# The long-term effects of a 16 week diet/activity intervention in postmenopausal women on bodyweight and physical activity behavior.

12 months follow-up measurement of the SHAPE-2 study

## Masterthesis

Physiotherapy Science

Program in Clinical Health Sciences

Utrecht University

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"ONDERGETEKENDE


Martijn de Roon,


bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld."

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**SAMENVATTING (words 299)**

*Doelstelling:* Het doel van deze studie is om de langetermijneffecten 12 maanden na een 16 weken durend afvalprogramma bestaande uit een bewegingsprogramma of een dieet op lichaamsgewicht en dagelijkse fysieke activiteit en bij vrouwen na de overgang te bepalen.

*Methode:* 243 postmenopauzale vrouwen waren gerandomiseerd in een beweeggroep (N=98), dieet groep (N=97) of controle groep(N=48). Twaalf maanden na het afronden van het interventieprogramma werden alle vrouwen welke de eerste meting hadden voltooid benaderd voor een vervolgmeting. Uitkomstmaten waren lichaamsgewicht, fysieke activiteit gemeten met een accelerometer(ActiGraph®) en een bewegingsvragenlijst: de Physical Activity Scale for the Elderly(PASE). Daarnaast was kwaliteit van leven gemeten met behulp van de short form-36.

*Resultaten* 12 maanden na beëindiging van het interventieprogramma lieten alle groepen een afname in gewicht zien ten opzichte van baseline. Vrouwen uit de bewegingsgroep en dieetgroep waren ±3kg meer afgevallen dan de controlegroep(-6.24:0.06 en -6.12:0.12 95% betrouwbaarheidsinterval(BHI)). Zowel beweeggroep(39 punten) als dieetgroep(14 punten) scoorden hoger op de PASE wat betekent dat beide groepen significant actiever zijn geworden ten opzichte van baseline wat door de ActiGraph® werd bevestigd. De ActiGraph® liet bij vrouwen uit de beweeggroep bij follow up minder zittend activiteit, -1.5% (-2.73:-0.26 95%BHI), meer middelzware, +0.6% (0.07:1:17 95%BHI) en zware activiteiten, +0.21% (0.05:0.37 95%BHI) zien vergeleken baseline. In de categorieën middelzware en zware activiteiten waren resultaten van de beweeggroep significant hoger dan in de dieet- en controlegroep.

*Conclusie* Deze studie toont bij postmenopauzale vrouwen met overgewicht en een inactieve levensstijl aan dat deelname aan een 16 weken durend afvalprogramma leidt tot minder lichaamsgewicht en een actievere levensstijl 12 maanden na beëindiging van het programma.

*Klinische* relevantie Deze studie toont aan dat voor postmenopauzale vrouwen met een inactieve levensstijl en overgewicht een kortdurende interventie leidt tot een beter leefstijl ook op lange termijn waardoor de gezondheid op lange termijn kan worden verbeterd.

**ABSTRACT (299 words)**

*Aim* The aim of this study is to determine the long-term effects of a sixteen week weight loss program induced by exercise or diet on bodyweight and daily physical activity levels in postmenopausal women after a twelve month follow up period.

*Methods* 243 postmenopausal women with an inactive lifestyle were randomized into an exercise (N=98), diet (n=97), or control group (N=48). During 16 weeks subjects received an exercise or diet intervention to lose 5kg in bodyweight. 12 months after completing the intervention, women were contacted for a follow up measurement. Outcomes were: bodyweight, physical activity measured by the ActiGraph® accelerometer and physical activity scale for the elderly (PASE), and quality of life measured by the short form-36(SF-36).

*Results* All groups lost a significant amount of bodyweight compared to baseline. Both the exercise and diet group lost ±3kg of bodyweight more in addition to the control group, 6.24:0.06 and -6.12:0.19 95% confidence-interval (CI). Both the exercise (39 points) and diet group (14 points) scored higher on the PASE questionnaire, which means both groups were significantly more active compared to baseline which was confirmed by the ActiGraph®. The ActiGraph® showed that the exercise group was performing less sedentary, -1.5% (-2.73:-0.26 95%CI), more moderate, +0.6% (0.07:1:17 95%CI), and vigorous activities, +0.21% (0.05:0.37 95%CI) compared to baseline. In categories moderate and vigorous activities the exercise group scored significantly higher in addition to the diet and control group

*Conclusion* In conclusion, this study shows weight loss and increased levels of physical activity 12 months after completing a sixteen week exercise program in postmenopausal women with obesity and an inactive lifestyle.

*Clinical Relevance* This study shows that taking part in a short term exercise intervention leads to a long-term healthier lifestyle whereby long-term healthiness can be improved in postmenopausal women with obesity and an inactive lifestyle.

Keywords:

[Roon, M de]                [Long term effects of a 16 week weigh loss program]

**INTRODUCTION (257 words, 3135 total)**

Breast Cancer is a major health problem worldwide.(1-4) A family history with breast cancer, late age of menopause, early age at menarche, late age of first childbirth, and nulliparity are associated with a higher risk of developing breast cancer. (5-8) However, there are also few modifiable lifestyle risk factors to breast cancer. (6,9-11)

Reviews of numerous observational studies showed that increased levels of physical activity and obesity are associated with a lower risk of breast cancer.(6,9-11) The meta-analysis by Renehan et al has estimated that per $5kg/m^2$ increase in Body Mass Index (BMI) the risk of breast cancer is increased by 12%. (12) It is suggested that 25% of all breast cancer cases are caused by obesity and an inactive lifestyle.(1,2,7)

To reduce the prevalence of an inactive lifestyle, obesity and subsequently breast cancer risk in postmenopausal women, lifestyle changes are necessary. (9,13) It has been shown that taking part in an exercise intervention or weight loss program is a successful method to lose bodyweight and to become more physically active. (14-16) Positive short term effects of an exercise intervention to change an inactive lifestyle are well known.(17) However, limited research is performed to determine the long term effects after ending an exercise intervention or weight loss program on behavioural change in postmenopausal women as shown in the meta-analysis by Franz et al.(16,18) Therefore, the aim of this study is to determine the long-term effects of a sixteen week weight loss program induced by exercise or diet on daily physical activity levels and bodyweight in postmenopausal women.

**METHODS (1127 words)**

DESIGN:

This study is a continuation of a multicenter randomized controlled trial twelve months after ending the sixteen week intervention program.

INTERVENTION SHAPE-2

*Run-in period*

All participants started the SHAPE-2 study with a 6 week run-in period, in which they received an isocaloric diet, according to the Dutch Guideline for a Healthy Diet.(19,20) After the run-in period subjects were randomized into an exercise group, a diet group, or a control group.(20) The goals of the intervention programmes were to lose an equivalent amount of 5-6kg of body weight in 10-14 weeks' time under supervision of dieticians and physiotherapists.(20)

*Diet group*

The weight loss intervention was delivered by registered dieticians, experienced in treatment of overweight and motivational interviewing.(20) The diet group was prescribed a diet with a deficit of 500kcal/day as compared to the subject's energy requirements estimated at the run-in period.(20) During the intervention period, subjects received four group sessions and two face to face counsels with their designated dietician.(20) The group sessions were based on principles of cognitive behavioural therapy and motivational interviewing.(20-22) Furthermore, group sessions included nutritional education, behavioural change techniques and self-management training.(20) Adherence to the diet program was monitored by telephone contacts every other week.(20)

*Exercise group*

Women in the exercise group received four hours of moderate-to-vigorous exercise per week in group- and individual sessions.(20)

During two one-hour group sessions supervised by a physiotherapist, women received high intensity endurance training combined with strength training.(20) Endurance training was performed in circuits on a treadmill, cycle, or a cross trainer. Intensity of endurance training was determined by the heart rate.(20) Throughout the intervention period intensity of endurance training was gradually increased.(20) Each endurance training took 20-25 minutes and was performed at heart rates ranging from 40-75% of the maximum heart rate.(20) Intensity of strength training was determined by 20- and 15- repetition maximum tests and gradually increased during the intervention period.(20) Furthermore 2-hours of supervised or individual home-based Nordic walking was included.(20)

Additionally, during the exercise intervention period, subjects underwent a face-to-face counsel with their designated dietician that prescribed a caloric restriction of 250 kcal/day.(20) Adherence to the diet in the exercise group was monitored by telephone contacts every other week

*Control group*

Subjects in the control group were requested to maintain their weight by adhering to the baseline diet as described during the run-in period, and maintaining their habitual exercise pattern. Important for the follow-up measurement is that all subjects of the control group were offered an alternative weight loss program after the study. The control group can show other results at follow up then when they were not offered an alternative weight loss program after completing the intervention program. The weight loss program contained 4 dietary group sessions and several exercise classes such as Nordic walking and/or fitness.

RANDOMISATION

During the SHAPE-2 study a computer randomly assigned participants into an exercise intervention (N=98), diet (N=97) or control group (N=48) stratified per multicenter in block sizes of 5 initially in 2:2:1 ratio as described in the SHAPE-2 study protocol.(20)

PARTICIPANTS:

In order to be eligible to participate in this follow-up study, subject had to meet the SHAPE-2 study's eligibility criteria as shown in table 1, completed at least one of the physical activity measurements at baseline, and given informed consent (IC) to be approached for potential follow-up. Subjects were excluded for this follow-up study when they were unable to complete the questionnaires or did not wear the ActiGraph® for seven days.

| Inclusion criteria | Exclusion criteria |
|---|---|
| Female | Presently using sex hormones |
| 50-69 years of age | Use of beta-blockers or oral corticosteroids |
| Postmenopausal(last menses>12 months) | Smoking |
| Body Mass Index(BMI) 25-35m/kg$^2$ | Alcohol or drug abuse |
| Sedentary lifestyle(<2 hours/week of at least moderate intensive activities(>4MET)) | Diagnosed breast cancer(present or history) |
| Willingly to be randomly assigned to one of the three study arms. | Diagnosed with other cancer(present or <5 years of history), except non-melanoma skin cancer |
| Informed consent for all screening and study activities | Diabetes mellitus or other unstable (endocrine) related diseases |
| | Any disorder the might impede participation in the exercise program |
| | Follow, or intention to follow, a structured weight loss program elsewhere |
| | Investigators opinion(successful fulfilling of the program is highly unlikely) |

*Table 1: In- and exclusion criteria as used during the SHAPE-2 study*

## FOLLOW-UP STUDY

Eligible subjects for the follow-up measurement were contacted by telephone 12-13 months after completing the SHAPE-2 intervention program. Subjects were asked by the researcher if they were willing to participate in an additional measurement, consisting of wearing the ActiGraph® for seven consecutive days in their daily habit, completing two questionnaires, and to report their bodyweight. If subjects could not be contacted by telephone, questionnaires were sent by mail including a letter of consent and a return envelope.

## OUTCOMES

The primary study parameters are bodyweight and physical activity levels (behaviour) per study group 12 months after completion of the SHAPE-2 study.

During the SHAPE-2 study body weight was measured by a calibrated analogue balance and digital balance scales (SECA®).(20) In the follow-up measurement bodyweight was self-measured and self-reported by the subjects.

In order to compare the physical activity levels during the SHAPE-2 study after a 12 month follow-up, we used the same questionnaire, the Physical Activity Scale for the Elderly (PASE), and accelerometer, the ActiGraph®, as used in the SHAPE-2 study. The PASE is a brief self-administered 7-day recall questionnaire to measure changes in physical activity over time.(23) The PASE has shown to have an excellent test-retest reliability (ICC 0.89) and a reasonable validity ($r_s$ 0.68).(23,24) The ActiGraph® is a waist-worn accelerometer which measures movements by a 3-axis(x, y, and z) acceleration sensor.(25) The ActiGraph® has shown to be a valid method to measure physical activity intensity.(25) Subjects were instructed to wear the ActiGraph® for 7 days.

Secondary parameter was quality of life measured by the Short Form-36(SF-36) at 12 months of follow up. The SF-36 is known to be a valid and reliable method to measure quality of life with a Cronbach's Alpha of 0.76.(26) In this study quality of life is separated in a mental and physical component summary score which represents the subjects' mental and physical health status.(27,28) Both the mental and physical component summary score are compiled by questions of the SF-36 that contain a mental or physical component.(27,28)

## STATISTICAL ANALYSIS FOLLOW-UP STUDY

Baseline descriptive statistics were presented for main demographic variables for each intervention group. Data analysis was performed according to intention-to-treat principle. Normality of the data 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. Within group differences between baseline and follow-up and between end of study and follow-up for all outcomes were analyzed by the linear mixed method. Missing data in the within group analysis was imputed by the linear mixed method, estimated on complete cases per

intervention group. The linear mixed effect method has shown to be a reliably method to impute missing longitudinal self-reported data.(29) Between group differences, between baseline and follow up, for all outcomes were also analyzed by a linear mixed method. Missing data in the between group analysis was imputed by the linear mixed method, estimated on complete cases of all subjects.

Analysis from the ActiGraph® is separated into five categories: sedentary, light, lifestyle, moderate, and vigorous activities.(30) ActiGraph® is estimated in time spent per category as a percentage of the total wear time of an average day. All statistical analyses were performed with SPSS 22.0, with a two-sided significance level of α = 0.05.

## RESULTS (975 words)

Of all 243 women included in the SHAPE-2 study were contacted 7(2.9%) refused participation and 43 women could not be contacted by telephone, mail, or were lost to follow up, figure 1. In total, 193 subjects were available for the follow-up: 77 exercise group, diet group 78, and control group 38. We received filled out questionnaires of 193 (79%) subjects and ActiGraphs® of 163 subjects (67%). At baseline, all groups were comparable for demographic characteristics as shown in table 2. Groups did not differ in baseline characteristics. Baseline characteristics of non-responders were not significantly different from all subjects who completed the follow-up measurement (data now shown).

Table 3 presents the estimated model means per group of women for who information of at least one time point was available. Result of the within group analysis of the linear mixed method are shown in table 3. Table 4 shows group estimated model means, based on
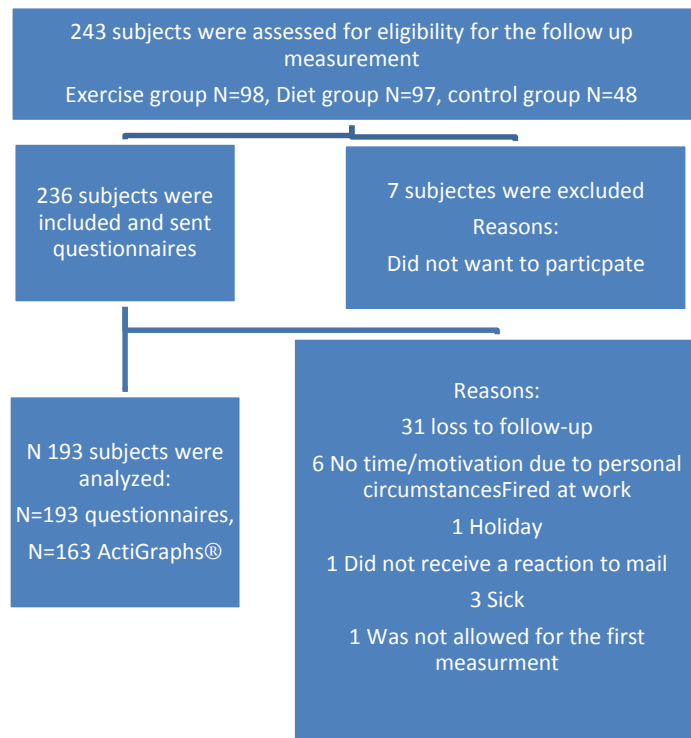


Figure 1: Flow chart of baseline measurement, randomization, intervention program, follow up measurement and drop-outs during follow up

Table 2:: Baseline demographic characteristics of the SHAPE-2 study

|  | Exercise group (N=98) Mean(sd) | Diet group (N=97) mean(sd) | Control group (N=48) mean(sd) |
|---|---|---|---|
| Age, years | 59(4.9) | 61(4.6) | 60(4.9) |
| Weight, kg | 80(9.0) | 80(8.6) | 81(10.0) |
| Length, cm | 166(5.2) | 165(6.0) | 165(6.0) |
| BMI, kg/cm$^2$ | 29.0(2.9) | 29.5(2.6) | 29.5(2.6) |
| Body fat % | 43.8(4.0) | 44.1(3.8) | 43.6(5.0) |
| Total fat, kg | 33.9(6.2) | 33.9(5.7) | 34.2(7.4) |
| Lean mass | 43.1(4.1) | 42.7(4.0) | 43.4(3.9) |
| Waist circumference, cm | 97.5(8.3) | 97.8(7.5) | 99.0(8.7) |
| Hip circumference, cm | 109.16(6.7) | 109.82(6.8) | 109.73(7.7) |
| VO$_2$ peak, ml/min | 1749(293) | 1742(310) | 1751(363) |
| VO$_2$ relative, ml/kg/min | 21.84(3.7) | 21.92(4.0) | 22.06(4.7) |
| Years since menopause | 10.9(7.7) | 10.7(6.1) | 11.4(7.8) |

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

[Roon, M de]          [Long term effects of a 16 week weigh loss program]

all groups, for each measurement. Also linear mixed between group effects during the entire study are shown.

**Bodyweight**

Figure 2 and table 3 show that both the exercise, 4.3kg, and diet group, 3.4kg, decreased in bodyweight during the intervention period but also slightly regained bodyweight during the follow-up period (1.3kg and 1.5kg respectively). Compared to baseline both groups lost a significant amount (P<0.001, -4.9:-3.7 95% confidence interval (CI) in the exercise group and P<0.001, -4.1:-2.7 95% CI in the diet group) of bodyweight compared to



*Figure 2: Weight change over time separated per group*

baseline as shown in table 3. Also, the control group lost a significant, P<0.001 (-2.8:-1.1 95% CI), amount of 2.0kg bodyweight during the follow-up period (table 3). However, the difference in body weight reduction at end of follow-up is still in favor of the exercise and diet group when comparing to the control group. As shown in table 4, both the exercise and the diet group lost 3.1kg (P=0.054, -6.24:0.06 95% CI) and 3.0kg (P=0.065, -6.12:0.19 95% CI) bodyweight compared to the control group at follow up since baseline. No significant differences were found between the exercise and the diet group (table 4) at 12 months follow up.



**PASE**

All groups became more physically active during the follow-up period as shown in figure 3 and table 3, compared to baseline and end of study. Within group differences showed an increased PASE score of 39 points (22.9:54.8 95% CI) compared to baseline
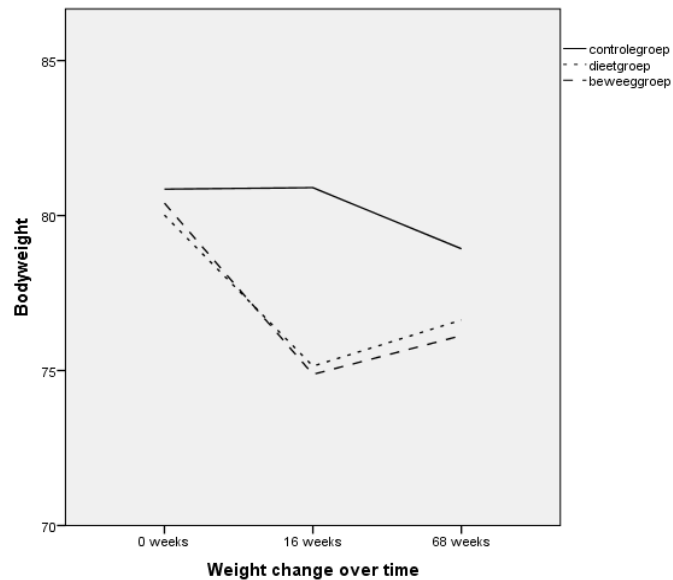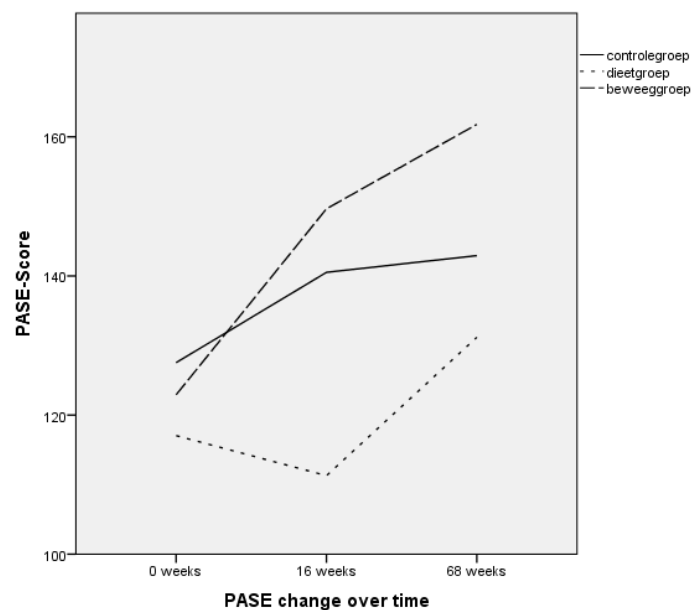
*Figure 2: PASE Score change over time separated per group*

(table 3). The diet group increased by 20 points compared to the end (5.74:34.00 95% CI) of study and 14 points (0.65:27.59 95% CI) compared to baseline (table 3). Between group analysis showed that the exercise group showed an increased PASE score when compared to the control group (difference of 8 points) and the diet group (difference of 25 points) (table 4). The diet group showed a significant (P=0.043, -33.72:-0.58 95% CI) 17 points decline at follow up compared to the control group compared to baseline (table 4).

**SF-36**

Quality of life scores of the SF-36 were subdivided into a physical and mental component summary score. The only significant difference, P=0.041(-4.28:-0.09 95% CI), was a decreased mental component score of 2.18 points at follow up for the exercise intervention compared to end of the study as shown in table 3. Beside the 0.12 increased score for the diet group in the mental component compared to baseline, all other domains showed a small deteriorating, however not significantly (table 3). No significant between group differences were found for both the physical and mental component of the quality of life as shown in table 4.

**ActiGraph®**

163 subjects wore an ActiGraph® during the follow up measurement of which 150 could be analyzed. 11 ActiGraphs® could not be analyzed because they did not record data correctly.

The exercise group spent 1.5% less time being sedentary during the day at follow up when compared to baseline(-2.73:-0.26 95% CI) (table 3). Also the exercise group showed more time spent in moderate, +0.6% (0.07:1:17 95%CI), and more vigorous activities, +0.21% (0.05:0.37 95%CI) per day when compared to baseline (table 3). However compared when compared to the end of study the exercise group showed less time spent in vigorous activities, -0.38% (-0.54:-0.23) per day as shown in table 3.

The diet group spent 1.2% (-2.26:-0.05) less time being sedentary during the day at follow up, when compared to the end of the study (table 3). Although, compared to baseline the difference was +0.3% (-0.84:1.42 95% CI) as shown in table 3. In the categories light, lifestyle, moderate, and vigorous activities no significant within group differences were shown within the diet group (table 3).

Like the diet group also the control group spent less time being sedentary during the day at follow up when compared to end of study, -1.9% (-3.75:-0.06) as shown in table 3. However, when compared to baseline no significant difference in time spent being sedentary during the day was shown, -1.5% (-3.31:0.32) (table 3). Furthermore the control group showed more time spent in light activities during the day when compared to end of study, +1% (0.09:1.98 95% CI), but when compared to baseline results did not significantly differ, +0.7% (-0.22:1.64 95% CI) (table 3). No significant differences where shown in the categories: lifestyle activities, moderate activities, and vigorous activities.

Only the exercise group showed significant between group differences when compared to the diet or control group as shown in table 4. The exercise group was spending less time being sedentary per day at follow up when compared to the diet group, -1.8% (-3.38:-0.26 95% CI), in comparison to baseline (table 4). Also the exercise group was spending more time per day at follow in light (+0.8%, -0.00:1.54 95% CI) and vigorous activities (+0.28%, 0.16:0.41 95% CI) when compared to the diet group in comparison to baseline (table 4). When compared to the control group, from baseline to follow, the exercise group spent more time in moderate (+0.8%, 0.12:1.45 95% CI) and vigorous activities (+0.23%, 0.07:0.39 95% CI) per day (table 4).

*Table 3: Within group differences of bodyweight, physical activity level and quality of life for all study groups. Baseline compared to follow-up (0-68 week) and end of study compared to follow up (16-68 weeks).*

| | Baseline 0 weeks‡ | End of study 16 weeks‡ | 12 month follow-up 68 weeks‡ | Within group difference (95% CI) 0-68 weeks* | P | Within group difference (95% CI) 16-68 weeks* | P |
|---|---|---|---|---|---|---|---|
| **N** | | | | | | | |
| Exercise | 98 | 93 | 77 | | | | |
| Diet | 97 | 94 | 78 | | | | |
| Control | 48 | 45 | 38 | | | | |
| | | | | | | | |
| **Bodyweight, kg** | | | | | | | |
| Exercise | 80.4 | 74.9 | 76.1 | -4.3(-4.88:-3.67) | <0.001 | 1.3(0.64:1.85) | <0.001 |
| Diet | 80.0 | 75.1 | 76.6 | -3.4 (-4.12:-2.65) | <0.001 | 1.5(0.75:2.22) | <0.001 |
| Control | 80.9 | 80.9 | 78.9 | -1.9(-2.73:-1.09) | <0.001 | -2.0(-2.79:-1.14) | <0.001 |
| | | | | | | | |
| **PASE score, points** | | | | | | | |
| Exercise | 123 | 150 | 162 | 39(22.93:54.75) | <0.001 | 12(-3.99:28.09) | 0.140 |
| Diet | 117 | 111 | 131 | 14(0.65:27.59) | 0.040 | 20(5.74:34.00) | 0.006 |
| Control | 128 | 141 | 143 | 15 (-0.57:31.55) | 0.058 | 3(-13.95:18.98) | 0.762 |
| | | | | | | | |
| **ActiGraph® Sedentary time %** | | | | | | | |
| Exercise | 72.7 | 71.7 | 71.2 | -1.5(-2.73:-0.26) | 0.018 | -0.5(-1.69:0.72) | 0.430 |
| Diet | 73.1 | 74.6 | 73.4 | 0.3(-0.84:1.42) | 0.614 | -1.2(-2.26:-0.05) | 0.041 |
| Control | 73.8 | 74.2 | 72.3 | -1.5(-3.31:0.32) | 0.104 | -1.9(-3.75:-0.06) | 0.043 |
| | | | | | | | |
| **ActiGraph® light activities %** | | | | | | | |
| Exercise | 15.1 | 15.1 | 15.5 | 0.4(-0.24:1.11) | 0.204 | 0.4(-0.26:1.06) | 0.234 |
| Diet | 14.7 | 14.2 | 14.6 | <-0.1(-0.63:0.57) | 0.919 | 0.4(-0.15:1.02) | 0.143 |
| Control | 15.0 | 14.7 | 15.7 | 0.7(-0.22:1.64) | 0.133 | 1.0(0.09:1.98) | 0.033 |
| | | | | | | | |
| **ActiGraph® lifestyle activities %** | | | | | | | |
| Exercise | 7.8 | 7.6 | 8.1 | 0.3(-0.16:0.79) | 0.188 | 0.5(0.01:0.93) | 0.048 |
| Diet | 7.7 | 7.1 | 7.4 | -0.4(-0.83:0.11) | 0.132 | 1.4(-0.16:0.76) | 0.194 |
| Control | 7.2 | 7.1 | 7.8 | 0.6(-0.11:1.31) | 0.095 | 0.7(-0.06:1.37) | 0.074 |
| | | | | | | | |
| **ActiGraph® moderate activities%** | | | | | | | |
| Exercise | 4.3 | 5.0 | 4.9 | 0.6(0.07:1.17) | 0.027 | -0.1(-0.37:0.41) | 0.641 |
| Diet | 4.4 | 4.1 | 4.4 | 0.1(-0.47:0.57) | 0.845 | 0.3(-0.19:0.83) | 0.217 |
| Control | 4.0 | 3.9 | 4.1 | 0.2(-0.43:0.78) | 0.568 | 0.3(-0.34:0.89) | 0.377 |
| | | | | | | | |
| **ActiGraph® vigorous activities %†** | | | | | | | |
| Exercise | -1.48 | -0.89 | -1.27 | 0.21(0.05:0.37) | 0.013 | -0.38(-0.54:-0.23) | <0.001 |
| Diet | -1.47 | -1.53 | -1.48 | <-0.01(-0.14:0.13) | 0.961 | 0.06(-0.08:0.19) | 0.073 |
| Control | -1.47 | -1.39 | -1.47 | <0.00(-0.17:0.17) | 0.998 | -0.07(-0.24:0.09) | 0.377 |
| | | | | | | | |
| **SF-36 Physical** | | | | | | | |
| Exercise | 53 | 54 | 53 | -0.1(-1.71:1.44) | 0.865 | -1.5(-3.15:0.69) | 0.060 |
| Diet | 53 | 53 | 52 | -0.7(-2.32:0.90) | 0.387 | -1.5(-3.07"0.18) | 0.081 |
| Control | 53 | 54 | 52 | -0.6(-2.93:1.84) | 0.650 | -1.9(-4.32:0.51) | 0.120 |
| | | | | | | | |
| **SF-36 mental** | | | | | | | |
| Exercise | 52 | 53 | 51 | -1.5(-3.60:0.54) | 0.147 | -2.2(-4.28:-0.09) | 0.041 |
| Diet | 52 | 52 | 52 | 0.1(-2.05:2.30) | 0.912 | -0.1(-2.31:2.08) | 0.919 |
| Control | 54 | 53 | 52 | -2.0(-4.38:0.42) | 0.104 | -1.4(-3.80:1.05) | 0.263 |

*Abbreviations: N, number of women; CI, confidence interval; PASE, Physical Activity Scale for the Elderly; SQUASH, Short Questionnaire to Assess Heath; SF-36 Short Form-36.*

*‡ Estimated means per group with linear mixed model taking into account all women with at least one measurement*

*\* Represents the overall within group effect over time for each questionnaire obtained with  linear mixed models, per intervention group*

*% Percentage per day based on a 10 hour day.*

*† A logarithmic transformation was applied to obtain normally distributed data*

Table 4: Between group differences in bodyweight, physical activity level and quality of life for baseline and end of study (16 weeks) results compared to follow-up (68 weeks) results

| | Baseline 0 weeks‡ | End of study 16 weeks‡ | 12 month follow-up 68 weeks‡ | Mean difference (95% CI) Intervention vs Control, 0-68 weeks* | P | Mean difference (95% CI) Exercise vs Diet, 0-68 weeks* | P |
|---|---|---|---|---|---|---|---|
| **Bodyweight, kg** | | | | | | | |
| Exercise | 80.4 | 74.9 | 76.1 | -3.09 (-6.24:0.06) | 0.054 | -0.13 (-2.67:2.43) | 0.922 |
| Diet | 80.0 | 75.1 | 76.6 | -2.97 (-6.12:0.19) | 0.065 | | |
| Control | 80.9 | 80.9 | 78.9 | | | | |
| **PASE score, points** | | | | | | | |
| Exercise | 123 | 150 | 162 | 7.8(-8.71:24.31) | 0.353 | 25.0(11.52:38.38) | <0.001 |
| Diet | 117 | 111 | 131 | -17.2(-33.72:-0.58) | 0.043 | | |
| Control | 128 | 141 | 143 | | | | |
| **ActiGraph® Sedentary time %** | | | | | | | |
| Exercise | 72.7 | 71.7 | 71.2 | -1.5(-3.44:0.46) | 0.134 | -1.8(-3.38:-0.26) | 0.023 |
| Diet | 73.1 | 74.6 | 73.4 | -0.3(-1.61:2.28) | 0.736 | | |
| Control | 73.7 | 74.2 | 72.3 | | | | |
| **ActiGraph® light activities %** | | | | | | | |
| Exercise | 15.1 | 15.1 | 15.6 | 0.1(-0.85:1.08) | 0.814 | 0.8(-0.00:1.54) | 0.050 |
| Diet | 14.7 | 14.2 | 14.6 | -0.7(-1.62:0.31) | 0.181 | | |
| Control | 15.0 | 14.7 | 15.6 | | | | |
| **ActiGraph® lifestyle activities %** | | | | | | | |
| Exercise | 7.8 | 7.6 | 7.8 | 0.5(-0.30:1.23) | 0.232 | -0.5(-0.16:1.07) | 0.147 |
| Diet | 7.7 | 7.1 | 7.4 | <0.1(-0.75:0.78) | 0.974 | | |
| Control | 7.2 | 7.1 | 8.1 | | | | |
| **ActiGraph® moderate activities%** | | | | | | | |
| Exercise | 4.3 | 5.1 | 4.9 | 0.8(0.12:1.45) | 0.021 | 0.4(-0.09:0.97) | 0.105 |
| Diet | 4.4 | 4.1 | 4.4 | 0.3(-0.32:1.01) | 0.309 | | |
| Control | 4.0 | 3.8 | 4.1 | | | | |
| **ActiGraph® vigorous activities %†** | | | | | | | |
| Exercise | -1.48 | -0.89 | -1.27 | 0.23(0.07:0.39) | 0.004 | 0.28(0.16:0.41) | <0.001 |
| Diet | -1.47 | -1.53 | -1.47 | -0.05(-0.21:0.11) | 0.539 | | |
| Control | -1.46 | -1.38 | -1.49 | | | | |
| **SF-36 Physical** | | | | | | | |
| Exercise | 53 | 54 | 53 | 0.45(-1.58:2.48) | 0.817 | 0.69(-0.94:2.31) | 0.407 |
| Diet | 53 | 53 | 52 | -0.24(-2.26:1.79) | 0.665 | | |
| Control | 53 | 54 | 52 | | | | |
| **SF-36 mental** | | | | | | | |
| Exercise | 52 | 53 | 51 | -1.04(-3.34:1.26) | 0.373 | 0.17(-1.67:2.01) | 0.856 |
| Diet | 52 | 52 | 52 | -1.21(-3.50:1.08) | 0.299 | | |
| Control | 54 | 53 | 52 | | | | |

*Abbreviations: N, number of women; CI, confidence interval; PASE, Physical Activity Scale for the Elderly; SQUASH, Short Questionnaire to Assess Heath; SF-36 Short Form-36.*

*\* 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*

*‡ Estimated means for all participants with linear mixed model taking into account all women with at least one measurement*

*⁺ Intercept between time/intervention is significant at the 0,05 level*

*† A logarithmic transformation was applied to obtain normally distributed data*

*% Percentage per day based on a 10 hour day.*

**DISCUSSION (769 words)**

Participation in the SHAPE-2 study resulted in a significant amount of weight loss 12 months after study completion compared to baseline in all groups. Both the exercise and the diet group lost 3 kilograms bodyweight more compared to the control group during 12 month follow up, which was borderline significant. Notably, also the control group lost a significant amount of 2 kilograms bodyweight during the follow-up period.

In addition, participation in the SHAPE-2 study resulted in a significantly higher physical activity level after a 12 month follow up period compared to baseline in women in the exercise and diet group. The control group showed a borderline significant increased physical activity level. Although, the exercise group showed a higher mean difference for the PASE score, from baseline to follow up, compared to control, results were not significantly different. The observed changes in physical activity level as shown in the PASE questionnaire are significantly supported by the ActiGraph®. The ActiGraph® showed that the exercise group was becoming less sedentary and more physically active at follow up when compared to baseline. Furthermore, no effects were seen on mental and physical quality of life, except for the exercise group where mental quality of life showed a minor decrease.

A notable result is that the control group lost a significant amount of bodyweight after completion of the SHAPE-2 study until follow up. The achieved weight loss might be explained by the offered weight loss program that start after the end of the study. Beside the offered weight loss program all participants were highly motivated to lose weight at baseline. The offered exercise component can also explain why the control group showed an increased physical activity level compared to baseline. Furthermore, despite our advice to the control group to maintain their natural behavior during the 16 week study period, the control group showed slightly higher levels of physical activity.

The achieved weight loss at follow up in all study groups of this study is comparable with the results of the meta-analysis in weight loss programs by Franz et al.(16) Franz et al showed in their meta-analysis that weight loss, induced by exercise and diet, can be maintained after a twelve month follow up period. (16) However, limited research is available on the effect of a weight loss intervention by exercise or diet in postmenopausal women with an inactive lifestyle.(14-16,18) Our study shows that, for this study population, a short-term exercise intervention is a successful method to lose bodyweight and increase the level of physical activity with a long-lasting effect. This was also found by Hertogh et al. (31) Hertogh et al showed a substantial difference in physical activity after a twelve month follow up period, between the exercise and the control group, after an exercise intervention trial in healthy sedentary postmenopausal women.(31)

Additionally to the similar results concerning the effects in weight loss and physical activity levels, this study also connects to the recommendations from earlier reviews in order to reduce breast cancer risks in postmenopausal women. (9,10) Numerous reviews recommended that losing a significant amount of body weight and becoming more physically active reduces the prevalence of an inactive lifestyle, obesity and subsequently breast cancer.(9,13)

The most important limitation in this study when assessing long term effect of lifestyle intervention programs, is that the control group was offered a weight loss program after the 16 study period. The offered weight loss program means the control strictly was not a control group anymore at follow up. A limitation for the follow up measurement is that weight was self-measured which could have led to observer bias or misclassification.

During our study we noted that measuring levels of physical activity by self-reported questionnaires had some limitations. In this study, self-reported questionnaires resulted several times into missing answers or incomplete questionnaires. We also noted that several subjects filled out the PASE questionnaire incorrectly by subdividing physical activities in the wrong intensity categories. Another limitation of this study is that not all subjects wore ActiGraph® because they did not want or were able to wear it. Furthermore, a limitation of the ActiGraph® itself, is that it cannot properly measure cycling or strength training. In the Netherlands where cycling is very common the ActiGraph® might, therefore, have shown an underestimated physical activity level.

An important strength of the SHAPE-2 study that physical activity was objectively observed by the ActiGraph®. Furthermore, there was good adherence during the intervention period, which makes studying root of long-term effects useful. Two other important strengths of this study are the relatively large study population and the high response rate (79%) for the follow up measurement.


**CONCLUSION (70 words)**

In conclusion, this study shows sustained weight loss and increased levels of physical activity 12 months after completing a 16 week weight loss program by diet or exercise in overweight and obese postmenopausal women with an inactive lifestyle. This study shows that taking part in a short-term exercise intervention leads to a long-term healthier lifestyle whereby long-term healthiness can be improved in postmenopausal women with obesity and an inactive lifestyle.

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**APPENDIX I**

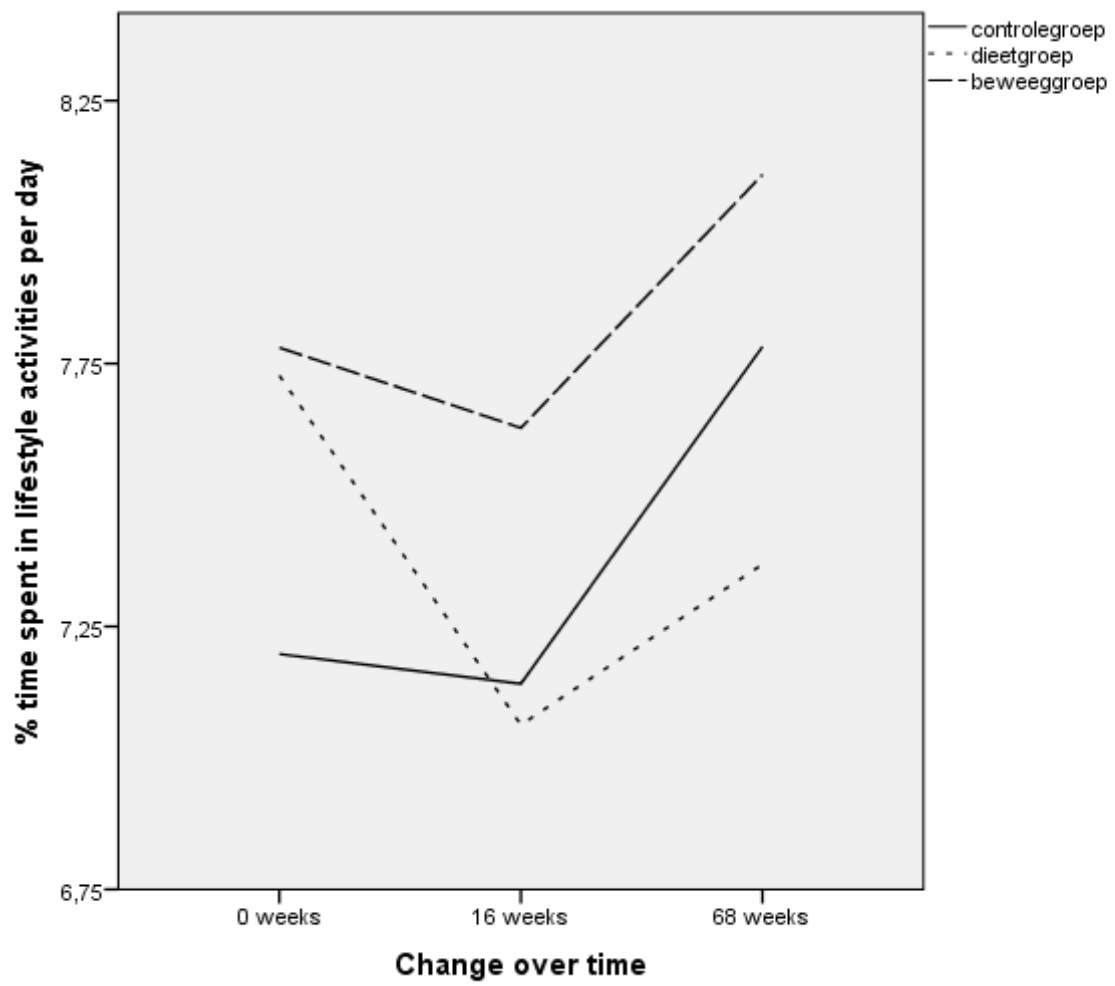*Weight change graph and histograms*
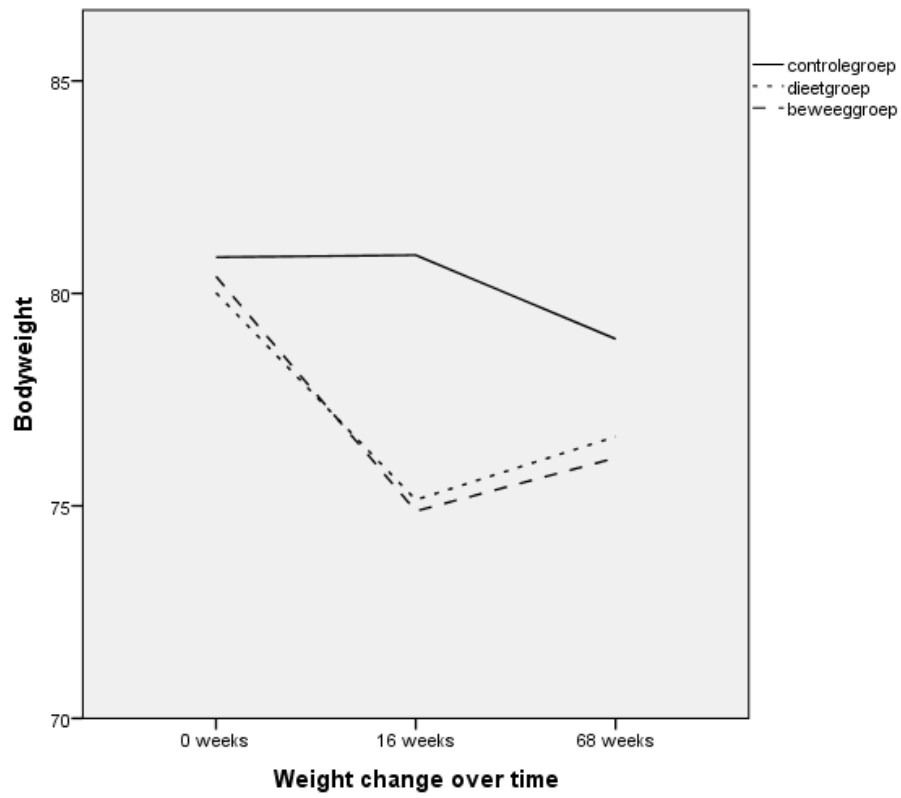


*Figure 3: Weight change over time separated per group*

[Roon, M de]     [Long term effects of a 16 week weigh loss program]

Mean = 80,33
Std. Dev. = 9,031
N = 243
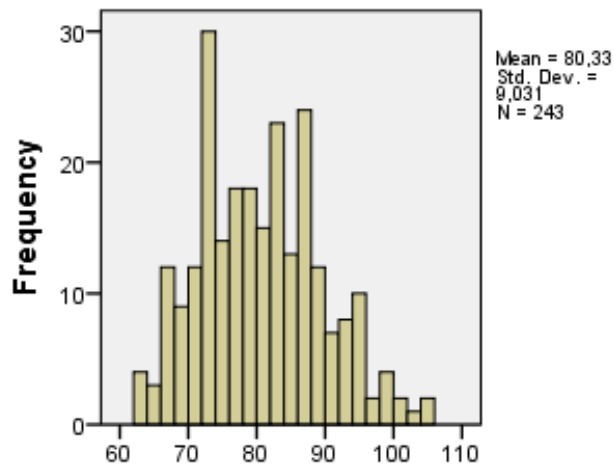
Bodyweight in kilograms at 0 weeks



Mean = 76,17
Std. Dev. = 9,342
N = 232
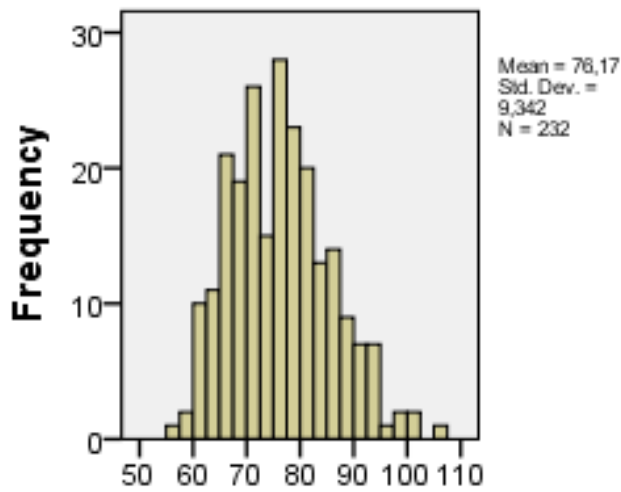
Bodyweight in kilograms at 16 weeks



Mean = 76,59
Std. Dev. = 9,718
N = 187
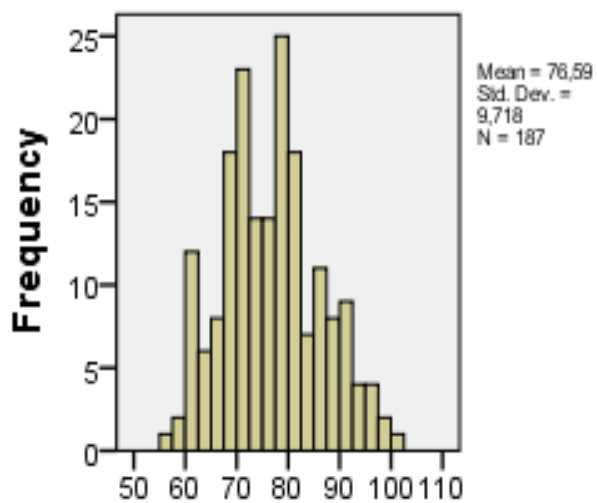
Bodyweight in kilograms at 68 weeks

[Roon, M de]                    [Long term effects of a 16 week weigh loss program]
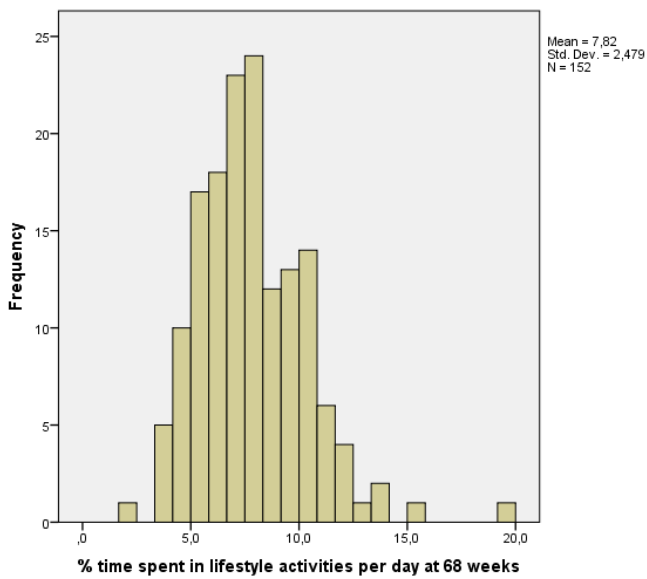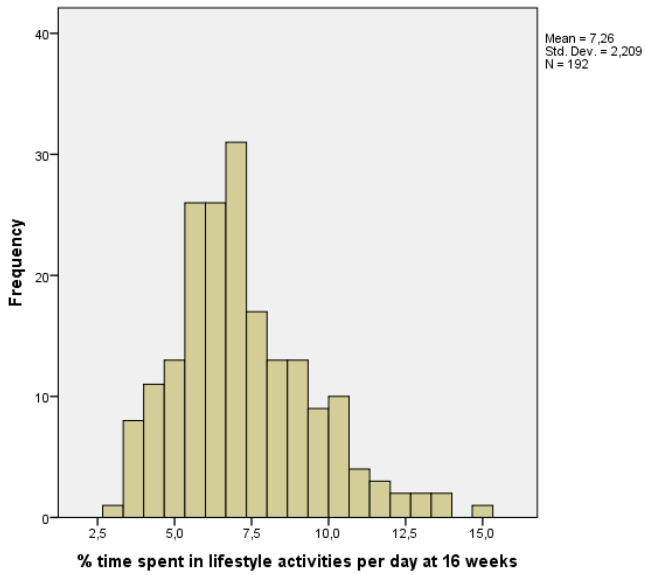
## APPENDIX II

*PASE change graph and histogram*
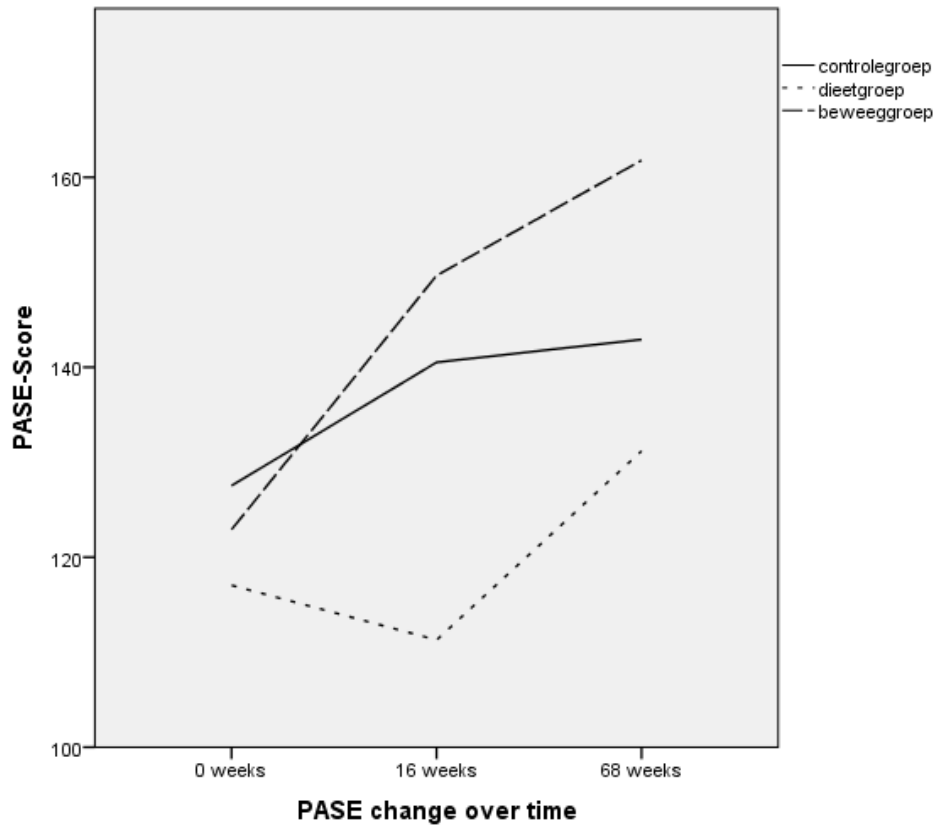


*Figure 4: PASE Score change over time separated per group*

[Roon, M de]                    [Long term effects of a 16 week weigh loss program]

PASE score at 0 weeks

Mean = 121,68
Std. Dev. = 53,582
N = 236



PASE score at 16 weeks

Mean = 133,42
Std. Dev. = 59,967
N = 209



PASE score at 68 weeks

Mean = 146,24
Std. Dev. = 68,627
N = 192

[Roon, M de]          [Long term effects of a 16 week weigh loss program]
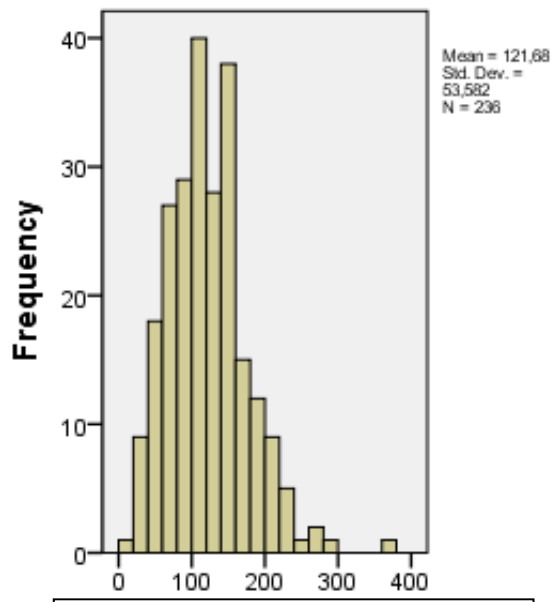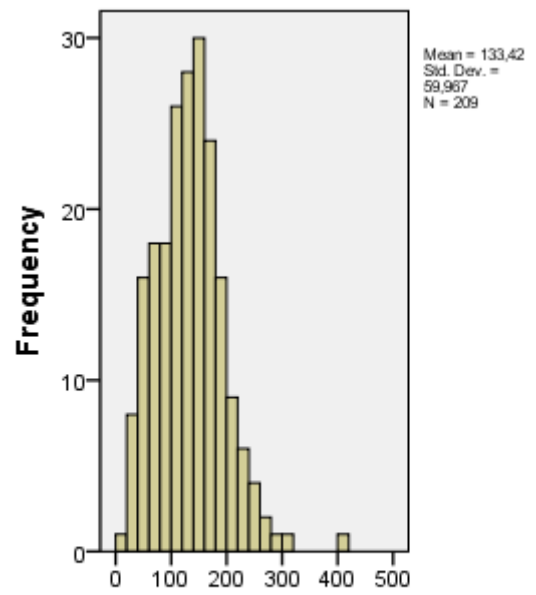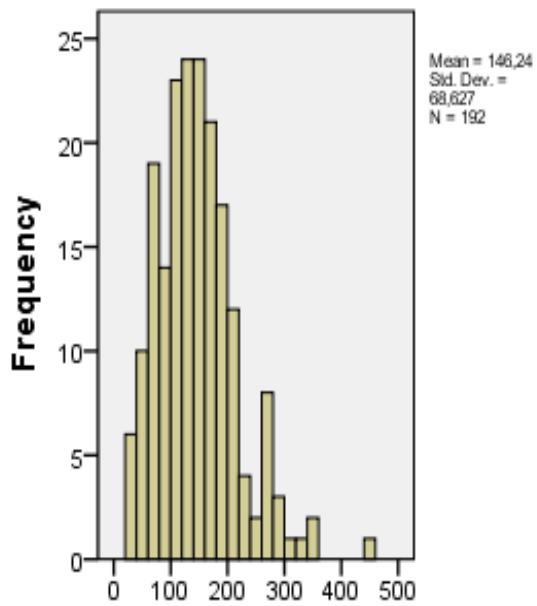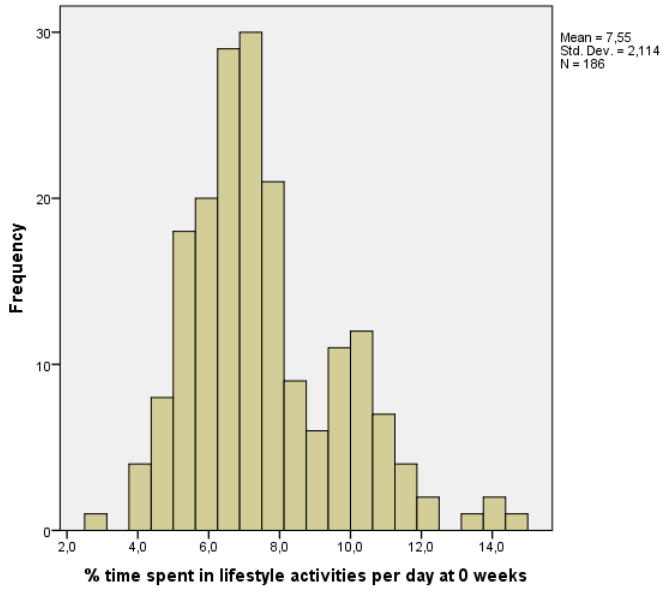
## APPENDIX III

*ActiGraph® change graph and histograms*

[Roon, M de]                    [Long term effects of a 16 week weigh loss program]

Mean = 73,30
Std. Dev. = 5,555
N = 186

% time spent sedentary per day at 0 weeks



Mean = 73,40
Std. Dev. = 5,835
N = 192

% time spent sedentary per day at 16 weeks



Mean = 72,17
Std. Dev. = 6,151
N = 152

% time spent sedentary per day at 68 weeks

[Roon, M de]                    [Long term effects of a 16 week weigh loss program]

Mean = 14,88
Std. Dev. = 2,837
N = 186

% time spent in light activities per day at 0 weeks



Mean = 14,68
Std. Dev. = 2,851
N = 192

% time spent in light activities per day at 16 weeks



Mean = 15,35
Std. Dev. = 3,171
N = 152

% time spent in light physical activities per day at 68 weeks

[Roon, M de]          [Long term effects of a 16 week weigh loss program]

Mean = 7,55
Std. Dev. = 2,114
N = 186

% time spent in lifestyle activities per day at 0 weeks



Mean = 7,26
Std. Dev. = 2,209
N = 192

% time spent in lifestyle activities per day at 16 weeks



Mean = 7,82
Std. Dev. = 2,479
N = 152

% time spent in lifestyle activities per day at 68 weeks

[Roon, M de]          [Long term effects of a 16 week weigh loss program]

Mean = 4,20
Std. Dev. = 2,084
N = 186

% time spent in moderate activities per day at 0 weeks



Mean = 4,43
Std. Dev. = 2,072
N = 192

% time spent in moderate activities per day at 16 weeks



Mean = 4,54
Std. Dev. = 2,233
N = 152

% time spent in moderate activities per day at 68 weeks

[Roon, M de]          [Long term effects of a 16 week weigh loss program]

Mean = -1,47
Std. Dev. = ,439
N = 185

Logaritmic transformation of % time spent per day in vigorous activities per day at 0 weeks



Mean = -1,23
Std. Dev. = ,634
N = 192

Logaritmic transformation of % time spent per day in vigorous activities per day at 16 weeks



Mean = -1,43
Std. Dev. = ,567
N = 149

Logaritmic transformation of % time spent per day in vigorous activities per day at 68 weeks

[Roon, M de]                    [Long term effects of a 16 week weight loss program]
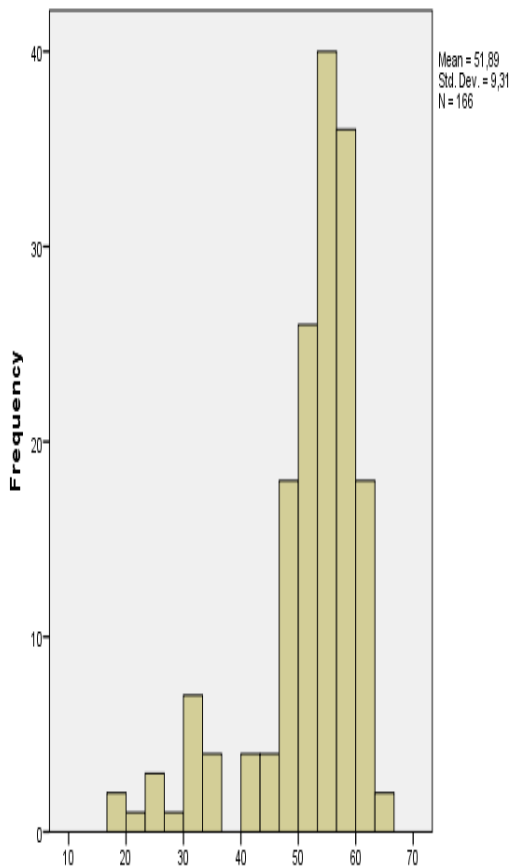
**APPENDIX IV**

*SF-36 change graph and histograms*

[Roon, M de]                    [Long term effects of a 16 week weigh loss program]

Mental component score at 0 weeks

Mean = 52,48
Std. Dev. = 7,805
N = 229



Mental component score at 16 weeks

Mean = 52,83
Std. Dev. = 7,286
N = 216



Mental component score at 68 weeks

Mean = 51,89
Std. Dev. = 9,31
N = 166

[Roon, M de]            [Long term effects of a 16 week weigh loss program]

SF-36 Phycical component score change over time

Mean = 52,85
Std. Dev. = 6,445
N = 229

Physical component score at 0 weeks



Mean = 54,02
Std. Dev. = 6,338
N = 216

Physical component score at 16 weeks



Mean = 62,30
Std. Dev. = 7,819
N = 166

Physical component score at 68 weeks