

Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Jingxuan Zhao

Date

**Reproductive Factors and Change in Weight/BMI During the Menopausal
Transition**

By

Jingxuan Zhao

Master of Public Health

Epidemiology

Lauren McCullough
Faculty Thesis Advisor

**Reproductive Factors and Change in Weight/BMI During the Menopausal
Transition**

By

Jingxuan Zhao

B.Sc., Peking University, 2015

Thesis Committee Chair: Lauren E. McCullough, PhD, MSPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2017

Abstract

Reproductive Factors and Change in Weight/BMI During Menopausal Transition

By Jingxuan Zhao

During the transition from peri-menopausal to post-menopausal, many women experience gains in weight and obesity. The reproductive period may be a critical time where changes in energy balance, maternal insulin resistance, and increased fat deposition in myocardial tissue occurs – influencing adult weight change. This study examined the association between reproductive characteristics (early menarche, age at first birth, parity, and lactation), and weight gain during the menopausal transition, overall, and in strata of race/ethnic groups.

We used the data from Study of Women's Health Across the Nation (SWAN), which included 1560. The outcomes of interest were the absolute changes in body mass index (BMI) and weight between baseline visit and visit 10. Weight and height were measured by study personnel. The exposures of interests, assessed via interviewer administered questionnaire, included menarche age, age at first birth, parity, lactation. Multiple linear regressions were conducted to evaluate the relation between change in obesity status and reproductive factors.

Women with a menarche age of 12 or 13 were less likely to experience gains in BMI compared with earlier menarche group (age 11) in all race/ethnicity groups ($\beta = -0.49$, 95% CI: [-0.97, -0.01] and $\beta = -0.5$, 95% CI: [-1.00, -0.05] for BMI and weight change, respectively). Women with 1 or 2 children had less gain in weight compared with women with no children ($\beta = -1.59$, 95% CI: [-3.16, -0.02] and $\beta = -1.47$, 95% CI: [-2.80, -0.14], respectively). We observed heterogeneity for the association between menarche age and BMI/weight change, parity and BMI/weight change, as well as lactation and BMI/weight change by race/ethnicity, with Chinese or Chinese American women more likely to experience gains in BMI or weight.

This study indicated that early menarche and null-parity were risk factors for weight gain and BMI increase during menopausal transition, particularly among Japanese or Japanese American women for parity and among African American for early menarche.

**Reproductive Factors and Change in Weight/BMI During Menopausal
Transition**

By

Jingxuan Zhao

B.Sc., Peking University, 2015

Thesis Committee Chair: Lauren McCullough

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2017

Acknowledgements

I would especially like to thank my thesis advisor, Dr. Lauren McCullough, for giving me advice on the topic, on data analysis, patiently reviewing my thesis and giving constructive feedback.

I would like to thank my parents and my boyfriend. Their love keeps me going.

Table of Contents

CHAPTER 1. INTRODUCTION AND BACKGROUND	1
1.1 Obesity	1
1.1.1 Obesity in the United States	1
1.1.2 Obesity and mortality	2
1.1.3 Obesity and chronic disease	2
1.2 BMI, weight gain and the menopausal transition.....	4
1.3 Risk factors for weight gain during menopausal transition	5
1.3.1 Psychological condition and weight gain during the menopausal transition	5
1.3.2 Life style and weight gain during the menopausal transition.....	5
1.4.1 Lactation: A candidate risk factor for weight gain during menopausal transition	8
1.4.2 Race/Ethnicity: A potential effect measure modifier	9
1.5 Significance of thesis.....	9
1.6 Specific Aims and Hypothesis:	11
CHAPTER 2 REPRODUCTIVE FACTORS AND CHANGE IN WEIGHT/BMI DURING MENOPAUSAL TRANSITION.....	12
2.1 Introduction	13
2.2 Methods.....	14
2.2.1 Population.....	14
2.2.2 Outcome assessment.....	15
2.2.4 Covariate assessment	16
2.2.5 Statistical methods.....	17
2.3 Results.....	17
2.3.1 Menarche age	18
2.3.2 Parity	19
2.3.3 Age at first birth	20
2.3.4 Lactation.....	20
2.4 Discussion.....	20

CHAPTER 3. FUTURE DIRECTIONS.....	28
3.1 Conclusion.....	28
3.2 Public Health Implications	28
3.3 Future Directions	29
Appendix 1. DAG and Pathways	35
Appendix 2. Backward Elimination for Model Selection	51

CHAPTER 1. INTRODUCTION AND BACKGROUND

1.1 Obesity

1.1.1 Obesity in the United States

The prevalence of overweight (body mass index [BMI] 25.0 kg/m²–29.9 kg/m²) and obesity (BMI greater than or equal to 30.0 kg/m²) has dramatically increased during the past few decades in the United States (1). The 2011–2012 National Health and Nutrition Examination Survey (NHANES) showed that 33.9% of adults are overweight, 35.1% are obese, and 6.4% are extremely obese (BMI greater than or equal to 40.0 kg/m²) (2). NHANES data indicates a steady increase of the obesity prevalence in the past four decades and a recent study suggests that this rate will remain on the rise (2). Between 1971 and 2012, the age-adjusted prevalence of obesity rose from 13.4% to 35.3% and the total population rate of extreme obesity rate increased from 0.9% to 6.6% (2).

The rise in the obesity prevalence exists among all age, gender, race/ethnicity and socioeconomic groups (3, 4). However, data have shown disparities in obesity rate among different groups (3, 5). The prevalence of obesity increased with age, and more than 70% of adults aged 60 years or older are obese or overweight (3). Between 2011-2012 two thirds of men and women were classified as overweight or obese however, women had a slightly higher obesity rate than men (36.1% vs. 33.5%) (2). Data from 1988 to 2012 showed large racial/ethnic disparities in obesity rate with non-Hispanic Blacks having the highest prevalence (2). The racial/ethnic difference was more pronounced among women compared to men (2, 5). Among women, the obesity prevalence for non-Hispanic Whites

was 32.8% while for the non-Hispanic Blacks it was 56.6% (2). Hispanics women has an obesity rate of 44.4%, while Non-Hispanic Asians had the lowest rate of obesity 11.4% (2).

1.1.2 Obesity and mortality

Studies suggested that people with excess weight experience shorter lifespan compared with their normal weight counterparts. A study of an average follow-up of seven years with more than 90,000 women indicated that extremely obese women had 2-fold risk of shorter life span (6). One prospective study examining the association between BMI and mortality among healthy non-smoking males and females aged 50-71 years showed a 20%-40% increase in death rate among the overweight group and 2-3-fold increase among the obese persons, when compared to people of normal weight (7). Another prospective study for a cohort of healthy, non-smoking White and Black U.S. adults estimated a 2-3-fold increase in mortality rate for obese and extremely obese people (8).

1.1.3 Obesity and chronic disease

Obesity, itself, is a chronic disease and a predictive factor for many other chronic diseases as well as disease-specific mortality (1).

1.1.3.1 Obesity and type II diabetes

The close relationship between diabetes and obesity has been described in numerous biological and epidemiologic studies. The colloquial term 'diabesity' demonstrates the intersect of these diseases (9). Type II diabetes mellitus is estimated to represent about 90% of all diabetes, and the frequency of type II diabetes closely mirrors that of obesity (10). Moreover, the trend of the increase in the prevalence of type II diabetes mellitus also

parallels the trend of the increase in the prevalence of obesity (11). Insulin resistance and insulin deficiency are the two pathophysiologic pathways that link obesity and type II diabetes mellitus (12). A meta-analysis found that the risk of developing diabetes is increased 7-fold (RR= 7.19) when comparing individuals with BMI>30 to those with BMI<25 (13). It is estimated about a 10-fold increase in diabetes incidence among people who are obese (14).

1.1.3.2 Obesity and cancer

Evidence has shown that excess body weight increase cancer risk at several sites, including breast, kidney, endometrium (15, 16). A study among postmenopausal women demonstrated that a 5 kg/m² in BMI was associated with a 10% increased risk of breast cancer (RR = 1.19, 95% CI = 1.05 to 1.34) (17). A case-control study including 810 cases and 3,106 controls observed a more than 2-fold increase the risk of renal cell (OR = 2.57, 95% CI = 2.02-3.28) and non-renal cell cancer (OR = 2.79, 95% CI = 1.70-4.60) among obese participants (18). Data support the positive association between BMI and endometrial cancer incidence. A case-cohort study showed that compared with women with BMI between 20 kg/m² and 22.9 kg/m², those with a BMI 30 kg/m² or greater had about a 4.5-fold increased risk of endometrial cancer (19).

1.1.3.3 Obesity and coronary heart disease

Accumulating evidence suggest that obesity is a strong risk factor for coronary heart disease (CHD). Obesity has been associated with hypertension, dyslipidemia, and insulin resistance (20). A meta-analysis of 21 cohort studies including more than 300,000 persons

with a total of 18,000 CHD events reported RRs for overweight and obesity were 1.32 (1.24-1.40) and 1.81 (1.56-2.10) compared to normal weight individuals (20). A cohort study with 16 years of follow-up including 2,771 CHD cases among men and 2,359 CHD cases among women found the RRs comparing BMI \geq 30.0 kg/m² with BMI 18.5 to 22.9 kg/m² were 2.13 (95% CI, 1.82–2.48) among men and 2.48 (95% CI, 2.20–2.80) among women (21).

1.2 BMI, weight gain and the menopausal transition

In the US population, the prevalence of obesity is higher among women than men (22). The reason for this disparity might be due to fluctuations in sex hormones during menarche, pregnancy, and menopause (22). Menopause transition, the period of time before the permanent cessation of menstrual function and the termination of reproductive capability, is a critical period for women health (23). The median age for menopausal transition is 51 years in North America (22). Women have relative high risk of experiencing weight gain and increased central body fat distribution during the menopausal transition and studies have shown that weight increases are primarily due to chronological aging, while changes in body fat distribution are due to ovarian aging (24). There are several changes that occur during the menopausal transition including: (1) increases in body mass and extracellular fluid; (2) decreases in bone and lean body mass; and (3) decreases in body protein (25). A cross sectional study including 53 healthy, middle aged, premenopausal women and 28 early-postmenopausal women found among early-postmenopausal women, total body fat

mass for was 28% higher (23 \pm 7 vs. 18 \pm 7 kg, P<0.01) and intra-abdominal was 49% greater (88.32 vs. 59.32 cm²) than that of premenopausal women (26). Many risk factors have been suggested to associate with weight gain during menopausal transition. These factors include life style, psychological conditions, and certain reproductive factors (e.g. early menarche and multi-parity).

1.3 Risk factors for weight gain during menopausal transition

1.3.1 Psychological condition and weight gain during the menopausal transition

Studies have shown a positive association between stress and weight gain during the menopausal transition. A meta-analysis of longitudinal studies on depression and weight control found that middle-age women suffering from stress were more likely to become obese (OR: 2.57, 95% CI: 2.27, 2.91) (27). Another study, based on the Penn Study of Ovarian Aging with 436 women aged 35-47 years, reported that depression was a major correlate of weight gain (OR: 1.9, 95% CI: 1.09, 3.31) (28). However, there are studies which report no association between psychological conditions and weight gain (29).

1.3.2 Life style and weight gain during the menopausal transition

Lifestyle factors including regular physical activity, smoking, and alcohol use have been associated with weight gain during the menopausal transition. Overall, an inverse association between physical activity and weight gain has been observed during the menopausal transition (24, 30, 31). A cohort study with 2-year follow-up among 232 women aged 40-50 years found that women who reported increased physical activity during follow-up gained the least weight (0.8 \pm 12.2 pounds) while those with the lowest

levels of physical activity had the most weight gain (5.3 ± 8.9 pounds) (24). Similarly, a prospective cohort study including 233 middle-age women with 20-months follow-up reported that physical activity uptake was associated with a 48% reduced likelihood (95% CI: 0.27, 0.98) of gaining abdominal fat (31).

The association between smoking and weight gain during the middle-aged women is unresolved, and may vary by former/current smoking status. A cross-sectional study with 617 women from southern Brazil found that smoking history was a risk factor for menopausal obesity with a prevalence ratio of 1.28 (95% CI: 1.07, 1.54) compared with nonsmokers (32). And this study found no relation between obesity during menopausal transition and current smoking status (PR: 0.80, 95% CI: 0.60, 1.05, compared with nonsmokers) (32). A cohort study with 5464 women showed that never-smokers and ex-smokers were associated with a weight gain of around 2.5 kg compared with current smokers ($P < 0.0001$) (33). Another study with 828 Japanese women aged 54 years showed that smoking history and smoking status were not associated with weight gain among middle-aged women (34).

Alcohol may also be associated with weight gain during the menopausal transition. One study based on Swedish middle-aged women concluded that alcohol users appeared to have less body fat and less central fat (33).

1.3.3 Reproductive factors and weight gain during the menopausal transition

Few previous studies have reported the role of early reproductive factors and weight

gain during the menopausal transition (29, 32, 34-37). These factors examined include early menarche, parity, and age at first birth.

1.3.3.1 Early menarche and weight gain during the menopausal transition

During the 20th century, the menarche age fell significantly especially in the developed countries and the prevalence of overweight and obesity for women increased in the same period (38). A study examined 1638 women participating in the Offspring and the Third Generation Framingham Heart Study cohort and found a significant inverse trend ($\beta=-0.6$, $P<0.0001$) between age at menarche and BMI (37). A prospective cohort study in China, with 75,039 non-pregnant women aged 40-70 years, reported adjusted weight gain for women whose menarche age was 14, 15, 16, 17 and 18 years compared to women with menarche at age ≤ 13 years was -0.9 (1.1, 0.7), -1.2 (1.4, 1.0), -1.5 (1.7, 1.3), -1.8 (2.0, 1.6), -1.8 (-2.0, -1.5), respectively (35). These data suggest that early menarche may enhance the incidence of obesity during the menopausal transition.

1.3.3.2 Parity and weight gain during the menopausal transition

Studies have demonstrated associations between multi-parity and weight gain during menopausal transition (23, 29, 32-35, 37, 39). A cross sectional analysis based on 5464 women aged 45-73 years showed a long-term change in weight for nulliparous, 1 child, 2 children, 3 children, 4 children and 5-8 children were 12.1kg (0.38kg), 13.0kg (0.30kg), 13.3kg (0.23kg), 13.0kg (0.34kg), 15.4kg (0.68kg) and 16.7kg (1.13kg), respectively, with $P<0.0001$ for the trend (33). Another cross sectional study with 617 women from South Brazil found women with 2 children and 3 or more had higher risk of general obesity

compared with nulliparous women or women with only one child (PR=1.44 [0.98-2.11] and 1.80 [1.43-2.27] respectively) (32). While associations in cross-sectional analyses appear to be consistent with the hypothesis that multi-parity is a risk factor for weight gain during the menopausal transition, temporal ambiguity limits causal inference.

1.3.3.3 Age at first birth and weight gain during the menopausal transition

An early first birth age may be a risk factor for weight gain and obesity during menopausal transition. A cohort study with 106 women ranging from 48 to 58 years at the Menox-outpatient clinic found an inverse association between age at first birth and obesity. The mean (SD) age for normal weight, overweight and obesity groups were 26.6 (5.1), 23.5 (4.8), 22.4 (3.2), respectively ($P<0.001$) (23). Similarly, a Chinese cohort study with 75,039 women also showed earlier age at first birth was related with higher risk of weight gain during the middle age.

1.4 Limitation for previous studies

1.4.1 Lactation: A candidate risk factor for weight gain during menopausal transition

Lactation (or breastfeeding) may similarly influence metabolism in women, but has not been investigated in association with weight gain during menopausal transition; albeit several studies have linked breastfeeding to weight change after pregnancy (40-42). One such study reported lactation was positively associated with abdominal fat cell diameter (39). This data may suggest that breastfeeding could be a predictor for weight change among middle-aged women.

1.4.2 Race/Ethnicity: A potential effect measure modifier

Most previous studies investigating associations between reproductive characteristics and weight/BMI changes were based on non-US cohorts primarily homogenous with respect to race and ethnicity. No previous study has investigated race/ethnicity as a potential effect measure modifier for the association between reproductive factors and weight gain during the menopausal transition.

1.5 Significance of thesis

The menopausal transition is a critical period for women health conditions and life quality. During the transition from peri-menopausal to post-menopausal, many women experience gains in weight and obesity (37, 43). Weight gain during the menopausal transition has been shown to be significantly associated with increased risk of chronic disease during adulthood (i.e., cardiovascular disease, breast cancer and diabetes) (36, 43, 44). The study of risk factors for menopausal transition obesity will play an important role in designing interventions to reduce risk of several chronic conditions. This proposed study will evaluate the association between reproductive characteristics, including early menarche, age after first birth, parity, and lactation and weight gain during the menopausal transition.

Previous studies have primarily been conducted on the association between reproductive factors and obesity status during menopausal transition period, rather than changes (which more likely reflect metabolic disturbances), as proposed in this study. Additionally, there is a dearth of literature on associations between lactation and changes

in weight across the menopausal transition despite evidence that suggests lactation may alter the metabolism of women (45). Several investigations have been conducted on the association between parity and young age at first birth with weight gain in mid-life (23, 33, 35), but to our knowledge none have investigated race/ethnicity as a potential effect measure modifier of the association (3, 5). There is substantial data to support racial/ethnic disparities with respect to obesity among US women (5, 46). It is therefore important to consider race/ethnicity in uncovering the drivers of weight and weight change during this important period of a women's life.

Study of Women's Health Across the Nation (SWAN) is a multi-site, prospective, longitudinal study aimed to investigate the health condition of women during the menopausal transition (47). This resource provides a unique opportunity to understand the drivers of weight gain during the menopausal transition and the opportunity to examine these associations in strata of race/ethnicity. The SWAN cross-sectional study consisted of women aged 40-55 years who were randomly selected from locations across the United States (47). To maximize heterogeneity of the study population each study site oversampled women of a specific racial or ethnic group (e.g., African-American, Chinese, Hispanic, Japanese and Caucasian). Women included in the SWAN cohort completed baseline data on socioeconomic status, physical conditions, medical treatment history and a host of other factors. These data were updated annually.

1.6 Specific Aims and Hypothesis:

Aim 1: To estimate the association between reproductive characteristics (early menarche, age at first birth, parity, and lactation), and weight gain (assessed via absolute change in BMI and weight [kg]) during the menopausal transition.

Hypothesis 1: Reproductive factors associate with weight gain during the menopausal transition.

Aim 2: To estimate the association between reproductive characteristics and weight gain during the menopausal transition by race/ethnicity.

Hypothesis 2: Race will modify the association between reproductive characteristics and weight gain during the menopausal transition.

CHAPTER 2 REPRODUCTIVE FACTORS AND CHANGE IN WEIGHT/BMI DURING MENOPAUSAL TRANSITION

Abstract

Background: During the transition from peri-menopausal to post-menopausal, many women experience gains in weight and obesity. The reproductive period may be a critical time where changes in energy balance, maternal insulin resistance, and increased fat deposition in myocardial tissue occurs – influencing adult weight change. This study examined the association between reproductive characteristics (early menarche, age at first birth, parity, and lactation), and weight gain during the menopausal transition, overall, and in strata of race/ethnic groups.

Methods: We used the data from Study of Women's Health Across the Nation (SWAN), which included 1560. The outcomes of interest were the absolute changes in body mass index (BMI) and weight between baseline visit and visit 10. Weight and height were measured by study personnel. The exposures of interests, assessed via interviewer administered questionnaire, included menarche age, age at first birth, parity, lactation. Multiple linear regressions were conducted to evaluate the relation between change in obesity status and reproductive factors.

Results: Women with a menarche age of 12 or 13 were less likely to experience gains in BMI compared with earlier menarche group (age 11) in all race/ethnicity groups ($\beta = -0.49$, 95% CI: [-0.97, -0.01] and $\beta = -0.5$, 95% CI: [-1.00, -0.05] for BMI and weight change, respectively). Women with 1 or 2 children had less gain in weight compared with

women with no children ($\beta = -1.59$, 95% CI: [-3.16, -0.02] and $\beta = -1.47$, 95% CI: [-2.80, -0.14], respectively). We observed heterogeneity for the association between menarche age and BMI/weight change, parity and BMI/weight change, as well as lactation and BMI/weight change by race/ethnicity, with Chinese or Chinese American women more likely to experience gains in BMI or weight.

Conclusion: This study indicated that early menarche and null-parity were risk factors for weight gain and BMI increase during menopausal transition, particularly among Japanese or Japanese American women for parity and among African American for early menarche.

2.1 Introduction

The menopausal transition is a critical period for women's health and quality of life. During the transition from peri-menopausal to post-menopausal, many women experience gains in weight and obesity (37, 43). Weight gain during the menopausal transition has been associated with increased risk of chronic disease during adulthood including cardiovascular disease, diabetes, and some cancers (36, 43, 44).

Reproductive characteristics may be a critical contributor to weight change during the menopausal transition. The reproductive period, itself, is associated with energy imbalance, maternal insulin resistance, and fat deposition in the myocardial tissue. While physiologic changes occurring during the reproductive period could be an important contributor to mid-

life weight change, limited epidemiologic data support these hypotheses. Several investigations have been conducted on the association between early menarche, parity and young age at first birth with weight gain in mid-life (23, 33, 35), but these studies have been limited to homogeneous populations of white women, despite accumulating evidence of racial/ethnic disparities with respect to obesity among US women (3, 5). In addition, lactation is also an important reproductive characteristic that influences the metabolism of women (45), but associations with weight gain during the menopausal transition are unknown. Finally, most previous study focused on weight change from adolescence up to the menopausal transition, but few studies have investigated weight change occurring during the menopausal transition period which likely represents the accumulation of visceral fat which is metabolically active and known to more strongly associate with chronic conditions like diabetes and cancer. The aims of this study are therefore to estimate the association between reproductive characteristics (early menarche, age at first birth, parity, and lactation), and weight gain (assessed as absolute changes in BMI or weight) during the menopausal transition, overall, and in strata of race/ethnic groups.

2.2 Methods

2.2.1 Population

Study of Women's Health Across the Nation (SWAN) is a multi-site, prospective, longitudinal study aimed to investigate the health condition of women during the menopausal transition (47). Women included in the SWAN cohort completed baseline data on reproductive factors, physical measures, socioeconomic status and physical conditions

(47). These data are updated annually (47). To maximize heterogeneity of the study population each study site oversampled women of a specific racial or ethnic group (e.g., African-American, Chinese, Hispanic, Japanese and Caucasian) (47). The multiethnic characteristics of the SWAN study population provide a unique opportunity to examine contributors to anthropometric characteristics during the menopausal transition by race/ethnicity. The eligibility criteria for women included in the parent study were aged 42-52 years, with an intact uterus and at least one ovary, not pregnant or breastfeeding, having at least one menstrual period in the previous 3 months, and not using reproductive hormones. A total of 3302 eligible women were enrolled into the longitudinal study population of SWAN and completed the baseline study (1,550 Caucasian, 935 African American, 286 Hispanic, 250 Chinese, and 281 Japanese).

This study is based on data from baseline visit and visit 10. We excluded women who missed visit 10 measurement (n=1063); women who had a hysterectomy or bilateral oophorectomy (n=209); women who were currently pregnant or breastfeeding (n=30); women with hormone therapy or took oral contraceptives within the previous 12 months (n=148); women who were still in pre-menopausal or early menopausal status by visit 10 (n=174); and women who reported cancers other than non-melanoma skin cancer (n=11). Thus, 1560 women remained eligible for this study.

2.2.2 Outcome assessment

The outcomes of interest were changes in body mass index (BMI) and changes in

weight. The changes were defined as the absolute difference in BMI or weight between visit 10 and baseline visit. Discalced weight and height were measured by the study personnel, and BMI was calculated by weight (kilograms) divided by height (meters) squared.

2.2.3 Exposure assessment

The exposures of interests were reproductive factors (menarche age, age at first birth, parity, lactation) and data ascertained via interviewer-administered questionnaire. Lactation was the average months of breastfeeding for each live birth, calculated by dividing the total months of breastfeeding across all reported live-births by the number of live births reported. Categorization of exposure variables was determined a priori and based on classifications in similar investigations: age at menarche (≤ 11 , 12, 13 and ≥ 14 years); age at first birth (≤ 25 , 26-30 and ≥ 31 years); parity (1, 2 and ≥ 3 children); and lactation (0, (0, 3], (3, 6] and >6 months).

2.2.4 Covariate assessment

Covariates for this study included race/ethnicity, age, education, family income, smoking status, alcohol consumption, and physical exercise. All the covariates were divided into several categories based on similar studies and available data. Education was categorized as high school or less, high school, college and post-college. Family income was divided into 4 groups: $< \$19,999$, $\$20,000$ - $\$49,000$, $\$50,000$ - $\$99,000$ and $> \$100,000$. Smoking status was assessed as never smokers, former smokers and current smokers.

Alcohol consumption was categorized as no, one or few drinks per day, and more than one drink per day. Physical exercise categories included less than, the same, and more frequent exercise compared to others.

2.2.5 Statistical methods

Descriptive methods were used to examine demographic and reproductive factor distributions of all women at baseline. Quantitative variables were estimated by mean and standard deviation; frequency and relative frequency were used for categorical ones. Multiple linear regression was performed to estimate the relation between reproductive factor and change in anthropometric characteristics using independent multivariate models for each exposure and of the outcomes of interest (BMI change and weight change). Directed acyclic graph (DAG) analyses were used to select covariates for consideration and backward elimination strategies employed to identify the final model based on a greater than 10% change in the beta estimate. The effect of each exposure was estimated overall, and within strata of race/ethnicity. Likelihood ratio test (a priori $p=0.05$) was used to examine the significance of the interaction between reproductive characteristics and race/ethnicity. Race/ethnicity was included in the overall model if it proved to be a confounder and was eliminated from the model if it was an effect measure modifier.

A letter of IRB exemption with signature was received for this study.

2.3 Results

The mean age at baseline was 46.18 years (standard deviation (SD)=2.65) for the 1560 women in the study. The mean BMI at baseline was 27.86 kg/m² (SD=7.32 kg/m²) and

28.81 kg/m² (SD=16.25 kg/m²) at visit 10. The mean weight at baseline was 74.03 kg (163.21 lb) (SD=21.25 kg [46.85lb]), and 76.38 kg (168.39 lb) (SD=20.78 kg [45.81 lb]) at visit 10. At baseline, 743 (47.63%) were at early peri-menopausal stage and 817 (52.37%) were at pre-menopausal stage; at visit 10 1434 (91.92%) were post-menopausal and 126 (8.08%) were at late peri-menopausal stage. Among the 1560 women, 740 (47.44%) were White non-Hispanic; 477 (30.58%) were African American; 166 (10.64%) were Chinese or Chinese American; 177 (11.35%) were Japanese or Japanese American; no Hispanic women were included in the study. (**Table 1**)

2.3.1 Menarche age

Among all the race/ethnicity groups, women with a menarche age of 12 or 13 were less likely to have an increase in BMI during the menopausal transition period compared to women with a menarche age of ≤ 11 ($\beta = -0.49$, 95% confidence interval (95% CI): (-0.97, -0.01); and $\beta = -0.5$, 95% CI: (-1.00, -0.05), respectively). For women with late menarche (age ≥ 14), no significant difference was observed compared to women with menarche age ≤ 11 . Race/ethnicity modified the relationship between menarche age and BMI change during the menopausal transition ($P=0.0008$). For African American women, a significant difference in BMI change was found between women with a menarche age of ≤ 11 and 12, and the latter group had less increase in BMI during the menopausal transition ($\beta = -1.45$, 95% CI: (-2.48, -0.42)). No other significant results were found for BMI change and menarche age for the other race/ethnicity groups. (Table 2)

A similar pattern was observed for weight change during the same time period. Women with a menarche age of 12 were less likely to gain weight compared with those with a menarche age of ≤ 11 for all race/ethnicity groups ($\beta = -1.42$, 95% CI: (-2.69, -0.14)). Race/ethnicity similarly modified the association between menarche age and weight change ($P < 0.0001$). African American women with a menarche age of 12 were less likely to gain weight compared with the early menarche (age ≤ 11) group ($\beta = -4.11$, 95% CI: (-6.79, -1.44)). Japanese or Japanese American with a menarche age of 13 were less likely to gain weight during the menopausal transition compared with menarche age ≤ 11 ones ($\beta = -2.40$, 95% CI: (-4.47, -0.33)). No other significant results were observed for weight change and menarche age for the other race/ethnic groups. (Table 3)

2.3.2 Parity

While no significant associations were observed among all race/ethnic groups combined, race/ethnicity was found to modify for the relationship between parity and BMI change ($P = 0.0036$). Women with 3 or more were less likely to have an increase in BMI compared with women with no children among Japanese or Japanese Americans ($\beta = -1.33$, 95% CI: (-2.31, -0.35)). Among White non-Hispanic women, women with 2 children had less increase in BMI compared to women with no children ($\beta = -0.74$, 95% CI: (-1.42, -0.06)). No other significant results were found among race groups. (Table 2).

Among all race/ethnicity groups, women with one child or 2 children were less likely to gain weight than women with no child ($\beta = -1.59$, 95% CI: (-3.16, -0.02); $\beta = -1.47$, 95%

CI: (-2.80, -0.14), respectively). Race/ethnicity modified the relationship between parity and weight change ($P=0.0024$). Both Japanese/Japanese American and White non-Hispanic women with more than 3 children has less weight gain compared to women with no children ($\beta= -2.80$, 95% CI: (-5.12, -0.48) and $\beta= -2.14$, 95% CI: (-3.92, -0.37), respectively). (Table 2, Table 3).

2.3.3 Age at first birth

We observed no meaningful associations between age at first birth and change in BMI or weight overall, or in strata of race/ethnic groups. (Table 2, Table 3).

2.3.4 Lactation

While we found no association between lactation and BMI or weight change during menopause transition overall, race/ethnicity did modify the relationship between lactation and BMI change ($P=0.0012$) as well as weight change ($P=0.0201$). Chinese or Chinese American women with lactation of greater than 6 months had less risk of gaining weight compared with those with no breastfeeding ($\beta= -2.08$, 95% CI: (-4.04, -0.12)). White non-Hispanic women were at higher risk of increasing weight with lactation compared with Chinese or Chinese American (Table 2, Table 3).

2.4 Discussion

Our study found that women with a menarche age of 12 or 13 were less likely to gain weight or increase in BMI compared with earlier menarche age among all race and ethnic groups. Additionally, women with 1 or 2 children had less gains in weight compared with women with no children. Overall, we found similar patterns of association for both BMI

and weight change – in addition to finding heterogeneity of the association by race/ethnic groups.

While previous studies have assessed weight or BMI at a single discrete time point during the menopausal transition, few have prospectively assessed changes in anthropometric characteristics which likely represents the accumulation of metabolically active visceral fat, which more strongly associates with chronic conditions like diabetes and cancer. This study examined the change in obesity status during the menopausal transition, and importantly assessed heterogeneity of the association between reproductive characteristics and weight or BMI change among different race/ethnic groups. There is accumulating evidence that declines in estrogen could cause weight gain during menopausal transition through its effects on energy imbalance (reduced energy consumption and increased energy intake) (48-51). Given the reproductive period is closely linked with available estrogen – the main goal of this study was to understand the effect of various reproductive characteristics on weight and BMI change overall, and by race/ethnic subgroups.

Our finding, of an inverse association between age at menarche and BMI/weight gains during the menopausal transition is consistent with one previous publication (34), and disagreement with another, which found no significant association between menarche age and weight gain during midlife (39). It is possible that early menarche subsequently leads to early menopause (52), the physiologic correlates of which lead to reduced lean body

mass and increased fat mass (53).

Our finding of an inverse association between parity and BMI/weight gain are largely inconsistent with the available literature where parity is positively associated with obesity (35, 39, 49). Data show that nulliparous women are more likely to have early natural menopause while increasing parity was linked to later menopause (52). Interestingly, we observed no association for women with 3 or more than 3 children, compared to non-parous women, which could be due to the competing effects of insulin resistance and age at menopause. Insulin resistance is greater in multigravid women than in non-parous women (54-56), and is associated with obesity during menopausal transition (48). However, women with multi-children tend to have late menopause which may offset these insulin-related effects.

Previous studies suggest early age at first birth and no lactation would trigger weight increase after pregnancy and during menopause (35, 56-58). However, among all women, we observed no association. It may be that these two factors only influence anthropometric characteristics immediately after pregnancy and have little impact on weight downstream.

This study, using 10-year longitudinal data from a multiethnic population, has several important strengths including complete assessment of weight and height by trained study personnel, reducing the likelihood of information bias. Moreover, our analyses focused on weight/BMI change during menopausal status, which had seldom assessed and may be biologically more relevant than weight at a single time point. Despite the strengths of this

study, there are important limitations that should be considered. While this study was well-powered to estimate effects overall, we were limitedly able to assess race/ethnic specific effects. Further, although this is the first study to consider potential modification by race/ethnicity, after applying exclusion criteria we were unable to include Hispanics in our analyses.

This study has several important public health implications. Understanding weight/BMI change during the menopausal transition is important because it may lead to reductions in obesity during the critical mid-life period. This results of this study showed that early menarche and nulliparity were risk factors for weight/BMI increase in menopause. Further studies should be conducted to understand the mechanisms underlying these observations. Additional insight could provide more targeted opportunities for education and intervention, and ultimately help to reduce the risk of obesity in midlife.

Table 1. Demographic characteristics for baseline visit (N=1560), Study of Women's Health Across the Nation (SWAN), 1996-2008

Demographic characteristics	Mean \pm SD or N (%)
Age	46.18 \pm 2.65
BMI	27.86 \pm 7.32
Menarche age at visit 0, year	
\leq 11	360 (23.23)
12	412 (26.58)
13	436 (28.13)
\geq 14	342 (22.06)
Age at first birth at visit 0, year	
\leq 22	669 (52.39)
23-28	344 (26.94)
\geq 29	264 (20.67)
Parity at visit 0	
0	282 (18.08)
1	252 (16.15)
2	552 (35.38)
\geq 3	474 (30.38)
Lactation, month	
0	410 (32.18)
(0, 3]	313 (24.57)
(3,6]	216 (16.95)
$>$ 6	335 (26.30)
Race/ Ethnicity	
Black,African American	477 (30.58)
Chinese or Chinese American	166 (10.64)
Japanese or Japanese American	177 (11.35)
Caucasion/White Non-Hispanic	740 (47.44)
Family income at visit 0	
$<$ \$19,999	156 (10.32)
\$20,000 - \$49,999	515 (34.08)
\$50,000 - \$99,999	599 (39.64)
$>$ \$100,000	241 (15.96)
Smoking status at visit 0	
Never	919 (59.99)
Former	377 (24.61)
Current	236 (15.40)

Table 1. Continued

Demographic characteristics	Mean \pm SD or N (%)
Alcohol consumption at visit 0	
No	735 (51.58)
One or fewer drinks/d	656 (46.04)
More than drink/d	34 (2.39)
Frequency of physical activity comparing to others at visit 0	
Less	649 (41.68)
The same	459 (29.48)
More	449 (28.84)

Table 2 Beta estimate for BMI change* from baseline visit to visit 10 associated with reproductive factors, stratified by race/ethnicity

Reproductive factors	race/ethnicity										P-Value
	Overall 1** Beta estimate (95% CI)		Black/African American Beta estimate (95% CI)		Chinese or Chinese American Beta estimate (95% CI)		Japanese or Japanese American Beta estimate (95% CI)		Caucasian/White Non-Hispanic Beta estimate (95% CI)		
	N		N		N		N		N		
Menarche age at visit 0, year											
≤11	275	ref.	94		15		37		129		0.0008
12	330	-0.49 (-0.97, -0.01)	91	-1.45 (-2.48, -0.42)	34	0.19 (-0.73, 1.11)	38	-0.40 (-1.20, 0.39)	167	-0.06 (-0.76, 0.64)	
13	339	-0.53 (-1.00, -0.05)	80	-0.62 (-1.70, 0.47)	40	-0.06 (-0.95, 0.82)	33	-0.69 (-1.51, 0.14)	186	-0.45 (-1.14, 0.24)	
≥14	250	0.05 (-0.46, 0.56)	74	0.00 (-1.12, 1.11)	48	-0.26 (-1.12, 0.61)	26	0.11 (-0.79, 1.00)	102	0.40 (-0.40, 1.20)	
Parity at visit 0											
0	204	ref.	30		21		18		135		0.0036
1	199	-0.53 (-1.14, 0.07)	59	-0.21 (-1.88, 1.46)	19	0.21 (-0.79, 1.21)	21	-0.25 (-1.33, 0.83)	100	-0.63 (-1.44, 0.18)	
2	436	-0.48 (-1.00, 0.04)	104	0.46 (-1.09, 2.00)	72	-0.07 (-0.85, 0.72)	57	-0.34 (-1.26, 0.58)	203	-0.74 (-1.42, -0.06)	
≥3	364	-0.33 (-0.87, 0.21)	151	0.15 (-1.36, 1.65)	25	0.34 (-0.62, 1.29)	38	-1.33 (-2.31, -0.35)	150	-0.21 (-0.94, 0.53)	
Age at first birth at visit 0, year											
≤25	506	ref.	224		36		34		194		0.2367
26-30	272	-0.41 (-0.91, 0.10)	47	-0.17 (-1.32, 0.99)	41	0.03 (-0.70, 0.76)	46	-0.55 (-1.36, 0.27)	138	-0.74 (-1.51, 0.03)	
≥31	221	0.01 (-0.55, 0.57)	26	0.27 (-1.32, 1.87)	39	0.06 (-0.68, 0.80)	36	0.12 (-0.78, 1.02)	120	-0.22 (-1.04, 0.60)	
Lactation, month											
0	314	ref.	156		36		10		112		0.0112
(0, 3]	238	0.06 (-0.48, 0.59)	80	-0.34 (-1.31, 0.63)	31	-0.12 (-0.90, 0.65)	39	0.00 (-1.26, 1.26)	88	0.69 (-0.24, 1.62)	
(3, 6]	173	-0.09 (-0.70, 0.51)	43	-0.66 (-1.95, 0.64)	24	-0.67 (-1.52, 0.17)	24	-0.68 (-1.98, 0.62)	82	0.73 (-0.24, 1.71)	
>6	272	0.08 (-0.47, 0.63)	33	-0.39 (-1.80, 1.01)	25	-0.75 (-1.55, 0.06)	43	0.14 (-1.11, 1.40)	171	0.62 (-0.26, 1.49)	

*

BMI change was defined as the absolute change in BMI, kg/m².

P for race/ethnicity as EMM: Likelihood ration test was used to calculate the P value, based on the model with race/ethnicity and its interaction term with each predictor and the reduced model.

Table 3 Beta estimate for weight change* from baseline visit to visit 10 associated with reproductive factors, stratified by race/ethnicity

Reproductive factors	race/ethnicity										P – Value
	Overall 1**		Black/African American		Chinese or Chinese American		Japanese or Japanese American		Caucasian/White Non-Hispanic		
	N	Beta estimate (95% CI)	N	Beta estimate (95% CI)	N	Beta estimate (95% CI)	N	Beta estimate (95% CI)	N	Beta estimate (95% CI)	
Menarche age at visit 0, year											
<=11	299	ref.	108		15		38		138		<0.0001
12	358	-1.42 (-2.69, -0.14)	103	-4.11 (-6.79, -1.44)	36	-0.57 (-2.93, 1.79)	38	-1.22 (-3.19, 0.74)	181	-0.08 (-1.95, 1.79)	
13	365	-1.22 (-2.51, 0.06)	91	-1.35 (-4.17, 1.46)	42	-0.92 (-3.23, 1.40)	33	-2.40 (-4.47, -0.33)	199	-1.02 (-2.86, 0.83)	
>=14	274	-0.03 (-1.40, 1.35)	87	-0.96 (-3.83, 1.92)	50	-1.12 (-3.41, 1.16)	27	0.16 (-2.00, 2.31)	110	1.10 (-1.03, 3.23)	
Parity at visit 0											
0	224	ref.	36		21		20		148		0.0024
1	211	-1.59 (-3.16, -0.02)	67	-1.72 (-5.88, 2.44)	21	0.79 (-1.56, 3.14)	21	-0.54 (-3.11, 2.03)	102	-1.63 (-3.77, 0.51)	
2	470	-1.47 (-2.80, -0.14)	117	0.37 (-3.45, 4.20)	76	-0.68 (-2.56, 1.20)	57	-0.07 (-2.25, 2.10)	220	-2.14 (-3.92, -0.37)	
>=3	400	-0.57 (-1.94, 0.79)	175	0.46 (-3.20, 4.12)	25	0.54 (-1.78, 2.85)	38	-2.80 (-5.12, -0.48)	162	-0.36 (-2.25, 1.53)	
Age at first birth at visit 0, year											
<=25	558	ref.	275		37		34		212		0.2733
26-30	294	-1.09 (-2.40, 0.23)	54	-1.04 (-4.04, 1.97)	46	0.04 (-1.74, 1.82)	46	-1.45 (-3.45, 0.55)	148	-1.66 (-3.63, 0.30)	
>=31	228	0.21 (0.75, 1.69)	30	1.23 (-2.78, 5.25)	39	0.18 (-1.69, 2.06)	36	0.39 (-1.81, 2.59)	123	-0.36 (-2.49, 1.76)	
Lactation, month											
0	349	ref.	185		37		10		117		0.0201
(0, 3]	253	0.52 (-0.87, 1.92)	85	-0.34 (-2.92, 2.24)	32	-0.38 (-2.31, 1.55)	39	0.07 (-3.03, 3.17)	97	1.98 (-0.40, 4.37)	
(3, 6]	184	0.19 (-1.40, 1.77)	49	-0.62 (-3.95, 2.72)	24	-1.70 (-3.84, 0.44)	24	-1.59 (-4.80, 1.62)	87	1.84 (-0.68, 4.36)	
>6	292	0.49 (-0.95, 1.92)	37	0.77 (-2.93, 4.47)	29	-2.08 (-4.04, -0.12)	43	0.24 (-2.84, 3.33)	183	1.36 (-0.90, 3.62)	

* Weight change was defined as the absolute change in weight, kg.

Likelihood ration test was used to calculate the P value, based on the model with race/ethnicity and its interaction term with each predictor and the reduced model.

CHAPTER 3. FUTURE DIRECTIONS

3.1 Conclusion

This study estimated the association between reproductive factors and weight/BMI change during menopausal transition. The reproductive factors examined in the study were menarche age, parity, age at first birth and lactation. We found that later age at menarche (e.g. age 12 or 13) was associated with reduced likelihood of weight gain or augmented BMI. Women with 1 or 2 children had less gain in weight or BMI compared with women with no children. For associations between menarche age, parity, and lactation, we found evidence of heterogeneity by race in both BMI and weight change models.

3.2 Public Health Implications

This study has several important public health implications. First, understanding weight/BMI change during the menopausal transition is important because it may lead to reductions in obesity during the critical mid-life period. While previous studies have assessed weight or BMI at a single discrete time point during the menopausal transition, few have prospectively assessed changes in anthropometric characteristics. Changes during this time likely represents the accumulation of visceral fat which is metabolically active and known to more strongly associate with chronic conditions like diabetes and cancer. This study examined the change in obesity status during the menopausal transition, and importantly assessed heterogeneity of the association between reproductive characteristics and weight or BMI change among different race/ethnic groups. We found that early menarche and nulliparity were risk factors for weight/BMI increase in menopause. These risk groups could be targeted for lifestyle intervention.

Additionally the increasing prevalence of obesity in the United States underscores the urgency in developing interventions to prevent weight gain during menopausal transition (4), and chronic conditions such as cancer, diabetes, and CHD (15, 16, 21). Investigating risk factors for weight/BMI gain during midlife may help identify mechanisms, beyond energy imbalance, that contribute to excess weight gain and could be targeted for biological or pharmacologic intervention. In the long term, this may decrease the prevalence of obesity-related chronic conditions.

3.3 Future Directions

First, to improve assessment of racial heterogeneity future studies with larger sample size are needed. For example, almost all of the sample sizes for Chinese or Chinese American and Japanese or Japanese American are less than 50. This led to unstable estimates with wide, imprecise, confidence intervals. Additionally, we had insufficient numbers of non-Hispanic women to estimate effects in this demographic group. Thus, future investigations in this group are warranted.

Second, future study can incorporate early life characteristics like birth weight and childhood obesity status into the study of the association between menarche age and weight/BMI change during menopausal transition. Previous studies had revealed that childhood obesity could trigger early menarche and early sexual maturation through hormone mechanism (59-61). Future analyses on the relation between menarche age and weight/BMI change during menopause stratified on early life characteristics should be conducted. The result will provide further findings on the hormone mechanism for puberty

and obesity in menopause.

Future analysis may also focus on abdominal obesity and body composition, as well as incorporate the use of circulating biomarkers (e.g. sex- and metabolic-hormone levels). In this study, we only conducted analyses on general obesity but not abdominal obesity or body composition. Thus, no findings on the change in body fat distribution or body fat could be concluded from this work. Some studies have demonstrated several reproductive factors, such as early menarche, multi-parity and early motherhood, were potential factors that might trigger abdominal and general obesity in women's life (62-65). However, no previous study has examined the changes in abdominal obesity status or body fat composition during menopausal transition which could be critical for a better understanding of the mechanism underlying the observed associations. In parallel, future studies may consider obtaining data on hormone levels during menarche, childbearing, time after birth, lactation and menopausal transition. It is well-established that changes in weight corresponds with levels of the sex hormones estrogen, androgen, and availability of sex-hormone binding globulin, particularly late in the postmenopausal transition (51). Moreover, hormonal changes during menopausal transition may trigger weight gain through its influence on metabolism (50, 51). Supplementing risk factor data with biomarker data may help clarify the causal pathway between reproductive characteristics and weight change during menopausal transition.

References:

1. Rippe JM, Crossley S, Ringer R. Obesity as a chronic disease: modern medical and lifestyle management. *J Am Diet Assoc* 1998;98(10 Suppl 2):S9-15.
2. F CD, C MD, O CL. Prevalence of Overweight, Obesity, and Extreme Obesity Among Adults: United States, 1960–1962 Through 2011–2012. *Division of Health and Nutrition Examination Surveys* 2014(2).
3. Gordon-Larsen P, Adair LS, Popkin BM. The relationship of ethnicity, socioeconomic factors, and overweight in US adolescents. *Obes Res* 2003;11(1):121-9.
4. Baskin ML, Ard J, Franklin F, et al. Prevalence of obesity in the United States. *Obes Rev* 2005;6(1):5-7.
5. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev* 2007;29:6-28.
6. McTigue K, Larson JC, Valoski A, et al. Mortality and cardiac and vascular outcomes in extremely obese women. *JAMA* 2006;296(1):79-86.
7. Adams KF, Schatzkin A, Harris TB, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med* 2006;355(8):763-78.
8. Calle EE, Thun MJ, Petrelli JM, et al. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999;341(15):1097-105.
9. Verma S, Hussain ME. Obesity and diabetes: An update. *Diabetes Metab Syndr* 2016.
10. Pereira SS, Alvarez-Leite JI. Low-Grade Inflammation, Obesity, and Diabetes. *Curr Obes Rep* 2014;3(4):422-31.
11. Hossain P, Kowar B, El Nahas M. Obesity and diabetes in the developing world--a growing challenge. *N Engl J Med* 2007;356(3):213-5.
12. Felber JP, Golay A. Pathways from obesity to diabetes. *Int J Obes Relat Metab Disord* 2002;26 Suppl 2:S39-45.
13. Abdullah A, Peeters A, de Courten M, et al. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. *Diabetes Res Clin Pract* 2010;89(3):309-19.
14. Ford ES, Williamson DF, Liu S. Weight change and diabetes incidence: findings from a national cohort of US adults. *Am J Epidemiol* 1997;146(3):214-22.
15. Bergstrom A, Pisani P, Tenet V, et al. Overweight as an avoidable cause of cancer in Europe. *Int J Cancer* 2001;91(3):421-30.
16. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. *Public Health* 2015;129(7):872-80.
17. Key TJ, Appleby PN, Reeves GK, et al. Body mass index, serum sex hormones, and breast cancer risk in postmenopausal women. *J Natl Cancer Inst* 2003;95(16):1218-26.
18. Pan SY, DesMeules M, Morrison H, et al. Obesity, high energy intake, lack of

- physical activity, and the risk of kidney cancer. *Cancer Epidemiol Biomarkers Prev* 2006;15(12):2453-60.
19. Schouten LJ, Goldbohm RA, van den Brandt PA. Anthropometry, physical activity, and endometrial cancer risk: results from the Netherlands Cohort Study. *J Natl Cancer Inst* 2004;96(21):1635-8.
 20. Bogers RP, Bemelmans WJ, Hoogenveen RT, et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. *Arch Intern Med* 2007;167(16):1720-8.
 21. Flint AJ, Hu FB, Glynn RJ, et al. Excess weight and the risk of incident coronary heart disease among men and women. *Obesity (Silver Spring)* 2010;18(2):377-83.
 22. Lovejoy JC, Champagne CM, de Jonge L, et al. Increased visceral fat and decreased energy expenditure during the menopausal transition. *Int J Obes (Lond)* 2008;32(6):949-58.
 23. Kirchengast S, Gruber D, Sator M, et al. Postmenopausal weight status, body composition and body fat distribution in relation to parameters of menstrual and reproductive history. *Maturitas* 1999;33(2):117-26.
 24. Choi J, Guiterrez Y, Gilliss C, et al. Physical activity, weight, and waist circumference in midlife women. *Health Care Women Int* 2012;33(12):1086-95.
 25. Cohn SH, Vaswani A, Zanzi I, et al. Changes in body chemical composition with age measured by total-body neutron activation. *Metabolism* 1976;25(1):85-95.
 26. Toth MJ, Tchernof A, Sites CK, et al. Effect of menopausal status on body composition and abdominal fat distribution. *Int J Obes Relat Metab Disord* 2000;24(2):226-31.
 27. Blaine B. Does depression cause obesity?: A meta-analysis of longitudinal studies of depression and weight control. *J Health Psychol* 2008;13(8):1190-7.
 28. Sammel MD, Grisso JA, Freeman EW, et al. Weight gain among women in the late reproductive years. *Fam Pract* 2003;20(4):401-9.
 29. Pimenta F, Maroco J, Ramos C, et al. Predictors of weight variation and weight gain in peri- and post-menopausal women. *J Health Psychol* 2014;19(8):993-1002.
 30. Terry MB, Ferris JS, Tehranifar P, et al. Birth weight, postnatal growth, and age at menarche. *Am J Epidemiol* 2009;170(1):72-9.
 31. Davidson LE, Tucker L, Peterson T. Physical activity changes predict abdominal fat change in midlife women. *J Phys Act Health* 2010;7(3):316-22.
 32. Theodoro H, Rodrigues AD, Mendes KG, et al. Reproductive characteristics and obesity in middle-aged women seen at an outpatient clinic in southern Brazil. *Menopause* 2012;19(9):1022-8.
 33. Lahmann PH, Lissner L, Gullberg B, et al. Sociodemographic factors associated with long-term weight gain, current body fatness and central adiposity in Swedish women. *Int J Obes Relat Metab Disord* 2000;24(6):685-94.
 34. Nagata C, Takatsuka N, Kawakami N, et al. Weight change in relation to natural

- menopause and other reproductive and behavioral factors in Japanese women. *Ann Epidemiol* 2002;12(4):237-41.
35. Wen W, Gao YT, Shu XO, et al. Sociodemographic, behavioral, and reproductive factors associated with weight gain in Chinese women. *Int J Obes Relat Metab Disord* 2003;27(8):933-40.
 36. Williams LT, Hollis JL, Collins CE, et al. The 40-Something randomized controlled trial to prevent weight gain in mid-age women. *BMC Public Health* 2013;13:1007.
 37. Trikudanathan S, Pedley A, Massaro JM, et al. Association of female reproductive factors with body composition: the Framingham Heart Study. *J Clin Endocrinol Metab* 2013;98(1):236-44.
 38. Bralic I, Tahirovic H, Matanic D, et al. Association of early menarche age and overweight/obesity. *J Pediatr Endocrinol Metab* 2012;25(1-2):57-62.
 39. Bjorkelund C, Lissner L, Andersson S, et al. Reproductive history in relation to relative weight and fat distribution. *Int J Obes Relat Metab Disord* 1996;20(3):213-9.
 40. Rooney BL, Schauburger CW. Excess pregnancy weight gain and long-term obesity: one decade later. *Obstet Gynecol* 2002;100(2):245-52.
 41. Hilson JA, Rasmussen KM, Kjolhede CL. Excessive weight gain during pregnancy is associated with earlier termination of breast-feeding among White women. *J Nutr* 2006;136(1):140-6.
 42. Dewey KG, Heinig MJ, Nommsen LA. Maternal weight-loss patterns during prolonged lactation. *Am J Clin Nutr* 1993;58(2):162-6.
 43. Wildman RP, Sowers MR. Adiposity and the menopausal transition. *Obstet Gynecol Clin North Am* 2011;38(3):441-54.
 44. Al-Safi ZA, Polotsky AJ. Obesity and menopause. *Best Pract Res Clin Obstet Gynaecol* 2015;29(4):548-53.
 45. Brumley J, Cain MA, Stern M, et al. Gestational Weight Gain and Breastfeeding Outcomes in Group Prenatal Care. *J Midwifery Womens Health* 2016.
 46. Wolfe WS, Sobal J, Olson CM, et al. Parity-associated body weight: modification by sociodemographic and behavioral factors. *Obes Res* 1997;5(2):131-41.
 47. Crawford S, Morganstein D, Neer R, et al. SWAN: A Multicenter, Multiethnic, Community- Based Cohort Study of Women and the Menopausal Transition. 2000.
 48. Davis S, Castelo-Branco C, Chedraui P, et al. Understanding weight gain at menopause. *Climacteric* 2012;15(5):419-29.
 49. Theodoro H, Rodrigues AD, Mendes KG, et al. Reproductive characteristics and obesity in middle-aged women seen at an outpatient clinic in southern Brazil. *Menopause* 2012;19(9):1022-8.
 50. Burger HG, Dudley EC, Robertson DM, et al. Hormonal changes in the menopause transition. *Recent Prog Horm Res* 2002;57:257-75.
 51. Lovejoy JC. The influence of sex hormones on obesity across the female life span.

- J Womens Health* 1998;7(10):1247-56.
52. Cramer DW, Xu H. Predicting age at menopause. *Maturitas* 1996;23(3):319-26.
 53. Jung SY, Vitolins MZ, Fenton J, et al. Risk profiles for weight gain among postmenopausal women: a classification and regression tree analysis approach. *PloS one* 2015;10(3):e0121430.
 54. Bastian LA, West NA, Corcoran C, et al. Number of children and the risk of obesity in older women. *Preventive medicine* 2005;40(1):99-104.
 55. Weng HH, Bastian LA, Taylor Jr DH, et al. Number of children associated with obesity in middle-aged women and men: results from the Health and Retirement Study. *Journal of Women's Health* 2004;13(1):85-91.
 56. Janney CA, Zhang D, Sowers M. Lactation and weight retention. *Am J Clin Nutr* 1997;66(5):1116-24.
 57. Dewey KG, Heinig MJ, Nommsen LA. Maternal weight-loss patterns during prolonged lactation. *The American Journal of Clinical Nutrition* 1993;58(2):162-6.
 58. Bobrow K, Quigley MA, Green J, et al. Persistent effects of women's parity and breastfeeding patterns on their body mass index: results from the Million Women Study. *International journal of obesity* 2013;37(5):712-7.
 59. Euling SY, Herman-Giddens ME, Lee PA, et al. Examination of US puberty-timing data from 1940 to 1994 for secular trends: panel findings. *Pediatrics* 2008;121 Suppl 3:S172-91.
 60. Ahmed ML, Ong KK, Dunger DB. Childhood obesity and the timing of puberty. *Trends Endocrinol Metab* 2009;20(5):237-42.
 61. Davison KK, Susman EJ, Birch LL. Percent body fat at age 5 predicts earlier pubertal development among girls at age 9. *Pediatrics* 2003;111(4):815-21.
 62. Blaudeau TE, Hunter GR, Sirikul B. Intra-abdominal adipose tissue deposition and parity. *Int J Obes (Lond)* 2006;30(7):1119-24.
 63. Gunderson EP, Sternfeld B, Wellons MF, et al. Childbearing may increase visceral adipose tissue independent of overall increase in body fat. *Obesity* 2008;16(5):1078-84.
 64. Olinto MT, Costa JS, Kac G, et al. [Abdominal obesity epidemiology amongst adult women resident in Southern Brazil]. *Arch Latinoam Nutr* 2007;57(4):349-56.
 65. Thurston RC, Sowers MR, Sternfeld B, et al. Gains in body fat and vasomotor symptom reporting over the menopausal transition: the study of women's health across the nation. *Am J Epidemiol* 2009;170(6):766-74.

Appendix 1. DAG and Pathways

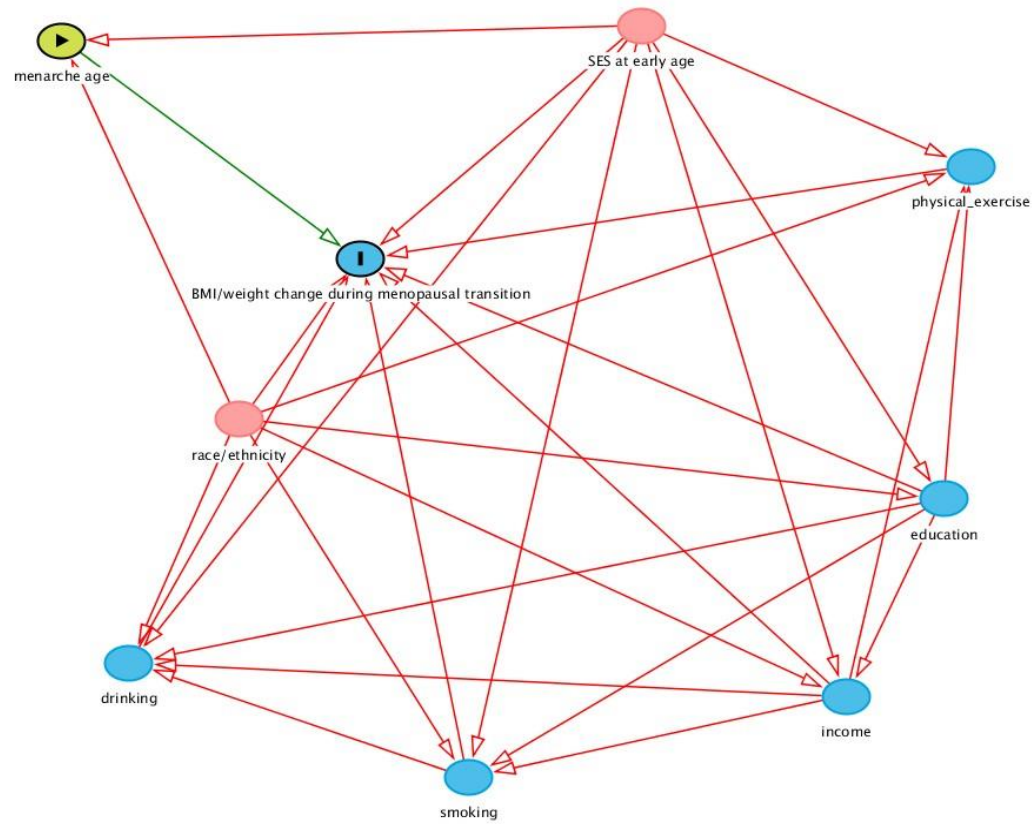


Figure 1. The DAG for menarche age and BMI/weight change during menopausal transition
Income, education, physical exercise, drinking and smoking are data collected during the early-stage of menopausal transition.

Table 1. Pathways for menarche age and BMI/weight change during menopausal transition.

No.	Pathways
1	Menarche age->weight/BMI change during menopausal transition
2	Menarche age->SES at early age->weight/BMI change during menopausal transition
3	Menarche age->race/ethnicity->weight/BMI change during menopausal transition
4	Menarche age->SES at early age->smoking->weight/BMI change during menopausal transition
5	Menarche age->SES at early age->drinking->weight/BMI change during menopausal transition
6	Menarche age->SES at early age->physical exercise->weight/BMI change during menopausal transition
7	Menarche age->SES at early age->education->weight/BMI change during menopausal transition
8	Menarche age->SES at early age->income->weight/BMI change during menopausal transition
9	Menarche age->race/ethnicity-> SES at early age->weight/BMI change during menopausal transition
10	Menarche age->race/ethnicity->smoking->weight/BMI change during menopausal transition
11	Menarche age->race/ethnicity->drinking->weight/BMI change during menopausal transition
12	Menarche age->race/ethnicity->physical exercise->weight/BMI change during menopausal transition
13	Menarche age->race/ethnicity->education->weight/BMI change during menopausal transition
14	Menarche age->race/ethnicity->income->weight/BMI change during menopausal transition
15	Menarche age->race/ethnicity-> SES at early age->smoking->weight/BMI change during menopausal transition
16	Menarche age->race/ethnicity-> SES at early age->drinking->weight/BMI change during menopausal transition
17	Menarche age->race/ethnicity->SES at early age->physical exercise->weight/BMI change during menopausal transition
18	Menarche age->race/ethnicity->SES at early age->education->weight/BMI change during menopausal transition
19	Menarche age->race/ethnicity->SES at early age->income->weight/BMI change during menopausal transition
20	Menarche age->SES at early age->smoking->drinking->weight/BMI change during menopausal transition
21	Menarche age->race/ethnicity->SES at early age->smoking->drinking->weight/BMI change during menopausal transition
22	Menarche age->race/ethnicity->smoking->drinking->weight/BMI change during menopausal transition
23	Menarche age->race/ethnicity->income->drinking->weight/BMI change during menopausal transition
24	Menarche age->race/ethnicity->income->smoking->weight/BMI change during menopausal transition
25	Menarche age->race/ethnicity->income->physical exercise->weight/BMI change during menopausal transition
26	Menarche age->SES at early age->income->drinking->weight/BMI change during menopausal transition
27	Menarche age->SES at early age->income->smoking->weight/BMI change during menopausal transition
28	Menarche age->SES at early age->income->physical exercise->weight/BMI change during menopausal transition
29	Menarche age->race/ethnicity->SES at early age->income->drinking->weight/BMI change during menopausal transition
30	Menarche age->race/ethnicity->SES at early age->income->smoking->weight/BMI change during menopausal transition
31	Menarche age->race/ethnicity->SES at early age->income->physical exercise->weight/BMI change during menopausal transition

Table 1. Continued

No.	Pathways
32	Menarche age->race/ethnicity ->income->smoking->drinking->weight/BMI change during menopausal transition
33	Menarche age-> SES at early age->income->smoking->drinking->weight/BMI change during menopausal transition
34	Menarche age->race/ethnicity->SES at early age->income->smoking->drinking->weight/BMI change during menopausal transition
35	Menarche age->race/ethnicity->education->drinking->weight/BMI change during menopausal transition
36	Menarche age->race/ethnicity->education->smoking->weight/BMI change during menopausal transition
37	Menarche age->race/ethnicity->education->physical exercise->weight/BMI change during menopausal transition
38	Menarche age->SES at early age->education->drinking->weight/BMI change during menopausal transition
39	Menarche age->SES at early age->education->smoking->weight/BMI change during menopausal transition
40	Menarche age->SES at early age->education->physical exercise->weight/BMI change during menopausal transition
41	Menarche age->race/ethnicity->SES at early age->education->drinking->weight/BMI change during menopausal transition
42	Menarche age->race/ethnicity->SES at early age->education->smoking->weight/BMI change during menopausal transition
43	Menarche age->race/ethnicity->SES at early age->education->physical exercise->weight/BMI change during menopausal transition
44	Menarche age->race/ethnicity ->education->smoking->drinking->weight/BMI change during menopausal transition
45	Menarche age-> SES at early age->education->smoking->drinking->weight/BMI change during menopausal transition
46	Menarche age->race/ethnicity->SES at early age->income->smoking->drinking->weight/BMI change during menopausal transition
47	Menarche age->race/ethnicity->education->income->drinking->weight/BMI change during menopausal transition
48	Menarche age->race/ethnicity->education->income->smoking->weight/BMI change during menopausal transition
49	Menarche age->race/ethnicity->education->income->physical exercise->weight/BMI change during menopausal transition
50	Menarche age->SES at early age->education->income->drinking->weight/BMI change during menopausal transition
51	Menarche age->SES at early age->education->income->smoking->weight/BMI change during menopausal transition
52	Menarche age->SES at early age->education->income->physical exercise->weight/BMI change during menopausal transition
53	Menarche age->race/ethnicity->SES at early age->education->income->drinking->weight/BMI change during menopausal transition
54	Menarche age->race/ethnicity->SES at early age->education->income->smoking->weight/BMI change during menopausal transition
55	Menarche age->race/ethnicity->SES at early age->education->income->physical exercise->weight/BMI change during menopausal transition
56	Menarche age->race/ethnicity ->education->income->smoking->drinking->weight/BMI change during menopausal transition

Table 1. Continued

No.	Pathways
57	Menarche age-> SES at early age->education->income->smoking->drinking->weight/BMI change during menopausal transition
58	Menarche age->race/ethnicity->SES at early age->income->smoking->drinking->weight/BMI change during menopausal transition

minimally sufficient adjustment set: {race/ethnicity, income, education, physical exercise, drinking, smoking}

Model: BMI/weight change at menopausal transition=menarche age + race/ethnicity + income + education + physical exercise + drinking + smoking + age

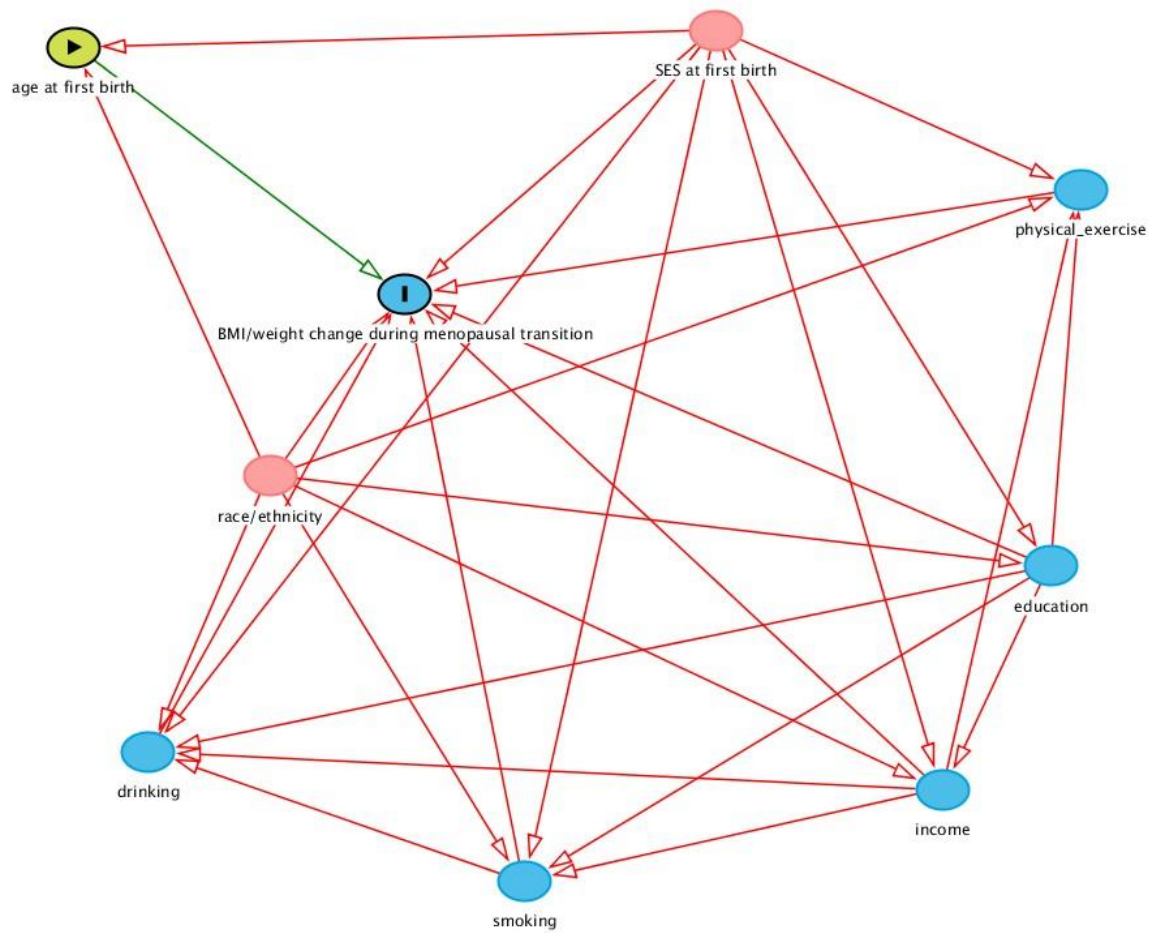


Figure 2. The DAG for age at first birth and BMI/weight change during menopausal transition
 Income, education, physical exercise, drinking and smoking are data collected during the early-stage of menopausal transition.

Table 2. Pathways for age at first birth and BMI/weight change during menopausal transition.

No.	Pathways
1	Age at first birth->weight/BMI change during menopausal transition
2	Age at first birth->SES at first birth->weight/BMI change during menopausal transition
3	Age at first birth->race/ethnicity->weight/BMI change during menopausal transition
4	Age at first birth->SES at first birth->smoking->weight/BMI change during menopausal transition
5	Age at first birth->SES at first birth->drinking->weight/BMI change during menopausal transition
6	Age at first birth->SES at first birth->physical exercise->weight/BMI change during menopausal transition
7	Age at first birth->SES at first birth->education->weight/BMI change during menopausal transition
8	Age at first birth->SES at first birth->income->weight/BMI change during menopausal transition
9	Age at first birth->race/ethnicity-> SES at first birth->weight/BMI change during menopausal transition
10	Age at first birth->race/ethnicity->smoking->weight/BMI change during menopausal transition
11	Age at first birth->race/ethnicity->drinking->weight/BMI change during menopausal transition
12	Age at first birth->race/ethnicity->physical exercise->weight/BMI change during menopausal transition
13	Age at first birth->race/ethnicity->education->weight/BMI change during menopausal transition
14	Age at first birth->race/ethnicity->income->weight/BMI change during menopausal transition
15	Age at first birth->race/ethnicity-> SES at first birth->smoking->weight/BMI change during menopausal transition
16	Age at first birth->race/ethnicity-> SES at first birth->drinking->weight/BMI change during menopausal transition
17	Age at first birth->race/ethnicity->SES at first birth->physical exercise->weight/BMI change during menopausal transition
18	Age at first birth->race/ethnicity->SES at first birth->education->weight/BMI change during menopausal transition
19	Age at first birth->race/ethnicity->SES at first birth->income->weight/BMI change during menopausal transition
20	Age at first birth->SES at first birth->smoking->drinking->weight/BMI change during menopausal transition
21	Age at first birth->race/ethnicity->SES at first birth->smoking->drinking->weight/BMI change during menopausal transition
22	Age at first birth->race/ethnicity->smoking->drinking->weight/BMI change during menopausal transition
23	Age at first birth->race/ethnicity->income->drinking->weight/BMI change during menopausal transition
24	Age at first birth->race/ethnicity->income->smoking->weight/BMI change during menopausal transition
25	Age at first birth->race/ethnicity->income->physical exercise->weight/BMI change during menopausal transition
26	Age at first birth->SES at first birth->income->drinking->weight/BMI change during menopausal transition
27	Age at first birth->SES at first birth->income->smoking->weight/BMI change during menopausal transition
28	Age at first birth->SES at first birth->income->physical exercise->weight/BMI change during menopausal transition
29	Age at first birth->race/ethnicity->SES at first birth->income->drinking->weight/BMI change during menopausal transition
30	Age at first birth->race/ethnicity->SES at first birth->income->smoking->weight/BMI change during menopausal transition
31	Age at first birth->race/ethnicity->SES at first birth->income->physical exercise->weight/BMI change during menopausal transition

Table 2. Continued

No.	Pathways
32	Age at first birth->race/ethnicity ->income->smoking->drinking->weight/BMI change during menopausal transition
33	Age at first birth-> SES at first birth->income->smoking->drinking->weight/BMI change during menopausal transition
34	Age at first birth->race/ethnicity->SES at first birth->income->smoking->drinking->weight/BMI change during menopausal transition
35	Age at first birth->race/ethnicity->education->drinking->weight/BMI change during menopausal transition
36	Age at first birth->race/ethnicity->education->smoking->weight/BMI change during menopausal transition
37	Age at first birth->race/ethnicity->education->physical exercise->weight/BMI change during menopausal transition
38	Age at first birth->SES at first birth->education->drinking->weight/BMI change during menopausal transition
39	Age at first birth->SES at first birth->education->smoking->weight/BMI change during menopausal transition
40	Age at first birth->SES at first birth->education->physical exercise->weight/BMI change during menopausal transition
41	Age at first birth->race/ethnicity->SES at first birth->education->drinking->weight/BMI change during menopausal transition
42	Age at first birth->race/ethnicity->SES at first birth->education->smoking->weight/BMI change during menopausal transition
43	Age at first birth->race/ethnicity->SES at first birth->education->physical exercise->weight/BMI change during menopausal transition
44	Age at first birth->race/ethnicity ->education->smoking->drinking->weight/BMI change during menopausal transition
45	Age at first birth-> SES at first birth->education->smoking->drinking->weight/BMI change during menopausal transition
46	Age at first birth->race/ethnicity->SES at first birth->income->smoking->drinking->weight/BMI change during menopausal transition
47	Age at first birth->race/ethnicity->education->income->drinking->weight/BMI change during menopausal transition
48	Age at first birth->race/ethnicity->education->income->smoking->weight/BMI change during menopausal transition
49	Age at first birth->race/ethnicity->education->income->physical exercise->weight/BMI change during menopausal transition
50	Age at first birth->SES at first birth->education->income->drinking->weight/BMI change during menopausal transition
51	Age at first birth->SES at first birth->education->income->smoking->weight/BMI change during menopausal transition
52	Age at first birth->SES at first birth->education->income->physical exercise->weight/BMI change during menopausal transition
53	Age at first birth->race/ethnicity->SES at first birth->education->income->drinking->weight/BMI change during menopausal transition
54	Age at first birth->race/ethnicity->SES at first birth->education->income->smoking->weight/BMI change during menopausal transition
55	Age at first birth->race/ethnicity->SES at first birth->education->income->physical exercise->weight/BMI change during menopausal transition
56	Age at first birth->race/ethnicity ->education->income->smoking->drinking->weight/BMI change during menopausal transition

Table 2. Continued

No.	Pathways
57	Age at first birth-> SES at first birth->education->income->smoking->drinking->weight/BMI change during menopausal transition
58	Age at first birth->race/ethnicity->SES at first birth->income->smoking->drinking->weight/BMI change during menopausal transition

Minimally sufficient adjustment set: {race/ethnicity, income, education, physical exercise, drinking, smoking}

Model: BMI/weight change at menopausal transition=age at first birth + race/ethnicity + income + education + physical exercise + drinking + smoking + age

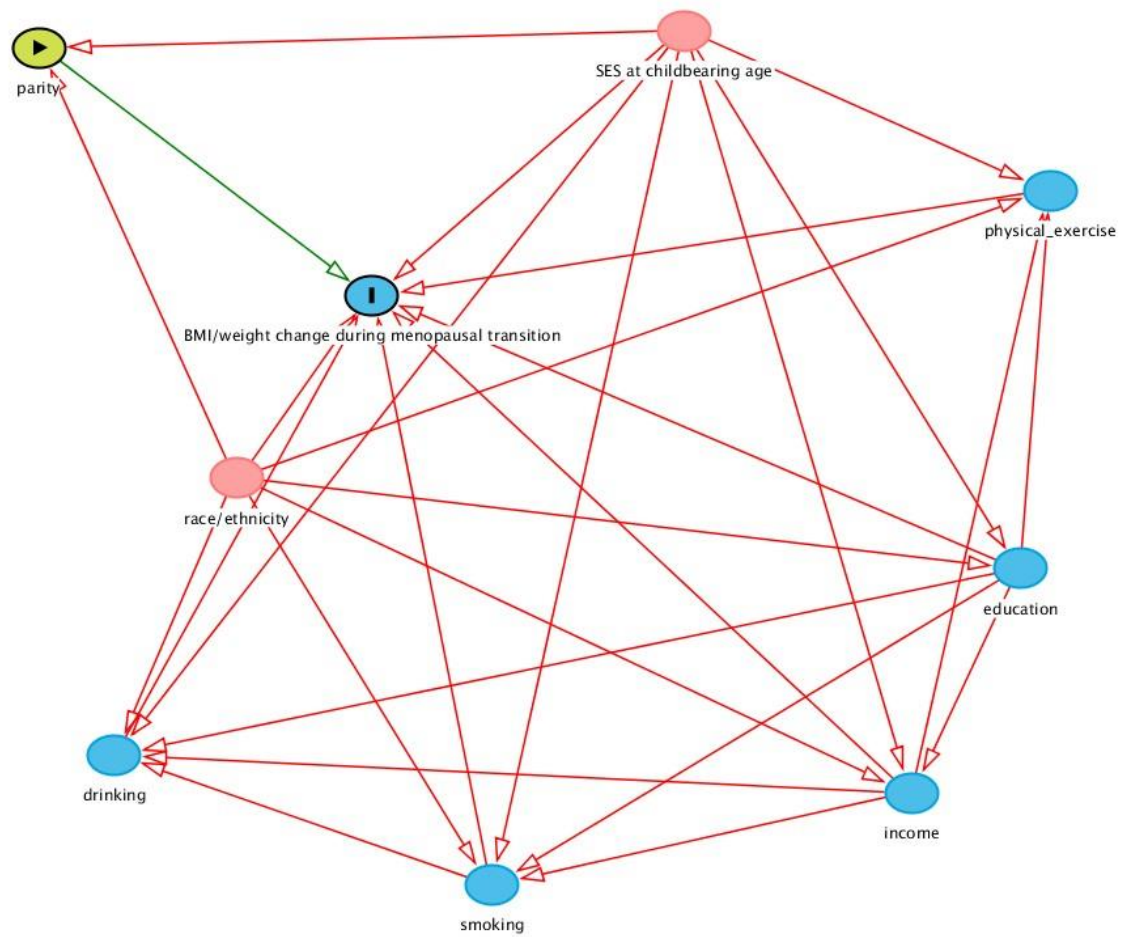


Figure 3. The DAG for parity and BMI/weight change during menopausal transition
 Income, education, physical exercise, drinking and smoking are data collected during the early-stage of menopausal transition.

Table 3. Pathways for parity and BMI/weight change during menopausal transition.

No.	Pathways
1	Parity->weight/BMI change during menopausal transition
2	Parity->SES at childbearing age->weight/BMI change during menopausal transition
3	Parity->race/ethnicity->weight/BMI change during menopausal transition
4	Parity->SES at childbearing age->smoking->weight/BMI change during menopausal transition
5	Parity->SES at childbearing age->drinking->weight/BMI change during menopausal transition
6	Parity->SES at childbearing age->physical exercise->weight/BMI change during menopausal transition
7	Parity->SES at childbearing age->education->weight/BMI change during menopausal transition
8	Parity->SES at childbearing age->income->weight/BMI change during menopausal transition
9	Parity->race/ethnicity->SES at childbearing age->weight/BMI change during menopausal transition
10	Parity->race/ethnicity->smoking->weight/BMI change during menopausal transition
11	Parity->race/ethnicity->drinking->weight/BMI change during menopausal transition
12	Parity->race/ethnicity->physical exercise->weight/BMI change during menopausal transition
13	Parity->race/ethnicity->education->weight/BMI change during menopausal transition
14	Parity->race/ethnicity->income->weight/BMI change during menopausal transition
15	Parity->race/ethnicity->SES at childbearing age->smoking->weight/BMI change during menopausal transition
16	Parity->race/ethnicity->SES at childbearing age->drinking->weight/BMI change during menopausal transition
17	Parity->race/ethnicity->SES at childbearing age->physical exercise->weight/BMI change during menopausal transition
18	Parity->race/ethnicity->SES at childbearing age->education->weight/BMI change during menopausal transition
19	Parity->race/ethnicity->SES at childbearing age->income->weight/BMI change during menopausal transition
20	Parity->SES at childbearing age->smoking->drinking->weight/BMI change during menopausal transition
21	Parity->race/ethnicity->SES at childbearing age->smoking->drinking->weight/BMI change during menopausal transition
22	Parity->race/ethnicity->smoking->drinking->weight/BMI change during menopausal transition
23	Parity->race/ethnicity->income->drinking->weight/BMI change during menopausal transition
24	Parity->race/ethnicity->income->smoking->weight/BMI change during menopausal transition
25	Parity->race/ethnicity->income->physical exercise->weight/BMI change during menopausal transition
26	Parity->SES at childbearing age->income->drinking->weight/BMI change during menopausal transition
27	Parity->SES at childbearing age->income->smoking->weight/BMI change during menopausal transition
28	Parity->SES at childbearing age->income->physical exercise->weight/BMI change during menopausal transition
29	Parity->race/ethnicity->SES at childbearing age->income->drinking->weight/BMI change during menopausal transition
30	Parity->race/ethnicity->SES at childbearing age->income->smoking->weight/BMI change during menopausal transition
31	Parity->race/ethnicity->SES at childbearing age->income->physical exercise->weight/BMI change during menopausal transition

Table 3. Continued

No.	Pathways
32	Parity->race/ethnicity ->income->smoking->drinking->weight/BMI change during menopausal transition
33	Parity-> SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition
34	Parity->race/ethnicity->SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition
35	Parity->race/ethnicity->education->drinking->weight/BMI change during menopausal transition
36	Parity->race/ethnicity->education->smoking->weight/BMI change during menopausal transition
37	Parity->race/ethnicity->education->physical exercise->weight/BMI change during menopausal transition
38	Parity->SES at childbearing age->education->drinking->weight/BMI change during menopausal transition
39	Parity->SES at childbearing age->education->smoking->weight/BMI change during menopausal transition
40	Parity->SES at childbearing age->education->physical exercise->weight/BMI change during menopausal transition
41	Parity->race/ethnicity->SES at childbearing age->education->drinking->weight/BMI change during menopausal transition
42	Parity->race/ethnicity->SES at childbearing age->education->smoking->weight/BMI change during menopausal transition
43	Parity->race/ethnicity->SES at childbearing age->education->physical exercise->weight/BMI change during menopausal transition
44	Parity->race/ethnicity ->education->smoking->drinking->weight/BMI change during menopausal transition
45	Parity-> SES at childbearing age->education->smoking->drinking->weight/BMI change during menopausal transition
46	Parity->race/ethnicity->SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition
47	Parity->race/ethnicity->education->income->drinking->weight/BMI change during menopausal transition
48	Parity->race/ethnicity->education->income->smoking->weight/BMI change during menopausal transition
49	Parity->race/ethnicity->education->income->physical exercise->weight/BMI change during menopausal transition
50	Parity->SES at childbearing age->education->income->drinking->weight/BMI change during menopausal transition
51	Parity->SES at childbearing age->education->income->smoking->weight/BMI change during menopausal transition
52	Parity->SES at childbearing age->education->income->physical exercise->weight/BMI change during menopausal transition
53	Parity->race/ethnicity->SES at childbearing age->education->income->drinking->weight/BMI change during menopausal transition
54	Parity->race/ethnicity->SES at childbearing age->education->income->smoking->weight/BMI change during menopausal transition
55	Parity->race/ethnicity->SES at childbearing age->education->income->physical exercise->weight/BMI change during menopausal transition
56	Parity->race/ethnicity ->education->income->smoking->drinking->weight/BMI change during menopausal transition

Table 3. Continued

No.	Pathways
57	Parity-> SES at childbearing age->education->income->smoking->drinking->weight/BMI change during menopausal transition
58	Parity->race/ethnicity->SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition

Minimally sufficient adjustment set: {race/ethnicity, income, education, physical exercise, drinking, smoking}

Model: BMI/weight change at menopausal transition=parity + race/ethnicity + income + education + physical exercise + drinking + smoking + age

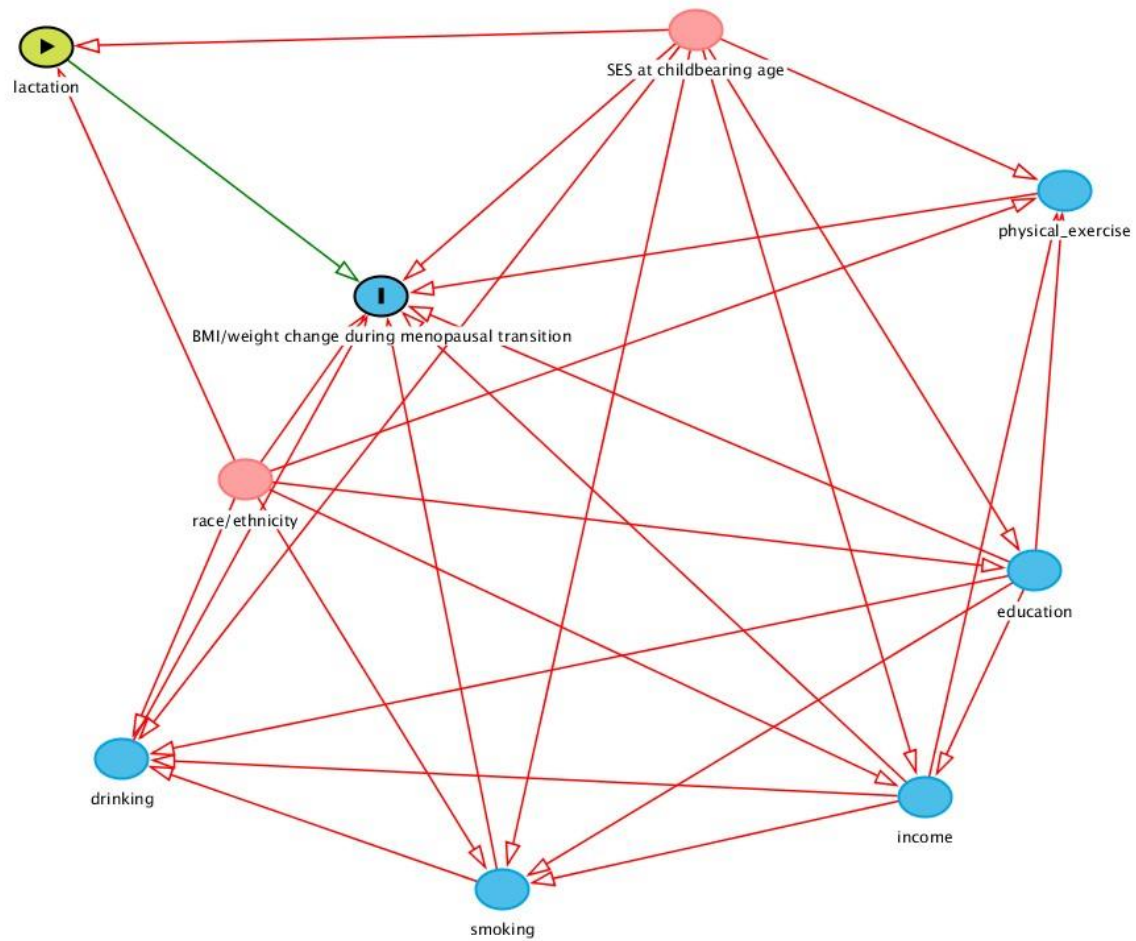


Figure 4. The DAG for lactation and BMI/weight change during menopausal transition
Income, education, physical exercise, drinking and smoking are data collected during the early-stage of menopausal transition.

Table 4. Pathways for lactation and BMI/weight change during menopausal transition.

No.	Pathways
1	Lactation->weight/BMI change during menopausal transition
2	Lactation->SES at childbearing age->weight/BMI change during menopausal transition
3	Lactation->race/ethnicity->weight/BMI change during menopausal transition
4	Lactation->SES at childbearing age->smoking->weight/BMI change during menopausal transition
5	Lactation->SES at childbearing age->drinking->weight/BMI change during menopausal transition
6	Lactation->SES at childbearing age->physical exercise->weight/BMI change during menopausal transition
7	Lactation->SES at childbearing age->education->weight/BMI change during menopausal transition
8	Lactation->SES at childbearing age->income->weight/BMI change during menopausal transition
9	Lactation->race/ethnicity->SES at childbearing age->weight/BMI change during menopausal transition
10	Lactation->race/ethnicity->smoking->weight/BMI change during menopausal transition
11	Lactation->race/ethnicity->drinking->weight/BMI change during menopausal transition
12	Lactation->race/ethnicity->physical exercise->weight/BMI change during menopausal transition
13	Lactation->race/ethnicity->education->weight/BMI change during menopausal transition
14	Lactation->race/ethnicity->income->weight/BMI change during menopausal transition
15	Lactation->race/ethnicity->SES at childbearing age->smoking->weight/BMI change during menopausal transition
16	Lactation->race/ethnicity->SES at childbearing age->drinking->weight/BMI change during menopausal transition
17	Lactation->race/ethnicity->SES at childbearing age->physical exercise->weight/BMI change during menopausal transition
18	Lactation->race/ethnicity->SES at childbearing age->education->weight/BMI change during menopausal transition
19	Lactation->race/ethnicity->SES at childbearing age->income->weight/BMI change during menopausal transition
20	Lactation->SES at childbearing age->smoking->drinking->weight/BMI change during menopausal transition
21	Lactation->race/ethnicity->SES at childbearing age->smoking->drinking->weight/BMI change during menopausal transition
22	Lactation->race/ethnicity->smoking->drinking->weight/BMI change during menopausal transition
23	Lactation->race/ethnicity->income->drinking->weight/BMI change during menopausal transition
24	Lactation->race/ethnicity->income->smoking->weight/BMI change during menopausal transition
25	Lactation->race/ethnicity->income->physical exercise->weight/BMI change during menopausal transition
26	Lactation->SES at childbearing age->income->drinking->weight/BMI change during menopausal transition
27	Lactation->SES at childbearing age->income->smoking->weight/BMI change during menopausal transition
28	Lactation->SES at childbearing age->income->physical exercise->weight/BMI change during menopausal transition
29	Lactation->race/ethnicity->SES at childbearing age->income->drinking->weight/BMI change during menopausal transition
30	Lactation->race/ethnicity->SES at childbearing age->income->smoking->weight/BMI change during menopausal transition

Table 4. Continued

No.	Pathways
31	Lactation->race/ethnicity->SES at childbearing age->income->physical exercise->weight/BMI change during menopausal transition
32	Lactation->race/ethnicity ->income->smoking->drinking->weight/BMI change during menopausal transition
33	Lactation-> SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition
34	Lactation->race/ethnicity->SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition
35	Lactation->race/ethnicity->education->drinking->weight/BMI change during menopausal transition
36	Lactation->race/ethnicity->education->smoking->weight/BMI change during menopausal transition
37	Lactation->race/ethnicity->education->physical exercise->weight/BMI change during menopausal transition
38	Lactation->SES at childbearing age->education->drinking->weight/BMI change during menopausal transition
39	Lactation->SES at childbearing age->education->smoking->weight/BMI change during menopausal transition
40	Lactation->SES at childbearing age->education->physical exercise->weight/BMI change during menopausal transition
41	Lactation->race/ethnicity->SES at childbearing age->education->drinking->weight/BMI change during menopausal transition
42	Lactation->race/ethnicity->SES at childbearing age->education->smoking->weight/BMI change during menopausal transition
43	Lactation->race/ethnicity->SES at childbearing age->education->physical exercise->weight/BMI change during menopausal transition
44	Lactation->race/ethnicity ->education->smoking->drinking->weight/BMI change during menopausal transition
45	Lactation-> SES at childbearing age->education->smoking->drinking->weight/BMI change during menopausal transition
46	Lactation->race/ethnicity->SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition
47	Lactation->race/ethnicity->education->income->drinking->weight/BMI change during menopausal transition
48	Lactation->race/ethnicity->education->income->smoking->weight/BMI change during menopausal transition
49	Lactation->race/ethnicity->education->income->physical exercise->weight/BMI change during menopausal transition
50	Lactation->SES at childbearing age->education->income->drinking->weight/BMI change during menopausal transition
51	Lactation->SES at childbearing age->education->income->smoking->weight/BMI change during menopausal transition
52	Lactation->SES at childbearing age->education->income->physical exercise->weight/BMI change during menopausal transition
53	Lactation->race/ethnicity->SES at childbearing age->education->income->drinking->weight/BMI change during menopausal transition

Table 4. Continued

No.	Pathways
54	Lactation->race/ethnicity->SES at childbearing age->education->income->smoking->weight/BMI change during menopausal transition
55	Lactation->race/ethnicity->SES at childbearing age->education->income->physical exercise->weight/BMI change during menopausal transition
56	Lactation->race/ethnicity ->education->income->smoking->drinking->weight/BMI change during menopausal transition
57	Lactation-> SES at childbearing age->education->income->smoking->drinking->weight/BMI change during menopausal transition
58	Lactation->race/ethnicity->SES at childbearing age->income->smoking->drinking->weight/BMI change during menopausal transition

Minimally sufficient adjustment set: {race/ethnicity, income, education, physical exercise, drinking, smoking}

Model: BMI/weight change at menopausal transition=lactation + race/ethnicity + income + education + physical exercise + drinking + smoking + age

Appendix 2. Backward Elimination for Model Selection

Table 1. Backward elimination for model selection for the association between menarche age and BMI change during menopausal transition

Model		Variables/ Categories	BMI change			
			beta estimate	<10%	<15%	95% CI
Fully adjusted model		menarche age, race, age, education, income, smoking, drinking, physical exercise				
		12	-0.490581		-0.97249	-0.008668
		13	-0.51542		-1.00039	-0.030453
	>=14	0.13329		-0.39288	0.659462	
1- drop age		menarche age, race, education, income, smoking, drinking, physical exercise		NO	NO	
		12	-0.50802		-0.99055	-0.025494
		13	-0.527924		-1.01365	-0.042199
	>=14	0.108315		-0.4183	0.634934	
1- drop education		menarche age, race, age, income, smoking, drinking, physical exercise		YES	YES	
		12	-0.520113		-1.00214	-0.038085
		13	-0.522498		-1.00723	-0.037763
	>=14	0.119904		-0.40587	0.645674	
1- drop income		menarche age, race, age, education, smoking, drinking, physical exercise		YES	YES	
		12	-0.490639		-0.97254	-0.008736
		13	-0.515354		-1.00031	-0.0304
	>=14	0.133185		-0.39296	0.659326	
1- drop smoking		menarche age, race, age, education, income, drinking, physical exercise		YES	YES	
		12	-0.457752		-0.93445	0.01895
		13	-0.506577		-0.98555	-0.0276
	>=14	0.144876		-0.37302	0.662769	

Table 1. Continued

Model	Variables/ Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
1- drop drinking	menarche age, race, age, education, income, smoking, physical exercise		NO	NO	
	12	-0.556478			-1.01436 -0.098596
	13	-0.654708			-1.1093 -0.20012
	>=14	0.022482			-0.47215 0.517117
1-drop physical exercise	menarche age, race, age, education, income, smoking, drinking		NO	NO	
	12	-0.49127			-0.97626 -0.006281
	13	-0.439565			-0.92659 0.047463
	>=14	0.196217			-0.33282 0.725253
1-drop race/ethnicity	menarche age, age, education, income, smoking, drinking, physical exercise		NO	NO	
	12	-0.495188			-0.97722 -0.013153
	13	-0.513518			-0.99742 -0.029615
	>=14	0.071478			-0.45003 0.59298
conclusion: drop income					
2- drop age	menarche age, race, education, smoking, drinking, physical exercise		NO	NO	
	12	-0.507905			-0.99043 -0.02538
	13	-0.528184			-1.01389 -0.042478
	>=14	0.108551			-0.41806 0.635156
2-drop education	menarche age, race, age, smoking, drinking, physical exercise		NO	NO	
	12	-0.520459			-1.0025 -0.038418
	13	-0.522108			-1.00685 -0.037361
	>=14	0.118083			-0.40757 0.643735
2- drop smoking	menarche age, race, age, education, drinking, physical exercise		YES	YES	
	12	-0.457939			-0.93463 0.018747
	13	-0.506445			-0.98542 -0.027475

Table 1. Continued

Model	Variables/ Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
2-drop drinking	>=14	0.144563			-0.37329 0.662412
	menarche age, race, age, education, smoking, physical exercise		NO	NO	
	12	-0.557233			-1.0151 -0.099368
	13	-0.654104			-1.10869 -0.199521
2-drop physical exercise	>=14	0.021142			-0.47342 0.515703
	menarche age, race, age, education, smoking, drinking		NO	NO	
	12	-0.492157			-0.97717 -0.007142
	13	-0.437953			-0.92497 0.049065
2-drop race/ethnicity	>=14	0.195545			-0.33353 0.724618
	menarche age, age, education, smoking, drinking, physical exercise		NO	NO	
	12	-0.495213			-0.97725 -0.013178
	13	-0.513879			-0.99769 -0.03007
	>=14	0.071486			-0.45002 0.592989
conclusion: drop smoking					
3- drop age	menarche age, race, education, drinking, physical exercise		NO	NO	
	12	-0.473521			-0.95084 0.003801
	13	-0.521476			-1.0011 -0.041849
	>=14	0.122086			-0.39626 0.640435
3- drop education	menarche age, race, age, drinking, physical exercise		YES	YES	
	12	-0.487846			-0.96473 -0.010963
	13	-0.514102			-0.9929 -0.035303
	>=14	0.132917			-0.38447 0.650305
3- drop drinking	menarche age, race, age, education, physical exercise		NO	NO	
	12	-0.529455			-0.98206 -0.076849
	13	-0.638138			-1.08678 -0.1895

Table 1. Continued

Model	Variables/ Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
3- drop physical exercise	>=14	0.014951			-0.47074 0.500638
	menarche age, race, age, education, drinking		NO	NO	
	12	-0.455182			-0.93486 0.024495
3-drop race/ethnicity	13	-0.425419			-0.90621 0.055368
	>=14	0.20822			-0.31238 0.728823
	menarche age, age, education, drinking, physical exercise		NO	NO	
	12	-0.464287			-0.94163 0.013052
	13	-0.522056			-0.9995 -0.044614
conclusion: drop education	>=14	0.062125			-0.451 0.575249
	menarche age, race, drinking, physical exercise		NO	NO	
	12	-0.503593			-0.9811 -0.026091
	13	-0.530382			-1.00979 -0.050977
	>=14	0.111176			-0.40673 0.629076
4- drop drinking	menarche age, race, age, physical exercise		NO	NO	
	12	-0.556996			-1.00984 -0.104151
	13	-0.642514			-1.09103 -0.193993
	>=14	0.008681			-0.47652 0.493884
4-drop physical exercise	menarche age, race, age, drinking		NO	NO	
	12	-0.487764			-0.96774 -0.00779
	13	-0.432683			-0.91342 0.048053
	>=14	0.194257			-0.32607 0.71458
4-drop race/ethnicity	menarche age, age, drinking, physical exercise		NO	NO	

Table 1. Continued

Model	Variables/ Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
12		-0.4916			-0.96915 -0.01405
13		-0.526873			-1.00425 -0.049496
>=14		0.048385			-0.46405 0.560823

Variables in the model: menarche age, race, age, drinking, physical exercise

Table 2. Backward elimination for model selection for the association between menarche age and weight change during menopausal transition

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	menarche age, race, age, education, income, smoking, drinking, physical exercise				
	12	-1.37803			-2.65841 -0.097646
	13	-1.26153			-2.55149 0.028432
	>=14	0.078843			-1.31277 1.470459
1- drop age	menarche age, race, education, income, smoking, drinking, physical exercise		NO	NO	
	12	-1.44473			-2.72893 -0.160533
	13	-1.28825			-2.5827 0.006196
	>=14	0.002081			-1.39359 1.397748
1- drop education	menarche age, race, age, income, smoking, drinking, physical exercise		YES	YES	
	12	-1.43205			-2.71054 -0.15355
	13	-1.25598			-2.54279 0.030831
	>=14	0.073685			-1.31471 1.46208
1- drop income	menarche age, race, age, education, smoking, drinking, physical exercise		NO	YES	
	12	-1.3783			-2.65903 -0.097565
	13	-1.25408			-2.54428 0.036114
	>=14	0.068243			-1.32353 1.460014
1- drop smoking	menarche age, race, age, education, income, drinking, physical exercise		NO	NO	
	12	-1.29904			-2.56712 -0.030969
	13	-1.2394			-2.51334 0.034535
	>=14	0.11429			-1.25786 1.486436
1- drop drinking	menarche age, race, age, education, income, smoking, physical exercise		NO	NO	

Table 2. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
1- drop physical exercise	12	-1.48761			-2.70502 -0.270205
	13	-1.52916			-2.74129 -0.317024
	>=14	-0.077657			-1.38799 1.232674
1- drop race/ethnicity	menarche age, race, age, education, income, smoking, drinking		NO	NO	
	12	-1.35559			-2.64438 -0.066797
	13	-1.03932			-2.3347 0.256066
1- drop conclusion: drop education	>=14	0.271465			-1.12752 1.670451
	menarche age, age, education, income, smoking, drinking, physical exercise		NO	NO	
	12	-1.36077			-2.63917 -0.082377
2- drop age	13	-1.22533			-2.51033 0.05967
	>=14	-0.011978			-1.39021 1.366255
	menarche age, race, income, smoking, drinking, physical exercise		NO	NO	
2- drop income	12	-1.50005			-2.7824 -0.217702
	13	-1.28817			-2.57946 0.003123
	>=14	-0.002502			-1.39503 1.390024
2- drop smoking	menarche age, race, age, income, drinking, physical exercise		NO	NO	
	12	-1.43641			-2.71553 -0.157298
	13	-1.25159			-2.53903 0.035845
2- drop smoking	>=14	0.048245			-1.34014 1.436627
	menarche age, race, age, income, drinking, physical exercise		NO	NO	
	12	-1.35391			-2.62021 -0.087621
	13	-1.23552			-2.50627 0.035233

Table 2. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
2-drop drinking	>=14	0.112082			-1.25699 1.48115
	menarche age, race, age, income, smoking, physical exercise		NO	NO	
	12	-1.53656			-2.75251 -0.320613
	13	-1.51875			-2.72826 -0.309251
2- drop physical exercise	>=14	-0.073516			-1.38096 1.233927
	menarche age, race, age, income, smoking, drinking		NO	NO	
	12	-1.42202			-2.70903 -0.135008
	13	-1.03997			-2.3325 0.252568
	>=14	0.256889			-1.13921 1.652985
2- drop race/ethnicity	menarche age, age, income, smoking, drinking, physical exercise		NO	NO	
	12	-1.41503			-2.69182 -0.138246
	13	-1.2228			-2.50515 0.059539
	>=14	-0.028141			-1.40253 1.346248

Variables in the model: menarche age, race, age, income, smoking, drinking, physical exercise

Table 3. Backward elimination for model selection for the association between parity and BMI change during menopausal transition

Model	Variables/Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	parity, race, age, education, income, smoking, drinking, physical exercise				
	1	-0.514071			-1.12025 0.092108
	2	-0.451295			-0.97671 0.074117
	>=3	-0.310172			-0.85846 0.238117
1- drop age	parity, race, education, income, smoking, drinking, physical exercise		NO	YES	
	1	-0.554222			-1.1595 0.051056
	2	-0.484673			-1.00942 0.040077
	>=3	-0.34967			-0.89686 0.197523
1- drop education	parity, race, age, income, smoking, drinking, physical exercise		YES	YES	
	1	-0.563697			-1.16416 0.036765
	2	-0.450251			-0.96389 0.06339
	>=3	-0.293341			-0.82872 0.242032
1- drop income	parity, race, age, education, smoking, drinking, physical exercise		YES	YES	
	1	-0.501477			-1.10268 0.099722
	2	-0.434223			-0.94898 0.080535
	>=3	-0.298726			-0.84247 0.245015
1- drop smoking	parity, race, age, education, income, drinking, physical exercise		NO	YES	
	1	-0.449936			-1.04807 0.148202
	2	-0.452492			-0.97006 0.065077
	>=3	-0.277254			-0.81959 0.265086
1- drop drinking	parity, race, age, education, income, smoking, physical exercise		NO	NO	

Table 3. Continued

Model	Variables/Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
1- drop physical exercise	1	-0.577119			-1.14683 -0.007406
	2	-0.483196			-0.97521 0.008819
	>=3	-0.412479			-0.92343 0.098471
	parity, race, age, education, income, smoking, drinking		YES	YES	
1- drop race/ethnicity	1	-0.530432			-1.14089 0.080026
	2	-0.456456			-0.98538 0.072471
	>=3	-0.333166			-0.88525 0.21892
	parity, age, education, income, smoking, drinking, physical exercise		NO	YES	
conclusion: drop income 2- drop age	1	-0.539398			-1.1434 0.064598
	2	-0.502234			-1.02517 0.020703
	>=3	-0.324129			-0.86232 0.214066
	parity, race, education, smoking, drinking, physical exercise		NO	YES	
2-drop education	1	-0.544711			-1.14467 0.055252
	2	-0.471916			-0.98555 0.041719
	>=3	-0.341006			-0.88332 0.201308
	parity, race, age, smoking, drinking, physical exercise		YES	YES	
2- drop smoking	1	-0.551175			-1.14926 0.046906
	2	-0.433856			-0.94265 0.074939
	>=3	-0.28593			-0.8204 0.248536
	parity, race, age, education, drinking, physical exercise		NO	NO	
2-drop drinking	1	-0.436293			-1.02972 0.157133
	2	-0.433874			-0.9412 0.07345
	>=3	-0.264522			-0.80233 0.273289
	parity, race, age, education, smoking, physical exercise		NO	NO	

Table 3. Continued

Model	Variables/Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
	1	-0.558762			-1.12432 0.006792
	2	-0.460839			-0.94563 0.023954
	>=3	-0.397322			-0.90512 0.110475
2- drop physical exercise	parity, race, age, education, smoking, drinking		YES	YES	
	1	-0.500985			-1.10657 0.104598
	2	-0.416539			-0.93488 0.101804
	>=3	-0.306523			-0.8542 0.24115
2- drop race/ethnicity	parity, age, education, smoking, drinking, physical exercise		YES	YES	
	1	-0.531486			-1.13188 0.068905
	2	-0.490368			-1.00386 0.023121
	>=3	-0.318453			-0.85457 0.217666
3- drop age	parity, race, education, smoking, drinking		NO	YES	
	1	-0.540793			-1.14502 0.063434
	2	-0.451984			-0.96903 0.065058
	>=3	-0.345314			-0.89147 0.20084
conclusion: drop physical exercise					
3-drop education	parity, race, age, smoking, drinking		YES	YES	
	1	-0.559344			-1.16191 0.04322
	2	-0.424219			-0.93672 0.088287
	>=3	-0.305419			-0.8438 0.232965
3- drop smoking	parity, race, age, education, drinking		NO	NO	
	1	-0.442854			-1.04048 0.15477
	2	-0.420766			-0.93154 0.09001
	>=3	-0.274708			-0.81628 0.266862

Table 3. Continued

Model	Variables/Categories	BMI change				
		beta estimate	<10%	<15%	95% CI	
3-drop drinking	parity, race, age, education, smoking		NO	NO		
	1	-0.560979			-1.13086	0.008905
	2	-0.435982			-0.92427	0.052303
	>=3	-0.409563			-0.92121	0.102081
3- drop race/ethnicity	parity, age, education, smoking, drinking		YES	YES		
	1	-0.534366			-1.13939	0.070659
	2	-0.477905			-0.99517	0.039361
	>=3	-0.329891			-0.87013	0.210344
conclusion: drop race/ethnicity						
4- drop age	parity, education, smoking, drinking		NO	NO		
	1	-0.573315			-1.17709	0.030465
	2	-0.513224			-1.02922	0.002774
	>=3	-0.366207			-0.90518	0.172763
4- drop education	parity, age, smoking, drinking		NO	NO		
	1	-0.606454			-1.20784	-0.005066
	2	-0.502377			-1.01252	0.007764
	>=3	-0.356117			-0.88541	0.173179
4- drop smoking	parity, age, education, drinking		NO	NO		
	1	-0.464904			-1.06216	0.132354
	2	-0.486834			-0.99684	0.02317
	>=3	-0.278012			-0.81193	0.255909
4-drop drinking	parity, age, education, smoking		NO	NO		
	1	-0.591031			-1.16046	-0.021603
	2	-0.496999			-0.9841	-0.009896
	>=3	-0.412633			-0.91861	0.09334

Variables in the model: parity, age, education, smoking, drinking

Table 4. Backward elimination for model selection for the association between parity and weight change during menopausal transition

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	parity, race, age, education, income, smoking, drinking, physical exercise				
	1	-1.46819			-3.07349 0.13711
	2	-1.27471			-2.65449 0.105062
	>=3	-0.490121			-1.93106 0.950815
1- drop age	parity, race, education, income, smoking, drinking, physical exercise		NO	NO	
	1	-1.66434			-3.26758 -0.061112
	2	-1.42237			-2.80168 -0.043056
	>=3	-0.662951			-2.10224 0.776343
1- drop education	parity, race, age, income, smoking, drinking, physical exercise		YES	YES	
	1	-1.59595			-3.18553 -0.006377
	2	-1.30414			-2.65401 0.045724
	>=3	-0.471162			-1.87741 0.935086
1- drop income	parity, race, age, education, smoking, drinking, physical exercise		NO	NO	
	1	-1.37512			-2.97175 0.221513
	2	-1.14215			-2.50028 0.215988
	>=3	-0.403051			-1.83548 1.029376
1- drop smoking	parity, race, age, education, income, drinking, physical exercise		NO	NO	
	1	-1.3707			-2.95524 0.213847
	2	-1.33816			-2.69743 0.021106
	>=3	-0.495832			-1.91972 0.928057
1- drop drinking	parity, race, age, education, income, smoking, physical exercise		NO	NO	

Table 4. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
	1	-1.61452			-3.12567 -0.103373
	2	-1.26256			-2.55928 0.034149
	>=3	-0.696621			-2.04403 0.650792
1- drop physical exercise	parity, race, age, education, income, smoking, drinking		YES	YES	
	1	-1.45396			-3.07121 0.163291
	2	-1.23567			-2.625 0.153654
	>=3	-0.51795			-1.96955 0.933652
1- drop race/ethnicity	parity, age, education, income, smoking, drinking, physical exercise		NO	NO	
	1	-1.56813			-3.16585 0.029589
	2	-1.39162			-2.76456 -0.018675
	>=3	-0.597109			-2.01049 0.816271
conclusion: drop physical exercise					
2- drop age	parity, race, education, income, smoking, drinking		NO	NO	
	1	-1.63835			-3.2529 -0.023799
	2	-1.37733			-2.76549 0.010816
	>=3	-0.679394			-2.12886 0.770073
2-drop education	parity, race, age, income, smoking, drinking		YES	YES	
	1	-1.59555			-3.19711 0.006007
	2	-1.27026			-2.62975 0.089236
	>=3	-0.512019			-1.92871 0.904669
2- drop income	parity, race, age, education, smoking, drinking		NO	NO	
	1	-1.32693			-2.93584 0.281977
	2	-1.05595			-2.42384 0.311942
	>=3	-0.400089			-1.84361 1.043433

Table 4. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
2- drop smoking	parity, race, age, education, income, drinking		YES	YES	
	1	-1.37225			-2.96806 0.223565
	2	-1.31016			-2.67841 0.058087
	>=3	-0.526753			-1.96067 0.907167
2-drop drinking	parity, race, age, education, income, smoking		NO	NO	
	1	-1.62156			-3.14524 -0.097872
	2	-1.20854			-2.51534 0.098262
	>=3	-0.739543			-2.09801 0.618924
2- drop race/ethnicity	parity, age, education, income, smoking, drinking		NO	NO	
	1	-1.55812			-3.16815 0.051922
	2	-1.36347			-2.74616 0.019221
	>=3	-0.623158			-2.04739 0.801078
conclusion: drop smoking					
3- drop age	parity, race, education, income, drinking		NO	NO	
	1	-1.53742			-3.13156 0.056731
	2	-1.44574			-2.81295 -0.078523
	>=3	-0.683357			-2.11523 0.748512
3-drop education	parity, race, age, income, drinking		YES	YES	
	1	-1.48401			-3.06335 0.095327
	2	-1.30161			-2.63975 0.036526
	>=3	-0.474183			-1.87213 0.923763
3- drop income	parity, race, age, education, drinking		NO	NO	
	1	-1.24282			-2.83054 0.344894
	2	-1.12723			-2.47454 0.220074

Table 4. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
3-drop drinking	>=3	-0.404006			-1.82968 1.021669
	parity, race, age, education, income		NO	NO	
	1	-1.57345			-3.07365 -0.073259
3- drop race/ethnicity	2	-1.31702			-2.59974 -0.034298
	>=3	-0.76955			-2.1071 0.567998
	parity, age, education, income, drinking		NO	NO	
	1	-1.44495			-3.03376 0.143858
	2	-1.43671			-2.79904 -0.074387
conclusion: drop education					
4- drop age	>=3	-0.571628			-1.97763 0.834371
	parity, race, income, drinking		NO	NO	
	1	-1.64874			-3.22639 -0.0711
4- drop income	2	-1.44381			-2.78034 -0.107283
	>=3	-0.635424			-2.0308 0.759948
	parity, race, age, drinking		NO	NO	
	1	-1.39761			-2.97514 0.179918
	2	-1.17407			-2.50473 0.156597
4-drop drinking	>=3	-0.427702			-1.82596 0.970559
	parity, race, age, income		NO	NO	
	1	-1.65046			-3.13781 -0.163106
	2	-1.26901			-2.52645 -0.011566
	>=3	-0.678765			-1.98471 0.627181
4- drop race/ethnicity	parity, age, income, drinking		NO	NO	

Table 4. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
1		-1.59157			-3.16229 -0.020848
2		-1.46932			-2.79761 -0.14103
>=3		-0.574165			-1.94244 0.794112

Variables in the model: parity, race, age, income, drinking

Table 5. Backward elimination for model selection for the association between age at first birth and BMI change during menopausal transition

Model	Variables/Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	age at first birth, race, age, education, income, smoking, drinking, physical exercise				
	26-30	-0.408502			-0.91271 0.095707
	>=31	0.005834			-0.55356 0.565232
1- drop age	age at first birth, race, education, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-0.371432			-0.87447 0.131601
	>=31	0.078946			-0.47456 0.632453
1- drop education	age at first birth, race, age, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-0.388637			-0.87606 0.098783
	>=31	0.025486			-0.5094 0.560373
1- drop income	age at first birth, race, age, education, smoking, drinking, physical exercise		NO	NO	
	26-30	-0.398348			-0.90146 0.104768
	>=31	0.013937			-0.54488 0.572755
1- drop smoking	age at first birth, race, age, education, income, drinking, physical exercise		NO	NO	
	26-30	-0.459853			-0.95539 0.035681
	>=31	-0.036155			-0.58758 0.515269
1- drop drinking	age at first birth, race, age, education, income, smoking, physical exercise		NO	NO	
	26-30	-0.356909			-0.83315 0.11933
	>=31	0.040418			-0.48245 0.56329
1- drop physical exercise	age at first birth, race, age, education, income, smoking, drinking		NO	NO	
	26-30	-0.401699			-0.90947 0.106074
	>=31	-0.018928			-0.58215 0.54429

Table 5. Continued

Model	Variables/Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
1- drop race/ethnicity	age at first birth, age, education, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-0.456582			-0.94238 0.029216
	>=31	-0.053873			-0.58671 0.478967

Variables in the model: age at first birth, race, age, education, income, smoking, drinking, physical exercise

Table 6. Backward elimination for model selection for the association between age at first birth and weight change during menopausal transition

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	age at first birth, race, age, education, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-1.08711			-2.402 0.227777
	>=31	0.21491			-1.25956 1.689376
1- drop age	age at first birth, race, education, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-0.940092			-2.2546 0.374412
	>=31	0.498601			-0.96508 1.962281
1- drop education	age at first birth, race, age, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-1.13715			-2.41292 0.138614
	>=31	0.117101			-1.29798 1.53218
1- drop income	age at first birth, race, age, education, smoking, drinking, physical exercise		NO	NO	
	26-30	-1.00135			-2.31269 0.309981
	>=31	0.27588			-1.19791 1.749675
1- drop smoking	age at first birth, race, age, education, income, drinking, physical exercise		NO	NO	
	26-30	-1.21882			-2.51226 0.074627
	>=31	0.092681			-1.36196 1.547326
1- drop drinking	age at first birth, race, age, education, income, smoking, physical exercise		NO	NO	
	26-30	-0.948915			-2.19503 0.2972
	>=31	0.287148			-1.0957 1.669994
1- drop physical exercise	age at first birth, race, age, education, income, smoking, drinking		NO	NO	
	26-30	-1.1186			-2.44311 0.205896
	>=31	0.127407			-1.35732 1.612135

Table 6. Continued

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
1- drop race/ethnicity	age at first birth, age, education, income, smoking, drinking, physical exercise		NO	NO	
	26-30	-1.13268		-	0.136455
	>=31	0.159294		-	1.569275

Variables in the model: age at first birth, race, age, education, income, smoking, drinking, physical exercise

Table 7. Backward elimination for model selection for the association between lactation and BMI change during menopausal transition

Model	Variables/Categories	BMI change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	lactation, race, age, education, income, smoking, drinking, physical exercise				
	(0, 3]	0.099549		-0.43911	0.638207
	(3,6]	-0.057055		-0.66935	0.55524
	>6	0.085073		-0.48453	0.654679
1- drop age	lactation, race, education, income, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.133392		-0.40415	0.670934
	(3,6]	-0.022206		-0.63359	0.589181
	>6	0.133416		-0.43346	0.700294
1- drop education	lactation, race, age, income, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.132676		-0.4046	0.669953
	(3,6]	-0.02889		-0.62839	0.570609
	>6	0.105548		-0.44445	0.65555
1- drop income	lactation, race, age, education, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.105911		-0.43229	0.644114
	(3,6]	-0.043244		-0.65342	0.56693
	>6	0.097448		-0.47033	0.66523
1- drop smoking	lactation, race, age, education, income, drinking, physical exercise		NO	NO	
	(0, 3]	0.020498		-0.51087	0.55187
	(3,6]	-0.111471		-0.71717	0.494223
	>6	0.02204		-0.53681	0.580887
1- drop drinking	lactation, race, age, education, income, smoking, physical exercise		NO	NO	

Table 7. Continued

Model	Variables/Categories	BMI change				
		beta estimate	<10%	<15%	95% CI	
1- drop physical exercise	(0, 3]	-0.100002			-0.60392 0.40392	
	(3,6]	-0.212108			-0.78896 0.364741	
	>6	-0.087251			-0.62736 0.452861	
	lactation, race, age, education, income, smoking, drinking			NO	NO	
	(0, 3]	0.068539			-0.47327 0.610349	
	(3,6]	-0.107388			-0.72309 0.508309	
1- drop race/ethnicity	>6	0.086544			-0.48686 0.659946	
	lactation, age, education, income, smoking, drinking, physical exercise			NO	NO	
	(0, 3]	0.055107			-0.47716 0.587377	
	(3,6]	-0.090694			-0.69565 0.514261	
	>6	0.08038			-0.46913 0.62989	

Variables in the model: lactation, race, age, education, income, smoking, drinking, physical exercise

Table 8. Backward elimination for model selection for the association between lactation and weight change during menopausal transition

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
Fully adjusted model	lactation, race, age, education, income, smoking, drinking, physical exercise				
	(0, 3]	0.589983			-0.82559 2.005559
	(3,6]	0.228115			-1.3786 1.834834
	>6	0.473991			-1.01981 1.967787
1- drop age	lactation, race, education, income, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.700659			-0.71617 2.117489
	(3,6]	0.3453			-1.26326 1.953857
	>6	0.670477			-0.8192 2.160156
1- drop education	lactation, race, age, income, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.619976			-0.78998 2.029935
	(3,6]	0.204044			-1.37127 1.779354
	>6	0.383768			-1.06112 1.828659
1- drop income	lactation, race, age, education, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.622691			-0.79338 2.038757
	(3,6]	0.318475			-1.28442 1.921374
	>6	0.566795			-0.92237 2.055959
1- drop smoking	lactation, race, age, education, income, drinking, physical exercise		NO	NO	
	(0, 3]	0.346538			-1.04834 1.741418
	(3,6]	0.052661			-1.53542 1.640747
	>6	0.283546			-1.18211 1.749198
1- drop drinking	lactation, race, age, education, income, smoking, physical exercise		NO	NO	

Table 8. Continues

Model	Variables/Categories	Weight change			
		beta estimate	<10%	<15%	95% CI
1- drop physical exercise	(0, 3]	0.104177			-1.22321 1.431566
	(3,6]	-0.145995			-1.66465 1.372663
	>6	0.094278			-1.32631 1.514868
	lactation, race, age, education, income, smoking, drinking		NO	NO	
	(0, 3]	0.512002			-0.91285 1.936855
	(3,6]	0.080551			-1.5359 1.697005
1- drop race/ethnicity	>6	0.463632			-1.04089 1.968149
	lactation, age, education, income, smoking, drinking, physical exercise		NO	NO	
	(0, 3]	0.523898			-0.87057 1.918366
	(3,6]	0.188773			-1.39647 1.774016
	>6	0.487216			-0.95033 1.924757

Variables in the model: lactation, race, age, education, income, smoking, drinking, physical exercise

Table 9. Summary for model selection*

Outcome	Exposure	race/ethnicity	age	education	income	smoking	drinking	physical exercise
BMI change	menarche age	Y	Y	N	N	N	Y	Y
	age at first birth	Y	Y	Y	Y	Y	Y	Y
	parity	N	Y	Y	N	Y	Y	N
	lactation	Y	Y	Y	Y	Y	Y	Y
weight change	menarche age	Y	Y	N	Y	Y	Y	Y
	age at first birth	Y	Y	Y	Y	Y	Y	Y
	parity	Y	Y	N	Y	N	Y	N
	lactation	Y	Y	Y	Y	Y	Y	Y

*Y indicates the variable should be included in the model; N indicates the variable should not be included in the model.