Determinants of long-term weight change among middle-aged Swedish women

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Keywords: weight change, women, longitudinal

Running Title: Determinants of long-term weight change

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Word count: 3463
Funding: This study was sponsored by grant K2012-69X-22062-01-3 from the Swedish Research Council
Disclosure: The authors declare no conflicts of interest
Author Contributions: DE contributed to data analyses, led the interpretation of the data and writing of the manuscript. PS and SS contributed to the study design, completed the main data analyses, and preparation of the manuscript. JO, HA, ML, EW contributed to the study design, interpretation of the data, and preparation of the manuscript. HA and EW coordinated data collection for Swedish Women's Lifestyle and Health study. EW conceived this specific study, coordinated data analysis plan, and coordinated publication efforts. All authors read and approved the final manuscript.
Study Importance:

1) What is already known about this subject:
   - It is well established that overweight and obesity are increasing in majority of countries worldwide; however, few longitudinal studies of the determinants of long-term weight change among women have been published.
   - Determinants of weight gain may vary across populations, age groups, sex, race, and ethnicity.

2) What this study adds:
   - Estimates of magnitude of weight gain over 12 year follow-up period among a Swedish population of women
   - Findings which suggest a number of determinants are important for weight management interventions for women (i.e., weight at start of middle age, cigarette smoking, physical activity)
   - One of few studies able to control for secular trend and aging in study of association between parity and long-term weight gain
ABSTRACT

Objective: To describe the determinants of 12-year weight change among middle-aged women in Sweden.

Methods: In 1991/1992, 49,259 women across Sweden were recruited into a cohort. In 2003, 34,402 (73%) completed follow-up. Lifestyle and health characteristics, including weight were collected and twelve-year weight change and substantial weight gain (≥+5.0 kilogram [kg]) were calculated; association between baseline characteristics and odds ratios (OR) with 95% confidence intervals (CI) of substantial weight gain were estimated.

Results: During the twelve-year follow-up, 81% of women experienced weight gain. Being above average weight (64.5 kg) at baseline [OR =1.20, 95% CI: 1.14, 1.26] and smoking 1-9 [OR=1.10, 95% CI: 1.01, 1.20], 10-19 [OR=1.30, 95% CI: 1.21, 1.39], or ≥20 cigarettes daily [OR=1.17, 95% CI: 1.04, 1.32] increased a woman’s odds of experiencing substantial weight gain (influenced by smoking cessation). In contrast, risk of substantial weight gain was reduced among women 45-50 years of age [OR=0.79, 95% CI: 0.73, 0.85], women reporting high alcohol consumption [OR=0.90, 95% CI: 0.83, 0.98], and those with medium [OR=0.93, 95% CI: 0.87, 1.00] or high [OR 0.83, 95% CI: 0.77, 0.90] physical activity levels.

Conclusions: The majority of women experienced weight gain during middle-age. Population-specific determinants of weight gain should guide obesity prevention efforts.
INTRODUCTION

Obesity is a major contributor to overall burden of disease by increasing the risk of numerous adverse health outcomes, such as diabetes, cardiovascular disease, cancer, and overall mortality. [1] In the majority of countries worldwide, the prevalence of overweight and obesity continues to increase among adults. [2] In Sweden, for example, approximately 46% of women over the age of twenty are now overweight or obese. [2] Despite the burden of overweight and obesity, large population-based studies on the cause of weight change are limited.

Published studies suggest, however, that a number of demographic, lifestyle, and health characteristics are associated with long term weight gain. [3-5] Among men and women in Australia, the mean weight increased over a twelve-year time period. Weight gain decreased, however, with advanced age and people aged 65 years and over lost, rather than gained weight. [3] In addition, weight gain was greatest for those with normal weight and lowest for those who were already obese at baseline. Weight gain was also lowest among those with highest levels of education. [3] Physical inactivity, high fat and protein diets, and alcohol consumption have also been related to weight gain over time. [4] In addition, menopausal status, parity, and age at menarche may be associated with weight gain or obesity in women. [5, 6, 7, 8] Studies of weight change among Swedish women are lacking.

The Swedish Women’s Lifestyle and Health (WLH) cohort provides an opportunity to study weight change over time in a large population-based sample of women. Our aims were to describe the twelve-year weight change among study participants and determine
the association between demographic, lifestyle, and health characteristics and weight change using data collected in 1991/1992 and again in 2003.

METHODS

Study Population

The WLH cohort has been described in detail elsewhere. [9] In short, 96,000 women between the ages of 29 and 49 years were randomly selected from the Swedish Population Registry based on their date of birth and invited to participate via a mailed questionnaire. During 1991-1992, a total of 49,259 (51%) women returned the baseline questionnaire (Q1) and were recruited into the cohort. A follow-up survey (Q2) was administered in 2003. The questionnaires captured data on a variety of demographic, lifestyle and health characteristics including education, height, weight, alcohol consumption, smoking, energy intake, physical activity (PA), age at menarche, menopausal status, parity and prevalent chronic disease.

The Swedish Data Inspection Board, the Regional Ethnical Committee of Uppsala University, and the Ethical Committee of the Karolinska Institutet approved the study. Consent was assumed by return of the mailed questionnaire.

Data

Weight change was calculated as the difference in weight at Q2 minus weight at Q1. For selected analyses, weight change was dichotomized as 0 (<5kg) and 1(≥5kg). Women were categorized into the following age categories: 29-34, 35-40, 41-44, and 45-50 years. Educational attainment was categorized as: <10 years and ≥ 10 years of schooling completed. Height was collected in centimeters (cm) and women were categorized as being below or above mean height of Q1 sample (166cm).
Women reported the number of glasses of beer, wine, and spirits consumed per week, per month, or per year. Reported alcohol consumption was converted to grams per day using food composition data from the Swedish National Food Administration and further categorized as: None, Low (<24 grams per week), and High (≥ 24 grams per week). [10] Smoking was categorized as: 0, 1-9, 10-19, or ≥ 20 cigarettes consumed per day. Energy intake was estimated based on total Kilojoule (Kj) consumed daily and categorized as: Low (<5000 Kj/day), Medium (5,000-8,700 Kj/day), and High (>8700 Kj/day). Respondents subjectively categorized their overall PA levels as Very Low, Low, Medium, High, or Very High.

Data on health characteristics, such as age at menarche, childbearing history, menopausal status and prevalent chronic disease was obtained from Q1 surveys. The survey specifically asked about the history of high blood pressure, diabetes mellitus, blood clots (extremities), cerebral hemorrhage, heart attack, rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, multiple sclerosis, and cancer. Parity was categorized as: None, one, or two or more children. Age at menarche was categorized as: <12 years and ≥ 12 years. Menopausal status was defined as: Yes (menopause had occurred at time of Q1) and No (menopause had not occurred at time of Q1). Chronic disease was categorized as: Yes (at least one disease reported) or No (no diseases reported). Using responses from Q2, we also grouped women into groups defined by changes in smoking or PA from Q1 to Q2.

Statistical Analyses
To test associations between baseline characteristics and reported mean weight at baseline and mean weight change at follow-up, we used analysis of variance techniques. The weight
change variable was also categorized into five approximately equal groups (quintiles) to graphically depict the distribution of weight change by individual baseline characteristics (Figure 1). We used multivariable logistic regression models to evaluate the association between baseline characteristics and substantial weight gain (<5kg or ≥5kg) in terms of odds ratios (OR) and 95% confidence intervals (CI). Ordinary linear regression model estimated the relationship between each baseline covariate on WC (continuous) in terms of regression coefficient β, fully adjusted for remaining variables to control for confounding. We also examined the impact of changes in smoking and PA on weight change using separate linear and logistic regression models.

There were no indications of violation of the assumptions (residual normality, homoscedasticity, and independence) for valid inference from the ordinary linear regression. All tests were two-sided on the nominal 5% level of significance.

To evaluate the potential bias that could arise due to dropout and missing data, we explored the impact of incomplete variables on results using two analytic techniques: Inverse Probability Weighting (IPW) and Multiple Imputation (MI). [11] For IPW, we re-fitted the model by weighting the observations according to (the inverse of) the probability of answering the second questionnaire, based on the answers in the first questionnaire. For MI we used Predictive Mean Matching (PPM) by chained equations implemented in the statistical software R package MICE to impute the missing information among the dropouts. [12] In brief, we started with the original Q1 cohort members (n=49,259) and removed study subjects with missing data on at least one covariate of interest (n=15,159), which resulted in a population of 41,309 women with complete covariate data. Among these, 12,177 subjects had missing data on weight at Q2; these were imputed via MI. We
compared the results on the effects of our covariates on weight change (as linear measure) obtained from a complete data analysis, MI, and also using IPW. The results of this missing data analyses are summarized in Figure 2. All statistical analyses in this study were based on complete data as we did not find evidence that our results were affected by missing data. Our statistical techniques assume data on approximate Gaussian or Binomial distribution. We checked these assumptions by graphical inspections of model residuals and calculated the model deviances.

All statistical analyses were performed in SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina) and R 3.2.3 (Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population

A total of 34,402 women (73% of baseline cohort) responded to the second survey in 2003; we excluded respondents who did not report their weight at baseline or at follow-up (n = 980), resulting in a final study population of 33,422 women. This study population and the original baseline cohort are similar across baseline characteristics. [Table 1] Baseline characteristics and mean weight change between Q1 and Q2 are summarized in Table 2. At baseline, women were, on average, 39.8 years of age and 81.6% reported ≥10 years of education. Alcohol consumption was reported by 87.7%, cigarette smoking by 27.2%, and low levels of PA by 13.9% of women. In addition, 18.8% of women reported at least one prevalent chronic disease and the majority (88.4%) were pre-menopausal. The majority (81%) of women in the study population experienced positive weight change during the 12-year time period [Figure 1].
Mean reported weight at Q1 varied by age, education, alcohol consumption, cigarette smoking status, energy intake levels, PA levels, height, and chronic disease, age at menarche, menopausal status, and parity. For example, older women weighed statistically significantly more at baseline than younger women (mean=63.6.2kg, standard deviation [SD] = ±10.4, mean=63.8kg, SD±10.7, mean=64.6kg, SD± 10.4, and mean=65.9kg, SD ± 10.7, p <0.001) for ages 29-34, 35-40, 41-44, and 45-50, respectively. Women with at least one chronic disease weighed more than women with no reported history of chronic disease; (mean=67.0kg, SD ±12.2) versus (mean=63.9kg, SD±10.1, p<0.001). Post-menopausal women were also heavier at Q1 (mean=66.5kg, SD±11.3), as compared to pre-menopausal women (mean=64.2kg, SD±10.4, p<0.001). [Table 2]

The difference in mean weight change between Q1 and Q2 was the lowest for women at the highest level of PA (5.0kg, SD±6.3) compared to women at medium (5.3kg, SD±6.9) or low (5.4kg, SD±8.2) levels of PA at Q1 (p<0.01). Post-menopausal women had lower weight gain (4.6 kg, SD±7.8) as compared to pre-menopausal women (5.3 kg, SD±7.0 (p<0.001). Non-smokers had lower weight gain (5.1 kg, SD=6.8) as compared to women who smoked 1-9 (5.4 kg, SD±6.7), 10-19 (5.8 kg, SD±7.9), and 20 or more (5.6 kg, SD±9.8) cigarettes per day (p<0.001). Nulliparous women (5.6kg, SD ± 8.1) had higher weight gain as compared to women who reported having one child (5.1kg, SD ±7.2) or women reporting two or more children (5.2kg, SD ±6.9). [Table 2]

**Determinants of substantial weight gain**

In a multivariable model, being above average weight and reporting any level of cigarette smoking at Q1 were both statistically significantly associated with an increased odds of
substantial weight gain between Q1 and Q2. Specifically, women who were above the weight of 64.5 kg at Q1 had a 19% (OR=1.20, 95% CI: 1.14, 1.26) greater odds of substantial weight gain between Q1 and Q2 as compared to women who weighed less than 64.5 kg at Q1. Women who smoked 1-9, 10-19, or ≥20 cigarettes daily experienced 10% (OR=1.10, 95% CI: 1.01, 1.19), 30% (OR=1.31, 95% CI: 1.21, 1.39), and 17% (OR=1.17, 95% CI: 1.04, 1.32) increased odds of substantial weight gain between Q1 and Q2 as compared to non-smokers at Q1, respectively [Table 3].

A number of characteristics were associated with decreased odds of substantial weight gain. For example, being 45-50 years of age at Q1 was associated with an estimated 21% lower odds (OR=0.79, 95% CI: 0.73, 0.85) of having substantial weight gain as compared to women 29 to 34 years of age. Women who reported a high level alcohol consumption, compared to those who reported none, had an estimated 10% lower odds (OR=0.90, 95% CI: 0.83, 0.98) of substantial weight gain. Medium level of PA was associated with a 7% lower odds (OR=0.93, 95% CI: 0.87, 1.00) and high level of PA was associated with a 17% lower odds (OR=0.83, 95% CI: 0.77, 0.90) of substantial weight gain compared to women who reported low levels. [Table 3].

*Association between baseline characteristics and weight change*

The average weight change that is associated with each baseline characteristic, whilst controlling for the other explanatory variables in the model is summarized in Table 4. Older age at Q1 (45-50 years) was associated with negative weight change at Q2 (-0.92 kg, 95% CI: -1.18, -0.66, p<0.001). High level of PA was also associated with a negative weight change (-0.37 kg, 95% CI: -0.63, -0.10, p<0.01) as compared to low levels of PA. In
addition, older age at menarche (≥12 years), (-0.29 kg, 95% CI: -0.53, -0.05, p<0.05) and being multiparous (-0.42 kg, 95% CI: -0.73, -0.12, p<0.05 [one child] and -0.39 kg, 95% CI: -0.63, -0.14, p<0.001 [two or more children]), were both negatively associated with weight change over time, in a multivariable model.

Smoking 10-19 or ≥20 cigarettes per day was associated with positive weight change between Q1 and Q2; specifically, (+0.75 kg, 95% CI: 0.51, 0.98, p<0.001) and (+0.47 kg, 95% CI: 0.06, 0.88, p<0.05), respectively, compared to non-smokers.

**Association between changes in smoking and PA levels and weight change**

The average unadjusted weight change among groups defined by changes in smoking or PA levels between baseline and follow-up are summarized in Table 5. Among women who reported smoking at baseline, those who reported being non-smokers at follow-up experienced more weight gain (+7.3 kg, SD±8.1), on average, than women who never smoked (+5.1 kg, SD±6.7) or women who continued (+5.3 kg, SD±8.1), or started smoking (+4.8 kg, SD±7.0). Women who increased their reported levels of PA from baseline to follow-up experienced lower weight gain (+4.2 kg, SD±6.7), on average, than women who decreased (+6.8 kg, SD±7.9) or did not change (+5.1 kg, SD±6.7) their PA levels.

Smoking cessation (OR=1.88, 95% CI: 1.68, 2.11) and decreasing PA (OR=1.58, 95% CI: 1.48, 1.68) were associated with increased odds of substantial weight gain as compared to women who reported no smoking at Q1 and Q2 and women who reported no changes in PA, respectively. [Table 5]

**Model assumptions**

Estimates and confidence intervals for baseline characteristics and weight change based on MI and IPW were similar to those obtain from a complete data set (results shown in Figure
2). Visual inspection of model residuals and deviances measures calculated for the logistic regression models supported the assumptions of data from approximate Gaussian and binomial distributions.

**DISCUSSION**

In this population-based cohort of over 33,000 women over eighty percent experienced weight gain over the 12-year study period. Women were on average 5 kg heavier at follow-up; this estimate is higher than the finding among 2,448 Australian women (mean age of 48.5 years at baseline), who were approximately 2.9 kg heavier at follow-up twelve years later. [3] In another study from Australia, the average weight gain was 3.3 kg over a twelve-year study period, but this cohort of women, was older (mean = 54 years), heavier (mean = 67.2 kg) at baseline and limited to non-smokers free of chronic disease. [4] Hence, our results are consistent with the ample evidence from population-based studies that adults are getting heavier over time. [13] Furthermore, women who were already above average weight at baseline had a statistically significantly higher risk of experiencing more than 5 kg increase in average weight; typically enough weight to progress from a lower to higher body mass index classification category. [14] According to our findings, middle-aged women gain on average 0.42 kg per year.

Two factors statistically significantly increased a woman’s odds of having substantial weight gain over time after controlling for a number of demographic, lifestyle, and health characteristics; being above average weight of cohort participants and smoking cigarettes at baseline. These findings suggest that weight management strategies targeting middle-aged women who are already above average weight or who smoke cigarettes may be justified. An inverse relationship between smoking and body mass index is well
established. [15] While we found that being a smoker at baseline was statistically significantly associated with a positive twelve-year weight change and women who smoked more cigarettes daily had an increased odds of experiencing substantial weight gain, our results on changes in smoking between Q1 and Q2 suggest that smoking cessation is an explanation for these results. The fear of post-cessation weight gain has indeed been reported as the main reason female smokers choose either not to attempt to quit or fail in their attempts to quit smoking. [16] Our findings that PA is negatively associated with subsequent weight gain are consistent with widely accepted notion that PA protects against weight gain. [17] Furthermore, our results suggest that increasing PA levels in middle-age may result in slightly lower absolute weight gain.

We did not find that postmenopausal women had a decreased odds of experiencing substantial weight gain over time as compared to pre-menopausal women. Our results differ with those from a small cohort of Czech women (n=146) which found that postmenopausal women (n=33) experienced greater weight gain as compared to all other groups of women (reproductive age, menopausal, and pre-menopausal). [5] Most of our women likely experienced menopausal changes during study period which may result in smaller weight changes between pre and post-menopausal groups at baseline. [18, 19] Our ability to control for potential confounding effects of other lifestyle characteristics, such as physical activity, may explain why we did not observe a positive association between menopausal status and long term weight gain given that lower levels of PA have been reported in postmenopausal women. [20] It is also possible that menopausal-related weight gain, may have already occurred prior to baseline given that postmenopausal women are likely to be older women and older women were already heavier (mean =65.9
kg for 45-50 year olds) than younger women (mean = 63.6 kg for 29-34 year olds) at baseline. The association between menopause and weight change during perimenopausal years is not well understood, but considered multifactorial and complex. [21]

Our finding that older age at menarche was negatively associated with weight change supports the theory that the timing of puberty may have potentially long lasting effects on health. [8] Earlier menarche has been associated with adverse health outcomes, including obesity, cardiovascular disease, select cancers, and mortality. [8] Furthermore, in a large pan-European cohort study, early age at menarche was associated with an increased risk of type 2 diabetes in adulthood and less than half of this increased risk was mediated by higher adult body mass index. [22] These findings suggest that strategies to prevent early age menarche, if possible, warrant consideration.

Studies on the association between parity and obesity or weight gain in women have generated mixed results; some reporting a positive [7, 23] while others report a negligible [6], or an inverse association [24]. A review of the literature on childbearing and obesity in women suggests that the majority of studies did not adequately control for important confounders, such as pre-pregnancy weight, gestational weight gain, secular trends, aging, and lifestyle and behavioral variables associated with body weight. [25] The longitudinal design of our study, however, allowed us to control for secular trend and aging on long term WC; we are also able to adjust for lifestyle variables, such as PA and smoking.

For a number of the characteristics we studied, we found no association with weight change. For example, level of educational attainment was not associated with weight change in alignment with one of the studies out of Australia. [4] Other studies, however, have reported a negative association between socio-demographic indicators, such as
education and weight gain. [3, 26] Our analyses of alcohol consumption, were limited by
the low levels of consumption reported; approximately two thirds of women reported less
than 24 grams of alcohol consumption weekly. Our lack of findings on association between
energy intake and subsequent weight change were also in alignment with those reported
elsewhere, and might be explained by the limitations of food frequency questionnaires in
assessing absolute energy intake as opposed to overall diet patterns. [4, 27] Moreover, we
assessed baseline diet, and there is a possibility that women have changed their diet over
time. Diet was not collected at follow-up.

Our study has a number of potential limitations. First, non-respondents of follow-up
survey reported higher prevalence of smoking, fewer years of education, and less PA at
baseline. [9] This healthy volunteer bias may affect the generalizability of our findings, but
we believe this bias to be small given our study population strongly resembles the original
cohort in terms of baseline demographic, lifestyle, and health characteristics. Second,
missing data due to loss to follow-up is a common limitation in cohort studies, however, we
have adequately addressed this potential limitation in our missing data analyses. Third,
exposure status for select variables may have changed given the twelve-year period
between baseline and follow-up, although we were able to explore the association between
changes in smoking and PA and weight change. Fourth, our data is self-reported and may
result in inaccurate reporting of lifestyle and health characteristics. Our estimates of weight
change may also be inflated if bias in self-reporting of weight has improved over time
although two recently published studies have yielded conflicting results on temporal
changes in self-reported weight. [28, 29]. Finally, the odds ratios we report may be
overestimates of the relative risk of experiencing substantial weight gain given that a high proportion of our sample (51%) experienced such.

There are numerous strengths of our study; a population-based cohort, several lifestyle and health characteristics studied, a long-follow-up period, and to our knowledge, the largest study related to weight change among women with data on over 33,000 participants.

CONCLUSION

Our findings indicate that if nothing changes, the great majority of women can expect to gain weight in middle-age; and, women who begin middle-age at an above average weight or as a cigarette smoker may be especially challenged in their weight management efforts.

Acknowledgements

Pouran Almstedt, Department of Medical Epidemiology and Biostatistics for data management. Karolinska Institutet, Stockholm, Sweden

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Figures

**Figure 1** - Categories of weight change by baseline participant characteristics: Swedish women’s lifestyle and health Study, 1991-2003

**Figure 2** - Estimated 95% confidence intervals for the effect of a selection of variables on weight change (as linear measure) between 1991 and 2003, based on the two questionnaires in the Swedish Women’s Lifestyle and Health Study, 1991-2003