



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

Martijn de Roon<sup>a,b</sup>, Willemijn A van Gemert<sup>a</sup>, Petra H Peeters<sup>a</sup>, Albertine J Schuit<sup>c,d</sup>, Evelyn M Monninkhof<sup>a,\*,1</sup>

<sup>a</sup> Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

<sup>b</sup> Physical Therapy Sciences, program in Clinical Health Sciences, University Medical Center Utrecht, Utrecht, The Netherlands

<sup>c</sup> Department of Health Science, VU University Amsterdam, The Netherlands

<sup>d</sup> National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

### ARTICLE INFO

#### Article history:

Received 18 April 2016

Received in revised form 7 November 2016

Accepted 5 December 2016

Available online 9 December 2016

#### Keywords:

Obesity

Body weight

Exercise

Diet

Physical activity

### ABSTRACT

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  $+2.2\%$ ,  $p = 0.695$  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 physical activity compared to the diet group, maintenance of weight loss did not differ between groups.

© 2016 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### 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).

\* Corresponding author at: University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, PO Box 85500, 3508 GA Utrecht, The Netherlands.

E-mail address: [E.Monninkhof@umcutrecht.nl](mailto:E.Monninkhof@umcutrecht.nl) (E.M. Monninkhof).

<sup>1</sup> Visiting address: Universiteitsweg 100, 3584 CG Utrecht, The Netherlands.

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 mainly 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/m<sup>2</sup>), 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 alcoholic 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 ( $\pm 4$  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 ( $t_2$ ) compared to baseline ( $t_0$ ) and at end of study ( $t_1$ ).

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 ( $r_s$  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 count 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 (5275–9498 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  $\geq 60$  min. Subjects were asked to wear the accelerometer for seven consecutive days around their waist at the height of where their 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/m<sup>2</sup> and the diet group  $-1.2$  kg/m<sup>2</sup> when comparing to baseline. Comparing the exercise group to the diet group, the exercise group decreased  $-0.6$  kg/m<sup>2</sup> 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.

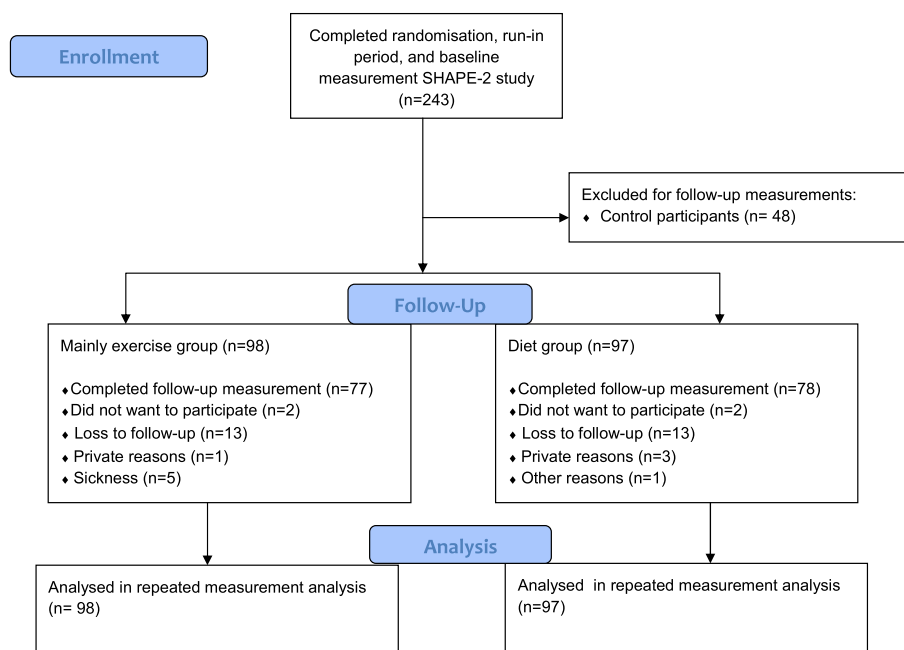


Fig. 1. Flow-chart showing the inclusion of participants into the follow-up study from the Sex Hormone And Physical Exercise-2 study.

**Table 1**  
Baseline characteristics of both intervention groups.

	Exercise group (N = 98) mean(sd)	Diet group (N = 97) mean(sd)
Age, years	59(4.9)	61(4.6)
Weight, kg	80(9.0)	80(8.6)
Length, cm	166(5.2)	165(6.0)
BMI, kg/cm <sup>2</sup>	29.0(2.9)	29.5(2.6)
Body fat %	43.8(4.0)	44.1(3.8)
Total fat, kg	33.9(6.2)	33.9(5.7)
Lean mass	43.1(4.1)	42.7(4.0)
Waist circumference, cm	97.5(8.3)	97.8(7.5)
Hip circumference, cm	109.2(6.7)	109.8(6.8)
VO <sub>2</sub> peak, ml/min	1749(293)	1742(310)
VO <sub>2</sub> relative, ml/kg/min	21.8(3.7)	21.9(4.0)
Years since menopause	10.9(7.7)	10.7(6.1)
Educational level <sup>a</sup>		
Low	33(33.6%)	27(27.8%)
Moderate	20(20.4%)	27(27.8%)
High	44(44.9%)	42(43.3%)
Alcohol (g/day)	4.3(0.0–10.0)	5.7(0.0–10.0)

Abbreviations: N, number of subjects; SD, standard deviation; kg, kilograms; cm, centimeters.

<sup>a</sup> Education levels: low = primary school and technical/professional school, middle = college degree, high = university degree.

#### 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; Yan 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; Catenacci and Wyatt, 2007).

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

**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 (t1) compared to follow-up (t2).

	Baseline 0 weeks <sup>a</sup> (t0)	End of study (t1)	12 month follow-up (t2)	% change baseline-12 m fup <sup>b</sup>	% change end of study-12 m fup <sup>b</sup>	Within group difference (95% CI) baseline-12 m fup <sup>b</sup>	<i>p</i>	Within group difference (95% CI) End of study-12 m fup <sup>b</sup>	<i>p</i>
N									
Mainly exercise	98	93	77						
Diet	97	94	78						
Bodyweight, kg									
Mainly exercise	80.4	74.9	76.1	−5.4%	+1.6%	−4.3 (−4.9;−3.7)	<0.001	1.3 (0.6;1.9)	0.001
Diet	80.0	75.1	76.6	−4.3%	+2.0%	−3.4 (−4.1;−2.7)	<0.001	1.5 (0.8;2.2)	<0.001
Body mass index, kg/m <sup>2</sup>									
Mainly exercise	29.0	27.0	27.5	−5.2%	+1.9%	−1.5 (−1.8;−1.3)	<0.001	0.5 (0.2;0.7)	<0.001
Diet	29.4	27.6	28.1	−4.4%	+1.8%	−1.2 (−1.5;−1.0)	<0.001	0.5 (0.3;0.8)	<0.001
PASE score, points									
Mainly exercise	123	150	162	+33%	+8.0%	39 (23;55)	<0.001	12 (−4;28)	0.140
Diet	117	111	131	+12%	+18%	14 (1;28)	0.040	20 (6;34)	0.006
Sitting time, average minutes per day									
Mainly exercise	351	342	355	+1.1%	+3.8%	4 (−30;37)	0.830	13 (−22;48)	0.458
Diet	394	377	370	−6.1%	−1.7%	−24 (−64;16)	0.232	−7 (−49;34)	0.723
ActiGraph® sedentary time <sup>c</sup>									
Mainly exercise	72.7	71.7	71.2	−2.1%	+0.1%	−1.5 (−2.7;−0.3)	0.018	−0.5 (−1.7;0.7)	0.430
Diet	73.1	74.6	73.4	+0.4%	−1.6%	0.3 (−0.8;1.4)	0.614	−1.2 (−2.3;−0.1)	0.041
ActiGraph® light activities <sup>c</sup>									
Mainly exercise	22.9	22.8	23.6	+3.1%	+3.5%	0.8 (−0.3;1.8)	0.165	0.9 (−0.3;1.9)	0.101
Diet	22.4	21.3	22.0	−1.8%	+3.3%	−0.4 (−1.3;0.5)	0.405	0.7 (−0.2;1.7)	0.110
ActiGraph® moderate and vigorous activities <sup>c</sup>									
Mainly exercise	4.4	5.5	5.1	+16%	−7.3%	0.7 (0.2;1.3)	0.012	−0.4 (−0.9;0.2)	0.207
Diet	4.5	4.2	4.6	+2.2%	+9.5%	0.1 (−0.4;0.7)	0.695	0.4 (−0.2;0.9)	0.168

Abbreviations: N, number of women; CI, confidence interval; PASE, Physical Activity Scale for the Elderly; SQUASH, Short Questionnaire to Assess Health.

Data is analysed using the linear mixed methods. All cases of which at least one measurement is available therefore is added in analyses.

<sup>a</sup> Estimated means per group with linear mixed model taking into account all women with at least one measurement

<sup>b</sup> Represents the overall within group effect over time for each questionnaire obtained with linear mixed models, per intervention group

<sup>c</sup> Percentage per day based on a 10-hour day.

**Table 3**  
Between group differences (exercise versus diet) in bodyweight, physical activity level and sitting time for baseline (t0) and end of study (t1) results compared to follow-up (t2) results.

	Mean difference (95% CI) Mainly exercise vs diet, baseline to follow-up <sup>c</sup>	<i>p</i>	Mean difference (95% CI) Mainly exercise vs diet, end-of-study to follow-up <sup>c</sup>	<i>p</i>
Bodyweight, kg <sup>a</sup>				
Mainly exercise	−0.13 (−2.67:2.43)		−0.40 (−3.07:2.27)	
Diet		0.922		0.769
Body mass index, kg/m <sup>2</sup>				
Mainly exercise	−0.6 (−1.3:0.2)		−0.6 (−1.4:0.2)	
Diet		0.160		0.168
PASE score, points				
Mainly exercise	25.0 (11.5:38.4)		34.2 (18.4:49.9)	
Diet		<0.001		<0.001
Sitting time, average minutes per day				
Mainly exercise	−31 (−75:14)		−22 (−70:27)	
Diet		0.173		0.378
ActiGraph® sedentary time <sup>b</sup>				
Mainly exercise	−1.8 (−3.38:−0.26)		−2.2 (−4.03:−0.35)	
Diet		0.023		0.020
ActiGraph® light activities <sup>b</sup>				
Mainly exercise	1.2 (−0.1:2.5)		1.3 (−0.2:2.8)	
Diet		0.059		0.098
ActiGraph® moderate and vigorous activities <sup>b</sup>				
Mainly exercise	0.6 (0.04:1.1)		0.9 (0.3:1.6)	
Diet		0.035		0.005

Abbreviations: N, number of women; CI, confidence interval; PASE, Physical Activity Scale for the Elderly; SQUASH, Short Questionnaire to Assess Health.

<sup>a</sup> Estimated means for all participants with linear mixed model taking into account all women with at least one measurement.

<sup>b</sup> Percentage per day based on a 10-hour day.

<sup>c</sup> Represents the overall between-group effect over time for each questionnaire obtained with linear mixed models analysis including baseline, end of study and follow-up measurement.

physical activity levels compared to baseline. These results are in accordance with the results of a meta-analysis by Gourlan et al. and an earlier study of our study group (van Gemert et al., 2015; Gourlan et al., 2011). Gourlan et al. summarized the long-term maintenance of interventions promoting physical activity levels in people with overweight and obesity; and they showed that exercise interventions, varying from three weeks to six months, were successful in maintaining physical activity levels after the intervention has ended (Gourlan et al., 2011). In order to extend the beneficial effects of the weight loss program, longer supervision from a dietician or physiotherapist may be recommended.

Our study has some limitations, which should be acknowledged. First, we could not compare the effects of the weight loss interventions at follow-up with a natural course since our control group was offered a weight loss program after the 16-week study period. Second, weight was self-measured at follow-up, which could have led to misclassification, usually an underestimation of the real weight (Pasalich et al., 2014; Schebendach et al., 2012). Third, since not all subjects could be contacted (13%), this might have led to selection bias. However, dropout at follow-up was equal in both groups (diet 19, mainly exercise 21) and baseline characteristics of non-responders were not significantly different from responders, except from age. Dropouts were slightly younger than participants (58 versus 60 year, respectively). It is unlikely that this difference in age biased our results.

Furthermore, a limitation of the ActiGraph® itself is that it cannot properly measure cycling or strength training (as experienced by the researchers during testing the accelerometer in advance of the study). It has been shown by Shiroma et al. (2015) that the correlation between self-measured accelerometer assessed MVPA is between 0.35 and 0.39 (Shiroma et al., 2015). A correlation of 0.40 is estimated for the IPAQ (sitting time) (Shiroma et al., 2015). Our own experiences with the accelerometer are also supported by Shiroma et al.: When the accelerometer is worn around the hip it does not measure stationary cycling, weight lifting or any other physical activities of the upper body (Shiroma et al., 2015). In The Netherlands, cycling is common and practiced on a daily basis by many women. The ActiGraph® might, therefore, have underestimated the level of physical activity and thereby potentially underestimated the positive study results.

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  $\beta$  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  $\pm 1.5$  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 92 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, Lydeke Zwart, Lizeth Vendrig, Marjon van de Meer, Gerry van Hemert, Karen Menninga, Joke Metselaars, Veronique Sauerwald, Renate Bloemen, Willemien Boersma, Silvia Achterberg, Petra Hemeltjen, Mirjam Floor, Roelof Peters and Jolanda Spruijt 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, performed data collection during the study period, and critically revised the data analysis and manuscript. Petra H. Peeters and Albertaine J Schuit critically revised the manuscript.

Trial registration: The SHAPE-2 study is registered in the register of clinicaltrials.gov, Identifier: NCT01511276

## References

- Baker, A., Sirois-Leclerc, H., Tulloch, H., 2016. The impact of long-term physical activity interventions for overweight/obese postmenopausal women on adiposity indicators, physical capacity, and mental health outcomes: a systematic review. *J. Obes.* 2016. <http://dx.doi.org/10.1155/2016/6169890>.
- Barte, J.C., ter Bogt, N.C., Bogers, R.P., et al., 2010. Maintenance of weight loss after lifestyle interventions for overweight and obesity, a systematic review. *Obes. Rev.* 11 (12): 899–906. <http://dx.doi.org/10.1111/j.1467-789X.2010.00740.x>.
- Bolszak, S., Casartelli, N.C., Impellizzeri, F.M., Maffiuletti, N.A., 2014. Validity and reproducibility of the Physical Activity Scale for the Elderly (PASE) questionnaire for the measurement of the physical activity level in patients after total knee arthroplasty. *BMC Musculoskelet. Disord.* 15 (46). <http://dx.doi.org/10.1186/1471-2474-15-46>.
- Brown, W., Bauman, A., Chey, T., Trost, S., Mummery, K., 2004. Comparison of surveys used to measure physical activity. *Aust. N. Z. J. Public Health* 28 (2), 128–134.
- Catenacci, V.A., Wyatt, H.R., 2007. The role of physical activity in producing and maintaining weight loss. *Nat. Clin. Pract. Endocrinol. Metab.* 3 (7):518–529. <http://dx.doi.org/10.1038/ncpendmet0554> [pii].
- Centers for Disease Control and Prevention, 2011. *Strategies to Prevent Obesity and Other Chronic Diseases: The CDC Guide to Strategies to Increase Physical Activity in the Community*. p. 1.
- Cnaan, A., Laird, N.M., Slasor, P., 1997. Using the general linear mixed model to analyse unbalanced repeated measures and longitudinal data. *Stat. Med.* 16 (20):80. [http://dx.doi.org/10.1002/\(SICI\)1097-0258\(19971030\)16:20<2349\(AID-SIM667>3.0.CO;2-E](http://dx.doi.org/10.1002/(SICI)1097-0258(19971030)16:20<2349(AID-SIM667>3.0.CO;2-E)).
- Franz, M.J., VanWormer, J.J., Crain, A.L., et al., 2007. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J. Am. Diet. Assoc.* 107 (10), 1755–1767 (doi:S0002-8223(07)01483-6 [pii]).
- Freedson, P.S., Melanson, E., Sirard, J., 1998. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med. Sci. Sports Exerc.* 30 (5), 777–781.
- Gourlan, M.J., Trouilloud, D.O., Sarrazin, P.G., 2011. Interventions promoting physical activity among obese populations: a meta-analysis considering global effect, long-term maintenance, physical activity indicators and dose characteristics. *Obes. Rev.* 12 (7):e633–e645. <http://dx.doi.org/10.1111/j.1467-789X.2011.00874.x>.
- Hanggi, J.M., Phillips, L.R., Rowlands, A.V., 2013. Validation of the GT3X ActiGraph in children and comparison with the GT1M ActiGraph. *J. Sci. Med. Sport* 16 (1):40–44. <http://dx.doi.org/10.1016/j.jsams.2012.05.012>.
- Health council of the Netherlands, 2006. *Guidelines for a Healthy Diet 2006* (2006/21E).
- Irwin, M.L., Yasui, Y., Ulrich, C.M., et al., 2003. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. *JAMA* 289 (3), 323–330 (doi:10.3989/joc21225 [pii]).
- Lambrinoudaki, I., Brincat, M., Erel, C.T., et al., 2010. EMAS position statement: managing obese postmenopausal women. *Maturitas* 66 (3):323–326. <http://dx.doi.org/10.1016/j.maturitas.2010.03.025>.
- Liu, R.D., Buffart, L.M., Kersten, M.J., et al., 2011. Psychometric properties of two physical activity questionnaires, the AQuAA and the PASE, in cancer patients. *BMC Med. Res. Methodol.* 11 (30). <http://dx.doi.org/10.1186/1471-2288-11-30>.
- Lynch, B.M., Neilson, H.K., Friedenreich, C.M., 2011. Physical activity and breast cancer prevention. *Recent Results Cancer Res.* 186:13–42. [http://dx.doi.org/10.1007/978-3-642-04231-7\\_2](http://dx.doi.org/10.1007/978-3-642-04231-7_2).
- Magkos, F., Fraterrigo, G., Yoshino, J., et al., 2016. Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. *Cell Metab.* 23 (4):591–601. <http://dx.doi.org/10.1016/j.cmet.2016.02.005>.
- Mendis, S., Davis, S., Norrving, B., 2015. Organizational update: the world health organization global status report on noncommunicable diseases 2014; one more landmark step in the combat against stroke and vascular disease. *Stroke* 46 (5):e121–e122. <http://dx.doi.org/10.1161/STROKEAHA.115.008097>.
- Nakade, M., Aiba, N., Suda, N., et al., 2012. Behavioral change during weight loss program and one-year follow-up: Saku Control Obesity Program (SCOP) in Japan. *Asia Pac. J. Clin. Nutr.* 21 (1), 22–34.
- Neilson, H.K., Friedenreich, C.M., Brockton, N.T., Millikan, R.C., 2009. Physical activity and postmenopausal breast cancer: proposed biologic mechanisms and areas for future research. *Cancer Epidemiol. Biomarkers Prev.* 18 (1):11–27. <http://dx.doi.org/10.1158/1055-9965.EPI-08-0756>.
- Ogden, C.L., Carroll, M.D., Kit, B.K., Flegal, K.M., 2014. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA* 311 (8):806–814. <http://dx.doi.org/10.1001/jama.2014.732>.
- Pasalich, M., Lee, A.H., Burke, L., Jancey, J., Howat, P., 2014. Accuracy of self-reported anthropometric measures in older Australian adults. *Australas. J. Ageing* 33 (3): E27–E32. <http://dx.doi.org/10.1111/ajag.12035>.
- Peters, S.A., Bots, M.L., den Ruijter, H.M., et al., 2012. Multiple imputation of missing repeated outcome measurements did not add to linear mixed-effects models. *J. Clin. Epidemiol.* 65 (6):686–695. <http://dx.doi.org/10.1016/j.jclinepi.2011.11.012>.
- Ryan, A.S., Ortmeier, H.K., Sorkin, J.D., 2012. Exercise with calorie restriction improves insulin sensitivity and glycogen synthase activity in obese postmenopausal women with impaired glucose tolerance. *Am. J. Physiol. Endocrinol. Metab.* 302 (1): E145–E152. <http://dx.doi.org/10.1152/ajpendo.00618.2010>.
- Sarwer, D.B., von Sydow Green, A., Vetter, M.L., Wadden, T.A., 2009. Behavior therapy for obesity: where are we now? *Curr. Opin. Endocrinol. Diabetes Obes.* 16 (5):347–352. <http://dx.doi.org/10.1097/MED.0b013e32832f5a79>.
- Sasaki, J.E., John, D., Freedson, P.S., 2011. Validation and comparison of ActiGraph activity monitors. *J. Sci. Med. Sport* 14 (5):411–416. <http://dx.doi.org/10.1016/j.jsams.2011.04.003>.
- Schebendach, J.E., Porter, K.J., Wolper, C., Walsh, B.T., Mayer, L.E., 2012. Accuracy of self-reported energy intake in weight-restored patients with anorexia nervosa compared with obese and normal weight individuals. *Int. J. Eat. Disord.* 45 (4):570–574. <http://dx.doi.org/10.1002/eat.20973>.
- Schuit, A.J., Schouten, E.G., Westerterp, K.R., Saris, W.H., 1997. Validity of the Physical Activity Scale for the Elderly (PASE): according to energy expenditure assessed by the doubly labeled water method. *J. Clin. Epidemiol.* 50 (5), 541–546.
- Shiroma, E.J., Cook, N.R., Manson, J.E., Buring, J.E., Rimm, E.B., Lee, I.M., 2015. Comparison of self-reported and accelerometer-assessed physical activity in older women. *PLoS One* 10 (12):e0145950. <http://dx.doi.org/10.1371/journal.pone.0145950>.
- van Gemert, W.A., Iestra, J.L., Schuit, A.J., et al., 2013. Design of the SHAPE-2 study: the effect of physical activity, in addition to weight loss, on biomarkers of postmenopausal breast cancer risk. *BMC Cancer* 13 (1) (doi:1471-2407-13-395 [pii]).
- van Gemert, W.A., Schuit, A.J., van der Palen, J., et al., 2015. Effect of weight loss, with or without exercise, on body composition and sex hormones in postmenopausal women: the SHAPE-2 trial. *Breast Cancer Res.* 17 (1):120. <http://dx.doi.org/10.1186/s13058-015-0633-9>.
- Wen, C.P., Wai, J.P., Tsai, M.K., et al., 2011. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet* 378 (9798):1244–1253. [http://dx.doi.org/10.1016/S0140-6736\(11\)60749-6](http://dx.doi.org/10.1016/S0140-6736(11)60749-6).
- Wiseman, M., 2008. The second World Cancer Research Fund/American Institute for Cancer Research expert report. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. *Proc. Nutr. Soc.* 67 (3):253–256. <http://dx.doi.org/10.1017/S002966510800712X>.
- Witham, M.D., Avenell, A., 2010. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. *Age Ageing* 39 (2):176–184. <http://dx.doi.org/10.1093/ageing/afp251>.
- Wu, T., Gao, X., Chen, M., van Dam, R.M., 2009. Long-term effectiveness of diet-plus-exercise interventions vs. diet-only interventions for weight loss: a meta-analysis. *Obes. Rev.* 10 (3):313–323. <http://dx.doi.org/10.1111/j.1467-789X.2008.00547.x>.
- Yan, T., Wilber, K.H., Aguirre, R., Trejo, L., 2009. Do sedentary older adults benefit from community-based exercise? Results from the active start program. *Gerontologist* 49 (6):847–855. <http://dx.doi.org/10.1093/geront/gnp113>.