Long-term effects of a weight loss intervention with or without exercise component in postmenopausal women: A randomized trial

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A R T I C L E   I N F O
Article history:
Received 18 April 2016
Received in revised form 7 November 2016
Accepted 5 December 2016
Available online 09 December 2016

Keywords:
Obesity
Body weight
Exercise
Diet
Physical activity

A B S T R A C T
The aim of this study was to determine the long-term effects of a weight loss intervention with or without an exercise component on body weight and physical activity.
Women were randomized to diet (n = 97) or exercise (N = 98) for 16 weeks. During the intervention, both groups had achieved the set goal of 5-6 kg weight loss. All women were re-contacted twelve months after study cessation for follow-up where body weight and physical activity were measured (PASE questionnaire and ActiGraph accelerometer).

At follow-up, body weight and physical activity (measured by the PASE questionnaire and accelerometer) were measured again. At follow-up, both mainly exercise (−4.3 kg, p < 0.001) and diet (−3.4 kg, p < 0.001) showed significantly reduced body weight compared to baseline. Both the mainly exercise and diet group were significantly more physically active at one year follow-up compared to baseline (PASE: +33%, p < 0.001 and +12%, p = 0.040, respectively; ActiGraph: +16%, p = 0.012, and +22%, p = 0.695 moderate-to-vigorous activity, respectively). Moreover, the increase in physical activity was statistically significantly when comparing exercise to diet (+0.6%, p = 0.035). ActiGraph data also showed significantly less sedentary time in mainly exercise group compared to baseline (−2.1%, p = 0.018) and when comparing exercise to diet (−1.8%, p = 0.023). No significant within group differences were found for the diet group.

This study shows largely sustained weight loss one year after completing a weight loss program with and without exercise in overweight postmenopausal women. Although the mainly exercise group maintained more physically active compared to the diet group, maintenance of weight loss did not differ between groups.

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1. Introduction

Obesity and a sedentary lifestyle are an increasing worldwide health problem (Ogden et al., 2014). The World Health Organization (WHO) reports that worldwide 39% of adults are overweight of which 13% are obese (Mendis et al., 2015). The prevalence of overweight and obesity is proportionally higher in postmenopausal women, compared to premenopausal women (Lambrinoudaki et al., 2010). It has been shown for obese postmenopausal women to have an increased risk for developing coronary heart diseases, stroke, venous thrombosis, osteoporosis, stroke, type 2 diabetes, and certain types of cancers, some of the leading causes of preventable death (Mendis et al., 2015; Lambrinoudaki et al., 2010; Wiseman, 2008). It is well known, aside from contributing factors as increasing age, lower energy expenditure due to a sedentary lifestyle and increased caloric intake, that menopause affects the body composition on hormonal levels, fat distribution and insulin resistance causing central obesity (Lambrinoudaki et al., 2010; Neilson et al., 2009). Since both physical inactivity and obesity increase with age and are affected by menopause, this postmenopausal group is a relevant population to study lifestyle interventions (Centers for Disease Control and Prevention, 2011; Lynch et al., 2011). It has been shown that taking part in an exercise intervention or weight loss program is a successful method to lose body weight and to become more physically active over the short-term (Ryan et al., 2012; Wu et al., 2009; Franz et al., 2007). As shown by Baker et al. interventions taking up to 1 year have shown to be successful but those interventions did not include a follow-up measurement after completing the supervised intervention period (Baker et al., 2016). Wu et al. did study sustainability of weight loss interventions in their meta-analysis, however, the included studies nor the results were aimed at postmenopausal women (Wu et al., 2009).

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So, there is a lack of knowledge on the long-term effects of a short-term weight loss intervention in postmenopausal women specifically. Therefore, the aim of this study is to determine sustainability of effects of a weight loss intervention with or without an exercise component on body weight and physical activity in postmenopausal women. Furthermore, we aimed to investigate whether effects are different when weight loss is induced by a hypocaloric diet or mainly by exercise.

2. Methods

This study is a post-intervention study in women who participated in the Sex Hormones And Physical Exercise (SHAPE)-2 study; a three-armed randomized controlled trial conducted from February 2012 to May 2013 in eight municipalities in and around Utrecht and Enschede in the Netherlands. The primary goal of the SHAPE-2 trial was to study the effects of 5–6 kg weight loss induced by a hypocaloric diet or mainly by exercise on postmenopausal serum sex hormone levels, associated with breast cancer risk (van Gemert et al., 2015; van Gemert et al., 2013). The main exercise intervention was combined with a small caloric intake restriction to ensure the intended weight loss in this short time-frame. However, the emphasis was on exercise and for clarity reasons, we refer to this group as ‘exercise group’ throughout the paper. The SHAPE-2 main results showed that weight loss in both intervention groups resulted in favourable effects on sex hormones. Weight loss induced mainly by exercise additionally resulted in maintenance of lean mass, greater fitness, greater fat loss and a larger effect on (some) sex hormones. Details of the study design are reported elsewhere (van Gemert et al., 2013). The study was approved by the ethical committee of the University Medical Center of Utrecht. All participants provided informed consent.

In short, women were eligible if they were aged 50–69 years, postmenopausal, overweight or obese (BMI 25–35 kg/m²), and insufficiently physically active (<2 h/week of ≥4 metabolic equivalents (MET) activity). Women were included via mass mailings and media publicity. Women who responded were contacted by telephone by a study nurse to assess their eligibility criteria. Main exclusion criteria were smoking, use of exogenous (sex) hormones, diabetes, or ever diagnosed with breast cancer.

Before the intervention started, all women started with a four to six-week run-in period during which a standardized diet was prescribed, (50–60% carbohydrates, 15–20% proteins, 20–35% fat, min. 25 g fiber, max. 1 alcohol consumption/day), aiming to remain weight stable (van Gemert et al., 2013; Health council of the Netherlands, 2006). After baseline measurements, women were stratified for municipality randomized by computer. Postmenopausal women (n = 243) were randomized to either a 16-week diet-induced weight loss group (‘diet group’, N = 97), weight loss mainly induced by exercise (‘mainly exercise group’, N = 98), or stable weight control group (‘control group’, N = 48). Both weight loss interventions aimed for 5–6 kg weight loss and were delivered by physiotherapists and/or dieticians.

In the intervention phase, the diet group was prescribed a diet with a deficit of 3500 kcal/week. Women in the mainly exercise group followed an intensive four hour/week exercise program; two one-hour group sessions of combined strength and endurance training at the physiotherapy centre and two one-hour sessions of moderate-to-vigorous Nordic walking per week. The average energy expenditure by exercise was approximately 2530 kcal/week. These women were also prescribed a relatively small caloric intake restriction of 1750 kcal/week to ensure the 5–6 kg weight loss goal within 14 weeks. The total targeted weekly energy deficit was, therefore, approximately 4280 kcal/week. This was an a priori decision, to ensure the 5–6 kg weight loss goal within 14 weeks. The targeted total average weekly deficit for the mainly exercise group is larger than the diet group to compensate for the gain in muscle mass (i.e., body weight) by the combined endurance and strength exercise program (van Gemert et al., 2013).

2.1. One-year post-intervention (follow-up) study

2.1.1. Study population

In order to be eligible to participate in the follow-up study of SHAPE-2 trial, subjects had to have given informed consent at baseline to be re-contacted in the future for invitation for additional research. These subjects were contacted by telephone one year (±4 weeks) after completing the SHAPE-2 intervention study. If subjects could not be contacted by telephone, questionnaires were sent by mail including a letter of consent and a return envelope. Subjects that could not be contacted by telephone or e-mail did not receive the accelerometer at follow-up.

The control group was excluded for analyses of the follow-up data since control subjects received a weight loss intervention after the intervention period. Therefore, the natural course during follow up could not be studied.

2.1.2. Outcomes

Primary outcomes are body weight and physical activity levels at follow-up (t2) compared to baseline (t0) and at end of study (t1). At baseline and end of study body weight was measured using an identical balance scale. At follow-up, body weight was self-reported by the participants.

Physical activity was assessed through the Physical Activity Scale for the Elderly (PASE) and an accelerometer, the ActiGraph®. Both methods were used also in the SHAPE-2 trial. The PASE is a brief self-administered seven-day recall questionnaire to measure changes in physical activity over time (Liu et al., 2011). The PASE has shown to have excellent test-retest reliability (ICC 0.89) and reasonable validity (r = 0.68) (Liu et al., 2011; Schuit et al., 1997). The PASE is evaluating the physical activity of the past 7 days in three life domains: recreational, household and work-related. Subjects rate their weekly frequency and daily duration for the following recreational activities: walking outside the home, light, moderate and strenuous activities and muscle strengthening. Whether household activities (light and heavy housework, home repairs, lawn work/yard care, outdoor gardening and caring for others) were performed was captured by answering yes or no. Finally, working for pay or as a volunteer was assessed by recording the amount of hours per week and the type of work performed. For each activity, a score was obtained by multiplying an activity frequency value by a task-specific weight provided by the scoring manual. The questionnaire data results in a PASE total score and categories ranging from very light activities to very vigorous activities. The PASE total score, which represents the overall physical activity level, is the sum of all activities together, and ranges between 0 and 400 or more (Bolszak et al., 2014). The results in all these categories will be counted together forming a continuous “PASE” score. A higher PASE score means a person is more physically active.

The ActiGraph® is a waist-worn accelerometer which measures movements by a three-dimensional/axis acceleration sensor (Hanggi et al., 2013). In our study we used the ActiGraph® wGT3X. The activity monitor measures activity in activity counts, which were recorded in 10 s intervals and transformed into 1-minute epochs. The 1-min epochs were used to compute the time spent in the different activity intensities i.e. sedentary (<100 counts per minute), light (100–759 counts per minute), lifestyle (760–1951 counts per minute), moderate (1952–5274 counts per minute), vigorous (5725–9498 counts per minute) and very vigorous (≥9499 counts per minute) (Sasaki et al., 2011; Freedson et al., 1998). All days with a wear-time minimum of 10 h are included in the analyses. Thus, also days with a wear-time >10 h are included. Days containing <10 h have been shown not to be representative for daily physical activity. The 10-hour day cut point is commonly used in literature. Data from the ActiGraph® was extracted using ActiLife® 6.8.1. For analyses, three categories were defined: sedentary time, light activities (light and lifestyle activities) and moderate to vigorous activities (moderate and very vigorous activities) based on the Freedson cut off points (Freedson et al., 1998). A non-wear period was
defined as periods of consecutive strings of zero count epochs lasting ≥60 min. Subjects were asked to wear the accelerometer for seven consecutive days around their waist at the height of where the belt is or would be. When the ActiGraph® was worn 4 days the results were included in analyses. The ActiGraph® outcomes were presented as the percentage of hours spent at a certain activity level of the total time the accelerometer was worn.

Two questions of the International Physical Activity Questionnaire (IPAQ) were added to measure subjects’ usual daily sitting time, during a week and a weekend day (Brown et al., 2004).

The dietary intake was not assessed at follow-up.

2.1.3. Statistical analysis

Baseline characteristics are presented for the diet and mainly exercise group. Data analysis was performed according to intention-to-treat principle. Normal distribution of the outcome data (physical activity and body weight) was evaluated by using histograms and Q-Q-plots. When data was not normally distributed, a log-transformation was applied to obtain a normal distribution. We analysed the differences between follow-up (t2) and baseline (t0); and between follow up (t2) and end of study (t1) within groups using mixed linear models. Between group differences (between the diet and mainly exercise group) comparing follow-up (t2) with baseline (t0) were also computed also using mixed linear models. The linear mixed effect method has shown to be a reliable method to handle missing longitudinal data (Cnaan et al., 1997; Peters et al., 2012). All statistical analyses were performed using SPSS 22.0, with a two-sided significance level of 0.05.

3. Results

195 women participating in the intervention groups of SHAPE-2 gave consent to re-contact them. We were unable to trace 26 (13%) women (lost to follow up) and 14 (7%) refused participation after contacting them (see Fig. 1). In total, 155 (80%) women filled in questionnaires. The accelerometer was worn by 132 subjects (68%), of which seven could not be analysed. Non-response at follow-up was equal in both groups (diet (19) and mainly exercise (21)). Non-responders were significantly younger than the responders (58 compared to 60). Other baseline characteristics did not differ between responders and non-responders.

At baseline (t0) groups were comparable for main characteristics (Table 1).

3.1. Body weight

At follow up, both the exercise (−4.3 kg, 95% confidence interval (CI) −4.9: −3.7) and diet group (−3.4 kg, 95% CI −4.1: −2.6) showed lower body weight compared to baseline but both groups also slightly regained body weight since the end of study (+1.3 kg and +1.5 kg, respectively) (Table 2). No statistically significant difference was observed between the mainly exercise and the diet group at follow-up (−0.13 kg, 95% CI −2.7:2.4) (Table 3).

At follow-up, BMI was significantly decreased in both groups: the mainly exercise group decreased −1.5 kg/m² and the diet group −1.2 kg/m² when comparing to baseline. Comparing the exercise group to the diet group, the exercise group decreased −0.6 kg/m² more over time (95% CI −1.3:0.2).

3.2. Physical activity level

Both intervention groups were more physically active at follow up compared to baseline as well as compared to end of study (Table 2). The mainly exercise group showed an increase in PASE score of +39 points (+33%) (95% CI 23:55) from baseline to follow up (Table 2). For the diet group this was +14 points (+12%) (95% CI 1:28) (Table 2).

Between-group analysis showed a higher PASE score for the mainly exercise group at follow up study when compared to the diet group (difference of +25 points) (Table 3). These results of the PASE questionnaire are supported by the ActiGraph® accelerometer (Tables 2 and 3); at follow up, the mainly exercise group spend less time with sedentary behaviour (−1.5% (95%CI −2.7:−0.3)) and more time with moderate and vigorous activities compared to baseline (+0.7% (95%CI 0.2:1.3)). Comparable results were found when comparing the mainly exercise group with diet: −1.8%(95%CI −3.4:−0.3) sedentary time and +0.6% (95%CI 0.0:1.1) moderate-to-vigorous activities. No statistically significant within and between-group differences were reported in sitting time measured by the IPAQ.

Fig. 1. Flow-chart showing the inclusion of participants into the follow-up study from the Sex Hormone And Physical Exercise-2 study.
Data is analysed using the linear mixed methods. All cases of which at least one measurement is available therefore is added in analyses.

Within group differences for both the mainly exercise and diet group in bodyweight, physical activity level and sitting time for baseline (t0) compared to follow-up (t2) and end of study (t12).

Table 2
Within group differences for both the mainly exercise and diet group in bodyweight, physical activity level and sitting time for baseline (t0) compared to follow-up (t2) and end of study (t12).

4. Discussion

This study shows largely sustained weight loss one year after completing a 16-week weight loss program with or without exercise component, in overweight postmenopausal women. Although both the mainly exercise and diet group regained weight after the intervention period, the reduction in body weight (−4.3 kg in the mainly exercise group and −3.4 kg in the diet group) was still statistically significant lower than at baseline and did not differ between groups. Women participating in the exercise program remained more physically active at follow-up than women in the diet only group.

Despite the mainly exercise group was still significantly more physically active one year after ending this program, maintenance of weight loss did not differ from the group with weight loss induced by a hypocaloric diet. This might be partly explained by the fact also the diet group showed increased physical activity after study completion. Another explanation could be that the food intake in the diet group remained lower at follow-up due to the dietary intervention program. It should be noted that the diet group shows statistically significant improvement in the PASE questionnaire between t1 and t2, but that the improvement in light and moderate-to-vigorous activities was, however positive, not statistically significant. This might be explained by due to limitations/differences in measuring physical activity by the PASE and by the ActiGraph®, which will be explained in the limitations section below.

The largely sustained weight loss of the intervention groups is comparable with results of other weight loss programs in elderly men and women (Franz et al., 2007; Barte et al., 2010; Witham and Avenell, 2010). These studies showed that in the first year after weight loss treatment, generally around two third of the lost body weight is sustained (Franz et al., 2007; Witham and Avenell, 2010; Sarwer et al., 2009). Limited data is available on potential differences in long-term effects between diet or exercise induced weight loss (Franz et al., 2007; Barte et al., 2010; Barte et al., 2010; Irwin et al., 2003; Nakade et al., 2012; Van et al., 2009). Our study shows that a short-term weight loss intervention, especially when exercises are included, is a successful method, to lose body weight and to increase the level of physical activity with a long-lasting effect. However, we only have data at one year after study end. Body weight and physical inactivity may increase in the future (Franz et al., 2007; Catacci and Wyatt, 2007).

We found that, in postmenopausal women with an inactive lifestyle, participation in an exercise intervention led to long-term higher

Table 1
Baseline characteristics of both intervention groups.

Table 2
Within group differences for both the mainly exercise and diet group in bodyweight, physical activity level and sitting time for baseline (t0) compared to follow-up (t2) and end of study (t12).
Abbreviations: N, number of women; CI, confidence interval; PASE, Physical Activity Scale for the Elderly; SQUASH, Short Questionnaire to Assess Health.

### Table 3

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean difference (95% CI)</th>
<th>p</th>
<th>Mean difference (95% CI)</th>
<th>p</th>
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<tbody>
<tr>
<td>Bodyweight, kg*</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mainly exercise vs diet, baseline to follow-up</td>
<td>−0.13 (−2.67:2.43)</td>
<td>0.922</td>
<td>−0.40 (−3.07:2.27)</td>
<td>0.769</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>−0.6 (−1.3:0.2)</td>
<td>0.160</td>
<td>−0.6 (−1.4:0.2)</td>
<td>0.168</td>
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<tr>
<td>PASE score, points</td>
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<tr>
<td>Mainly exercise vs diet, end-of-study to follow-up</td>
<td></td>
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<tr>
<td>Sitting time, average minutes per day</td>
<td>−31 (−75:14)</td>
<td>0.173</td>
<td>−22 (−70:27)</td>
<td>0.378</td>
</tr>
<tr>
<td>ActiGraph® sedentary time b</td>
<td>−1.8 (−3.38:−0.26)</td>
<td>0.023</td>
<td>−2.2 (−4.03:−0.35)</td>
<td>0.020</td>
</tr>
<tr>
<td>ActiGraph® light activities b</td>
<td>1.2 (−0.1:2.5)</td>
<td>0.059</td>
<td>1.3 (−0.2:2.8)</td>
<td>0.098</td>
</tr>
<tr>
<td>ActiGraph® moderate and vigorous activities b</td>
<td>0.6 (0.04:1.1)</td>
<td>0.035</td>
<td>0.9 (0.3:1.6)</td>
<td>0.005</td>
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<tr>
<td>Diet</td>
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Important strengths of the SHAPE-2 study are the high response rate (80%) among the SHAPE-2 participants for the 12-month follow up study and the relatively large study population. Also, intended weight loss by mainly exercise could be directly compared to intended weight loss by diet alone. Results on self-reported physical activity levels were supported by results of objectively measured data of the ActiGraph® (when data from the ActiGraph® was split into the same five categories as the PASE).

The increased physical activity levels and the highly maintained weight loss might have beneficial effects on multiple obesity related diseases. Magkos et al. have shown in their study the beneficial effects of 5% weight loss (Magkos et al., 2016). They found that subject with 5% weight loss had significantly decreased body fat, including abdominal fat and fat in the liver. Subjects also had decreased plasma levels of glucose, insulin, triglycerides and leptin, which are risk factors for heart diseases and type-2 diabetes (Magkos et al., 2016). They also showed improved function of insulin-secreting β cells, as well as the ability of fat, liver, and muscle tissue to respond to insulin. The increased physical activity is also of great importance. At follow up, the participants from the mainly exercise group were ±1.5 h per week more physically active. This might for example affect breast cancer risk and extend the life expectancy. Were Wu et al. showed that the relative risk for breast cancer was 0.95 for every 2 h per week increase in moderate and vigorous recreational activities, Wen et al. showed that at least 52 min of exercise per week in inactive people reduces the risk of all-cause-mortality with 14% (Wu et al., 2009; Wen et al., 2011).

### 5. Conclusion

In conclusion, this study shows largely sustained weight loss one year after completing a 16-week weight loss program by a hypocaloric diet only or mainly exercise in overweight and obese postmenopausal women with an inactive lifestyle. The exercise group became more physically active at follow-up than the diet group. However, maintenance of weight loss at follow-up did not differ between taking part in the exercise or diet group. This study indicates that taking part in a short-term weight loss intervention leads to healthier lifestyle one year after participation.
Conflict of interest

We have no financial or non-financial competing interests to disclose.

Acknowledgments

This work was supported by the Dutch Cancer Society [Grant number UU 2010-4843 to EM] and the Dutch Pink Ribbon Foundation [Grant numbers PR110032, PR110039 to EM]. The support from the sponsors was unconditional, and the data collection, design, management, analysis, interpretation and reporting were performed without their interference. Results of the present study do not constitute endorsement by American College of Sports Medicine.

We would like to thank Manon de Leeuw, Fien Stern, Lyddeke Zwart, Lizeth Vendrig, Marjan van der Meer, Gerry van Hemert, Karen Menninga, Joke Metselaars, Veronique Sauerwald, Renate Bloemen, Willemien Boersma, Silvia Achterberg, Petra Hemelijtjen, Mirjam Floor, Roelof Peters and Jolanda Spruit who have collected or contributed to the running of the study. Prof. Huub van den Bergh contributed to select the most reliable statistical analysis.

Martijn de Roon carried out the follow-up measurement, analysis, interpreted the data and drafted the manuscript. Willemijn A. van Gemert and Evelyn M. Monninkhof putted up the study design, per-