Published in final edited form as:
Menopause. 2008 ; 15(5): 924–933. doi:10.1097/gme.0b013e3181786adc.

Dietary and lifestyle predictors of age at natural menopause and reproductive span in the Shanghai Women's Health Study

Tsogzolmaa Dorjgochoo, MD, PhD[1], **Asha Kallianpur, MD, MPH**[1], **Yu-Tang Gao, MD**[2], **Hui Cai, MD, PhD**[1], **Gong Yang, MD, MPH**[2], **Honglan Li, MD**[2], **Wei Zheng, MD, PhD**[1], and **Xiao Ou Shu, MD, PhD**[1]

1*Vanderbilt Epidemiology Center, Department of Medicine, School of Medicine, Vanderbilt University and Vanderbilt-Ingram Cancer Centerm*

2*Department of Epidemiology, Shanghai Cancer Institute, Shanghai, China*

Abstract

Objectives: Modifiable factors predicting the onset of menopause, a transition with important implications for women's health, have not been fully characterized. We evaluated the impact of dietary, lifestyle and reproductive factors on age at natural menopause and reproductive span in Chinese women.

Design: Study participants were Chinese women aged 40–70 who experienced natural menopause and participated in a population-based, prospective study, the Shanghai Women's Health Study (n=33,054). Dietary intakes at the baseline survey were assessed by food-frequency questionnaire. Regression (β) coefficients, calculated by multivariable linear regression, were used to estimate the effects of dietary, lifestyle, and reproductive patterns on age at menopause and the number of reproductive years, adjusting for potential confounding factors.

Results: Early menarche, younger age at first-live birth, older age at last live-birth, longer duration of breastfeeding, and higher parity were associated with longer reproductive years (P_{trend}<0.01 for all). Higher body-mass index at age 20, mid-life weight gain, and leisure-time physical activity during adolescence and adulthood predicted later menopause and longer reproductive span (P_{trend}<0.01 for all). Total intakes of calories, fruits, protein, and possibly carbohydrates were positively associated with later menopause (P_{trend} <0.05 for all) and longer reproductive span [P_{trend} <0.05, except for carbohydrates (P_{trend} =0.06)], and long-term tea consumption predicted longer reproductive span (P_{trend} =0.03). Vegetable, fat, soy, and fiber intakes did not significantly affect reproductive span or age at menopause. Smoking was inversely related to both age at menopause and reproductive span (P_{trend} <0.01).

Conclusions: In addition to reproductive factors, intakes of fruit, protein, smoking, and tea consumption, lifetime patterns of physical activity, and weight gain influenced the onset of menopause and/or reproductive span in Chinese women.

Keywords

Age at onset of menopause; Dietary intake; Physical activity; Reproductive span; Smoking; Tea; Weight gain

Corresponding author contact information: Xiao Ou Shu, M.D., Ph.D. Vanderbilt Epidemiology Center Institute of Medicine & Public Health Vanderbilt University Medical Center 2525 West End Avenue, Suite 600 Nashville, TN 37203-1738 E-mail: Xiao-ou.shu@vanderbilt.edu Tel: 615-936-0713 Fax: 615-936-8291.

INTRODUCTION

Menopause marks the natural cessation of reproductive capacity in women as well as the onset of increased risk for many chronic health problems.[1-3] Early menopause (at age 40-45) is associated with the development of osteoporosis, obesity and other features of the metabolic syndrome, and cardiovascular disease,[4-6] whereas delayed menopause (occurring at age 55-60) is associated with an increased risk of estrogen-responsive cancers.[7,8]

Considerable research has been published regarding lifestyle and reproductive factors that may predict the age of onset of menopause in women of different racial/ethnic and socioeconomic backgrounds.[9-12] The results of these studies, primarily conducted in Western countries, have been largely inconsistent. Several factors reported to affect the timing of menopause include educational level, occupation, marital status, age at menarche, parity, oral contraceptive use, and smoking.[13-15] A few studies have suggested that physical activity and diet influence the age at which natural menopause occurs.[16,17] Some studies have observed earlier menopause among malnourished women or women with a low body-mass index (BMI), while overweight or obese women may experience menopause at a later age.[17-20] However, other studies have shown no such correlations.[14,21] The few prospective cohort and cross-sectional studies that have investigated the effects of dietary fat and protein intake on menopause have had somewhat inconsistent results.[22-25] A German cohort study reported that higher total intakes of fat, meat and protein all correlated with later onset of menopause.[25] In Japanese women, an inverse association was observed between the intake of vegetables and the age at onset of menopause,[24] but no effect of fat intake was observed, in contrast to findings from an earlier cross-sectional study in the same population.[16] Finally, in a recent interventional study, women who followed a low-fat, high-carbohydrate diet showed no demonstrable change in the timing of menopause compared to control women who followed their usual diet.[22]

Some of the inconsistent findings in prior studies may be due to small sample sizes, selection bias in some instances, and the genetic and environmental heterogeneity among the populations studied. We examined the role of specific dietary nutrients as well as reproductive and lifestyle factors on the age of onset of natural menopause and on the duration of regular menses in a large, population-based cohort of urban Chinese women.

METHODS

Study population

The Shanghai Women's Health Study (SWHS) is a prospective cohort study that was designed to investigate associations of diet and lifestyle with chronic diseases. The study comprises 74,942 women from urban Shanghai, aged 40-70 years at recruitment (March 1997 - May 2000). Details regarding subject recruitment methods and baseline surveys have been published elsewhere.[26] Briefly, baseline assessment of women included a self-administered questionnaire to elicit information regarding socioeconomic and demographic characteristics, lifestyle factors, medical, surgical, and reproductive history. A separate questionnaire was administered by trained personnel during an in-person interview to obtain detailed information on dietary habits, weight history, physical activity, and standardized anthropometric measurements. A total of 37,256 (49.6%) women were postmenopausal at study recruitment. Women who reported cessation of menstruation as a result of hysterectomy, bilateral ovariectomy or the use of HRT were excluded (n=4,202). The remaining 33,054 women who had experienced natural menopause (44.1% of all subjects and 88.7% of all postmenopausal women) were included in the current study. The study protocols were approved by all institutes involved in the study, and written informed consent was obtained from all subjects.

Outcome ascertainment

The primary outcomes in this study were age at onset of natural menopause and the total number of reproductive years as of the baseline recruitment. Menopausal status was defined as the absence of menstruation for ≥12 months, according to the World Health Organization definition of menopause. The age at which menopause occurred and the reasons for its occurrence [natural menopause, hysterectomy, or hormone replacement therapy (HRT)] were recorded. The number of reproductive years, or reproductive span, was defined as the duration between age at menarche and age at menopause.

Ascertainment of exposures

Reproductive factors—Data on other reproductive variables, which were obtained by self-administered questionnaire or via in-person interview, included: age at menarche, number of pregnancies, number of abortions, miscarriages and stillbirths, number of live births, ages at first and last live births, duration of breastfeeding for each live birth, usual length and regularity of menstrual cycles, and ever-use of birth control methods (contraceptive pills, injections, intrauterine devices, and tubal ligation).[26]

Anthropometrics and physical activity—Current weight and height were estimated by two measurements taken by interviewers using standard protocols. Data on recalled weight and height at age 20 and 50 years were collected. BMI was calculated as (weight, kg)/(height, meter^2). Information about physical activity patterns during adolescence and adulthood was ascertained from all participants through the validated SWHS Physical Activity Questionnaire (PAQ).[27] Exercise during adolescence (age 13-19) and adulthood was defined as participation in leisure-time or sports activities at least once per week for more than 3 months continuously. In addition, regular exercise during adolescence was defined by the time spent (years) and duration (hours per week) of participation in the 3 most common types of exercise in school, both of which were summarized as the average duration of exercise during adolescence (hrs/wk/yr). Participants were also asked to rate the amount of time spent on exercise in adolescence and adulthood (in the past 5 years) in comparison to other people using Likert-type responses (*i.e.*, more than average, a little more than average, about average, a little less than average, and less than average). From the above responses, a single lifetime physical activity variable was created with four groups: 1) low activity during adolescence and adulthood, 2) low activity during adolescence but medium-high during adulthood, 3) moderate-high activity during adolescence but low during adulthood, and 4) moderate-high activity during adolescence and adulthood.

Dietary factors and smoking—Dietary intake data were collected during in-person interviews using a validated food-frequency questionnaire (FFQ) that included 77 food items/groups commonly consumed over the 12 months preceding the interview.[28] During the face-to-face interview, each participant was first asked about how often, on average, during the previous year she had consumed a specific food or food group (the possible responses were daily, weekly, monthly, yearly, or never), followed by a question on the amount consumed in grams per unit of time. Intake of nutrients was then calculated by multiplying the amount of food consumed by the nutrient content per gram of food according to the Chinese Food Composition Tables.[29] We also collected information on changes in eating habits with respect to main food groups such as red meat, vegetables and fruits in the 5 years preceding the interview compared to the past year.

Smoking was defined as smoking ≥1 cigarette per day for >6 months continuously at some point during a woman's life. Regular drinking of beer or wine and tea ≥3 times/week for >6 months continuously was defined as regular consumption of alcohol or tea, respectively.

Statistical Analysis—Age at menopause and reproductive years were normally distributed in this study population. The age-adjusted mean age at onset of menopause or mean number of reproductive years by demographic variables were calculated. Multivariable linear regression analysis was used to estimate adjusted mean differences and their 95% confidence intervals (CI) for age at natural menopause and number of reproductive years associated with exposures of interest. Variables adjusted for in models with non-reproductive outcome variables included age (continuous), educational level (no formal education/elementary, middle, high school, and college or higher), type of occupation (manual worker, clerical/ administrative, and professional), age at menarche (≤11, 12-13, 14-15 and ≥16 years), number of live births (nulliparous, 1, 2, 3, and ≥4), oral contraceptive use (never/ever), weight gain between the ages 20 and 50 years (in quartiles), lifetime physical activity pattern, cigarette smoking (never/ever), and total energy intake (continuous). Additional adjustment for tea or alcohol use, regular exercise (yes/no), family income, current employment (yes/no), total months of breastfeeding, age at last live birth, menstrual cycle pattern, and years between age at menarche and first live birth did not appreciably alter the results. Therefore, these variables were not included in the final model. Tests for trend were performed by entering the categorical variables as continuous parameters in the model.

The Bonferroni correction was applied to account for multiple comparisons, in order to reduce the frequency of false-positive results. All statistical tests were two-sided and were performed using SAS statistical software, version 9.1 (SAS Institute, Cary, NC).

RESULTS

The mean age of the study population was 60.2 years. The age at which natural menopause occurred ranged from 40.6-50.0 years with an overall mean of 49.2±3.7. The number of reproductive years ranged from 31.6 to 36.7 with a mean of 34.0±4.1. Only 4.7% of women had experienced a menopause at age of ≤45.4 years (data not shown).

The distributions of socioeconomic and demographic factors in relation to age at natural menopause and reproductive span are shown in Table 1. The latest onset of menopause and longest reproductive span were reported by women in the cohort who were 55-59 years of age. Socioeconomic and demographic factors associated with later menopause and longer reproductive span (adjusted for age at enrollment to account for potential confounding by birth cohort) included: higher educational level, higher income group, a professional occupation, current employment, and married status.

Reproductive factors

Associations of reproductive factors with age at menopause onset and reproductive span are presented in Table 2. The mean age at menarche was 15.2±1.8 years (range 14-16 years) in this study population. Approximately 0.7% of women experienced early menarche (at age ≤11 years) and 42.1% experienced late menarche (at age ≥16 years). Older age at menarche was significantly associated with later menopause and shorter reproductive span (P_{trend}<0.01). Number of live births was positively associated with later menopause and extended reproductive span (P_{trend}<0.01). After proper adjustments, younger age at first and older age at last live birth and longer duration of breastfeeding were each associated with slightly delayed menopause and more reproductive years (P_{trend}<0.01). Menstrual irregularity was related to fewer reproductive years (P_{trend}<0.01), but not to menopausal age. A significant proportion (24.5%) of women in the cohort had used birth control methods (oral contraceptive pill, intrauterine device, or tubal ligation), and their use was positively associated with the timing of menopause and with the number of reproductive years (P_{values}<0.01 for all methods,Table 2). The time between menarche and the first live-birth was negatively associated with menopausal age and positively associated with reproductive span (P_{values} <0.01). Self-reported

abortions and miscarriages or stillbirths had no detectable effect on age at menopause or number of reproductive years (data not shown).

Anthropometrics and physical activity

As shown in Table 3, the recalled weights of women at 20 years of age ranged from 45.0 to 54.0 kg with a mean of 49.4±6.6 kg. Weight ≥54 kg and BMI ≥21.4 at age 20 predicted a slightly later onset of menopause and longer reproductive span (P_{trend}<0.01 for both factors). Overall, women reported gaining an average of 7.5 kg between ages 20 and 50, and greater weight gain during this age period was associated with slightly later menopause and a longer reproductive capacity (P_{trend}<0.01). More than half of the women in this study reported low exercise participation during their lifetime (54.4% in adolescence and 57% in adulthood, data not shown). Presented in Table 4 are the associations of physical activity with age at menopause and reproductive span. Women who reported moderate-to-high exercise participation and more intensive exercise during adolescence were significantly more likely to experience later menopause and more reproductive years than their less physically active counterparts (P_{values}<0.05). Overall, women who exercised at moderate to high levels during both adolescence and adulthood were more likely to have later menopause and a longer reproductive span (P_{values}<0.01).

Dietary factors and smoking

Associations between dietary factors and reproductive outcomes are presented in Table 5. Total energy intake was significantly associated with older age at menopause and longer reproductive span (P_{trend}<0.01 for both outcomes). Higher intakes of total fruit, protein and carbohydrates were positively associated with slightly later menopause and longer reproductive span (P_{trend}<0.05 for all factors, except for carbohydrates and reproductive span with P_{trend}<0.06). Intake of total fiber also tended to predict later menopause, but the association did not reach statistical significance (P_{trend}=0.09). Intakes of total vegetables, soy, fiber, and fat had no discernible impact on the timing of menopause or the number of reproductive years. We also examined mean differences in the age at menopause and in reproductive span across dietary exposure categories, using the residual method to adjust for total energy intake [30], but the results did not differ from the results presented. Additionally, we conducted analyses among study participants who reported that their dietary habits in the 5 years prior to enrollment had not changed or had only slightly changed compared with their dietary habits within a year prior to enrollment. Associations of dietary red meat, vegetable and fruit intakes with reproductive outcomes in this analysis were similar to our initial findings for these dietary intakes (data not shown).

Among the 4.4% of women who reported ever smoking, those who had smoked for ≥28 years were significantly more likely to have experienced early menopause and fewer reproductive years (Table 6). Similarly, current smokers were more likely to have experienced earlier menopause and a shorter reproductive span compared to former smokers (P_{values} <0.01 for both factors). In contrast, women who regularly drank tea for ≥19 years were more likely to have had an extended reproductive span P_{trend}=0.03). Alcohol consumption, which was rare in this cohort, was not associated with menopausal age or reproductive span.

Application of the Bonferroni correction for multiple statistical tests did not significantly change any of our results; initially significant *p*-values remained significant (data not shown).

DISCUSSION

Menopause marks an important transition for a woman and has significant implications for the risk of cardiovascular diseases and cancer. Identifying predictors, particularly modifiable

factors, for onset of menopause would thus have a significant impact on etiological research and the prevention of these chronic diseases. The current study is one of very few studies to systematically evaluate the effects of a wide variety of factors on the timing of menopause as well as on the duration of reproductive life in Chinese women. Age at menopause and the reproductive span in this population were associated with specific dietary factors and with patterns of physical activity and weight gain during adolescence and adulthood, although the magnitude of these effects was small (on the order of several months to <1.5 years). The mean age at natural menopause in this population was similar to the mean age at menopause that has been reported for Asian women in other studies (49.0-50.0).[31,32] The mean number of reproductive years in our study population was 34.0±4.1, slightly less than that of women in the United States.[33]

Consistent with many studies,[10,11,34,35] various socioeconomic factors predicted the age of menopause and reproductive span in Chinese women. Lower educational attainment and manual work were associated with an earlier age at menopause and fewer reproductive years, whereas married status, and increased parity predicted slightly later menopause and a longer reproductive span as demonstrated in other studies.[9,36] Socioeconomic factors may impact the onset of menopause through effects on dietary pattern and quality, physical activity, obesity, and access to contraceptives, but the precise nature of these relationships is unclear.

With regard to reproductive factors such as parity, fewer cumulative menstrual cycles in parous women may be associated with a larger reserve of oocytes and longer exposure to estrogen.[37,38] A similar mechanism may explain our finding, in accord with previous studies, that oral contraceptives slightly delayed menopause and prolonged the reproductive span.[39] However, other studies have reported no such effects,[13,25] or opposite effects with oral contraceptives.[11,39] We also observed that women who reported having lifelong menstrual cycle irregularity tended to have earlier menopause and fewer reproductive years in this study, consistent with most previous studies.[40,41] Increased duration of breastfeeding was associated with delayed onset of menopause and longer reproductive span in this study, possibly because prolonged breastfeeding can prevent follicle depletion and preserve ovarian function.[42,43] Similarly, later age at menarche may have resulted in delayed exhaustion of ovarian follicles and later menopause in this study,[15,25] although other studies have found either no association or an inverse association between age at menarche and the timing of menopause.[13,44] In this study, later age at first live birth was associated with earlier menopause and fewer reproductive years,[45] supporting the concept that a decline in follicle count and/or sex hormone levels may lead to both reduced fertility, earlier menopause, and fewer overall reproductive years. Not all studies have reported the same association between age at first live birth and onset of menopause, however.[42]

Few studies,[20,46,47] including this one, have investigated the effects of weight gain and physical activity during adolescence, young adulthood, and the reproductive years on the timing of menopause and overall reproductive span. Our study suggests that weight gain between ages 20 and 50 and increased BMI during early adulthood (at age 20) may predict a later age at menopause and more reproductive years. We also found that higher LTPA during both adolescence and adulthood was associated with later age at menopause and a longer reproductive span, similar to other reports.[46,48] Although severe weight loss or vigorous exercise may suppress ovarian function by lowering estrogen levels and increasing sex-hormone-binding globulin levels, the mechanisms underlying the associations between moderate premenopausal weight gain or physical activity and onset of menopause remain to be determined.[25,49,50]

The effects of nutrition on sex hormone levels and reproductive function have been investigated in animal models.[51,52] The results of the few published studies conducted on the impact of

diet on the timing of menopause have been inconsistent.[16,22,24,25] In our study, high intake of total calories was significantly associated with delayed age at menopause and a longer reproductive span. Other studies have also associated aging, menstrual irregularity and infertility in women with total energy consumption.[53-55] High fruit intake may delay the onset of menopause and increase the overall reproductive span due to the antioxidant content of fruit; oxidative stress has been implicated in menopause onset and the age-related decline in fertility via the adverse effects of reactive oxygen species on the number and quality of ovarian follicles produced [56,57] High protein intake and, to a lesser extent, high carbohydrate intake among the Chinese women in this study predicted a delay in menopause and an increase in the reproductive span. The European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study found a similar association with protein intake, but carbohydrate intake was inversely related to age at natural menopause.[25] Other studies failed to find any association. [22,24] In contrast to previous studies [16,25] but consistent with some other reports,[22-24] our results failed to support any association between total fat, saturated fat, or red meat intake and the onset of menopause. Although two previous prospective studies found that early menopause was associated with high vegetable intake,[24,25] we did not substantiate that observation. Contrary to a report of a positive relationship between soy intake and the onset of menopause, [16] we observed no significant impact of dietary soy products on either the age at which menopause occurred or on the overall number of reproductive years in the women in our study. These results concur with two other studies that failed to find such an association.[24,25] Similarly, our study findings are consistent with prior reports that dietary fiber does not significantly alter sex hormone levels in premenopausal women.[58,59]

To our knowledge, this is the first study to investigate the relationship between tea consumption and reproductive outcomes. Regular tea consumption predicted an extended reproductive span, although the assessment of tea consumption in this study did not distinguish between types of tea. Recently, the antioxidant effects of tea have been extensively investigated,[60] and it has been suggested that some constituents of green and black tea, such as tea flavonoids (e.g., epigallocatechin gallate, or EGCG), exert non-steroidal estrogenic effects that counteract degenerative processes.[56,61] However, studies exploring these effects remain inconclusive, [62,63] and this issue requires further study.

Polycyclic, aromatic hydrocarbons present in cigarette smoke may be toxic to ovarian follicles, resulting in earlier ovarian failure and menopause.[64,65] We found an inverse association between smoking and age at menopause, supporting some prior reports that smoking, and particularly a long smoking history, predict earlier onset of menopause and a shorter reproductive span.[62,66] However, the prevalence of smoking in our study population is low, which limited our ability to evaluate the dose-response relationship previously observed.[11, 14] Similarly, the effects of alcohol on reproductive outcomes could not be adequately evaluated in our study, because very few women (2.4%) reported regular alcohol consumption.

Our study represents the first large, population-based study to comprehensively evaluate a variety of factors, including diet and physical activity, on the age at natural menopause and number of reproductive years among Asian women. Many previous epidemiological studies on the timing of menopause were small or were conducted among highly selected populations such as clinic-based populations. The high response rate (92%) in this study further enhances the validity and generalizability of our findings; the detailed and comprehensive exposure assessments and strict quality control procedures are other noticeable strengths. However, several methodological limitations should also be considered. Assessments of some exposures, including menstrual and reproductive history, dietary intakes, and patterns of weight gain and physical activity, were entirely based on self-report and may therefore be subject to misclassification. Information on maternal menstrual history, which has been shown to influence both age at menarche and menopause in Chinese women, was not available. Dietary

intakes and physical activity were assessed at enrollment, after menopause had occurred. Changes in dietary intake and physical activity after menopause may therefore have influenced the study results. However, analyses in a subset of the cohort that reported a stable dietary pattern over the 5 years prior to study enrollment showed similar associations. Continued follow-up of the premenopausal women in this cohort and/or future prospective studies are therefore needed to verify our findings. Finally, given the large sample size of the study, some of the significant small differences may not have clinical significance.

CONCLUSIONS

Consistent with the literature, we found in this Chinese population that delayed onset of menopause and longer reproductive span were associated with earlier age at first live birth, longer duration of breastfeeding, and oral contraceptive use, as well as high intakes of calories, fruits, protein, and possibly carbohydrates. Novel findings include positive associations with weight gain, a pattern of lifelong physical activity, and tea consumption. Future studies incorporating repeated, prospective measurements of these exposures and correlations with sex hormone levels are needed to replicate these associations and to explore their underlying mechanisms and significance of the associations.

ACKNOWLEDGEMENTS

This study was supported by research grants R01CA70867 and HL079123 from the National Institutes of Health, USA.

Sources of support: This study was supported by research grants R01CA70867 and HL079123 from the National Institutes of Health, USA.

REFERENCES

1. Research on the menopause in the 1990s. Report of a WHO Scientific Group. World Health Organ Tech Rep Ser 1996;866:1–107. [PubMed: 8942292]
2. Wilson MM. Menopause. Clin Geriatr Med 2003;19:483–506. [PubMed: 14567003]
3. Cui R, Iso H, Toyoshima H, et al. Relationships of age at menarche and menopause, and reproductive year with mortality from cardiovascular disease in Japanese postmenopausal women: the JACC study. J Epidemiol 2006;16:177–184. [PubMed: 16951536]
4. Gordon T, Kannel WB, Hjortland MC, et al. Menopause and coronary heart disease. The Framingham Study. Ann Intern Med 1978;89:157–161. [PubMed: 677576]
5. Jacobsen BK, Heuch I, Kvale G. Age at natural menopause and stroke mortality: cohort study with 3561 stroke deaths during 37-year follow-up. Stroke 2004;35:1548–1551. [PubMed: 15178828]
6. Sternfeld B, Bhat AK, Wang H, et al. Menopause, physical activity, and body composition/fat distribution in midlife women. Med Sci Sports Exerc 2005;37:1195–1202. [PubMed: 16015138]
7. Pike MC, Pearce CL, Wu AH. Prevention of cancers of the breast, endometrium and ovary. Oncogene 2004;23:6379–6391. [PubMed: 15322512]
8. Iwasaki M, Otani T, Inoue M, et al. Role and impact of menstrual and reproductive factors on breast cancer risk in Japan. Eur J Cancer Prev 2007;16:116–123. [PubMed: 17297387]
9. Luoto R, Kaprio J, Uutela A. Age at natural menopause and sociodemographic status in Finland. Am J Epidemiol 1994;139:64–76. [PubMed: 8296776]
10. Castelo-Branco C, Blumel JE, Chedraui P, et al. Age at menopause in Latin America. Menopause 2006;13:706–712. [PubMed: 16837893]
11. Gold EB, Bromberger J, Crawford S, et al. Factors associated with age at natural menopause in a multiethnic sample of midlife women. Am J Epidemiol 2001;153:865–874. [PubMed: 11323317]
12. Palmer JR, Rosenberg L, Wise LA, et al. Onset of natural menopause in African American women. Am J Public Health 2003;93:299–306. [PubMed: 12554590]

13. van Noord PA, Dubas JS, Dorland M, et al. Age at natural menopause in a population-based screening cohort: the role of menarche, fecundity, and lifestyle factors. Fertil Steril 1997;68:95–102. [PubMed: 9207591]
14. Hardy R, Kuh D, Wadsworth M. Smoking, body mass index, socioeconomic status and the menopausal transition in a British national cohort. Int J Epidemiol 2000;29:845–851. [PubMed: 11034967]
15. Parazzini F. Determinants of age at menopause in women attending menopause clinics in Italy. Maturitas 2007;56:280–287. [PubMed: 17069999]
16. Nagata C, Takatsuka N, Inaba S, et al. Association of diet and other lifestyle with onset of menopause in Japanese women. Maturitas 1998;29:105–113. [PubMed: 9651899]
17. Evans EM, Racette SB. Menopause and risk for obesity: how important is physical activity? J Womens Health (Larchmt) 2006;15:211–213. [PubMed: 16536685]
18. Douchi T, Yamamoto S, Nakamura S, et al. The effect of menopause on regional and total body lean mass. Maturitas 1998;29:247–252. [PubMed: 9699196]
19. Elias SG, van Noord PA, Peeters PH, et al. Caloric restriction reduces age at menopause: the effect of the 1944-1945 Dutch famine. Menopause 2003;10:399–405. [PubMed: 14501600]
20. Kato I, Toniolo P, Akhmedkhanov A, et al. Prospective study of factors influencing the onset of natural menopause. J Clin Epidemiol 1998;51:1271–1276. [PubMed: 10086819]
21. Brambilla DJ, McKinlay SM. A prospective study of factors affecting age at menopause. J Clin Epidemiol 1989;42:1031–1039. [PubMed: 2809660]
22. Martin LJ, Greenberg CV, Kriukov V, et al. Intervention with a low-fat, high-carbohydrate diet does not influence the timing of menopause. Am J Clin Nutr 2006;84:920–928. [PubMed: 17023721]
23. Torgerson DJ, Avenell A, Russell IT, et al. Factors associated with onset of menopause in women aged 45-49. Maturitas 1994;19:83–92. [PubMed: 7968648]
24. Nagata C, Takatsuka N, Kawakami N, et al. Association of diet with the onset of menopause in Japanese women. Am J Epidemiol 2000;152:863–867. [PubMed: 11085398]
25. Nagel G, Altenburg HP, Nieters A, et al. Reproductive and dietary determinants of the age at menopause in EPIC-Heidelberg. Maturitas 2005;52:337–347. [PubMed: 16011884]
26. Zheng W, Chow WH, Yang G, et al. The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. Am J Epidemiol 2005;162:1123–1131. [PubMed: 16236996]
27. Matthews CE, Shu XO, Yang G, et al. Reproducibility and validity of the Shanghai Women's Health Study physical activity questionnaire. Am J Epidemiol 2003;158:1114–1122. [PubMed: 14630608]
28. Shu XO, Yang G, Jin F, et al. Validity and reproducibility of the food frequency questionnaire used in the Shanghai Women's Health Study. Eur J Clin Nutr 2004;58:17–23. [PubMed: 14679362]
29. Yang, G.; Wang, G.; Pan, X. Chinese Food Composition Tables. Peking University Medical Press; Beijing: 2002.
30. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986;124:17–27. [PubMed: 3521261]
31. Chang C, Chow SN, Hu Y. Age of menopause of Chinese women in Taiwan. Int J Gynaecol Obstet 1995;49:191–192. [PubMed: 7649328]
32. Loh FH, Khin LW, Saw SM, et al. The age of menopause and the menopause transition in a multiracial population: a nation-wide Singapore study. Maturitas 2005;52:169–180. [PubMed: 16257608]
33. Nichols HB, Trentham-Dietz A, Hampton JM, et al. From menarche to menopause: trends among US Women born from 1912 to 1969. Am J Epidemiol 2006;164:1003–1011. [PubMed: 16928728]
34. Ayatollahi SM, Ghaem H, Ayatollahi SA. Sociodemographic factors and age at natural menopause in Shiraz, Islamic Republic of Iran. East Mediterr Health J 2005;11:146–154. [PubMed: 16532683]
35. Lawlor DA, Ebrahim S, Smith GD. The association of socio-economic position across the life course and age at menopause: the British Women's Heart and Health Study. BJOG 2003;110:1078–1087. [PubMed: 14664879]
36. Kaczmarek M. The timing of natural menopause in Poland and associated factors. Maturitas 2007;57:139–153. [PubMed: 17307314]
37. Nikolaou D, Templeton A. Early ovarian ageing. Eur J Obstet Gynecol Reprod Biol 2004;113:126–133. [PubMed: 15063947]

38. Santoro N, Brockwell S, Johnston J, et al. Helping midlife women predict the onset of the final menses: SWAN, the Study of Women's Health Across the Nation. Menopause 2007;14:415–424. [PubMed: 17303963]
39. de VE, den T,I, van Noord PA, et al. Oral contraceptive use in relation to age at menopause in the DOM cohort. Hum Reprod 2001;16:1657–1662. [PubMed: 11473959]
40. Bromberger JT, Matthews KA, Kuller LH, et al. Prospective study of the determinants of age at menopause. Am J Epidemiol 1997;145:124–133. [PubMed: 9006309]
41. Reynolds RF, Obermeyer CM. Age at natural menopause in Spain and the United States: results from the DAMES project. Am J Hum Biol 2005;17:331–340. [PubMed: 15849704]
42. Cassou B, Derriennic F, Monfort C, et al. Risk factors of early menopause in two generations of gainfully employed French women. Maturitas 1997;26:165–174. [PubMed: 9147348]
43. Chang SH, Kim CS, Lee KS, et al. Premenopausal factors influencing premature ovarian failure and early menopause. Maturitas 2007;58:19–30. [PubMed: 17531410]
44. Thomas F, Renaud F, Benefice E, et al. International variability of ages at menarche and menopause: patterns and main determinants. Hum Biol 2001;73:271–290. [PubMed: 11446429]
45. te Velde ER, Pearson PL. The variability of female reproductive ageing. Hum Reprod Update 2002;8:141–154. [PubMed: 12099629]
46. 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;27:933–940. [PubMed: 12861234]
47. Ortega-Ceballos PA, Moran C, Blanco-Munoz J, et al. Reproductive and lifestyle factors associated with early menopause in Mexican women. Salud Publica Mex 2006;48:300–307. [PubMed: 16913454]
48. Matthews KA, Abrams B, Crawford S, et al. Body mass index in mid-life women: relative influence of menopause, hormone use, and ethnicity. Int J Obes Relat Metab Disord 2001;25:863–873. [PubMed: 11439301]
49. De Souza MJ, Miller BE, Loucks AB, et al. High frequency of luteal phase deficiency and anovulation in recreational women runners: blunted elevation in follicle-stimulating hormone observed during luteal-follicular transition. J Clin Endocrinol Metab 1998;83:4220–4232. [PubMed: 9851755]
50. Jasienska G, Ziomkiewicz A, Thune I, et al. Habitual physical activity and estradiol levels in women of reproductive age. Eur J Cancer Prev 2006;15:439–445. [PubMed: 16912573]
51. Sprangers SA, Piacsek BE. Chronic underfeeding increases the positive feedback efficacy of estrogen on gonadotropin secretion. Proc Soc Exp Biol Med 1997;216:398–403. [PubMed: 9402145]
52. Lujan ME, Krzemien AA, Reid RL, et al. Developing a model of nutritional amenorrhea in rhesus monkeys. Endocrinology 2006;147:483–492. [PubMed: 16195399]
53. Meydani M. Nutrition interventions in aging and age-associated disease. Ann N Y Acad Sci 2001;928:226–235. [PubMed: 11795514]
54. Loucks AB. Energy availability and infertility. Curr Opin Endocrinol Diabetes Obes 2007;14:470–474. [PubMed: 17982354]
55. Fujiwara T. Diet during adolescence is a trigger for subsequent development of dysmenorrhea in young women. Int J Food Sci Nutr 2007;58:437–444. [PubMed: 17710588]
56. Flora SJ. Role of free radicals and antioxidants in health and disease. Cell Mol Biol (Noisy -le-grand) 2007;53:1–2. [PubMed: 17535753]
57. Agarwal A, Gupta S, Sharma RK. Role of oxidative stress in female reproduction. Reprod Biol Endocrinol 2005;3:28. [PubMed: 16018814]
58. Gann PH, Chatterton RT, Gapstur SM, et al. The effects of a low-fat/high-fiber diet on sex hormone levels and menstrual cycling in premenopausal women: a 12-month randomized trial (the diet and hormone study). Cancer 2003;98:1870–1879. [PubMed: 14584069]
59. Kaneda N, Nagata C, Kabuto M, et al. Fat and fiber intakes in relation to serum estrogen concentration in premenopausal Japanese women. Nutr Cancer 1997;27:279–283. [PubMed: 9101558]
60. Park OJ, Surh YJ. Chemopreventive potential of epigallocatechin gallate and genistein: evidence from epidemiological and laboratory studies. Toxicol Lett 2004;150:43–56. [PubMed: 15068824]

61. Fujiki H, Suganuma M, Okabe S, et al. Mechanistic findings of green tea as cancer preventive for humans. Proc Soc Exp Biol Med 1999;220:225–228. [PubMed: 10202393]

62. Midgette AS, Baron JA. Cigarette smoking and the risk of natural menopause. Epidemiology 1990;1:474–480. [PubMed: 2090286]

63. Kinney A, Kline J, Levin B. Alcohol, caffeine and smoking in relation to age at menopause. Maturitas 2006;54:27–38. [PubMed: 16260101]

64. Matikainen T, Perez GI, Jurisicova A, et al. Aromatic hydrocarbon receptor-driven Bax gene expression is required for premature ovarian failure caused by biohazardous environmental chemicals. Nat Genet 2001;28:355–360. [PubMed: 11455387]

65. Mattison DR, Shiromizu K, Nightingale MS. Oocyte destruction by polycyclic aromatic hydrocarbons. Am J Ind Med 1983;4:191–202. [PubMed: 6301272]

66. Kinney A, Kline J, Kelly A, et al. Smoking, alcohol and caffeine in relation to ovarian age during the reproductive years. Hum Reprod 2007;22:1175–1185. [PubMed: 17261576]

Table 1

Mean age at the onset of natural menopause and mean reproductive span according to socioeconomic and demographic factors

	No. of women n=33,054	Proportion (%)	Age at menopause (y) * Mean (SD)	*p* value	Reproductive span * (y) Mean (SD)	*p* value
Age group (y)						
40-44	179	0.5	40.6 (2.1)		26.1 (2.9)	
45-49	1385	4.2	45.4 (2.4)		30.6 (2.8)	
50-54	5523	16.7	48.8 (2.7)		33.9 (3.3)	
55-59	6901	20.9	50.0 (3.4)		35.2 (3.8)	
60-64	9072	27.5	49.6 (3.8)		34.3 (4.3)	
65-70	9994	30.2	49.1 (3.9)	<0.01	33.5 (4.3)	<0.01
Education						
College/above	4637	14.0	50.2 (3.7)		35.9 (4.1)	
High school	6812	20.6	49.6 (3.7)		35.0 (4.1)	
Middle school	7408	22.4	49.0 (3.7)		33.9 (4.1)	
Elementary school/below	14186	43.0	48.7 (4.0)	<0.01	33.0 (4.4)	<0.01
Family income						
High	8405	25.4	49.6 (3.8)		34.8 (4.2)	
Middle	12753	38.6	49.1 (3.7)		33.9 (4.1)	
Low	11889	36.0	48.9 (3.5)	<0.01	33.5 (4.6)	<0.01
Occupation						
Professional	9710	29.6	49.8 (3.7)		35.2 (4.1)	
Clerical & administrative	5710	17.4	49.1 (3.6)		33.8 (4.1)	
Manual worker	17405	53.0	48.8 (3.7)	<0.01	33.4 (4.1)	<0.01
Marital status						
Never married	194	0.6	48.2 (3.7)		33.4 (4.1)	
Presently married	27554	83.3	49.2 (3.7)		34.1 (4.1)	
Widowed	4622	14.0	48.9 (3.8)		33.5 (4.2)	
Separated/Divorced	684	2.1	49.1 (3.7)	<0.01	34.0 (4.1)	<0.01
Currently employed						
No	25386	76.8	49.1 (3.8)		33.9 (4.2)	
Yes	7668	23.2	49.4 (3.9)	*p*<0.01	34.4 (4.5)	*p*<0.01

Note: *p* values were derived from ANOVA

* Adjusted for age at enrollment (continuous) except for the 'age group' variable

Table 2

Adjusted mean differences in age at onset of natural menopause and in reproductive span according to reproductive factors

	No. of women (n=33,054)	Age at natural menopause (years)			Reproductive span (years)		
		Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$	Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$
Age at menarche (y)							
≤11	216	48.9 (4.3)	0.00 (referent)		38.1 (4.3)	0.00 (referent)	
12-13	6066	49.2 (3.7)	0.40 (0.1, 0.9)		36.4 (3.7)	−1.47 (−2.0, −1.0)	
14-15	12858	49.2 (3.6)	0.51 (0.0, 1.0)		34.7 (3.7)	−3.11 (−3.6, −2.6)	
≥16	13911	49.2 (3.8)	0.55 (0.1, 1.0)	<0.01	32.2 (4.0)	−5.43 (−5.9, −4.9)	<0.01
Delay from menarche to first live birth (y)**							
<8	15917	49.3 (3.8)	0.00 (referent)		33.3 (4.2)	0.00 (referent)	
≥8	16097	49.2 (3.6)	−0.19 (−0.3, −0.1)	*p*<0.01	34.7 (3.9)	0.91 (0.8, 1.0)	*p*<0.01
Age at first live birth (y)**							
<20	6882	49.3 (3.9)	0.00 (referent)		34.0 (4.3)	0.00 (referent)	
20-24	13951	49.2 (3.6)	−0.16 (−0.3, 0.0)		33.9 (4.1)	−0.61 (−0.7, −0.5)	
25-29	8865	49.1 (3.6)	−0.32 (−0.4, −0.2)		34.2 (4.1)	−0.81 (−1.0, −0.7)	
≥30	2319	49.0 (3.5)	−0.49 (−0.7, −0.3)	<0.01	34.2 (3.9)	−0.86 (−1.1, −0.6)	<0.01
Number of live births							
0	1037	48.3 (3.8)	0.00 (referent)		33.2 (4.3)	0.00 (referent)	
1	6177	48.3 (3.6)	0.30 (0.0, 0.6)		33.6 (4.0)	0.29 (0.0, 0.6)	
2	11234	49.6 (3.5)	1.23 (1.0, 1.5)		34.6 (4.0)	1.18 (0.9, 1.5)	
3	7174	49.5 (3.7)	1.10 (0.8, 1.3)		34.0 (4.2)	1.06 (0.8, 1.3)	
≥4	7432	49.2 (4.0)	0.73 (0.5, 1.0)	<0.01	33.5 (4.3)	0.73 (0.4, 1.0)	<0.01
Cumulative breastfeeding (months)**							
No breastfeeding	3015	48.8 (3.8)	0.00 (referent)		34.0 (4.2)	0.00 (referent)	
≤12	7236	48.8 (3.6)	0.14 (0.0, 0.3)		34.1 (4.0)	0.04 (−0.1, 0.2)	
≤24	8888	49.5 (3.5)	0.75 (0.6, 0.9)		34.5 (3.9)	0.56 (0.4, 0.7)	
≤36	5515	49.4 (3.7)	0.63 (0.5, 0.8)		33.9 (4.2)	0.44 (0.3, 0.4)	
>36	7363	49.2 (3.9)	0.45 (0.3, 0.6)	<0.01	33.5 (4.4)	0.25 (0.1, 0.4)	<0.01
Age at last live birth (y)**							
<25	4185	49.2 (3.7)	0.00 (referent)		34.3 (4.1)	0.00 (referent)	
25-29	15926	49.1 (3.7)	−0.26 (−0.4, −0.1)		33.9 (4.1)	−0.57 (−0.7, −0.4)	
30-34	9750	49.2 (3.7)	−0.36 (−0.5, −0.2)		34.0 (4.2)	−0.79 (−0.9, −0.6)	
≥35	2156	49.6 (3.7)	−0.17 (−0.4, 0.0)	<0.01	34.4 (4.2)	−0.62 (−0.8, −0.4)	<0.01
Menstrual cycle regularity							
Always regular	11029	49.2 (3.7)	0.00 (referent)		34.0 (4.1)	0.00 (referent)	
Sometimes regular	19870	49.2 (3.7)	−0.02 (−0.1, 0.1)		34.0 (4.1)	−0.04 (−0.1, 0.1)	
Irregular	2153	49.0 (4.1)	−0.14 (−0.3, 0.0)	0.17	33.6 (4.6)	−0.40 (−0.6, −0.2)	<0.01
Oral contraceptive (OC) use							
Never	24654	49.1 (3.8)	0.00 (referent)		33.9 (4.2)	0.00 (referent)	
Ever	8400	49.4 (3.4)	0.48 (0.4, 0.6)	*p*<0.01	34.4 (3.8)	0.50 (0.4, 0.6)	*p*<0.01
Intrauterine device (IUD) use							
Never	23521	49.2 (3.8)	0.00 (referent)		33.9 (4.3)	0.00 (referent)	
Ever	9533	49.0 (3.5)	0.18 (0.1, 0.3)	*p*<0.01	34.0 (3.8)	0.11 (0.0, 0.2)	*p*=0.047
Tubal sterilization							
No	23694	49.1 (3.6)	0.00 (referent)		34.0 (4.1)	0.00 (referent)	
Yes	9360	49.3 (3.8)	0.21 (0.1, 0.3)	*p*<0.01	33.9 (4.3)	0.23 (0.1, 0.3)	*p*<0.01

Note:

$P_{for\ trend}$ values were derived from multivariable linear regression by entering the categorical variables as continuous parameters in the model

p values for dichotomous variables were driven from the linear regression model

p values <0.01 did not change after Bonferroni corrections

* Adjusted for age (continuous), education, occupation, income, marital status, current employment (yes/no), energy intake (kcal, continuous), weight gain between age 20 and 50 yrs (categorized), cigarette smoking (never/ever), and leisure-time physical activity patterns in adolescence and adulthood (categorized)

** Among parous women only

Table 3

Adjusted mean differences in age at onset of menopause and in reproductive span according to anthropometric factors

	No. of women**	Age at natural menopause (y)			Reproductive span (y)		
		Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$	Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$
Weight at age 20 (kg, Q_{1-4})	n=27,165						
<45.0	5803	49.1 (3.7)	0.00 (referent)		33.9 (4.2)	0.00 (referent)	
45.0-48.0	7141	49.2 (3.6)	0.15 (0.0, 0.3)		34.2 (4.0)	0.19 (0.1, 0.3)	
49.0-53.0	7298	49.3 (3.6)	0.21 (0.1, 0.3)		34.2 (4.0)	0.25 (0.1, 0.4)	
≥54.0	6923	49.2 (3.7)	0.30 (0.2, 0.54)	<0.01	34.1 (4.2)	0.31 (0.2, 0.5)	<0.01
Height at age 20 (m, Q_{1-4})	n=26,104						
<1.55	5869	49.1 (3.7)	0.00 (referent)		34.0 (4.2)	0.00 (referent)	
1.55-1.57	5477	49.3 (3.7)	0.13 (0.0, 0.3)		34.3 (4.1)	0.14 (0.0, 0.3)	
1.58-1.60	7792	49.2 (3.6)	0.05 (−0.1, 0.2)		34.2 (4.0)	0.06 (−0.1, 0.2)	
≥1.61	6966	49.2 (3.7)	0.06 (−0.1, 0.2)	0.69	34.1 (4.1)	0.03 (−0.1, 0.2)	0.96
BMI at age 20 (kg/m^2, Q_{1-4})	n=24,648						
<18.0	6166	49.1 (3.7)	0.00 (referent)		34.0 (4.1)	0.00 (referent)	
18.0-19.4	6053	49.2 (3.6)	0.10 (0.0, 0.2)		34.3 (4.1)	0.12 (0.0, 0.3)	
19.5-21.3	6305	49.3 (3.6)	0.20 (0.1, 0.3)		34.2 (4.0)	0.24 (0.1, 0.4)	
≥21.4	6124	49.2 (3.7)	0.22 (0.1, 0.4)	<0.01	34.1 (4.2)	0.24 (0.1, 0.4)	<0.01
Weight gain between ages 20 and 50 years (kg, Q_{1-4})†	n=25,926						
<2.0	6073	49.0 (3.7)	0.00 (referent)		33.7 (4.2)	0.00 (referent)	
2.0-6.9	6661	49.3 (3.7)	0.25 (0.1, 0.4)		34.1 (4.1)	0.26 (0.1, 0.4)	
7.0-12.4	6283	49.3 (3.6)	0.36 (0.2, 0.5)		34.3 (4.0)	0.40 (0.3, 0.5)	
≥12.5	6912	49.2 (3.7)	0.44 (0.3, 0.6)	<0.01	34.3 (4.1)	0.48 (0.4, 0.6)	<0.01

Note: *p* values <0.01 did not change after Bonferroni corrections

*Adjusted for age (continuous), education, occupation, age at menarche (categorized), number of live births (categorized), past use of oral contraceptives (never/ever), weight gain between age 20 and 50 years (categorized) except for the same variable, cigarette smoking (ever/never), leisure-time physical activity pattern in adolescence and adulthood (categorized), and energy intake (continuous)

**Number of women with information on anthropometric factors at age 20

†Weight gain for women <50 years was defined as recalled weight gain between age 20 and current age; for women ≥50 years, weight gain was defined as recalled weight gain between ages 20 and 50

Menopause. Author manuscript; available in PMC 2009 September 1.

Table 4

Adjusted mean differences in at age of onset of menopause and reproductive span according to patterns of leisure-time physical activity (LTPA)

	No. of women n=33,054	Age at natural menopause (y)			Reproductive span (y)		
		Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$	Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$
Self-rated adolescent LTPA (age 13-19 y)	N=32,597						
Low	17510	49.1 (3.8)	0.00 (referent)		33.6 (4.2)	0.00 (referent)	
Moderate-High	15087	49.3 (3.6)	1.35 (0.0, 2.7)	*p*=0.048	34.4 (4.0)	1.04 (−0.3, 2.4)	*p*=0.14
Intensity of LTPA, hrs/wk/yr† (age 13-19 y)	N=33,054						
None	14289	49.1 (3.9)	0.00 (referent)		33.4 (4.3)	0.00 (referent)	
<1.2	4675	48.7 (3.7)	0.06 (−0.1, 0.2)		33.6 (4.0)	0.16 (0.0, 0.3)	
1.2-1.9	1831	49.0 (3.6)	0.16 (0.0, 0.4)		34.1 (4.0)	0.26 (0.0, 0.5)	
2.0-3.9	8283	49.4 (3.5)	0.35 (0.2, 0.5)		34.8 (3.9)	0.45 (0.3, 0.6)	
≥4.0	3976	49.5 (3.5)	0.47 (0.2, 0.7)	<0.01	34.9 (3.8)	0.56 (0.3, 0.8)	<0.01
Self-rated adolescent/adult LTPA	N=32,481						
Low/Low	10373	49.1 (3.8)	0.00 (referent)		33.6 (4.2)	0.00 (referent)	
Low/Moderate-High	7068	49.1 (3.9)	−0.10 (−0.2, 0.0)		33.6 (4.3)	−0.08 (−0.2, 0.0)	
Moderate-High/Low	8073	49.1 (3.6)	0.09 (0.0, 0.2)		34.3 (4.0)	0.11 (0.0, 0.2)	
Moderate-High/Moderate-High	6967	49.5 (3.5)	0.23 (0.1, 0.3)	<0.01	34.6 (3.9)	0.28 (0.1, 0.4)	<0.01

Note:

$P_{for\ trend}$ were derived from multivariable linear regression by entering the categorical variables as continuous parameters in the model

p values for dichotomous variables were driven from the linear regression model

p values <0.01 did not change after Bonferroni corrections

* Adjusted for age (continuous), education, occupation, age at menarche (categorized), number of live births (categorized), past use of oral contraceptives (never/ever), weight gain between age 20 and 50 (categorized), cigarette smoking (ever/never), leisure-time physical activity pattern in adolescence and adulthood (categorized) except for the same variable, and energy intake (continuous)

Table 5

Adjusted mean differences in age at onset of menopause and in number of reproductive years according to dietary intakes

	No. of women n=33,054	Age at natural menopause (y)			Reproductive span (y)		
		Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$	Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$
Total energy (kcal/day)							
≤1281.5	5486	48.9 (3.8)	0.00 (referent)		33.5 (4.3)	0.0 (referent)	
1281.6-1458.6	5519	49.1 (3.7)	0.21 (0.1, 0.3)		33.9 (4.2)	0.24 (0.1, 0.4)	
1458.7-1608.3	5489	49.3 (3.6)	0.35 (0.2, 0.5)		34.2 (4.0)	0.40 (0.3, 0.5)	
1608.4-1774.4	5519	49.3 (3.6)	0.37 (0.2, 0.5)		34.2 (4.1)	0.39 (0.3, 0.5)	
1774.4-2005.0	5520	49.3 (3.6)	0.38 (0.2, 0.5)		34.2 (4.1)	0.42 (0.3, 0.6)	
>2005.1	5521	49.2 (3.7)	0.39 (0.3, 0.5)	<0.01	34.0 (4.2)	0.40 (0.3, 0.5)	<0.01
Total vegetables (g/day)							
≤139.6	5487	49.0 (3.9)	0.00 (referent)		33.7 (4.3)	0.00 (referent)	
140.0-194.7	5519	49.1 (3.6)	0.08 (0.0, 0.2)		33.9 (4.0)	0.05 (−0.1, 0.2)	
194.8-250.1	5487	49.2 (3.7)	0.11 (0.0, 0.2)		34.0 (4.1)	0.09 (0.0, 0.2)	
250.2-318.4	5521	49.2 (3.7)	0.13 (0.0, 0.3)		34.1 (4.2)	0.11 (0.0, 0.3)	
318.5-423.4	5520	49.2 (3.7)	0.11 (0.0, 0.3)		34.1 (4.2)	0.06 (−0.1, 0.2)	
>423.5	5520	49.2 (3.7)	0.06 (−0.1, 0.2)	0.39	34.1 (4.2)	0.00 (−0.1, 0.2)	0.83
Total fruits (g/day)							
≤73.3	5485	48.9 (3.9)	0.00 (referent)		33.4 (4.4)	0.00 (referent)	
73.4-142.4	5520	49.1 (3.7)	0.10 (0.0, 0.2)		33.8 (4.2)	0.13 (0.0, 0.3)	
142.5-209.3	5487	49.3 (3.6)	0.22 (0.1, 0.4)		34.1 (4.1)	0.23 (0.1, 0.4)	
209.4-283.6	5521	49.2 (3.7)	0.10 (0.0, 0.2)		34.1 (4.1)	0.13 (0.0, 0.3)	
283.7-383.1	5521	49.3 (3.6)	0.24 (0.1, 0.4)		34.3 (4.0)	0.26 (0.1, 0.4)	
>383.2	5520	49.2 (3.7)	0.13 (0.0, 0.3)	0.04	34.1 (4.2)	0.15 (0.0, 0.3)	0.03
Red meat (g/day)							
≤17.4	5485	49.1 (3.8)	0.00 (referent)		33.7 (4.2)	0.00 (referent)	
17.5-27.9	5516	49.2 (3.7)	0.11 (0.0, 0.2)		34.0 (4.2)	0.11 (0.0, 0.2)	
28.0-38.1	5492	49.1 (3.7)	0.00 (0.1, 0.1)		33.9 (4.1)	0.00 (−0.1, 0.1)	
38.2-50.9	5519	49.2 (3.6)	0.06 (−0.1, 0.2)		34.1 (4.0)	0.07 (−0.1, 0.2)	
51.0-70.8	5517	49.2 (3.7)	0.04 (−0.1, 0.2)		34.1 (4.1)	0.04 (−0.1, 0.2)	
>70.9	5523	49.2 (3.7)	−0.05 (−0.2, 0.1)	0.37	34.1 (4.1)	−.0.05 (−0.2, 0.1)	0.47
Total fat (g/day)							
≤16.0	5481	49.0 (3.8)	0.00 (referent)		33.4 (4.2)	0.00 (referent)	
16.1-21.1	5529	49.1 (3.7)	0.02 (−0.1, 0.1)		33.7 (4.2)	0.03 (−0.1, 0.2)	
21.2-25.6	5486	49.2 (3.7)	0.08 (−0.1, 0.2)		34.0 (4.2)	0.11 (0.0, 0.2)	
25.7-30.8	5514	49.2 (3.6)	0.05 (−0.1, 0.2)		34.2 (4.1)	0.09 (−0.1, 0.2)	
30.9-38.2	5523	49.3 (3.6)	0.08 (−0.1, 0.2)		34.3 (4.1)	0.12 (0.0, 0.3)	
>38.3	5521	49.2 (3.7)	−0.07 (−0.2, 0.1)	0.90	34.2 (4.2)	−0.03 (−0.2, 0.1)	0.66
Saturated fat (g/day)							
≤4.2	5487	48.9 (3.8)	0.00 (referent)		33.4 (4.2)	0.00 (referent)	
4.3-5.8	5529	49.2 (3.7)	0.15 (0.0, 0.3)		33.8 (4.2)	0.17 (0.0, 0.3)	
5.9-7.3	5494	49.2 (3.7)	0.09 (0.0, 0.2)		34.0 (4.1)	0.12 (0.0, 0.3)	
7.4-9.0	5499	49.2 (3.6)	0.06 (−0.1, 0.2)		34.1 (4.1)	0.12 (0.0, 0.3)	
9.1-11.4	5516	49.3 (3.6)	0.10 (0.0, 0.3)		34.4 (4.0)	0.16 (0.0, 0.3)	
>11.5	5528	49.3 (3.7)	0.01 (−0.2, 0.2)	0.80	34.3 (4.2)	0.06 (−0.1, 0.2)	0.64
Total protein (g/day)							
≤45.7	5490	48.9 (3.8)	0.00 (referent)		33.4 (4.2)	0.00 (referent)	
45.8-54.2	5514	49.1 (3.8)	0.17 (0.0, 0.3)		33.8 (4.2)	0.19 (0.0, 0.3)	
54.3-61.7	5492	49.2 (3.6)	0.21 (0.1, 0.4)		34.0 (4.1)	0.24 (0.1, 0.4)	
61.8-70.3	5508	49.3 (3.6)	0.26 (0.1, 0.4)		34.2 (4.0)	0.30 (0.1, 0.5)	
70.4-82.6	5527	49.3 (3.7)	0.26 (0.1, 0.4)		34.3 (4.1)	0.30 (0.1, 0.5)	
>82.7	5523	49.3 (3.8)	0.24 (0.0, 0.4)	0.02	34.3 (4.2)	0.28 (0.1, 0.5)	<0.01
Total soy (g/day)							

	No. of women n=33,054	Age at natural menopause (y)			Reproductive span (y)		
		Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$	Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$
≤39.9	5486	49.0 (3.7)	0.00 (referent)		33.6 (4.2)	0.00 (referent)	
40.0-68.6	5519	49.2 (3.6)	0.16 (0.0, 0.3)		34.0 (4.1)	0.16 (0.0, 0.3)	
68.7-103.9	5488	49.2 (3.7)	0.12 (0.0, 0.3)		34.0 (4.2)	0.12 (0.0, 0.3)	
104.0-166.5	5522	49.3 (3.6)	0.20 (0.1, 0.3)		34.2 (4.0)	0.22 (0.1, 0.4)	
166.6-295.1	5519	49.3 (3.7)	0.17 (0.0, 0.3)		34.0 (4.1)	0.16 (0.0, 0.3)	
>295.2	5520	49.2 (3.8)	0.07 (−0.1, 0.2)	0.30	34.0 (4.3)	0.08 (−0.1, 0.2)	0.26
Total fiber (g/day)							
≤6.8	5479	48.9 (3.8)	0.00 (referent)		33.5 (4.2)	0.00 (referent)	
6.9-8.6	5525	49.1 (3.7)	0.10 (0.0, 0.2)		34.0 (4.1)	0.12 (0.0, 0.3)	
8.7-10.2	5497	49.2 (3.6)	0.22 (0.1, 0.3)		34.0 (4.1)	0.22 (0.1, 0.4)	
10.3-11.9	5499	49.3 (3.7)	0.25 (0.1, 0.4)		34.2 (4.1)	0.23 (0.1, 0.4)	
12.0-14.4	5533	49.2 (3.7)	0.15 (0.0, 0.3)		34.2 (4.1)	0.15 (0.0, 0.3)	
>14.5	5521	49.2 (3.8)	0.13 (0.0, 0.3)	0.09	34.2 (4.2)	0.11 (−0.1, 0.3)	0.20
Total carbohydrates (g/day)							
≤223.9	5485	49.0 (3.8)	0.00 (referent)		33.7 (4.3)	0.00 (referent)	
224.0-253.5	5521	49.2 (3.7)	0.14 (0.0, 0.3)		34.0 (4.2)	0.17 (0.0, 0.3)	
253.6-277.8	5486	49.2 (3.6)	0.22 (0.1, 0.4)		34.1 (4.1)	0.21 (0.1, 0.4)	
278.9-305.6	5523	49.3 (3.7)	0.24 (0.1, 0.4)		34.2 (4.1)	0.27 (0.1, 0.4)	
305.7-346.7	5518	49.2 (3.7)	0.20 (0.0, 0.4)		34.1 (4.1)	0.22 (0.0, 0.4)	
>346.8	5521	49.2 (3.7)	0.24 (0.0, 0.5)	0.04	33.9 (4.1)	0.21 (0.0, 0.5)	0.06

Note : Dietary intakes categorized into sixths (from low to high)

*Adjusted for age (continuous), education, occupation, age at menarche (categorized), number of live births (categorized), past use of oral contraceptives (never/ever), weight gain between age 20 and 50 (categorized), cigarette smoking (ever/never) except for the same variable, leisure-time physical activity pattern in adolescence and adulthood (categorized), and energy intake (continuous) except for the same variable

Table 6

Adjusted mean differences in age at onset of menopause and in number of reproductive years according to smoking, tea and alcohol consumption

	No. of women n=33,054	Age at natural menopause (y)			Reproductive span (y)		
		Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$	Mean (SD)	Mean difference β(95% CI)*	$P_{for\ trend}$
Smoking status							
Never smoked	31615	49.2 (3.7)	0.00 (referent)		34.0 (4.1)	0.00 (referent)	
Former smoker	271	48.9 (4.0)	−0.40 (−0.8, 0.0)		33.3 (4.5)	−0.51 (−0.9, 0.0)	
Current smoker	1167	48.4 (4.1)	−0.76 (−1.0, −0.5)	<0.01	32.8 (4.4)	−0.78 (−1.0, −0.6)	<0.01
Years of smoking :							
<28 years**	686	48.6 (3.8)	−0.51 (−0.8, −0.2)		33.2 (4.1)	−0.53 ((−0.8, −0.2)	
≥28 years	752	48.3 (4.3)	−0.86 (−1.1, −0.6)	<0.01	32.6 (4.7)	−0.90 (−1.2, −0.6)	<0.01
Regular alcohol consumption							
Never	32252	49.2 (3.7)	0.00 (referent)		33.8 (4.7)	0.00 (referent)	
Ever	802	49.1 (4.2)	−0.05 (−0.3, 0.2)	*p*=0.73	34.0 (4.1)	−0.06 (−0.3, 0.2)	*p*=0.65
Regular tea use							
Never	24968	49.1 (3.7)	0.00 (referent)		33.9 (4.1)	0.00 (referent)	
Ever	8089	49.3 (3.7)	0.08 (0.0, 0.2)	*p*=0.09	34.4 (4.1)	0.10 (0.0, 0.2)	*p*=0.04
Years of tea consumption							
<19 years**	3931	49.2 (3.7)	0.07 (−0.1, 0.2)		34.3 (4.1)	0.08 (0.0, 0.2)	
≥19 years	4154	49.3 (3.7)	0.09 (0.0, 0.2)	0.10	34.5 (4.1)	0.12 (0.0, 0.2)	0.03

Note : Years of smoking or years of tea consumption categorized into median distribution

$P_{for\ trend}$ values were derived from multivariable linear regression by entering the categorical variables as continuous parameters in the model

p values for dichotomous variables were driven from the linear regression model

p values <0.01 did not change after Bonferroni corrections

* Adjusted for age (continuous), education, occupation, age at menarche (categorized), number of live births (categorized), past use of oral contraceptives (never/ever), weight gain between age 20 and 50 years (categorized), cigarette smoking (ever/never) except for the same variable, adolescence-adult leisure time-physical activity pattern (categorized), and energy intake (continuous) except for the same variable

** 'never smoked' and 'never regular tea use' categories are used as a referent