conner's adult ADHD Rating Scale	Negative (100%)	Cross-sectional	(292)
	Binge eating	—	Positive (100%)	Cross-sectional	(290)
Personality/ emotions	Psychologically secure (vs. healthy lifestyle habits or high risk)	Cluster analysis based on composite of GHQ-12, IPAQ, NCI fruit and vegetable screener, TFEQ, and SECI	Negative (100%)	Cross-sectional	(98)

Abbreviations: ADHD, Attention Deficit Hyperactivity Disorder; DHQ, Diet History Questionnaire; EAT, Eating Attitudes Test; EDI, Eating Disorder Inventory; FFQ, Food Frequency Questionnaire; FRS, Figure Rating Scale

* Percentage calculated per study; direction of majority (>50%) is shown

† Association for change in waist circumference

Table S19. Factors associated with hip circumference

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Positive (100%)	Cross-sectional	(77)
	Sex (male)	—	Negative (100%)	Prospective†	(62)
Physical activity	Physical activity	Pedometer	Negative (100%)	Cross-sectional	(170)
Body image	Body dissatisfaction	EDI	Negative (75%)**	Cross-sectional	(203)
Eating attitude	Disordered eating	EAT-26	Positive (100%)	Cross-sectional	(198)

Abbreviations: EAT, Eating Attitudes Test; EDI, Eating Disorder Inventory
* Percentage calculated per study; direction of majority (>50%) is shown
** Of the individual EDI items assessed within the study
† Association for change in hip circumference

Table S20. Factors associated with waist-to-hip ratio

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Age	—	Positive (100%)	Cross-sectional	(77)
Ethnicity (vs. European)	African	—	Negative (100%)	Prospective	(285)
Eating attitude	Disordered eating	EAT-26	Positive (100%)	Cross-sectional	(198)

Abbreviations: EAT, Eating Attitudes Test; EDI, Eating Disorder Inventory
* Percentage calculated per study; direction of majority (>50%) is shown

Table S21. Factors associated with corpulence index

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
University campus life	Fourth year (vs. other years) undergraduate study	—	Positive (100%)	Cross-sectional	(182)

Abbreviations: EAT, Eating Attitudes Test; EDI, Eating Disorder Inventory
* Percentage calculated per study; direction of majority (>50%) is shown

Table S22. Factors associated with body surface area

Phenotypic category	Trait	Method of measurement	Direction of effect*	Study cohort type	Reference
Demographics	Sex (male)	—	Positive (100%)	Cross-sectional	(245)

* Percentage calculated per study; direction of majority (>50%) is shown

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Chapter 3: Rationale and design of GENEiUS: a prospective observational study on the genetic and environmental determinants of body mass index evolution in Canadian undergraduate students

Rita E. Morassut,[1] Christine Langlois,[1] Akram Alyass,[1] Adeola F. Ishola,[1] Fereshteh T. Yazdi,[1] Alexandra J. Mayhew,[1] Hudson Reddon,[1] James MacKillop,[2] Marie Pigeyre,[1,3] David Meyre[1,4]

Affiliations

[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

[2]Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada

[3]Department of Nutrition, University of Lille, CHRU Lille, Lille, 59000, France

[4]Department of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario, Canada

Correspondence to: Dr David Meyre; meyred@mcmaster.ca

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3.1 Abstract

Introduction: Obesity is a global epidemic and is a risk factor for developing other comorbidities. Young adulthood is a critical period for body weight change and establishing healthy lifestyle behaviours. The 'Freshman 15' suggests that undergraduate students gain 15 lbs (6.8 kg) during their first year of university, although evidence estimates a more modest weight gain of approximately 3–5 lbs (1.4–2.3 kg). Previous studies have only investigated weight change in the first year and do not study potential risk factors. Genetic and EnviroNmental Effects on weight in University Students (GENEiUS) is a prospective observational study which will investigate the environmental and biological determinants of weight change in undergraduate students over 4 years.

Methods and analysis: The GENEiUS study will recruit 2500 multiethnic undergraduates aged 17–25 years at McMaster University at the start of their first year and will follow them every 6 months for 4 years. Primary outcomes are obesity traits: body mass index, waist circumference, waist-to-hip ratio, body fat mass and body fat percentage. The contribution of well-established and novel genetic variants for obesity traits and heritability values will be derived from whole-genome single-nucleotide polymorphism genotyping arrays. Civil status, age, sex, ethnicity, length of residence in Canada, religiosity, energy intake, physical activity, exercise motivation, electronic screen time, sleep patterns, history of assault, smoking status, alcohol consumption, medication and drug use, stress, impulsivity, body image perception, self-esteem, anxiety, eating disorders and depression will be investigated for their effect on obesity traits. The findings of

the GENEiUS study will be used to help design obesity prevention programme in North American universities with multiethnic populations.

Ethics and dissemination: Ethical approval of the study protocol has been obtained from the Hamilton Integrated Research Ethics Board. Study results will be disseminated through scientific publications, scholarly meetings, and collaborative meetings with university administration and student groups.

3.2 Strengths and limitations of this study

- This is the first adequately powered study to investigate genetic associations of weight change in undergraduate students.
- This is the first study to investigate an exhaustive number of potential risk factors for weight change in undergraduate students.
- While most studies investigating weight changes in undergraduates have taken place over 6–8 months, this study will follow students throughout their studies for 4 years.
- Validated questionnaires will be used to measure the majority of parameters in order to decrease participant burden and limit cost.
- This study is sufficiently powered to identify genetic and environmental predictors of weight change in undergraduate students; however, it is not powered to assess gene–environment interactions.

3.3 Introduction

3.3.1 Obesity in young adulthood

Obesity has become a global epidemic and affects one in five adults in Canada (1, 2). This is of great concern to public health as obesity is a major risk factor for depression, osteoarthritis, type 2 diabetes, hypertension, cardiovascular disease, and some cancers (3, 4). The high prevalence, associated co-morbidities, and increased mortality make obesity a monumental economic burden accounting for $7.1 billion in Canadian health care costs (5). Adolescence and young adulthood may be critical periods for the development of obesity as elevated body mass index (BMI) during this time is associated with obesity later in adulthood (6). When comparing the prevalence of obesity in Canadian adults from 2010 to 2014, the largest increase was observed amongst individuals aged 18-19 (7). While education status is negatively correlated with BMI in the general population from high-income countries, young adults with higher education gain more weight and are more likely to be obese than those without university education in the United States (8-10).

The “Freshman 15” is a popular theory which suggests that university undergraduate students gain 15 pounds (6.8 kg) during their first year of post-secondary education, although the average weight gain is estimated to be 3-5 pounds (1.4-2.3 kg) (11-13). It should be noted these studies are limited by small sample sizes, high female to male ratios, and may be susceptible to volunteer bias due to high dropout rates. Furthermore, sex- and ethnicity-specific subgroup analyses are scarce. Most studies are also only conducted over one year and there are limited and conflicting reports over weight change afterward. While one study suggests that students gain weight consistently, another describes stabilization after the first year of undergraduate education (14, 15). Overall, students tend to weigh more in the fourth year compared to the first year and it is unclear whether this can be attributed to continued physical development and maturation or the accumulation of fat mass (16, 17). The entire duration of undergraduate studies may therefore be a critical period for weight change in young adults and this study will provide insight into the genetic and environmental determinants of weight change among this population.

3.3.2 Predictors of undergraduate weight change

The etiology of obesity is complex and depends on a variety of biological, environmental, lifestyle, and socioeconomic factors (18, 19). There is limited evidence on factors influencing weight in undergraduate students. Excessive consumption of calorie-dense foods, the number of meals consumed during the evening and weekends, and recent dieting have all been associated with weight gain in undergraduate students (20-22). Evidence suggests that a lack of healthy food options on campus and buffet-style meal plan design may facilitate the development of unhealthy eating patterns among students (23, 24). Further, the increased expenses of university tuition and living away from home limit a student's budget to purchase healthy foods which often cost more (23, 24). First year students tend to make unhealthier food choices and increase alcohol consumption as each academic semester progresses, especially near exam-time (25-28). These poor eating habits coupled with decreased physical activity and increased sedentary behaviour from internet usage may partially explain the mean weight gain of 3-5 pounds in first year (29). Their low motivation to exercise may also be detrimental as greater motivation promotes weight loss in both the short and long term (24, 30).

Undergraduate students sleep less and more erratically than high-school students (27). Sleep and BMI have a U-shaped relationship such that short and long sleep durations are associated with elevated BMI (31). In undergraduates, a decrease in the quantity but not the quality of sleep is related to weight gain (20). Students are also subject to greater stress as they transition to undergraduate studies due to an increased academic workload and by living away from home and away from social support systems. Stress has previously been associated with both weight gain and weight loss in undergraduate students (28). Interestingly, BMI may moderate the effect of stress on weight change in students as high stress has been associated with weight gain among those with high baseline BMI and weight loss in those with low baseline BMI (32). Weight may also be influenced by adverse experiences. History of sexual assault has been linked to obesity and elevated BMI in some studies (33, 34). This is of particular concern to university students as 14-44% report experiencing some form of sexual assault since starting undergraduate studies (35).

Undergraduate students have described lack of self-control as a barrier to making healthy dietary choices (23). Impulsivity in the context of weight maintenance, as measured by delayed discounting, reflects preferences for small immediate pleasures compared to larger rewards later in life. Steeper delayed discounting, indicating more impulsive choices, has been associated with obesity, especially in adolescents (36). Further, impulsive personality traits have been positively associated with BMI in university students indirectly through compulsive eating behaviours (37).

Psychiatric conditions may also impact the weight of undergraduate students. Bulimia nervosa and binge eating disorder, have been associated with elevated BMI (38). Young adults are especially at risk for pathological eating since the prevalence of eating disorders appears to increase from 0.3% in adolescence to 1% in young adulthood (39). Although there is weak evidence, disordered eating habits have been associated with overweight and obesity in university students (40). Further, among female but not male students, weight gain has been associated with greater disordered eating behaviour over four years (14). Both depression and anxiety have been associated with obesity (4, 41). These conditions are of major concern on university campuses since it is estimated that 18.3% and 14.7% of Canadian students have anxiety and depression, respectively (42). Limited studies show that depression appears to be associated with obesity in male, but not female, undergraduate students (14, 43). Finally, other psychological factors including body image dissatisfaction and low self-esteem have been associated with overweight and obesity in adolsecents (44). Few studies have investigated these in undergraduate students, and there are conflicting reports whether they are related to weight change (45, 46).

Among those aged 15-24 in Canada, approximately 71% report a religious affiliation (47). Religiosity has been associated with healthy lifestyle behaviors in adolescents (48). While religiosity has been shown to have protective effects on cardiometabolic traits like diabetes and hypertension, it has been associated with elevated BMI (49, 50). One study found increased incidence of obesity in religious young adults (51). Therefore, the effect of religiosity on weight in undergraduates warrants further investigation. Further, birthplace and length of residence may also contribute to weight change in undergraduate students. In the United States, foreign-born immigrants tend to have lower BMI than those born in the United States, yet experience an increase in BMI with length of residence (52).

Genome-wide association studies (GWAS) have identified many single nucleotide polymorphisms (SNPs) associated with BMI, waist-to-hip ratio (WHR), and body fat percentage (%BF), however these markers are not specific to university students (53-55). To the best of our knowledge, only one study from the United Kingdom has explored the genetic causes of weight gain in university. It found that *FTO* SNP rs9939609, the most important genetic contributor to obesity in European populations, showed a nominal association with weight gain at the end of the first academic year (56). However, the study suffered from several limitations: high drop-out rate (78%), low statistical power (*N=310*), and limited follow-up duration.

To design effective obesity prevention programs in universities, a better understanding of its causes in undergraduate students is needed. The Genetic and EnviroNmental Effects on weight in University Students (GENEiUS) study will investigate the genetic and environmental determinants of obesity trait evolution in undergraduate students at McMaster University (Hamilton, Ontario, Canada) over the four year course of their studies.

3.3.3 Study objectives

The primary objectives of this study are to (1) describe BMI level and change over four years, (2) to investigate the heritability and genetic determinants of BMI level and change, and (3) to investigate the social, cultural, lifestyle, and environmental determinants of BMI level and change in undergraduate students. Secondary objectives of the GENEiUS study include the investigation of genetic and environmental determinants of additional obesity traits (waist circumference, WHR, %BF, body fat mass) and endophenotypes.

3.4 Methods and study design

3.4.1 Participant selection and recruitment

The GENEiUS Study is a longitudinal prospective observational study in Hamilton, Ontario. Undergraduate students from McMaster University will be followed every six months over four years beginning in September of their first year of study. First year students enrolled at McMaster University between the ages of 17 and 25 are eligible to participate in the study (57). Individuals who are pregnant, have given birth, or have a medical condition which can impact BMI for a long period of time (e.g. bariatric surgery, immobilization from injury, etc.) will be excluded from the study.

Beginning in September 2015, first year students are invited to participate from September and October of each year. Recruitment will be conducted via advertising through presentations, information tables, posters, flyers, and social media. Interested students will be given detailed information about the study in person, via email, or by phone. Approximately 500 participants will be recruited per year for about five years until a goal of 2500 participants is reached. Students will be evaluated for eligibility to participate at the baseline visit and provide informed consent prior to enrollment. Participants will be reimbursed with a gift card upon completion of each study appointment.

3.4.2 Data collection

Participants will be assessed every six months for four years, once in September or October and again in March or April of each academic year (Table 1). At the baseline visit only, a saliva sample will be obtained in addition to information on age, sex, ethnicity, birthplace, and country of residence history. Weight, height, waist circumference (WC), hip circumference (HC), %BF, and body fat mass (BFM) will be measured at baseline and all follow-up appointments. Socioeconomic status, civil status, sexual orientation, medical history, medication and drug use, smoking status, energy intake, meal plan type, alcohol consumption, physical activity, electronic screen time, method commuting to campus, living status on or off campus, sleep health, stress, history of abuse, impulsivity, eating disorders, body dissatisfaction, self-esteem, depression, anxiety, religiosity will be measured at all time-points using online, self-reported questionnaires. Participants will complete their questionnaires and one food recall at their baseline visit with instruction from a research assistant. After receiving this initial training, follow-up questionnaires and food recalls will be completed online outside of study appointments at the participant's leisure to minimize burden. All questionnaires and food recalls will be completed within three weeks of a participant's study appointment.

3.4.3 Outcomes

The obesity trait outcome variables are BMI, WC, WHR, %BF, and BFM. Trained research personnel will perform all anthropometric measurements in duplicate to reduce intra-rater variability. Participants will wear light clothing and remove shoes before being weighed. Weight will be measured to the nearest 0.1 kg using a digital scale (Seca, Hamburg, Germany). Height will be measured to the nearest 0.1 cm using a portable stadiometer (Seca 225, Hamburg, Germany). WC will be measured after a normal exhalation at the midpoint of the last palpable rib and the superior portion of the iliac crest to the nearest 0.1 cm and HC will be measured at the widest part of the buttocks to the nearest 0.1 cm using a stretch-resistant tape measure, as previously described by the World Health Organization (58). WHR will be calculated as WC divided by HC. BMI (kg/m^2) will be calculated by dividing weight by squared height. Bioelectric impedance analysis (BIA) will be used to assess BFM to the nearest 0.1 kg and %BF to the nearest

0.1%. Participants will remove jewelry before stepping barefoot onto the BIA device (Tanita SC-331S, Illinois, USA).

3.4.4 Predictor variables

A variety of genetic and environmental predictors of weight will be measured. Potential risk factors for obesity including age, sex, ethnicity, socioeconomic status, civil status, sexual orientation, smoking status, medical conditions, medication or drug use, living status on or off campus, method of commuting to campus, meal plan type (of the several meal plan choices offered both on- and off-residence), time spent using electronic devices, birthplace, and history of country residence will be evaluated through online, self-reported questionnaires.

3.4.4.1 DNA extraction, whole-genome genotyping and whole-exome sequencing

Deoxyribonucleic acid (DNA) will be collected from a saliva sample. Saliva will be collected and preserved using the Norgen saliva collection kit (RU4500, Norgen Biotek Corporation, Thorlord, Canada) as per the manufacturer's instructions and stored at room temperature. Before purification, saliva samples will be incubated overnight at 50°C. DNA will be purified from 4 mL of preserved saliva using the Chemagen 500 MSM I (PerkinElmer chemagen Technologie GmbH, Baesweiler, Germany) as per the manufacturer's instructions. Two types of genetic experiments will be performed in the present study using Illumina microarray genotyping and next generation sequencing platforms at the McMaster Genome Facility. Genotyping of whole-genome SNP arrays for each participant will be done to study the association of common and low frequency genetic variants (minor allele frequency > 0.005) with obesity traits. We plan to use the Illumina Infinium Multi-Ethnic Global-8 microarray because it combines a relatively high density of SNPs (1.7 million) with a SNP tagging strategy adapted to ethnically diverse populations. Whole-exome sequencing (WES) will be used to study the association of rare coding variants with obesity traits. WES will be performed on a subset of participants who have extreme decreases in BMI (≤10th percentile), maintain BMI (45th to 55th percentile), and extreme increases in BMI (≥90th percentile) between baseline and 1-year post baseline. We also plan to use the Illumina TrueSeq Exome kit for DNA library preparation and HiSeq 1500 for DNA sequencing, as per the manufacturer's instructions.

3.4.4.2 Energy intake

Energy intake will be assessed with a 3-day 24-hour food recall, which was selected for its validity, reliability, and minimal participant burden (59). Participants will recall their energy intake from two weekdays and one weekend day using the 2016 Canadian adaptation of the Automated Self-Administered 24-hour Recall (ASA24-Canada-2016) (60). Three-day total energy intake will be averaged to give a mean value per day in kcal. Values for nutrient intake including total carbohydrates (g), protein (g), and fats (g), including saturated fat, monounsaturated fat, and polyunsaturated fat will be reported.

3.4.4.3 Alcohol consumption

The self-reported version of the Alcohol Use Disorders Identification Test (AUDIT) will be used as a validated measure of alcohol consumption (61). The AUDIT is a 10-item questionnaire with each question rated on a 5-point scale from 0 to 4 and summed to give a total global score out of 40. Higher scores indicate greater risk of dangerous drinking habits. A score of 8 or more indicates harmful alcohol use with possible alcohol dependence.

3.4.4.4 Physical activity

Physical activity will be assessed using a 16-item, self-reported version of the Global Physical Activity Questionnaire (GPAQ). The GPAQ was selected for its use in broad populations and its ability to assess physical activity and sedentary time at work, for recreation, and during transportation (62). Although the GPAQ is traditionally delivered in-person or via telephone interview, self-reported administration has been shown to be a comparable alternative and self-reported version will be used in this study for its feasibility (63). The GPAQ will be scored by calculating Total Metabolic Equivalent of Task minutes per week as previously described by the World Health Organization (64).

3.4.4.5 Exercise motivation

The exercise regulations questionnaire (BREQ-2) is a 19-item, self-reported questionnaire which measures motivation towards exercising in 5 domains: external regulation, identification, introjection, and amotivation (65). Each item is scored on a 5-point scale from 0 (*not true for me*) to 4 (*very true for me*). The mean score of each subscale will be calculated and used in analysis. Higher scores indicate greater motivation.

3.4.4.6 Sleep

Sleep health will be measured by the Pittsburg Sleep Quality Index (PSQI) as a reliable measure for sleep quality in university students (66, 67). The PSQI is a 24-item, self-reported questionnaire which measures 7 domains of sleep health over the past month: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. Each domain is scored on a 4-point scale from 0 (*not during the past month*) to 3 (*three or more times per week*) and summed to give a total global score out of 21. Higher scores indicate poorer sleep quality.

3.4.4.7 Stress

Hair cortisol concentration (ρg/mg) will be measured as a biochemical marker for exposure to physical stressors and ongoing chronic stress (68). Hair strands will be cut as close to the scalp as possible from the posterior vertex position. At least 10 mg of hair from the most proximal 3 cm, representing the last 3 months of hair growth, will be analyzed (69). Cortisol will be extracted as previously described and measured using enzyme-linked immunosorbent assay (70).

3.4.4.8 History of abuse

The Sexual and Physical Abuse Questionnaire (SPAQ) is a 9-item, self-reported questionnaire and will be used as a validated measure of physical and sexual abuse (71). It assesses abuse at four time-points (1) <6 years old, (2) >6 but <12 years old, (3) >12 but <16 years old, and (4) >16 years old. Positive answers indicate a history of abuse. Due to the potentially triggering nature of this questionnaire, participants will be provided with contact information for local legal and support resources at the time of data collection.

3.4.4.9 Impulsivity

To measure impulsive personality traits, the Short UPPS-P Impulsive Behaviour Scale will be used and was selected for its use in university students (72, 73). It is a 20-item, self-reported questionnaire with subscales to measure negative urgency, positive urgency, lack of perseverance, lack of premeditation, and sensation seeking. Items are scored on a 4-point scale from 1 (*strongly* *agree*) to 4 (*strongly disagree*) with higher scores indicating more impulsive behaviour. Mean scores from each subscale will be calculated and summed to give a total global score from 5 to 20.

A computer-administered Delay Discounting Task (DDT) will be used to measure impulsive choice (74). This is a 5-item task whereby participants are asked to choose between an immediate reward of $100 or a delayed reward of $1000. Monetary values will be held constant while temporal delays will be adjusted up or down, ranging from 1 hour to 25 years, depending on the choice made by each participant. This task will result in 32 potential Effective Delay 50% (ED_{50}) scores approximately evenly spaced on a logarithmic scale. Temporal discounting rates, *k*-values, will be generated for each participant by calculating the inverse of ED_{50}. Higher *k*-values reflect greater impulsivity.

3.4.4.10 Eating disorders

Eating disorders will be evaluated using the Eating Disorder Diagnostic Scale (EDDS) developed for use in community populations (75). The EDDS is a 22-item, self-reported questionnaire which assesses Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for diagnosing anorexia nervosa, bulimia nervosa, and binge-eating disorder in respondents. It will be scored as previously described (75). Scores will be analyzed dichotomously by eating disorder diagnosis and continuously by total global score.

3.4.4.11 Body dissatisfaction

Concern about body image will be measured using the 8-item Body Shape Questionnaire (BSQ-8C) for its use in community populations (76, 77). The BSQ-8 is a self-reported questionnaire which assesses body shape concerns over the last four weeks on a 6-point scale from 1 (*never*) to 6 (*always*). Higher scores indicate greater body dissatisfaction.

3.4.4.12 Self-esteem

Self-worth will be measured using the Rosenberg self-esteem scale for its wide use in general populations (78). It is a self-reported questionnaire which measures self-esteem on a 4-point scale from 1 (*strongly disagree*) to 4 (*strongly agree*). Higher scores indicate higher self-esteem.

3.4.4.13 Depression

Depressive symptoms will be evaluated by the Center for Epidemiological Studies Depression Scale Revised (CESD-R) for its validated use in university students (79, 80). The CESD-R is a 20-item, self-reported questionnaire with subscales to measure sadness, loss of interest, appetite, sleep, thinking and concentration, guilt, fatigue, agitation, and suicidal ideation during the past week. The CESD-R is scored using a frequency 5-point scale for each item from 0 (*not at all or less than one day*) to 4 (*nearly every day for two weeks*). Higher scores indicate greater depressive symptoms. A cumulative score of at least 16 out of 60 indicates risk of clinical depression. A major depressive episode is characterized by loss of interest or sadness nearly every day for the past two weeks, and symptoms in another four DSM symptom groups occurring nearly every day for the past two weeks.

3.4.4.14 Anxiety

The 7-item Generalized Anxiety Disorder scale (GAD-7) is a valid measure of anxiety (81). The GAD-7 is a self-reported questionnaire which assesses anxious symptoms in the last two weeks on a 4-point scale from 0 (*Not at all*) to 3 (*Nearly every day*). Higher scores indicate greater anxiety. Scores of 10 or greater indicate risk of an anxiety disorder.

3.4.4.15 Religiosity

Participants will be asked to self-report their religious affiliation as Christian, Jewish, Muslim, Hindu, Buddhist, Sikh, Traditional (aboriginal) spirituality, or No religion (47). Religiosity will be measured by the Duke University Religion Index (DUREL) as a widely used, validated tool for assessing religious involvement (82, 83). The DUREL is a 5-item, self-reported questionnaire with subscales to measure organizational religious association, non-organizational religious association, and intrinsic religiosity. Items measuring organizational and non-organizational religious association are assessed on a 6-point scale from 1 to 6 with higher scores reflecting more frequent religious attendance. Items measuring intrinsic religiosity are assessed on a 5-point scale from 1 (*Definitely not true*) to 5 (*Definitely true of me*). Individual subscales scores will be summed and analyzed separately.

3.4.5 Sample size calculation

Most previous studies investigating weight change in undergraduate students have used sample sizes between 75 and 200 participants (11). With a sample size of 2000, there is at least 80% power to detect effect sizes of 0.8 kg/m^2 across a range of allele frequencies at the 5% significance level for BMI level (Table 2). For reference, the risk allele of *FTO* increases BMI level by approximately 0.4 kg/m^2 and has a minor allele frequency of 0.4 in Europeans, although these differ by ethnicity (84). For BMI change, there is at least 80% power to detect effect sizes of 0.1 kg/m^2 across a range of allele frequencies at the 5% level of significance (Table 3). To account for a 20% dropout rate, an additional 500 individuals will be recruited for a final sample size of 2500 (13). Dropout is defined as missing two consecutive appointments since it reflects one full academic year. Sample size estimates for GWAS, exome-wide association study for rare variants, and associations for binary environmental traits are included for reference for BMI level (Supplementary Tables S1-S3) and BMI change (Supplementary Tables S4-S6). Our targeted sample size will provide a reasonable to good statistical power for these analyses.

3.4.6 Statistical methods

Descriptive statistics at baseline will illustrate the distribution of sex, age, sexual orientation, civil status, socioeconomic status, ethnicity, proportion born in Canada, distribution of economic status of birth country (high/middle/low income), residence status on/off-campus, meal plan type (yes/no, high/medium/low cost), total and carbohydrate/fat/protein energy intake, alcohol consumption, physical activity, exercise motivation, electronic screen time, sleep quality, hair cortisol concentrations, history of sexual assault, impulsive personality traits, impulsive choice, disordered eating, body dissatisfaction, self-esteem, depressive symptoms, anxiety, religiosity, religious affiliation, BMI, WC, WHR, BFM, and %BF. Continuous variables will be reported by mean and standard deviation. Categorical variables will be reported by count and percentage. Subgroup analyses (e.g. ethnicity) on obesity outcomes will be performed if there is a significant interaction between the predictor and the subgroup factor.

3.4.6.1 Analysis of environmental risk factors

The effect of potential environmental risk factors on obesity traits (i.e. BMI, WC, WHR, %BF, BFM) at baseline will be tested using linear regression models with adjustments for age, sex, and ethnicity. For variables such as sleep health which are evaluated by scaled questionnaires, the cumulative global score will be used in the analyses to increase power. The effect of each potential environmental risk factor at baseline and during follow-up on the evolution of obesity traits at 1 year (interim) and 3.5 year (final) post-baseline visit will be tested using mixed effects linear regression models with adjustment for age, sex, ethnicity, and baseline BMI. Multivariate hierarchical stepwise mixed regression models will be used to assess the independent effect of each environmental risk factor on obesity trait trajectories. Collinearity and sensitivity analyses will be conducted to ensure stability of the model. Mediation and interaction analyses will be conducted when there is scientific rationale or biological plausibility for a relationship between variables.

3.4.6.2 Analysis of genetic risk factors

All analyses will investigate associations with genetic variants at baseline, 1 year and 3.5 years post-baseline. Heritability estimates for obesity trait level and change will be calculated. GWAS will be performed to identify genetic variants associated with obesity trait level and change. Significance of genetic variants will be tested at the genome-wide level of significance ($p<5x10^{-8}$). Gene-based association tests for SNPs will also be performed for obesity traits. WES analysis will be performed to identify rare genetic coding variants associated with obesity trait level and change. Significance of SNPs and exonic variants will be tested at the gene-based level of significance ($p<2.5x10^{-6}$) (85). Hypothesis-free whole genome approaches (GWAS and WES) do not have the power to detect all the genetic variants contributing to obesity because of the multiple testing burden from the Bonferroni correction (86, 87). Testing a subset of strong candidate genes or SNPs reduces the number of tests conducted and has the potential to lead to the identification of obesity genes missed by conventional approaches (88). These strategies will be conducted in GENEiUS. Genome-wide Complex Trait Analysis will be used to assess the heritability of obesity traits and change in obesity traits from SNP variants previously identified by GWAS (89). The PLINK software will be used for GWAS (90). Autosomal and X chromosome SNPs will be imputed using the all ancestry 1000 Genomes Project reference panel and the miniMAC or IMPUTE2 software (91, 92). Gene-based association of SNPs with obesity trait level and change will be assessed using VEGAS2 software (93). Variant annotation and filtering from whole-exome sequences will be performed using the KGGSEQ framework (94).

The association of well-established GWAS SNPs for BMI, WC, WHR, and %BF, or a combination of pathogenic mutations in previously identified monogenic genes, with obesity trait level and change at baseline will be performed using linear regression models with adjustment of age, sex, and ethnicity/population structure (53-55). The self-reported ethnicity will be verified using principal component analysis from the EIGENSTRAT software (95). Adjustment for ethnicity/population structure will be achieved by adding the 10 first principal components of EIGENSTRAT analysis in the regression model. A p-value threshold of 0.05 will be considered significant given the high prior likelihood of association. SNP variants will be analyzed individually and cumulatively as a gene score using additive, dominant, and recessive modes of inheritance. An unweighted gene score, which estimates the effect of all obesity susceptibility genetic variants on obesity traits, will be calculated by summing the alleles positively correlated with individual obesity traits (96). Missing genotype values will be imputed using the method of the mean in the calculation of the gene score. This imputation will be performed for each SNP individually using the arithmetic average of the coded genotypes observed for all the successfully genotyped individuals in each ethnic group. An allelic burden test of functional mutations for previously identified obesity genes will be conducted to investigate the cumulative effect obesity genes mutations on obesity trait level and change. All models will be adjusted for age, sex, ethnicity/population structure. Interim and final analyses will also be conducted to determine the effect of predisposing obesity genetic variants on individual obesity traits and changes in obesity traits with adjustment for age, sex, ethnicity, and baseline BMI.

3.4.6.3 Prediction models of weight change

Models will be created to assess the utility of genetic variants and environmental factors on predicting weight status. Support vector machine learning models will be used to determine the optimal combination of predictive SNPs for incident occurrence of overweight and/or obesity (97). Receiver operating characteristic curve and net reclassification improvement analyses will include environmental and genetic factors to estimate their ability to predict overweight, overweight/obese, or obese status in undergraduate students (98, 99). Optimal predictive values for continuous environmental traits will be determined by polychotomization as previously described (100). Internal validation of the prediction models will involve training-testing split methods (101).

3.5 Discussion

Weight changes occurring in young adulthood may be important for the development of chronic obesity (6). However, this age group has been poorly studied. The GENEiUS study is the first adequately powered observational study design aiming to investigate genetic and environmental associations of weight change in undergraduate students. The majority of past studies investigating undergraduate weight gain have only followed students until the end of their first academic year (i.e. 6-8 months) therefore little is known about weight changes throughout undergraduate studies (11). The GENEiUS study aims to fill this knowledge gap by following students prospectively over their first four years of undergraduate study. The longitudinal nature of GENEiUS will permit the study of temporal relationships between obesity risk factors and strengthen the ability to make causal inferences regarding determinants of undergraduate weight change. This study includes the measurement of many well-established risk factors for obesity such as energy intake, physical exercise, and sleep duration (102). GENEiUS will also investigate novel potential risk factors like exercise motivation, history of abuse, religiosity, stress measured by hair cortisol and the effect of immigration. Only few studies in undergraduate students have included the measurement of WHR, %BF, or BFM (11). Since BMI may be a biased estimate of body fat, the inclusion of these measures in GENEiUS will provide a better estimation of adiposity (103). While it may be argued that measurement of additional cardio-metabolic outcomes (e.g. T2D, hypertension, dyslipidemia, fatty liver, atherosclerosis) may be important, these co-morbidities are mainly driven by obesity in young adults at the population level (104-106). For this reason, evolution of obesity-related traits will be our main focus. The heterogeneous nature of the sample population consisting of multi-ethnic students from a variety of undergraduate programs will also help to increase the generalizability of findings in North America and perhaps identify ethnic-specific effects.

While the GENEiUS study design has many strengths in its design, it also has limitations. First, it is restricted to measurement of only two time-points each year from September to October and from March to April, without inclusion of a summer assessment. Since few students remain on campus during this period, a summer time-point will be avoided. Further, while the great use of validated questionnaires will provide strong estimates for various environmental factors, many of these do not represent the criterion measure for their respective traits. For instance, the GPAQ overestimates moderate-to-vigorous physical activity when compared to accelerometer data (107). These short, validated questionnaires delivered online were selected by balancing accuracy and feasibility given the large sample size of the study. Although dual-energy X-ray absorptiometry is a more precise measure of adiposity, BIA will be used in the present study to increase access to the equipment, decrease participant burden and limit cost (108). BIA is limited by its sensitivity to fluid changes, the position in which participants stand, and equations for %BF and BFM may not be generalizable to all ethnicities (109). Further, this study is only conducted at one institution and thus results may not be generalizable to other universities. The single center design however, results in less variability of certain environmental factors including type of cafeteria food, food accessibility, and access to physical fitness facilities to be held constant. Finally, the GENEiUS study is not sufficiently powered to find gene-environment interactions which require samples of up to 100,000 (110). Certain subgroup analyses with a low number of individuals, such as Aboriginal Peoples in ethnic-specific analyses, may also be underpowered to find associations (111).

Overall, the GENEiUS study is the first to investigate the genetic and environmental determinants of weight change in undergraduate students. It will assess a wide range of well-studied and novel potential risk factors. It will contribute to the limited knowledge of weight change throughout undergraduate studies as it will follow participants longitudinally. The prospective nature of this observational study will help to make causal inferences for weight change in undergraduate students. Since the duration of obesity is associated with higher morbidity and mortality, understanding the determinants of weight gain in young adulthood may lead to major improvements in the quality of life and life expectancy, as well as decrease the burden that obesity places on public health infrastructure.

3.5.1 Ethics and dissemination

Prior to enrollment, a member of the research team will explain the consent form in plain language and each student then will be asked to read and provide written informed consent. The informed consent states the voluntary nature of participation and that withdrawal from the study may be done at any time. All methods and procedures for this study (#0524) were reviewed and approved by the Hamilton Integrated Research Ethics Board. Outcomes for this research will be published in peer-reviewed journals and presented at scholarly regional, national, and international meetings. Meetings will occur with university leaders like the associate dean of education, administration, and student groups at McMaster University to facilitate knowledge translation to the local stakeholders and student population.

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Competing interests: None declared.

3.6 Figures and tables

Table 1. Study timeline, outcomes risk factor variables, and measurements

		Measurement	Sep-Oct Year 1	Mar-Apr Year 1	Sep-Oct Year 2	Mar-Apr Year 2	Sep-Oct Year 3	Mar-Apr Year 3	Sep-Oct Year 4	Mar-Apr Year 4
	Informed consent		X							
Anthropometric outcomes	Weight	Electronic scale	X	X	X	X	X	X	X	X
	Height	Stadiometer	X	X	X	X	X	X	X	X
	Waist circumference	Stretch-resistant measuring tape	X	X	X	X	X	X	X	X
	Hip circumference	Stretch-resistant measuring tape	X	X	X	X	X	X	X	X
	BMI	Calculated weight (kg)/height(m)^2	X	X	X	X	X	X	X	X
	WHR	Calculated waist circumference (m)/hip circumference (m)	X	X	X	X	X	X	X	X
	BFM	BIA	X	X	X	X	X	X	X	X
	%BF	BIA	X	X	X	X	X	X	X	X
Genetics	DNA sample	Norgen saliva kit (RU4500)	X							
Cultural, environmental, lifestyle, social factors	Age, sex, ethnicity	Self-reported	X							
	Birthplace, changes in country of residence	Self-reported	X							
	Sexual orientation, civil status	Self-reported	X	X	X	X	X	X	X	X
	Socioeconomic status	Parent's education, parent's income, postal code	X	X	X	X	X	X	X	X
	Meal plan type	Self-reported	X	X	X	X	X	X	X	X
	Commuting method	Self-reported	X	X	X	X	X	X	X	X
	Living status on/off campus	Self-reported	X	X	X	X	X	X	X	X
	Medical history	Self-reported	X	X	X	X	X	X	X	X
	Medication and drug use	Self-reported	X	X	X	X	X	X	X	X
	Smoking history	Self-reported	X	X	X	X	X	X	X	X

	Time using electronic devices	Self-reported	X	X	X	X	X	X	X	X
	Energy intake	ASA24-Canada-2016 3-day food recall	X	X	X	X	X	X	X	X
	Alcohol consumption	AUDIT	X	X	X	X	X	X	X	X
	Physical activity	GPAQ	X	X	X	X	X	X	X	X
	Exercise motivation	BREQ-2	X	X	X	X	X	X	X	X
	Sleep health	PSQI	X	X	X	X	X	X	X	X
	Stress	Hair cortisol concentration (ρg/mg)	X	X	X	X	X	X	X	X
	History of assault	SPAQ	X	X	X	X	X	X	X	X
	Impulsive personality traits	SUPPS-P	X	X	X	X	X	X	X	X
	Impulsive choice	DTT	X	X	X	X	X	X	X	X
	Eating disorders	EDDS	X	X	X	X	X	X	X	X
	Body dissatisfaction	BSQ-8C	X	X	X	X	X	X	X	X
	Self-esteem	Rosenberg self-esteem scale	X	X	X	X	X	X	X	X
	Depression	CESD-R	X	X	X	X	X	X	X	X
	Anxiety	GAD-7	X	X	X	X	X	X	X	X
	Religiosity	DUREL	X	X	X	X	X	X	X	X

ASA24, Automated self-administered 24-hour; AUDIT, Alcohol Use Disorders Identification Test; BFM, body fat mass; BIA, bioelectric impedance analysis; BMI, body mass index; BREQ-2, Exercise regulations questionnaire; BSQ-8C, 8-item Body Shape Questionnaire; CESD-R, Center for Epidemiologic Studies Depression Scale Revised; DDT, delay discounting task; DNA, deoxyribonucleic acid; DUREL, Duke University Religion Index; EDDS, Eating Disorder Diagnostic Scale; GAD-2, 2-item Generalized Anxiety Disorder scale; GPA, grade point average; GPAQ, Global Physical Activity Questionnaire; PSQI, Pittsburg Sleep Quality Index; SPAQ, Sexual and Physical Abuse Questionnaire; UPPS-P, impulsive behaviour scale; WHR, waist-to-hip ratio; %BF, body fat percentage.

Table 2. Sample size estimates for BMI level

Table 2. Sample sizes needed in a cohort design to detect significant associations of genetic variants with BMI level with 80% power and a two-sided P of 0.05 by beta coefficient and allele frequency for risk allele.

	Minor allele frequency					
Allelic beta	0.01	0.05	0.1	0.2	0.3	0.4
0.10	513741	107071	56508	31784	24215	21188
0.20	128432	26765	14112	7943	6051	5294
0.30	57079	11893	6275	3528	2687	2351
0.40	32105	6688	3528	1983	1510	1321
0.50	20546	4279	2257	1268	965	844
0.60	14267	2970	1566	879	669	585
0.70	10481	2181	1149	645	490	429
0.80	8023	1669	879	493	374	327
0.90	6339	1316	694	389	295	258
1.00	5134	1067	561	314	238	208
1.50	2279	472	257	137	104	90
2.00	1280	264	137	75	57	49
2.50	818	167	86	47	35	30
3.00	567	115	59	31	23	19
3.50	415	83	42	22	16	13

Table 3. Sample size estimates for BMI change

Table 3. Sample sizes needed in a cohort design to detect significant associations of genetic variants with BMI change with a power of 80% and a two-sided P of 0.05 by beta coefficient and allele frequency for risk allele.

	Minor allele frequency					
Allelic beta	0.01	0.05	0.1	0.2	0.3	0.4
0.01	>1000000	669216	353196	198671	151367	132446
0.02	802722	167301	88296	49665	37839	33109
0.03	356763	74354	39240	22071	16815	14713
0.04	200678	41822	22071	12413	9457	8274
0.05	128432	26765	14124	7943	6051	5294

0.06	89188	18586	9807	5515	4201	3675
0.07	65525	13654	7204	4051	3085	2699
0.08	50166	10453	5515	3100	2361	2066
0.09	39637	8258	4357	2449	1865	1631
0.10	32105	6688	3528	1983	1510	1321
0.20	8023	1669	879	493	374	327
0.30	3564	740	389	217	164	143
0.40	2003	414	217	120	91	79
0.50	1280	264	137	75	57	49
0.60	888	182	94	51	38	33
0.70	651	133	68	36	27	23
0.80	498	101	51	27	19	16
0.90	392	79	40	20	14	12
1.00	317	63	31	16	11	9

Table S1. Sample size estimates for BMI level by GWAS

Table S1. Sample size estimates for BMI level by GWAS. Sample sizes needed in a cohort design to detect significant associations of genetic variants identified by GWAS with BMI level with 80% power and a two-sided P of $5x10^{-8}$ by beta coefficient and allele frequency for risk allele.

	Minor allele frequency					
Allelic beta	0.01	0.05	0.1	0.2	0.3	0.4
0.10	>1000000	469717	247898	139435	106232	92951
0.20	5633426	117416	61962	34846	26545	23225
0.30	250402	52175	27529	15477	11788	10313
0.40	140844	29341	15477	8699	6623	5793
0.50	90134	18772	9899	5561	4233	3701
0.60	71982	14987	7900	4435	3375	2950
0.70	52879	11006	6799	3253	2474	2162
0.80	40481	8421	4435	2486	1889	1651
0.90	31981	6650	3500	1960	1489	1300
1.00	25901	5383	2831	1584	1202	1049
1.50	11500	2381	1247	693	523	455
2.00	6460	1331	693	381	285	247
2.50	4127	844	436	236	175	150
3.00	2860	580	297	158	115	98

3.50	2096	421	212	110	78	66

Table S2. Sample size estimates for BMI level by exome-wide association study

Table S2. Sample size estimates for BMI level by exome-wide association study. Sample sizes needed in a cohort design to detect significant gene-based associations of rare exonic variants with BMI level with 80% power and a two-sided P of 2.5×10^{-6} by beta coefficient and allele frequency for risk allele.

	Minor allele frequency							
Allelic beta	0.001	0.005	0.01	0.05	0.1	0.2	0.3	0.4
0.10	>1000000	>1000000	>1000000	420158	221743	124724	95024	83144
0.20	>1000000	>1000000	503980	105028	55424	31169	23744	20774
0.30	>1000000	445730	223983	46671	24624	13844	10545	9225
0.40	>1000000	250716	125984	26245	13844	7781	5925	5182
0.50	986563	160453	80624	16792	8855	4974	3786	3311
0.60	554935	111421	55984	11656	6145	3450	2625	2295
0.70	407703	81856	41127	8560	4510	2530	1924	1682
0.80	312144	62667	31484	6550	3450	1934	1470	1284
0.90	246629	49512	24873	5172	2722	1525	1158	1011
1.00	199767	40102	20144	4186	2202	1232	935	816
1.5	88777	17814	8945	1852	970	539	407	354
2.0	49930	10014	5025	1035	539	296	222	192
2.5	31950	6403	3210	657	339	184	136	117
3.0	22183	4442	2225	451	231	123	89	76
3.5	16293	3259	1630	327	165	86	61	51

Table S3. Sample size estimates for environmental traits with BMI level

Table S3. Sample size estimates for environmental traits with BMI level. Sample sizes needed in a cohort design to detect significant associations of binary environmental traits with BMI level with 80% power and a two-sided P of 0.05 by beta coefficient and prevalence of environmental exposure.

	Prevalence of environmental exposure					
Beta	0.01	0.05	0.10	0.20	0.30	0.40
0.10	>1000000	214147	113020	63572	48435	42380
0.20	256869	53534	28252	15890	12106	10592

0.30	114162	23791	12554	7060	5378	4705
0.40	64214	13380	7060	3970	3023	2645
0.50	41096	8562	4517	2539	1934	1691
0.60	28537	5945	3136	1762	1342	1173
0.70	20965	4366	2303	1294	985	861
0.80	16051	3342	1762	989	753	658
0.90	12681	2640	1391	781	594	519
1.0	10271	2138	1126	632	480	420
1.5	4563	948	498	279	211	184
2.0	2565	531	279	155	117	102
2.5	1640	339	177	98	74	64
3.0	1138	234	122	67	50	43
3.5	835	171	88	48	35	31

Table S4. Sample size estimates for BMI change by GWAS

Table S4. Sample size estimates for BMI change by GWAS. Sample sizes needed in a cohort design to detect significant associations of genetic variants identified by GWAS with BMI change with 80% power and a two-sided P of $5x10^{-8}$ by beta coefficient and allele frequency for risk allele.

	Minor allele frequency					
Allelic beta	0.01	0.05	0.1	0.2	0.3	0.4
0.01	>1000000	>1000000	>1000000	>1000000	763714	668247
0.02	>1000000	>1000000	445491	250580	190914	167047
0.03	>1000000	909187	197985	111358	84839	74232
0.04	>1000000	511409	111358	62630	47714	41747
0.05	647996	327294	71262	40076	30530	26711
0.06	449991	227282	49481	27825	21195	18543
0.07	330601	166997	36348	20437	15567	13618
0.08	253112	127837	27825	15643	11914	10422
0.09	199985	101003	21981	12355	9409	8230
0.10	161984	81809	17801	10004	7618	6663
0.20	40481	20437	4435	2486	1889	1651
0.30	17981	9072	1960	1094	829	723
0.40	10105	5094	1094	606	457	398
0.50	6460	3253	693	381	285	247
0.60	4480	2253	475	258	192	165

0.70	3286	1650	344	184	135	115
0.80	2511	1259	258	136	98	83
0.90	1980	990	200	103	73	61
1.00	1600	798	158	79	54	44

Table S5. Sample size estimates for BMI change by exome-wide association study

Table S5. Sample size estimates for BMI change by exome-wide association study. Sample sizes needed in a cohort design to detect significant gene-based associations of rare exonic variants with BMI change with 80% power and a two-sided P of 2.5×10^{-6} by beta coefficient and allele frequency for risk allele.

	Minor allele frequency							
Allelic beta	0.001	0.005	0.01	0.05	0.1	0.2	0.3	0.4
0.01	>1000000	>1000000	>1000000	>1000000	>1000000	779603	593980	519730
0.02	>1000000	>1000000	>1000000	656505	346482	194889	148483	129921
0.03	>1000000	>1000000	>1000000	291772	153983	86609	65984	57734
0.04	>1000000	>1000000	787478	164115	86609	48711	37109	32469
0.05	>1000000	>1000000	503980	105028	55424	31169	23744	20774
0.06	>1000000	696461	349982	72931	38484	21641	16484	14422
0.07	>1000000	511682	257125	53578	28270	15895	12107	10592
0.08	>1000000	391753	196858	41017	21641	12166	9266	8106
0.09	>1000000	309530	155539	32405	17096	9610	7318	6401
0.10	>1000000	250716	125984	26245	13844	7781	5925	5182
0.20	312144	62667	31484	6550	3450	1934	1470	1284
0.30	138722	27844	13984	2902	1525	851	644	562
0.40	78024	15655	7860	1626	851	472	356	309
0.50	49930	10014	5025	1035	539	296	222	192
0.60	34669	6949	3485	714	369	201	149	128
0.70	25467	5102	2556	520	267	143	105	90
0.80	19595	3902	1953	395	201	106	76	65
0.90	15400	3080	1540	309	155	80	57	47
1.00	12471	2492	1245	247	123	61	42	34

Table S6. Sample size estimates for environmental traits with BMI change

Table S6. Sample size estimates for environmental traits with BMI change. Sample sizes needed in a cohort design to detect significant associations of binary environmental traits with BMI level with 80% power and a two-sided P of 0.05 by beta coefficient and prevalence of environmental exposure.						
Minor allele frequency						
Allelic beta	0.01	0.05	0.1	0.2	0.3	0.4
0.01	>1000000	>1000000	706395	397346	302739	264896
0.02	>1000000	334606	176596	99333	75682	66221
0.03	713531	148712	78485	44146	33634	29429
0.04	401359	83649	44146	24830	18917	16552
0.05	256869	53534	28252	15890	12106	10592
0.06	178380	37175	19618	11034	8406	7354
0.07	131053	27311	14412	8105	6174	5402
0.08	100337	20909	11034	6205	4726	4135
0.09	79278	16520	8717	4902	3734	3266
0.10	64214	13380	7060	3970	3023	2645
0.20	16051	3342	1762	989	753	658
0.30	7131	1483	781	438	332	290
0.40	4010	833	438	244	185	162
0.50	2565	531	279	155	117	102
0.60	1780	368	192	106	80	70
0.70	1307	269	140	77	58	50
0.80	999	205	106	58	43	37
0.90	789	161	83	45	33	29
1.0	638	130	67	36	26	22

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Chapter 4: Conclusion

4.1 Summary of conclusions and methodological limitations

Undergraduate students represent an at-risk group for elevated BMI and the development of obesity later in adulthood (1-3). While the weight changes over first year have been well-studied, less is known about changes throughout the entire duration of undergraduate education (i.e. 4 years) or about the causes of these weight changes (4-6). The systematic review described in Chapter 2 summarized a list of factors associated with obesity traits including demographics, genetics, calendar year, diet/nutrition, eating habits, physical activity, sedentary activity, weight loss interventions, lifestyle, sleep, stress, university campus life, substance use, medical history, psychiatric illness/disorders, body image, eating attitude, eating regulation, personality/emotions, and social/cultural influences. Although a broad range of factors were identified, the strength of associations or quality of evidence cannot be inferred as no meta-analysis or risk of bias assessment was conducted. Furthermore, most of the associations were identified from observational study designs, especially cross-sectional, which limit any inferences of causality. Hence there is a need to conduct high quality longitudinal studies to replicate these findings and investigate variables which have yet to be studied.

We used the knowledge gained from this systematic review to inform the variables we selected for measurement in the GENEiUS study, a prospective observational study, described in Chapter 3. The GENEiUS study aims to identify the genetic and environmental determinants of BMI change in undergraduate students. This is the first adequately powered study to investigate genetics of weight change in undergraduate students and will capture information for an extensive amount of environmental variables (7). In addition, the measurement of adiposity through BIA will provide better insight on the changes in body composition over the four years, which many previous studies have lacked (4). Although this study finds strength through use of validated questionnaires, these tools may not be as accurate as their respective gold-standard measurement tools. Additionally, this study may be underpowered to find associations in subgroups under-represented at university, such as Africans or Aboriginal Peoples.

4.2 Sources of bias

4.2.1 Factors associated with obesity traits in undergraduate students: a systematic review

Systematic reviews can be affected by multiple sources for bias. First, bias can be introduced in the design of the search strategy. To capture as many relevant papers as possible, we employed a broad search strategy and consulted with an expert information specialist (LEB) to keep our search as sensitive as possible. The blind review of titles and abstracts by two reviewers allowed for an unbiased selection of papers to assess for full-text. Full-text review and data extraction were performed by a single individual which could have introduced some bias. However, a subject expert (DM) was consulted whenever there was uncertainty about the eligibility of a paper or an outcome. We also did not extract any data on variables which were not associated with obesity trait outcomes. By not capturing data for non-associations, we may have misclassified the direction of effect (i.e. positive, no association, negative, complex, uncertain). No meta-analysis was conducted so the strength of associations cannot be inferred.

4.2.2 Rationale and design of GENEiUS: a prospective observational study on the genetic and environmental determinants of body mass index evolution in Canadian undergraduate students

The GENEiUS study, as a prospective observational study, is subject to several potential sources of bias. We intend to recruit a broad sample of undergraduates for the GENEiUS study. We have made efforts to minimize sampling bias by only excluding individuals if they were not between the ages of 17 and 25, were not undergraduate students, were pregnant, or had a medical condition which prevents normal physical activity. This is very generalizable to the undergraduate population at McMaster as most students are in the aforementioned age range (8). We are uncertain of pregnancy rates or the prevalence of exercise-restrictive medical conditions, therefore we do not know what proportion of students will not be represented in our study. In terms of recruitment, we currently recruit via flyers, social media, and in-class announcements. This non-probabilistic approach to recruitment was selected for its convenience and feasibility, however it could yield a sample which is not wholly representative of the entire undergraduate population (9). Additionally, volunteer bias could arise such that individuals who are healthier or take more initiative in their health preferentially choose to enroll in GENEiUS over those who are less health-conscious (9). Similarly, those participants who stay enrolled in the study and who do not drop-out or become “non-responders” (i.e. participants who are enrolled but do not respond to some questionnaires) could also be healthier (9). This could ultimately skew our results as these individuals may gain less weight thus leading to an underestimation of the mean weight gain. Information bias could arise from random and systematic errors in measurement (9).

An example of random error would be an individual's random variation in responses to a questionnaire administered over multiple testing periods, for which the responses should not change with time (i.e. SPAQ childhood history subsection). On the other hand, a systematic error would be measuring participants on a mis-calibrated scale, for example recording everyone as 0.2 kg heavier. In order to minimize the observer bias between the multiple research assistants measuring the anthropometric outcomes, all research assistants are trained according to a standard protocol by the study coordinator. Finally, the aim of GENEiUS is to identify which genetic and environmental factors influence BMI change in undergraduates. To strengthen our inferences of causality, we need to limit the effect of confounders on our predictors and outcomes of interest (9). Since the GENEiUS study measures a wide variety of genetic lifestyle variables, this allows us to adjust for potential confounders during data analysis.

4.3 Feasibility of the GENEiUS study and practical considerations

The GENEiUS study began in its preliminary phases with the collection of a limited number of variables and outcomes. This included measuring weight, height, HC, WC, diet through a food frequency questionnaire, depression, and lifestyle factors. As GENEiUS has grown in size and as we have changed the study protocol, we have learned valuable information which we hope will increase compliance and retention as the study continues. First, we transitioned from delivering questionnaires on paper to delivering them on Limesurvey, an online platform. This enables participants to complete questionnaires outside of the lab at their convenience which limits burden. Laboratory appointments are now shortened as only anthropometry needs to be measured and biological samples need to be collected in-person. These shortened appointments also allow the research team to see more participants per day and limits the strain on research assistants, which are critical since GENEiUS aims to recruit 2500 individuals. When we transitioned from a food frequency questionnaire to the 3-day recall using the online ASA24-Canada-2016, we noticed participants had difficulty completing the questionnaire initially. Now we ensure all participants complete their first food recall in the laboratory during their first appointment. This gives participants the ability to ask questions and get clarification from research assistants. We also send participants reminder emails with detailed instructions attached to increase compliance and remind them of how to complete the form. Finally, with the transition to online questionnaires we found some participants complete the in-lab portion but not the online one. To increase motivation and compliance to study protocol, we will implement a two-step gift card in the future. Currently participants receive one gift card for their participation each visit. Moving forward we will send participants one gift card after the completion of the in-lab appointment and another after the online questionnaires are completed.

4.4 Ethical considerations with the GENEiUS study

The GENEiUS study collects a broad range of information on each participant including genetics and some information about their mental health. Capturing genetic information raises some ethical issues on how to handle situations in which the investigators find a genetic mutation that could adversely affect a participant's health. As is presently stated in the information sheet, the GENEiUS study will not inform participants about the results of their genetic analyses. However, we are currently in the process of consulting with the Hamilton Integrated Research Ethics Board to revise this protocol. We plan to only reveal the results of genes for which we are actively looking, have well-described implications on health, and have possibility for treatment. This includes conditions such as proopiomelanocortin (POMC) deficiency and leptin deficiency which are caused by mutations in *POMC* and in *LEP*, respectively (10-12). POMC deficiency can be treated by hydrocortisone replacement therapy to address the adrenal insufficiency, setmelanotide to reduce hunger and stimulate weight loss, and lifestyle counselling to manage weight (10, 13). Similarly, leptin deficiency is treated with leptin replacement therapy to manage weight, reduce hunger, reduce insulin concentrations, and promote fertility (11, 12). However, it is unlikely we will come across many such conditions since *POMC* deficiency is usually diagnosed in infancy and forms of syndromic obesity are usually marked by mental impairments, thus hindering this population from attending higher education institutions (10, 14). In addition, leptin deficiency is extremely rare with only 20 individuals identified to date (11). As per the recommendations by the Tri-Council Panel on Research Ethics, participants have the right not to receive information about their gene status, especially since the knowledge of genetic conditions predisposing to disease could affect eligibility for insurance or employment (15).

The GENEiUS study uses validated questionnaires which assess risk for anxiety (GAD-7), depression (CESD-R), and eating disorders (EDDS). If at any point in time during the study a participant is scoring in the clinical range for any of the aforementioned questionnaires, a member of the study team will approach the participant to disclose this information and provide resources available to get medical help or counselling. It is also possible that through answering the questionnaires themselves, students may experience harm. In particular, the SPAQ asks questionnaires about recent and prior experiences of abuse. Some participants may be triggered by the nature of these items so we have given participants the option to skip the questionnaire without reading it. We also provide an information sheet with contact information for counselling resources at McMaster University and in the Hamilton community at the beginning of the Limesurvey session and immediately before the SPAQ as well as at the time of their confirmation email for booking their follow-up appointment as a pdf attachment.

4.5 Future directions

The systematic review described in Chapter 2 reveals gaps in knowledge by identifying variables which have been under-investigated or not yet studied. It as highlights the need to do subgroup analysis and more complex non-linear analysis on some variables. Many associations were identified for cross-sectional studies but far fewer factors were investigated in longitudinal studies. In addition, the most commonly reported outcomes for changes in obesity traits in longitudinal studies were BMI change and weight change. These measures do not reveal changes in body composition. Thus, there is a clear need to conduct more studies investigating what causes the change in more precise adiposity measures (e.g. %BF). Together this information will help design high quality longitudinal studies investigating the determinants of body composition change in undergraduates, such as the GENEiUS study. The information from longitudinal studies will hopefully reveal factors influencing adiposity and identify subgroups at-risk in the undergraduate population. Using this knowledge, universities can design more effective obesity prevention programs in the future.

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