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Association of bilateral oophorectomy and body fatness in a representative sample of US women

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Abstract

Objective—Preclinical studies suggest that abrupt hormone deprivation caused by oophorectomy, leads to obesity and its metabolic sequelae. The purpose of the current study was to examine the association between oophorectomy and body fatness in a nationally representative sample of women.

Methods—The association between prior oophorectomy and nine adiposity measures was examined using data from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994). The analytic population included cancer-free women age 40 or older (N=3549) who underwent standardized body measurements and reported on whether or not they had a bilateral oophorectomy. Multivariate linear and polytomous logistic regressions were used to evaluate the association of oophorectomy with multiple measures of adiposity.

Results—Mean percent body fat, skinfold thickness, waist circumference and body mass index were significantly higher in women with oophorectomy before age 40 compared to those with intact ovaries, but no difference was observed in women with oophorectomy at an older age. Women who underwent an early oophorectomy were nearly three times more likely than women with intact ovaries to have percent body fat in the highest tertile compared to the lowest tertile (OR=2.82, 95% CI 1.39–5.75). Excluding hormone therapy (HT) users yielded stronger associations.

Conclusion—Bilateral oophorectomy in young women is strongly associated with an increase in percent body fat, a well-established risk factor for cancer and other chronic diseases. Measuring body fat in addition to BMI may provide a more comprehensive assessment of adiposity in these women.

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Introduction

Each year approximately 300,000 women have their ovaries removed, both for benign gynecologic conditions as well as for cancer prevention (1). In the general population, oophorectomy has been associated with a decrease in breast and ovarian cancer (2–6), and in some studies, an increase in all-cause mortality, primarily related to cardiovascular disease (7–9). Estrogen is believed to play a major role but the exact mechanisms underlying this association have not been clearly elucidated.

During natural menopause the ovaries gradually stop producing estrogen, while androgen production continues (10). This change in hormonal milieu is associated with increased central abdominal adiposity (11, 12). Animal studies have consistently demonstrated a relationship between bilateral oophorectomy and increased adiposity (13–15) and insulin resistance (13, 16, 17) and higher total and LDL-cholesterol (13, 18). A few clinical studies and two population based studies have examined the association of oophorectomy with weight, body mass index (BMI), and waist circumference (WC), however the results have been inconsistent (12, 19–24). No study has specifically evaluated body fat as measured by bioelectrical impedance analysis (BIA). BIA measures the opposition of body tissue to the flow of a small electric current, which can be used to estimate total body water, fat free mass, and percent body fat.(25, 26)

The current study examines the association between bilateral oophorectomy, and percent body fat, skinfold thickness, waist circumference and body mass index, in a nationally representative sample of U.S women.

Methods

Study Population

The Third National Health and Nutrition Examination Survey (NHANES III), conducted from 1988 to 1994, is a cross-sectional, nationally representative survey of the US population that included interviews, physical examinations, and blood testing. Details of the study design and methods have been published (27).

Our study population included women aged 40 years and older who completed both the interview and the exam (N=5076). Women were excluded if they did not answer the survey question about oophorectomy (N=324), reported unilateral oophorectomy or unknown type of oophorectomy (N=376), were missing age at oophorectomy (N=7), had oophorectomy performed <25 years(N=15), reported a hysterectomy at a younger age than oophorectomy (N=43), reported a prior reproductive cancer (breast N=94, cervical N=27, uterine N=39, ovarian N=11), were missing information on weight, height, or waist or buttocks circumference (N=244), missing self-reported weight at age 25 (N=342) or were pregnant (N=5). This yielded a study population of 3549 women. Analyses of percent body fat include only women who additionally underwent bioelectrical impedance analysis (BIA) (N=3303), and analyses of skinfolds include only women with complete skinfold measures (N=3369). For brevity, ‘oophorectomy’ will denote ‘bilateral oophorectomy’ for the remainder of the manuscript.

Adiposity Measures

Survey staff conducted standardized body measurements that included weight, height, waist circumference (WC), buttocks circumference, and skinfolds. Detailed protocols were used to ensure accuracy and reliability of anthropometric measures (28). Skinfold measures were performed in duplicate, and if the difference in measures was outside a specific tolerance range, the skinfold measures were repeated. Body mass index (BMI) and waist-hip ratio (WHR) were calculated from these measures ($BMI = \text{weight(kg)}/\text{height(m)}^2$, $WHR = \text{waist circumference (cm)}/\text{buttocks circumference(cm)}$). Bioelectrical impedance analysis (BIA) was performed on study participants, and percent body fat was calculated from BIA resistance and weight using prediction equations described previously (25). Women were also asked to report their weight at age 25, and weight 10 years ago. BMI at age 25 was calculated from self-reported weight at age 25 and height measured at interview. BMI 10 years ago was calculated from self-reported weight 10 years ago and height measured at interview.

Statistical Analyses

Weighted means and proportions of descriptive statistics were calculated by oophorectomy status. We defined hormone therapy (HT) users as women who reported ever using estrogen or female hormone pills. Detailed information about type of HT was not ascertained. We categorized menopausal status at interview in the following manner: premenopausal women reported a menstrual period or pregnancy in the last year, postmenopausal women reported bilateral oophorectomy or no menstrual period in the last year. For the subgroup of women whose menopause status could not be determined from reports of menstrual bleeding (N=557), women <51 years were categorized as premenopausal, and women ≥51 years were considered postmenopausal, consistent with the median age of menopause in our study population and the average age of menopause in the US (29). Oophorectomy status was categorized as intact ovaries, oophorectomy <40 years, and oophorectomy ≥40 years. Since menopause status at oophorectomy was not available, we chose an age cutoff of 40 years since women <40 years are likely to be premenopausal. Participants were asked about their leisure time physical activity in the past month, which was classified by rate of energy expenditure using a standardized coding scheme (30). Moderate or vigorous physical activity was categorized: no physical activity, physical activity <3 times per week, 3–7 times per week, and >7 times per week.

We examined the correlations among adiposity measures. Means for adiposity measures were standardized to the 2000 Standard Population using the direct method with 5 year age intervals. Distributions of adiposity measures were examined graphically and with the exception of skinfolds, no significant departures from normality were observed. The calipers used to measure skinfolds had an upper limit of 50 cm and participants with skinfolds larger than 50 cm were noted. Therefore, tobit regression for censored data was used to analyze skinfold data. Multivariate linear or tobit regression was conducted to examine the association of oophorectomy with adiposity, adjusted for age at interview, race/ethnicity, income, parity, smoking status, education, alcohol, oral contraceptive use, and BMI at age 25. Regressions of weight were additionally adjusted for height. We did not adjust for physical activity in the final models because there was no difference in activity by

oophorectomy status, and inclusion of physical activity in the models did not significantly alter effect estimates. In addition, though region was associated with oophorectomy status, it was not associated with measures of adiposity. Adjusting for region in the multivariate model did not meaningfully change effect estimates, so region was not included in the final multivariate models. Because of the high correlations between adiposity measures, we did not mutually adjust models for other measures (31). Weight, BMI, WC, and percent body fat were all highly correlated with one another ($r^2 = 0.76\text{--}0.93$). Subscapular, suprailiac, and tricep skinfold measurements were highly correlated with each other ($r^2 = 0.75\text{--}0.81$) and weight, BMI, WC and percent body fat ($r^2 = 0.66\text{--}0.78$).

Additionally, the following sensitivity analyses were performed for linear and tobit regression models: stratifying by HT use, limiting the study population to women younger than age 70, stratifying by time since oophorectomy (15 years prior to interview or >15 years prior to interview) and by race, using various categories for age at oophorectomy, limiting the study population to postmenopausal women aged 50–65, examining adiposity in women with hysterectomy only at a young age, and adjusting for number of calories and grams of fat consumed from 24 hour dietary recall.

Finally, to compare across adiposity measures, we divided each adiposity measure into tertiles, and used polytomous logistic regression to examine the odds of adiposity in the highest tertile for women with oophorectomy <40 compared to women with intact ovaries. All analyses incorporated examination sampling weights using survey commands in Stata IC 10 (College Station, TX). NHANES III was approved by the IRB of the National Center for Health Statistics, and since the data was de-identified for use by researchers outside CDC, this study was exempt from review by the Johns Hopkins School of Public Health IRB.

Results

Table 1 compares the descriptive characteristics for 502 women who had an oophorectomy to 3047 women with intact ovaries. Women with oophorectomy were slightly older, less educated, drank less alcohol, and were more likely to reside in the southern states of the US than women with intact ovaries. The median age at oophorectomy was 43 years (range 26–79), and the median time since oophorectomy was 17 years. Nearly all women with oophorectomy also had a hysterectomy. Additionally, over 70% of women with oophorectomy reported past or current HT use, compared to 18% of women with intact ovaries.

Table 2 displays the age-standardized mean for all nine adiposity measures by oophorectomy status. Women who reported having an oophorectomy <40 years had significantly higher adiposity measures compared to those with intact ovaries, including mean WC, percent body fat, tricep and thigh skinfolds. Older women who underwent oophorectomy had similar adiposity to women with intact ovaries.

Table 3 displays the results of a multivariate linear regression examining the association between oophorectomy and multiple adiposity measures. Overall, after adjusting for age at interview, race, income, education, parity, smoking, alcohol, oral contraceptives, and BMI at

age 25, women with oophorectomy had significantly higher body fat when compared to women with intact ovaries. When stratified by age at oophorectomy, women who had their ovaries removed at <40 years were on average 6.82 lbs heavier, had 1.23 kg/m² greater BMI, 2.36% greater body fat, and 3.10 cm greater WC than women with intact ovaries. Significant differences were not observed in women with oophorectomy performed at an older age. When we excluded women who reported using HT, the magnitude of the associations between oophorectomy and adiposity measures (percent body fat, weight, BMI, WC) was even stronger. In HT non-users, oophorectomy <40 years was significantly associated with higher percent body fat ($\beta=2.89\%$, $p=0.017$). Weight, BMI, and WC were also higher in non-HT users with oophorectomy <40 years, but these estimates did not reach statistical significance, likely due to the small sample size in this subgroup (N=56).

Table 4 displays the results of tobit regression for skinfold measures by oophorectomy status. Tobit regression estimates linear relationships in the presence of censored values, and was therefore used to account for women with skinfold thickness too large to be measured with calipers (>50mm). Oophorectomy at a young age was significantly associated with greater skinfold thickness across all four measures. After excluding HT users, oophorectomy was more strongly associated with tricep, suprailiac and subscapular skinfold thickness.

We performed sensitivity analyses using various age categories for oophorectomy, and found the strongest association with adiposity measures among women with oophorectomy performed younger than 40. Effect estimates for women with oophorectomy <40 years were even stronger when the analysis was limited to women <70 years at interview or to postmenopausal women age 50–65 years. A similar pattern was observed for both non-Hispanic white and non-Hispanic black women, with oophorectomy <40 years being associated with increased adiposity. However, the beta estimates were larger for black women with oophorectomy than white women with oophorectomy. Of note, black women with oophorectomy were less likely to be HT users than white women with oophorectomy (57% vs. 73%, respectively) and black women had significantly higher self-reported BMI at age 25 than white women. Women with hysterectomy alone before age 40 years did not have significantly higher adiposity compared to women with intact ovaries and uterus, which supports the conclusion that increased adiposity among women with oophorectomy at a young age is due to removal of the ovaries rather than the uterus. Furthermore, women with oophorectomy at a young age reported consuming slightly fewer calories and grams of fat in 24 hour dietary recall than women with intact ovaries, however adjusting for calorie and fat consumption did not meaningfully alter our observed results.

Polytomous logistic regression was used to compare the association of early oophorectomy across different adiposity measures (Table 5). We chose to examine tertiles rather than clinically defined cut points because a large proportion of women in our study population had measurements above such cutoffs. Women with oophorectomy <40 years were nearly three times more likely to have body fat and suprailiac skinfolds in the highest tertile compared to women with intact ovaries. They were also more than twice as likely to have weight and BMI in the highest tertile as women with intact ovaries.

Discussion

To our knowledge this is the first population-based study to evaluate the relationship between oophorectomy and body fat. Women with oophorectomy at a young age had significantly higher age-adjusted mean percent body fat, skinfold thickness, BMI, and WC compared to women with intact ovaries after adjusting for potential confounders including age, race, and BMI at age 25 years. When adiposity measures were compared across tertiles, early oophorectomy was most strongly associated with percent body fat and suprailiac skinfold thickness. Women with oophorectomy were nearly three times more likely to be in the highest tertile of body fat and suprailiac skinfold thickness compared to those with intact ovaries. Associations between oophorectomy and adiposity measures were even stronger among women who never used HT. In subgroup analyses among women with early oophorectomy, percent body fat was the only measure to reach statistical significance. These results are consistent with the hypothesis that estrogen deprivation is key factor driving increased adiposity in this group.

To our knowledge no other study has examined the relationship between oophorectomy and body fat. BMI is the most commonly used adiposity measure, however it does not differentiate between lean and fat mass. Several studies have found percent body fat as measured by BIA to be more predictive of CVD, diabetes, and mortality than BMI (32–36), and that percent body fat is associated with such outcomes even among those with normal BMI.(37–44) In a population based study in Norway comparing 263 women aged 40–69 years with oophorectomy to 789 age-matched controls with intact ovaries (23), women who had an oophorectomy prior to age 50 were more likely to have BMI 30 kg/m^2 (30% vs. 21%, $p=0.003$) and WC $>88\text{cm}$ (41% vs. 32%, $p=0.005$) compared to age matched controls with intact ovaries (23). This result is consistent with ours, given that it examined women with similar ages at oophorectomy and excluded HT users. A limited number of studies have examined changes in adiposity before and after oophorectomy. In a longitudinal study of 2,500 women age 42–52 years who had BMI $<30 \text{ kg/m}^2$ and intact ovaries at baseline, those who had surgical menopause over 9 years of follow-up ($N=162$) were significantly more likely to develop severe obesity (BMI 35 kg/m^2 , HR=5.07, 95% CI 2.29–11.20) than women who remained premenopausal after adjusting for HT use (12). In this study only 60% of women in the surgical menopause group had an oophorectomy. A study of 1962 premenopausal women aged 42–52 at baseline found that BMI increased for all women over the menopause transition, however the rate of increase in BMI was greatest for women with bilateral oophorectomy and hysterectomy compared to women with hysterectomy alone or natural menopause after adjusting for HT use.(24) Two small studies ($N<25$) with short follow-up found no significant differences in weight, BMI, or WHR before and after oophorectomy performed in premenopausal women (21, 22). To our knowledge no existing studies have specifically measured percent body fat or skinfold thickness in women with oophorectomy.

Because of the cross-sectional design of NHANES III we cannot determine causality between oophorectomy and body fat. However, we did not see evidence that heavier women were more likely to undergo an oophorectomy in NHANES III. Women with oophorectomy <40 years reported similar weight at age 25 to women with intact ovaries. Nevertheless we

adjusted for BMI at age 25 in all multivariate models. In addition, women who had an oophorectomy within 10 years of interview reported similar weight 10 years ago as women with intact ovaries. For all these reasons it is unlikely that our findings are completely explained by weight prior to oophorectomy. Studies of hysterectomy and adiposity in two British birth cohorts suggest that women who are overweight or obese may have increased likelihood of hysterectomy, regardless of oophorectomy status (45, 46). Overweight and obese women have increased risk of gynecological conditions such as fibroids, endometriosis, and menstrual problems which may increase the likelihood of gynecologic surgery (45).

A few limitations of the data should be considered. Self-report of oophorectomy has not been validated in NHANES III, however three previous studies suggest that self-report of oophorectomy status is valid (6, 47, 48). The validation study conducted in the Cancer and Steroid Hormone (CASH) study is most relevant to NHANES III, since it was a population based survey with cancer-free controls recruited with random-digit dialing (48). This study found 90% agreement between self-report of oophorectomy and medical records, and agreement was high regardless of age or hysterectomy status. Though it is not possible to validate self-report of oophorectomy in NHANES III, in order for our results to be due to reporting bias alone, women with higher adiposity would need to be significantly more likely to mis-report oophorectomy status than lean women. Given the relatively large magnitude of associations we observed, the reporting bias would need to be rather large to fully explain our results. Another limitation of our study is the lack of information on type of HT. The ideal comparison to examine HT use would be to compare women with oophorectomy plus hysterectomy to women with hysterectomy alone, since both groups would be likely to be using estrogen only therapy since these women are no longer at risk for uterine cancer. However, given the small number of women with hysterectomy alone who used HT (N~200) we could not make meaningful conclusions based on this analysis. Because of this differential treatment pattern and because HT use may mask the effect of oophorectomy on adiposity, we repeated our analysis excluding HT users and still observed strong associations.

Despite these limitations, NHANES III provides a large, nationally representative sample with more than 500 women who had an oophorectomy, allowing analysis of differences by age at oophorectomy. Body measurements were performed by study personnel in a standardized fashion, eliminating issues of reporting bias and increasing precision of measurements. We were able to demonstrate the association between early oophorectomy and body fat as well as other adiposity measures. Lastly we had information on important confounders such as BMI at age 25, parity, smoking, alcohol, oral contraceptive use, physical activity, calories and fat consumption that were included as adjustment factors.

In conclusion, we demonstrated a relationship between oophorectomy at a young age and increased body fatness after a median follow-up of 17 years. Our results strongly suggest that evaluating body fat in addition to BMI would be informative in this population.

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References

1. Jacoby VL, Vittinghoff E, Nakagawa S, Jackson R, Richter HE, Chan J, et al. Factors associated with undergoing bilateral salpingo-oophorectomy at the time of hysterectomy for benign conditions. *Obstet Gynecol.* 2009 Jun; 113(6):1259–67. [PubMed: 19461420]
2. Nichols HB, Visvanathan K, Newcomb PA, Hampton JM, Egan KM, Titus-Ernstoff L, et al. Bilateral oophorectomy in relation to risk of postmenopausal breast cancer: confounding by nonmalignant indications for surgery? *Am J Epidemiol.* 2011 May 15; 173(10):1111–20. [PubMed: 21430192]
3. Parazzini F, Braga C, La Vecchia C, Negri E, Acerboni S, Franceschi S. Hysterectomy, oophorectomy in premenopause, and risk of breast cancer. *Obstet Gynecol.* 1997 Sep; 90(3):453–6. [PubMed: 9277661]
4. Titus-Ernstoff L, Longnecker MP, Newcomb PA, Dain B, Greenberg ER, Mittendorf R, et al. Menstrual factors in relation to breast cancer risk. *Cancer Epidemiol Biomarkers Prev.* 1998 Sep; 7(9):783–9. [PubMed: 9752986]
5. Irwin KL, Lee NC, Peterson HB, Rubin GL, Wingo PA, Mandel MG. Hysterectomy, tubal sterilization, and the risk of breast cancer. *Am J Epidemiol.* 1988 Jun; 127(6):1192–201. [PubMed: 3369418]
6. Brinton LA, Schairer C, Hoover RN, Fraumeni JF Jr. Menstrual factors and risk of breast cancer. *Cancer Invest.* 1988; 6(3):245–54. [PubMed: 3167610]
7. Parker WH, Broder MS, Chang E, Feskanich D, Farquhar C, Liu Z, et al. Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study. *Obstet Gynecol.* 2009 May; 113(5):1027–37. [PubMed: 19384117]
8. Rocca WA, Grossardt BR, de Andrade M, Malkasian GD, Melton LJ 3rd. Survival patterns after oophorectomy in premenopausal women: a population-based cohort study. *Lancet Oncol.* 2006 Oct; 7(10):821–8. [PubMed: 17012044]
9. Rivera CM, Grossardt BR, Rhodes DJ, Brown RD Jr, Roger VL, Melton LJ 3rd, et al. Increased cardiovascular mortality after early bilateral oophorectomy. *Menopause.* 2009 Jan-Feb;16(1):15–23. [PubMed: 19034050]
10. Burger H. The menopausal transition--endocrinology. *J Sex Med.* 2008 Oct; 5(10):2266–73. [PubMed: 18624962]
11. Lovejoy JC, Champagne CM, de Jonge L, Xie H, Smith SR. Increased visceral fat and decreased energy expenditure during the menopausal transition. *Int J Obes (Lond).* 2008 Jun; 32(6):949–58. [PubMed: 18332882]
12. Sutton-Tyrrell K, Zhao X, Santoro N, Lasley B, Sowers M, Johnston J, et al. Reproductive hormones and obesity: 9 years of observation from the Study of Women's Health Across the Nation. *Am J Epidemiol.* 2010 Jun 1; 171(11):1203–13. [PubMed: 20427327]
13. Saengsirisuwan V, Pongseeda S, Prasannarong M, Vichaiwong K, Toskulkao C. Modulation of insulin resistance in ovariectomized rats by endurance exercise training and estrogen replacement. *Metabolism.* 2009 Jan; 58(1):38–47. [PubMed: 19059529]
14. Rogers NH, Perfield JW 2nd, Strissel KJ, Obin MS, Greenberg AS. Reduced energy expenditure and increased inflammation are early events in the development of ovariectomy-induced obesity. *Endocrinology.* 2009 May; 150(5):2161–8. [PubMed: 19179442]
15. Hong J, Stubbins RE, Smith RR, Harvey AE, Nunez NP. Differential susceptibility to obesity between male, female and ovariectomized female mice. *Nutr J.* 2009; 8:11. [PubMed: 19220919]
16. Pighon A, Paquette A, Barsalani R, Chapados NA, Rabasa-Lhoret R, Yasari S, et al. Resistance training attenuates fat mass regain after weight loss in ovariectomized rats. *Maturitas.* 2009 Sep 20; 64(1):52–7. [PubMed: 19683884]

17. Siri PW, Ginsberg HN. Ovariectomy leads to increased insulin resistance in human apolipoprotein B transgenic mice lacking brown adipose tissue. *Metabolism*. 2003 Jun; 52(6):659–61. [PubMed: 12800087]
18. Zoth N, Weigt C, Laudenbach-Leschowski U, Diel P. Physical activity and estrogen treatment reduce visceral body fat and serum levels of leptin in an additive manner in a diet induced animal model of obesity. *J Steroid Biochem Mol Biol*. 2010 Oct; 122(1–3):100–5. [PubMed: 20298783]
19. Ozdemir S, Celik C, Gorkemli H, Kiyici A, Kaya B. Compared effects of surgical and natural menopause on climacteric symptoms, osteoporosis, and metabolic syndrome. *Int J Gynaecol Obstet*. 2009 Jul; 106(1):57–61. [PubMed: 19394614]
20. Cagnacci A, Zanin R, Cannoletta M, Generali M, Caretto S, Volpe A. Menopause, estrogens, progestins, or their combination on body weight and anthropometric measures. *Fertil Steril*. 2007 Dec; 88(6):1603–8. [PubMed: 17481628]
21. Verhoeven MO, van der Mooren MJ, Teerlink T, Verheijen RH, Scheffer PG, Kenemans P. The influence of physiological and surgical menopause on coronary heart disease risk markers. *Menopause*. 2009 Jan-Feb; 16(1):37–49. [PubMed: 18791484]
22. Nar A, Demirtas E, Ayhan A, Gurlek A. Effects of bilateral ovariectomy and estrogen replacement therapy on serum leptin, sex hormone binding globulin and insulin like growth factor-I levels. *Gynecol Endocrinol*. 2009 Dec; 25(12):773–8. [PubMed: 19905995]
23. Dorum A, Tonstad S, Liavaag AH, Michelsen TM, Hildrum B, Dahl AA. Bilateral oophorectomy before 50 years of age is significantly associated with the metabolic syndrome and Framingham risk score: a controlled, population-based study (HUNT-2). *Gynecol Oncol*. 2008 Jun; 109(3):377–83. [PubMed: 18407340]
24. Gibson CJ, Thurston RC, El Khoudary SR, Sutton-Tyrrell K, Matthews KA. Body mass index following natural menopause and hysterectomy with and without bilateral oophorectomy. *Int J Obes (Lond)*. 2012 Sep 25. Epub ahead of print. 10.1038/ijo.2012.164
25. Chumlea WC, Guo SS, Kuczmarski RJ, Flegal KM, Johnson CL, Heymsfield SB, et al. Body composition estimates from NHANES III bioelectrical impedance data. *Int J Obes Relat Metab Disord*. 2002 Dec; 26(12):1596–609. Research Support, U.S. Gov't, P.H.S. [PubMed: 12461676]
26. Bioelectrical impedance analysis in body composition measurement: National Institutes of Health Technology Assessment Conference Statement. *Am J Clin Nutr*. 1996 Sep; 64(3 Suppl):524S–32S. Consensus Development Conference Consensus Development Conference, NIH Review. [PubMed: 8780375]
27. Ezzati TM, Massey JT, Waksberg J, Chu A, Maurer KR. Sample design: Third National Health and Nutrition Examination Survey. *Vital Health Stat*. 1992 Sep; 2(113):1–35.
28. NHANES III Anthropometric Procedures [videotape]. Washington, DC: US Department of Health and Human Services; 1996. April 1, 2011:[Available from: http://www.cdc.gov/nchs/nhanes/nhanes3/anthropometric_videos.htm]
29. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD, et al. Factors Associated with Age at Natural Menopause in a Multiethnic Sample of Midlife Women. *American Journal of Epidemiology*. 2001 May 1; 153(9):865–74. [PubMed: 11323317]
30. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc*. 1993 Jan; 25(1):71–80. [PubMed: 8292105]
31. Hu, FB. Obesity epidemiology. Oxford ; New York: Oxford University Press; 2008. Measurement of Adiposity and Body Composition; p. 53–83.
32. Bohm A, Heitmann BL. The use of bioelectrical impedance analysis for body composition in epidemiological studies. *Eur J Clin Nutr*. 2013 Jan; 67(Suppl 1):S79–85. [PubMed: 23299875]
33. Marques-Vidal P, Bochud M, Mooser V, Paccaud F, Waeber G, Vollenweider P. Obesity markers and estimated 10-year fatal cardiovascular risk in Switzerland. *Nutr Metab Cardiovasc Dis*. 2009 Sep; 19(7):462–8. Research Support, Non-U.S. Gov't. [PubMed: 19185476]
34. Singh RB, Niaz MA, Beegom R, Wander GS, Thakur AS, Rissam HS. Body fat percent by bioelectrical impedance analysis and risk of coronary artery disease among urban men with low rates of obesity: the Indian paradox. *J Am Coll Nutr*. 1999 Jun; 18(3):268–73. [PubMed: 10376784]

35. Heitmann BL, Hills AP, Frederiksen P, Ward LC. Obesity, leanness, and mortality: effect modification by physical activity in men and women. *Obesity* (Silver Spring). 2009 Jan; 17(1): 136–42. Research Support, Non-U.S. Gov't. [PubMed: 18997669]
36. Lahmann PH, Lissner L, Gullberg B, Berglund G. A prospective study of adiposity and all-cause mortality: the Malmö Diet and Cancer Study. *Obes Res*. 2002 May; 10(5):361–9. Research Support, Non-U.S. Gov't. [PubMed: 12006635]
37. De Lorenzo A, Martinoli R, Vaia F, Di Renzo L. Normal weight obese (NWO) women: an evaluation of a candidate new syndrome. *Nutr Metab Cardiovasc Dis*. 2006 Dec; 16(8):513–23. [PubMed: 17126766]
38. Allison DB, Zhu SK, Plankey M, Faith MS, Heo M. Differential associations of body mass index and adiposity with all-cause mortality among men in the first and second National Health and Nutrition Examination Surveys (NHANES I and NHANES II) follow-up studies. *Int J Obes Relat Metab Disord*. 2002 Mar; 26(3):410–6. Research Support, Non-U.S. Gov't Research Support, U.S. Gov't, P.H.S. [PubMed: 11896498]
39. Heitmann BL, Erikson H, Ellsinger BM, Mikkelsen KL, Larsson B. Mortality associated with body fat, fat-free mass and body mass index among 60-year-old Swedish men—a 22-year follow-up. The study of men born in 1913. *Int J Obes Relat Metab Disord*. 2000 Jan; 24(1):33–7. Research Support, Non-U.S. Gov't. [PubMed: 10702748]
40. Bigaard J, Frederiksen K, Tjønneland A, Thomsen BL, Overvad K, Heitmann BL, et al. Body fat and fat-free mass and all-cause mortality. *Obes Res*. 2004 Jul; 12(7):1042–9. Research Support, Non-U.S. Gov't. [PubMed: 15292467]
41. Cepeda-Valery B, Pressman GS, Figueredo VM, Romero-Corral A. Impact of obesity on total and cardiovascular mortality—fat or fiction? *Nat Rev Cardiol*. 2011 Apr; 8(4):233–7. Review. [PubMed: 21263454]
42. Gomez-Ambrosi J, Silva C, Galofre JC, Escalada J, Santos S, Millan D, et al. Body mass index classification misses subjects with increased cardiometabolic risk factors related to elevated adiposity. *Int J Obes (Lond)*. 2012 Feb; 36(2):286–94. Research Support, Non-U.S. Gov't. [PubMed: 21587201]
43. Gomez-Ambrosi J, Silva C, Galofre JC, Escalada J, Santos S, Gil MJ, et al. Body adiposity and type 2 diabetes: increased risk with a high body fat percentage even having a normal BMI. *Obesity* (Silver Spring). 2011 Jul; 19(7):1439–44. Comparative Study Research Support, Non-U.S. Gov't. [PubMed: 21394093]
44. De Lorenzo A, Bianchi A, Maroni P, Iannarelli A, Di Daniele N, Iacopino L, et al. Adiposity rather than BMI determines metabolic risk. *Int J Cardiol*. 2011 Nov 14. Epub head of print. 10.1016/j.ijcard.2011.10.006
45. Cooper R, Hardy R, Kuh D. Is adiposity across life associated with subsequent hysterectomy risk? Findings from the 1946 British birth cohort study. *BJOG*. 2008 Jan; 115(2):184–92. discussion 92. [PubMed: 18081600]
46. Cooper R, Kuh D, Hardy R, Power C. Is there an association between hysterectomy and subsequent adiposity? *Maturitas*. 2007 Nov 20; 58(3):296–307. [PubMed: 17945444]
47. Colditz GA, Stampfer MJ, Willett WC, Stason WB, Rosner B, Hennekens CH, et al. Reproducibility and validity of self-reported menopausal status in a prospective cohort study. *Am J Epidemiol*. 1987 Aug; 126(2):319–25. [PubMed: 3605058]
48. Irwin KL, Wingo PA, Lee NC. Agreement of self-reported ovarian number following gynecologic surgery with medical record reports. *J Clin Epidemiol*. 1990; 43(2):181–7. Comparative Study Research Support, U.S. Gov't, P.H.S. [PubMed: 2303847]

Table 1

Baseline Characteristics of Women 40 yrs in NHANES III 1988–1994, N=3549

	Intact Ovaries N=3047	Oophorectomy N=502	p-value*
Age at Interview, yrs, mean $\pm$ SD	56.8 $\pm$ 0.5	60.8 $\pm$ 0.7	<0.001
Age at Ooph, yrs, median (range)	---	43 (26–79)	
Time Since Ooph, yrs, median (range)	---	17 (0–56)	
Race (%)			
Non-Hispanic White	81.5	86.0	0.036
Non-Hispanic Black	8.6	9.4	
Mexican American	3.2	1.8	
Other	6.8	2.9	
Income			
Less than \$20,000	33.2	39.1	0.097
\$20,000 or more	64.9	59.7	
Missing	1.9	1.3	
Insurance			
Insured	90.5	92.3	0.498
Un-insured	7.2	6.5	
Missing	2.3	1.2	
Education			
<12 yrs	24.4	30.1	0.009
12 yrs	36.8	40.5	
>12 yrs	38.2	29.1	
Missing	0.6	0.3	
Region			
Northeast	20.9	18.7	0.028
Midwest	25.1	21.9	
South	31.6	40.2	
West	22.4	19.3	
Parity (%)			
≥ 2	75.9	69.2	0.094
1	12.2	16.2	
Nulliparous	11.9	14.6	
Hysterectomy	15.0	98.8	<0.001
Age at Hysterectomy, yrs	41.5	43.0	0.070
Ever Used Birth Control	48.8	37.6	<0.001

	Intact Ovaries N=3047	Oophorectomy N=502	p-value*
HT (Estrogen Pills)	18.9	70.7	<0.001
Postmenopausal	58.0	100.0	<0.001
Smoking			
Never	54.9	53.5	0.767
Former	25.9	25.6	
Current	19.1	20.9	
Current Alcohol Use			
12 drinks past yr	38.6	29.0	0.004
<12 drinks past yr	61.4	71.0	
Diagnosed Diabetes	8.0	8.4	0.807
Weight at age 25, lbs	126.4	126.0	0.747
Physical Activity			
No reported Physical Activity	19.6	23.2	0.348
0.1–2.9 times per week	30.6	28.4	
3–7 times per week	24.1	21.2	
>7 times per week	25.7	27.3	

* P-value from two-sided t-test or Pearson chi squared test

Abbreviations: yrs = years and r, year

Table 2

Weighted Age Standardized Mean Adiposity Measures, NHANES III 1988–1994*

	Intact Ovaries N=3047	Oophorectomy N=502	p-value	Oophorectomy <40 yrs N=169	p-value	Oophorectomy 40 yrs N=333	p-value
Weight (lbs)	154.9	157.0	0.357	159.4	0.134	152.8	0.542
Body Mass Index (kg/m ²)	27.2	27.5	0.458	28.2	0.065	26.6	0.309
Waist Circumference (cm)	91.9	93.4	0.090	94.6	0.038	92.4	0.699
Body Fat (%) [†]	36.2	37.2	0.051	38.5	<0.001	35.8	0.675
Waist-Hip Ratio	0.889	0.893	0.573	0.895	0.417	0.891	0.837
Skinfolds (mm) [‡]							
Triceps	24.8	26.3	0.012	27.0	0.012	25.2	0.582
Subscapular	22.5	24.0	0.054	23.7	0.280	24.1	0.207
Suprailiac	21.8	23.7	0.014	24.2	0.057	23.1	0.256
Thigh	33.8	35.1	0.099	37.3	0.006	33.5	0.780

* Age standardized to the US Standard Population 2000 using 5 year age intervals, p-values for oophorectomy vs. intact ovaries, p-values from Wald test compared to intact ovaries

[†] Excludes missing BIA measure, N=3303 total, 467 oophorectomy

[‡] Skinfold means include women too big for calipers set to 50mm, excludes missing skinfold measures N=3369, 461 oophorectomy

Abbreviations: yrs, years

Linear Regression, Difference in Mean Weight, BMI, Percent Body Fat, and Waist Circumference by Oophorectomy Status, NHANES III 1988–1994

Table 3

		Weight [†]		Body Mass Index		Percent Body Fat [‡]		Waist Circumference	
N		β^*	p-value	β^*	p-value	β^*	p-value	β^*	p-value
Total Population (N=3549)									
No Ooph	3047	Reference		Reference		Reference		Reference	
Total Ooph	502	2.26 lbs	0.259	0.47 kg/m ²	0.183	0.95%	0.040	1.27 cm	0.111
Age at Ooph <40 yrs	169	6.82 lbs	0.008	1.23 kg/m²	0.007	2.36%	<0.001	3.10 cm	0.010
Age at Ooph 40 yrs	333	-0.37 lbs	0.889	0.03 kg/m ²	0.946	0.17%	0.784	0.21 cm	0.822
HRT non users (N=2683)									
No Ooph	2507	Reference		Reference		Reference		Reference	
Total Ooph	176	5.89 lbs	0.007	1.04 kg/m²	0.007	1.73%	0.006	2.76 cm	0.004
Age at Ooph <40 yrs	56	9.58 lbs	0.132	1.65 kg/m ²	0.150	2.89%	0.017	3.86 cm	0.218
Age at Ooph 40 yrs	120	3.86 lbs	0.279	0.71 kg/m ²	0.253	1.15%	0.164	2.15 cm	0.162

* Multivariate model adjusted for age at interview, race, income, parity, smoking status, education, alcohol, oral contraceptive use, BMI at age 25;

[†] Additionally adjusted for height;

[‡] Excludes missing BIA measure (N=3303), Abbreviations: Ooph, oophorectomy, yrs, years

Tobit Regression, Difference in Mean Skinfold Thickness by Oophorectomy Status, NHANES III 1988–1994

Table 4

		Tricep [§]		Subscapular [§]		Suprailiac [§]		Thigh [§]	
N		β^*	p-value	β^*	p-value	β^*	p-value	β^*	p-value
Total Population (N=3278)									
No Ooph	2829	Reference		Reference		Reference		Reference	
Total Ooph	449	1.44 mm	0.016	1.45 mm	0.028	1.63 mm	0.009	1.12 mm	0.216
Age at Ooph <40 yrs	149	3.29 mm	<0.001	2.38 mm	0.010	3.55 mm	0.001	3.63 mm	0.015
Age at Ooph 40 yrs	300	0.44 mm	0.497	0.94 mm	0.214	0.59 mm	0.383	-0.20 mm	0.841
HRT non users (N=2487)									
No Ooph	2326	Reference		Reference		Reference		Reference	
Total Ooph	161	1.41 mm	0.007	1.83 mm	0.026	2.31 mm	0.004	0.86 mm	0.438
Age at Ooph <40 yrs	52	2.69 mm	0.064	3.55 mm	0.060	3.96 mm	0.033	2.05 mm	0.277
Age at Ooph 40 yrs	109	0.69 mm	0.449	0.85 mm	0.476	1.36 mm	0.247	0.19 mm	0.894

* Multivariate model adjusted for age at interview, race, income, parity, smoking status, education, alcohol, oral contraceptive use, BMI at age 25

§ Tobit Regression, Analysis limited to women with complete skinfold measures (N=3278), Abbreviations: Ooph, oophorectomy, yrs, years

Table 5

Polytomous Logistic Regression* of tertiles of adiposity for women with oophorectomy <40 compared to women with intact ovaries, NHANES III 1988–1994 N=3549

Weight [†]		BMI		% Body Fat [‡]		WC		
Tertiles	OR	95% CI	Tertiles	OR	95% CI	Tertiles	OR	95% CI
<135.7 lbs	1.00	Reference	<24.0 kg/m ²	1.00	Reference	<33.8%	1.00	Reference
135.7–164.7 lbs	1.41	0.66–3.03	24.0–28.7 kg/m ²	1.23	0.70–2.15	33.8–39.7%	2.86	1.45–5.64
>164.7 lbs	2.49	1.13–5.46	28.8 kg/m ²	2.28	1.21–4.31	>39.7%	2.82	1.39–5.75

Tricep [§]		Subscapular [§]		Suprailiac [§]		Thigh [§]					
OR	95% CI	Tertiles	OR	95% CI	Tertiles	OR	95% CI				
<20.6 cm	1.00	Reference	<17.5 cm	1.00	Reference	<29.4 cm	1.00				
20.6–27.9 cm	1.32	0.63–2.74	17.6–25.9 cm	1.30	0.71–2.38	15.5–26.4 cm	1.81	0.85–3.88	29.4–38.5 cm	1.16	0.60–1.20
>27.9 cm	2.28	1.28–4.06	>25.9 cm	2.10	1.16–3.79	>26.4 cm	2.83	1.33–6.03	>38.5 cm	2.38	1.33–4.26

* Multivariate models adjusted for age at interview, race, income, parity, smoking, education, alcohol, oral contraceptive use, BMI at age 25

[†] Additionally adjusted for height.

[‡] Excludes missing BIA measure (N=3303).

[§] Analysis limited to women with complete skinfold measures (N=3278)