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CHAPTER 8

Weight change in patients with coronary artery disease: observations from the RESPONSE 2 trial

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Manuscript in preparation

ABSTRACT

Background

Effective weight loss programmes as part of secondary prevention programmes are limited. The aim of this secondary analysis was to study the effects of the weight loss component as part of a comprehensive intervention in patients with coronary artery disease (CAD) and to identify predictors of weight loss.

Methods

The RESPONSE 2 trial was a multicentre (n=15) randomised controlled trial of nurse-coordinated referral of patients (with a BMI>27 kg/m^2) and their partners to community-based lifestyle programmes in the Netherlands, compared to usual care alone. The intervention consisted of lifestyle programmes to achieve weight loss (Weight Watchers™), increasing physical activity (Philips DirectLife™), and smoking cessation (Luchtsignaal™). The outcome of this secondary analysis was weight loss and predictors of successful weight loss (≥ 5% of baseline weight) at 12 months follow-up.

Results

In total, 536 patients had BMI>27 kg/m^2 and were motivated to achieve weight loss (intervention n=280, control n=256). Patients in the intervention group lost 2.4 kg (±7.1) compared to 0.2 kg (±4.6) patients in the control group lost (p<0.001). Predictors of successful weight loss were higher age, (OR 1.05; 95% C.I. 1.02-1.09 per 1 year) and participation in the weight loss programme (OR 3.75 95% C.I. 1.86-7.59). Weight gain occurred in 36% of participants in the intervention (mean 4.4 kg (±3.3)) compared to 41% in the control group, (mean 4.0 kg (±2.5)) (p=0.33).

Conclusion

Among CAD patients with BMI>27 kg/m^2 who were motivated to work on weight loss, this weight loss programme, as part of a comprehensive lifestyle programme, was effective in achieving weight loss. Weight gain was highly prevalent, and prevention of weight gain may be as important as attempts at weight loss.

INTRODUCTION

Overweight is a global health problem in patients with established cardiovascular disease (CVD). Overweight is highly prevalent (70-80%)1 and weight loss of 5-10% is associated with a clinically significant loss of CVD.2 3 Other weight loss interventions have been able to achieve effective weight loss (5-10%), but few interventions are community-based and widely available in many countries.4

In the setting of primary prevention, referral to a commercial weight loss programme (WW, formerly Weight Watchers) in primary care has been shown to be effective in achieving weight loss. An advantage of such a commercial intervention is that it is widely available in many countries, at low cost.5 We recently investigated this weight loss programme in the RESPONSE-2 trial.6 We found that in patients with coronary artery disease (CAD) a combination of nurse-coordinated care and referral to a comprehensive set of up to three widely available community-based lifestyle programmes, on top of usual care, is more effective in improving at least one lifestyle-related risk factor (LRF) compared to usual care alone. The programmes included weight loss (WW) promoting physical activity (Philips DirectLife™) and smoking cessation (Luchtsignaal™), and referral was dependent on the patients' risk profile and preferences. The observed difference in the primary outcome (a statistically significant improvement in at least one LRF without deterioration in any of the other two) was mainly driven by weight loss. Therefore, the aim of this secondary analysis was to evaluate the effect of the weight loss component of the intervention and possible predictors of successful weight loss.

METHODS

Study Design

The RESPONSE 2 trial was a multicentre randomised controlled trial conducted in 15 secondary and tertiary hospitals in the Netherlands. Study methods and main results have been published and are summarized below. 7 6 The institutional committees on human research of all recruiting hospitals approved the protocol, and written informed consent was obtained from all patients. (Dutch trials register: NTR3937. Registered 8 April 2013, http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=3937).

Patient Population

Eligible patients (age>18 years) had been hospitalized for coronary artery disease (CAD), i.e. myocardial infarction or unstable angina pectoris, and/or underwent percutaneous coronary interventions or coronary artery bypass graft surgery. For the main trial, eligible patients had at least one of the following LRFs: (1) current smoking or stopped

< 6 months before hospital admission (2) overweight (BMI>27 kg/m^2) (3) self-reported physical inactivity (<30 minutes of physical activity of moderate intensity 5 times per week), and willingness to attend the lifestyle programmes. Patients were not analysed if outcome data on LRF were not available at 12 months follow-up.

Patients were excluded if they met any of the following criteria: 1) surgery expected within 8 weeks after inclusion 2) limited life expectancy (≤2 years) 3) congestive heart failure New York Heart Association class III or IV 4) visits to outpatient clinic and/or lifestyle programmes not feasible 5) no access to a computer or internet 6) presence of depressive symptoms (Hospital Anxiety and Depression Scale (HADS) questionnaire >14). For the current analysis we excluded patients with a BMI<27 kg/m^2, as weight loss in individuals with lower BMI's was not a part of the study protocol.

Randomisation

Patients were randomised at the end of the baseline post discharge interview through an automated online protocol to the intervention group or the control group in a 1:1 fashion, stratified by hospital.

Intervention

Patients were offered participation in up to three of the lifestyle programmes detailed below. Patient preference was leading in the choice of programme(s), the total number of programmes followed, and the sequence and duration. In addition, partners were encouraged to participate in the programme, independent of the partners' risk profile. All programmes were offered free of charge.

Weight loss programme

The weight loss programme offered in the RESPONSE 2 trial by WW is a behaviour change program that promotes a healthy pattern of eating, using the ProPoints system to address the total energy value in each product, regular physical activity, and group support. Patients were encouraged to attend weekly workshops (formerly called meetings) and had the option to use digital tools to monitor food intake, physical activity and weight change8

Physical activity programme

Philips DirectLife™ (DL) is an internet-based coaching activity health programme that includes a personal accelerometer, comparable to a small USB device. The programme monitors daily physical activities, provides feedback and offers personalised, internet-based coaching.9

Smoking cessation counselling

Luchtsignaal™ (LS) is an existing national smoking cessation programme in The Netherlands, offering up to seven personalised telephone counselling sessions by professionals during a period of three months. The programme is based on the stages of change concept from the trans-theoretical model and uses strategies from motivational interviewing, action and coping planning, self-control training and relapse prevention.10

Usual Care

All patients received usual care, which included regular visits to the cardiologist or other specialists, and cardiac rehabilitation, according to national and international guidelines.11-13 Usual care also included up to four visits, with a minimum of one, to a nurse-coordinated case management (NCCM) programme that addressed 1) healthy lifestyles, 2) biometric risk factors, and 3) medication adherence.11 14 15

Nurses contributing to the study were registered nurses with a minimum of a four years bachelor's degree in nursing, and with experience in cardiovascular care. They were trained for the study in motivational interviewing and referral strategies, and the nurses were offered participation in the lifestyle programmes themselves.

Programme referral

During NCCM visit(s), nurses documented the patients' LRFs, participation in the cardiac rehabilitation programme and results from physical examination. Patients in the intervention group were asked about their willingness to participate in one or more of the lifestyle programmes (motivation). If patients indicated that they were motivated for short-term improvement (specified as within one month), immediate referral to relevant lifestyle programmes was offered. If this time frame was between one and three months, referral was deferred to the next nurse visit, with a repeated assessment of motivation.

Data collection and measurements

We collected demographic and medical data at baseline (first visit after discharge) and at 12 months, including cardiovascular history, smoking status, dietary status, level of physical activity, medication use and cardiac rehabilitation participation. Height and weight were measured in light clothes without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m2).

Waist circumference was measured at the superior edge of the iliac crest. Body fat composition was assessed using an impedance scale (Tanita scale SC-240-MA). Regular physical activity was self-reported and estimated by measuring the 6-minute walking distance (6MWD) test as per protocol.16 17 Smoking status was assessed by self-report and by urinary cotinine test (UltiMed one step; Dutch Diagnostic, Zutphen, The Netherlands; detection limit 200 ng/ml). Blood pressure was measured twice by an automated

sphygmomanometer and the average of these two was used. Fasting blood samples were analysed for lipid profiles, glucose and HbA1c. Weight change was categorized in three groups; weight gain (≥ 1kg weight gain), unchanged (< 1 kg weight gain and < 1kg weight loss) and weight loss (≥ 1kg weight loss). Successful weight loss was defined according to the ESC prevention guidelines as a BMI<25kg/m^2 and/or ≥ 5% weight loss with respect to baseline weight.

Outcomes

The primary outcome in this analysis was weight change from baseline to 12 months follow-up. Secondary outcomes were changes in body fat percentage, waist circumference, blood pressure, lipid profiles, glucose and HbA1c% levels, ≥5% weight loss, sufficient level of physical activity, number of LRFs per patient, number of WW meetings attended, participation in other programmes (DirectLife™ and Luchtsignaal™), completion of the programmes and partner participation.

Statistical methods

Continuous variables with a normal distribution were presented as means with standard deviation, and continuous variables with a non-normal distribution as median with interquartile range. Categorical variables were presented as frequencies and percentages. Comparisons between groups were made by independent samples t-tests, one-way ANOVA (and Bonferroni corrected for multiple testing) and Fisher's exact tests, as appropriate. A multivariable logistic regression model was developed to determine independent predictors of successful weight loss. A set of variables assumed to influence weight change were selected a priori, consisting of age, gender, level of education, smoking status, baseline weight, physical inactivity at baseline, only overweight as risk factor at baseline, participation in WW, LS and/or DL programme, and partner participation in WW. All variables were first tested in a univariable model, and variables with a significance of $p<0.10$ were included in the final multivariable model. All statistical tests were two-tailed and a p-value of <0.05 was used to indicate statistical significance. Analyses were performed using IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Figure 1 presents the trial profile. From April 2013 to July 2015, 2031 patients with CAD were screened for enrolment, 994 were ineligible based on exclusion criteria (depressive symptoms (n=271), severe comorbidity (n=227), no internet or computer access (n=65), inability to attend follow-up visits (n=75) or inability to provide written informed consent (n=89)); 213 patients declined participation. In total, 824 patients provided

informed consent and were randomised, of whom 609 patients had a BMI>27kg/m^2. Five hundred and thirty-six patients attended the 12 months follow-up visit and were included in this analysis. (Figure 1) Patients who did not attend the 1 year follow-up visit (27 interventions, 46 controls, p=0.014) were younger (55.9 vs. 58.7 years, p=0.02), had a higher diastolic blood pressure (83 vs 70 mmHg, p=0.03) and higher triglycerides (1.3 vs. 1.1 mmol/L, p=0.04) as compared with those who completed the 12 months follow-up visit.

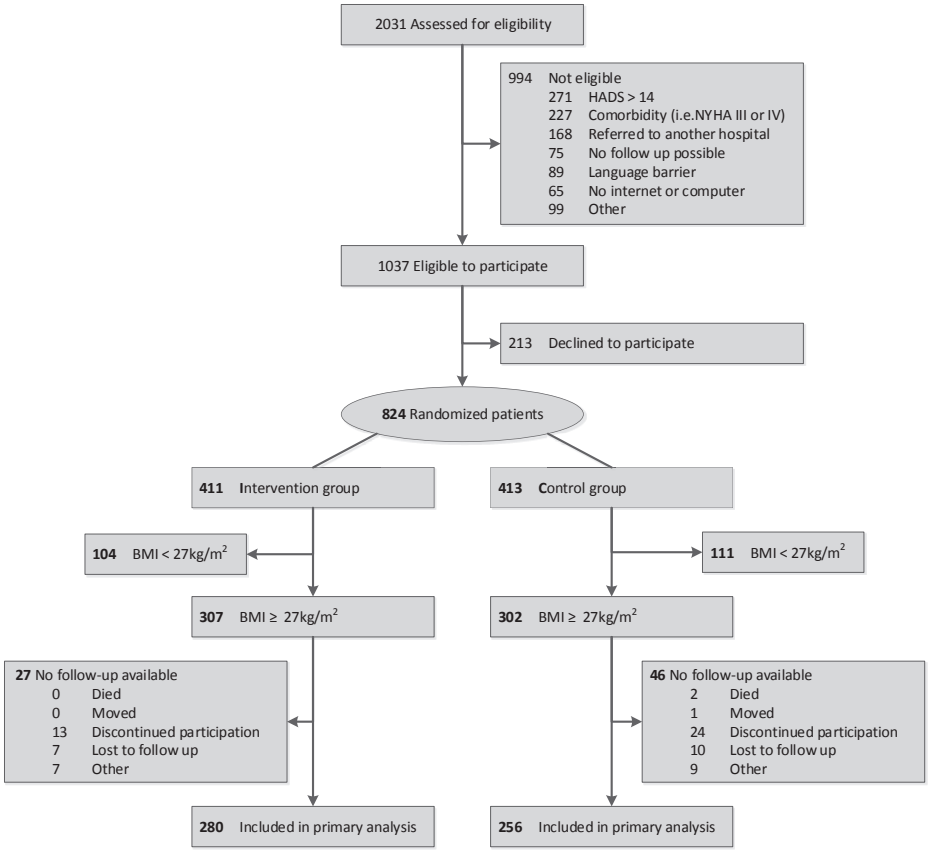

Figure 1. study flowchart
HADS= Hospital Anxiety and Depression Scale, BMI=Body Mass Index,

Baseline characteristics are presented in Table 1. Patients had a mean age of 58.4 (±9.1) years, 23% were female, and 82% were living with a partner. The majority of patients (63%) had no previous history of cardiovascular disease. In total, 38% of the patients smoked at the index event. Mean BMI was 31 kg/m^2 and 62% of patients did not meet the criterion for adequate physical activity. At baseline, the use of preventive medication

was high (98% used antiplatelet therapy, 86% used beta blockers, 75% used ACE inhibitors or ARBs, and 97% used lipid lowering drugs). Most of the patients (90%) attended cardiac rehabilitation.

Table 1. Baseline patient characteristics

	Intervention (n= 307)		Control (n= 302)	
Demographics				
Age, mean (SD), years	58.1	(± 9.0)	58.7	(± 9.2)
Female	71	(23)	71	(24)
Caucasian	289	(94)	279	(92)
Higher education (>13 years)	133	(43)	110	(36)
Relationship (married or cohabitating)	254	(83)	247	(82)
Index event				
ST elevation myocardial infarction	129	(42)	120	(40)
Non-ST elevation myocardial infarction	110	(36)	102	(34)
Unstable angina	27	(9)	32	(11)
Stable angina with intervention	41	(13)	48	(16)
Previous cardiovascular disease				
Myocardial infarction	67	(22)	71	(24)
Percutaneous coronary intervention	53	(17)	51	(17)
Coronary artery bypass surgery	15	(5)	14	(5)
Stroke	6	(2)	12	(4)
Peripheral artery disease	20	(7)	14	(5)
No known previous cardiovascular disease	195	(64)	186	(62)
Cardiovascular risk factors				
Diabetes Mellitus	54	(18)	57	(19)
History of hypertension	116	(38)	138	(46)
History of dyslipidaemia	81	(26)	79	(26)
Clinical data, mean (SD)				
BMI, kg/m^2	31.7	(±3.6)	31.3	(±3.5)
Weight, kg	98.1	(±13.5)	96.9	(±14.2)
Fat percentage, (n=273 and n=261)	33.4	(±8.5)	32.6	(±9.0)
Waist circumference, cm	112	(±10)	110	(±10)
Blood pressure, mm Hg				
Systolic	134	(±18)	136	(±17)
Diastolic	80	(±10)	80	(±11)
Cholesterol, mmol/L				
Total cholesterol	4.10	(±0.93)	4.10	(±1.16)
LDL-cholesterol	2.22	(±0.78)	2.16	(±0.82)
HDL-cholesterol	1.12	(±0.37)	1.14	(±0.36)

Table 1. Baseline patient characteristics (continued)

	Intervention (n= 307)		Control (n= 302)	
Triglycerides	1.81	(±1.17)	1.80	(±1.10)
Cardiovascular risk factors levels				
Systolic blood pressure < 140 mmHg	196	(64)	181	(60)
LDL-cholesterol < 1.8 mmol/L	91	(30)	95	(31)
Smoking at index event	119	(39)	112	(37)
Weight category				
BMI >27 <30 kg/m^2	120	(39)	135	(45)
BMI >30 < 35 kg/m^2	135	(44)	120	(40)
BMI >35 <40 kg/m^2	43	(14)	38	(13)
BMI >40 kg/m^2	9	(3)	9	(3)
Physically inactive	192	(63)	187	(62)
Medication				
Antiplatelet	305	(99)	293	(97)
β-Blockers	257	(84)	264	(87)
ACE inhibiter/ARB	236	(77)	222	(74)
Lipid lowering drugs	296	(96)	294	(97)

Values are n (%) unless otherwise indicated
BMI: body mass index, LDL: lower density lipoprotein, HDL: lower density lipoprotein, ACE: angiotensin-converting enzyme, ARB angiotensin receptor blockers

Table 2 presents the outcomes. Patients in the intervention group lost significantly more weight in 12 months compared with the control group (2.4 kg ±7.1 vs 0.2 kg ±4.6, p<0.001, respectively). Comparable results were seen for decreases in waist circumference (3.7 cm ±6.8 in the intervention group and 1.7 cm ±5.4 in the control group; p<0.001), and body fat percentage (-1.3% ±7.6 in the intervention group and +0.2% ±6.5 in the control group; p=0.04)]. We observed a significantly higher rate of ≥5% weight loss in the intervention group as compared with the control group (32% vs 16%, p<0.001). Weight loss to a BMI<25kg/m^2 was achieved in 4% of patients in the intervention group compared with none in the control group (p=0.002).

Figure 2 presents waterfall plots of the weight change of all individual patients by randomisation group. The individual weight change in the intervention group ranged from +23 kg to -25 kg and from +13 kg to -15 kg in the control group. Weight loss was observed in 54% of the patients in the intervention group compared with 41% of the patient in the control group. In individuals who successfully lost > 1 kg, mean weight loss was 7.5 kg (±5.5) and 4.5 kg (±3.0) (p<0.001), respectively. Notably, a considerable number of patients gained weight: 36% in the intervention group and 41% in the control group, with a mean weight gain in these individuals of 4.4 kg (±3.3) in the intervention

Table 2. Outcomes

	Baseline		Change at 12 months				Change at 12 months
	Intervention	Control	Intervention	Control	Mean Difference	p value	Patients followed WW
	(n=280)	(n=256)	(n=280)	(n=256)	(95% C.I.)	for difference	(n=182)
Primary outcome							
Weight, kg	97.8 (13.7)	96.5 (14.2)	-2.4 (7.1)	-0.2 (4.6)	-2.2 (-3.2 to -1.1)	<0.001	-3.7 (7.6)
Secondary outcome							
BMI, kg/m^2	31.7 (3.5)	31.2 (3.5)	-0.8 (2.3)	-0.1 (1.5)	-0.7 (-1.0 to -0.3)	<0.001	-1.2 (2.5)
Fat percentage, %	33.4 (8.5)	32.3 (8.7)	-1.3 (7.6)	0.2 (6.5)	-1.4 (-2.8 to -0.1)	0.04	-1.2 (7.5)
Waist circumference, cm	111.6 (10.1)	109.9 (10.1)	-3.7 (6.8)	-1.7 (5.4)	-2.0 (-3.1 to -0.1)	<0.001	-4.8 (7.3)
Blood pressure, mmHg							
Systolic	134.2 (18.4)	134.9 (17.5)	-2.1 (18.09	2.0 (18.5)	-4.0 (-7.2 to -0.8)	0.01	-2.6 (18.7)
Diastolic	79.2 (9.6)	79.0 (10.3)	-0.3 (10.9)	1.8 (11.5)	-2.0 (-3.9 to -0.1)	0.04	-0.5 (11.2)
Cholesterol, mmol/L							
Total	4.1 (0.9)	4.1 (1.2)	-0.02 (0.93)	-0.06 (1.24)	0.04 (-0.15 to 0.23)	0.65	-0.01 (0.87)
LDL-C	2.2 (0.8)	2.1 (0.8)	0.03 (0.86)	-0.00 (0.90)	0.03 (-0.12 to 0.19)	0.68	0.03 (0.78)
HDL-C	1.1 (0.4)	1.2 (0.4)	0.06 (0.34)	0.03 (0.32)	0.02 (-0.04 to 0.08)	0.45	0.09 (0.25)
Triglycerides	1.8 (1.2)	1.7 (1.0)	-0.15 (0.90)	-0.05 (1.1)	-0.10 (-0.27 to 0.08)	0.30	-0.22 (0.89)

Values are mean (SD), unless otherwise indicated

BMI: body mass index, LDL: lower density lipoprotein, HDL: lower density lipoprotein, WW: Weight Watchers

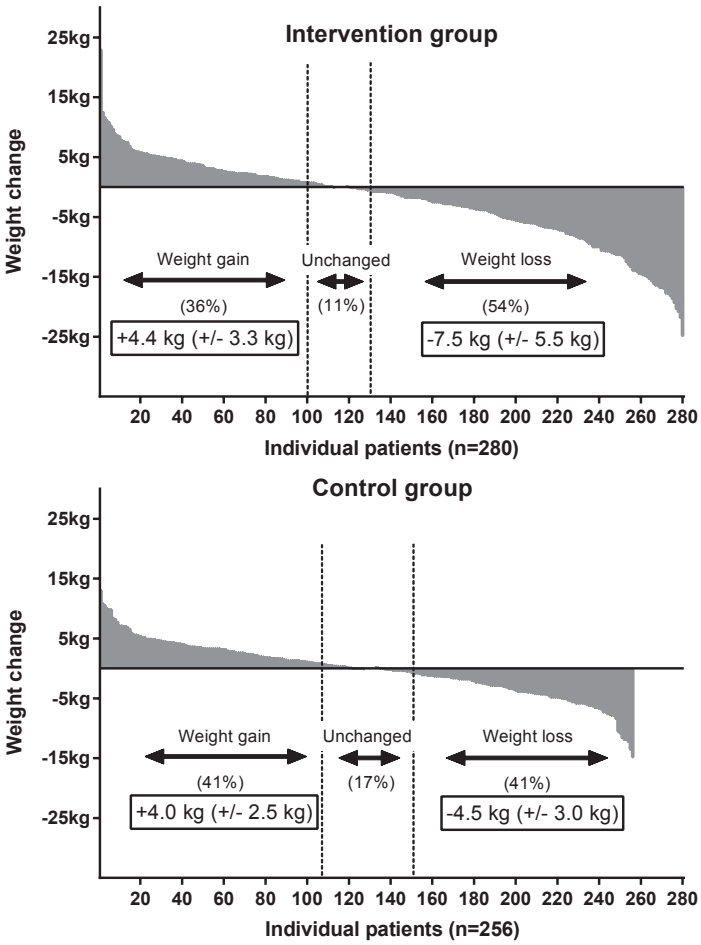

Figure 2. Waterfall plots; Weight change at 12 months by randomization group.

group and 4.0 kg (±2.5) in the control group (p=0.33). Of these patients with weight gain in the intervention group 41% (41/100) had successfully stopped smoking compared to 12% (13/106) in the control group (p=0.04). In all patients who stopped smoking weight gain was 0.9 kg (±7.4) in the intervention group (n=65) compared to 1.8 kg (±5.2) in the control group (n=45) (p = 0.16)

In total, 182 patients (65%) in the intervention group followed the weight reduction programme. The median number of weight loss programme meetings attended in the intervention group was 12 (range 0 to 50). In total, 81 (45%) partners attended the weight loss programme. There was a significant relationship between the number of meetings attended and the change in weight loss (p<0.001) (figure 3). Patient characteristics, programme attendance, intensity/duration of the programme, and partner participation in patients with and without successful weight loss are shown in Appendix I.

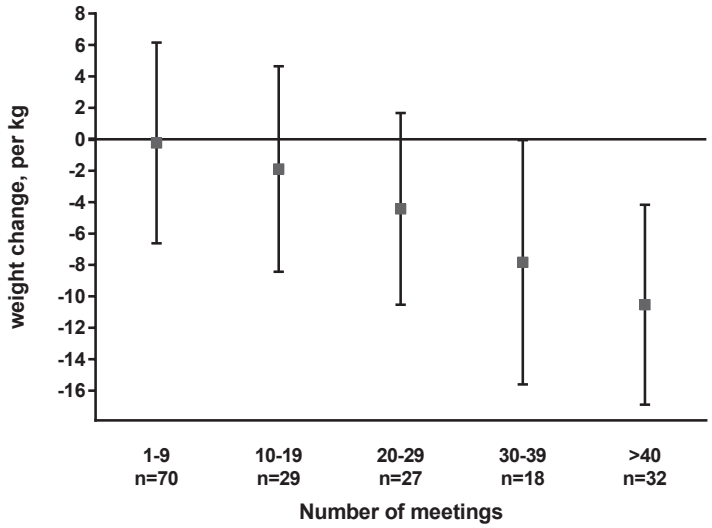

Figure 3. Mean weight change at 12 months per category of group meetings followed during one year. Error bars indicate Standard Deviation (SD) (p<0.001)

In the multivariable logistic regression analysis successful weight loss predictors were higher age, (OR 1.06; 95% C.I. 1.02-1.10 per 1 year) and participation in the WW programme (OR 3.28 95% C.I. 1.18-9.13) (table 3).

Table 3. Predictors of successful weight reduction (BMI<25 and/or ≥5% of baseline weight)

	Univariable			Multivariable		
	OR	95% C.I.	p value	OR	95% C.I.	p value
Patient characteristics						
Age	1.05	(1.02-1.09)	0.001	1.06	(1.02-1.10)	0.004
Female	1.57	(0.88-2.80)	0.12	2.30	(0.94-5.63)	0.07
Higher education (>13 years)	0.67	(0.40-1.12)	0.13			
Relationship	1.24	(0.62-2.50)	0.54			
Lifestyle risk factors						
Weight at baseline	1.01	(0.99-1.02)	0.57			
Physically active at baseline	0.89	(0.53-1.49)	0.65			
Smoking at baseline visit	0.34	(0.14-0.84)	0.02	0.85	(0.29-2.47)	0.76
Only overweight at baseline	1.71	(0.97-3.04)	0.07	1.21	(0.56-2.62)	0.62
Lifestyle programs						
Participation WW	4.30	(2.27-8.14)	<0.001	3.28	(1.18-9.13)	0.02
Participation DL	1.06	(0.64-1.76)	0.82			
Participation LS	0.30	(0.10-0.88)	0.03	0.51	(0.13-1.34)	0.32
Participation of partner WW	2.97	(1.62-5.46)	0.01	1.44	(0.82-3.91)	0.14

WW: Weight Watchers, DL: DirectLife, LS: Luchtsignaal

DISCUSSION

The main finding of our study is that in patients with CAD and overweight, referral to a community-based commercial weight-loss programme as part of a comprehensive lifestyle intervention, results in significantly more successful weight loss (≥5% of baseline weight) compared with controls (32% vs 16%, p<0.001). In the intervention group, 4% achieved a BMI<25 kg/m^2, compared to none in the control group. Mean weight loss was 2.4 kg (SD ±7.1) in the intervention group versus 0.2 kg (SD ±4.6) in the control group

While the relatively large number of patients who managed to lose weight in the first year after their coronary event or procedure is encouraging, the number of patients who gained weight, despite being offered participation in a weight loss programme, is alarming. Both in the intervention and control groups, a considerable number of patients gained ≥1 kg (36% vs 41%) in the first 12 months. This was seen on top of a high level of usual care, with all patients attending nurse-coordinated outpatient clinics, where LRFs were discussed during each visit, and the majority of patients (90%) attending cardiac rehabilitation. Weight gain in patients with CAD has been associated with a number of factors, such as age, smoking status, presence of pre-existing obesity and depression.18 One central factor in weight gain among CAD patients is smoking cessation. Patients who stop smoking after a myocardial infarction have been shown to gain an average of 4.8kg (±8.6) in the first year after their acute coronary event.19 In another secondary analysis of RESPONSE-2 on smoking behaviour, we found that smokers who successfully quit had a mean weight increase of 2.0 kg (±6.8) and 3.0 kg (±5.1) in the intervention and control group, respectively (p=0.29)20. In this secondary analyses we found in patients with a BMI>27 who stopped smoking a smaller amount of weight gain [+0.9 kg (±7.4) interventions vs +1.8 kg (±5.2) controls (p = 0.16)]. Overall, weight gain in patients who stopped smoking in the RESPONSE2 trials was slightly lower than what has previously been reported. The fact that patients were allowed to stop smoking before addressing their weight issue might have contributed to the patterns of weight gain in quitters. However, weight gain was also seen in non-smokers, and the number of individuals with weight gain after a coronary event or revascularisation remains a cause of concern.

Community-based commercial weight loss programmes have been demonstrated to be effective in primary prevention. In primary prevention, Jebb et al. showed that participants with at least one risk factor for obesity-related disease, referred by a health-care professional to the same weight loss programme as used in our trial lost 4.1 kg (S.E. ±0.31) compared to the control group, who lost 1.8 kg (S.E. ±0.19).5 Our study is consistent with these findings that this commercial weight loss programme can be successfully offered to patients with CAD. The mean weight loss was lower in our study, but the difference in weight loss between the intervention and control group was similar: 2.3 kg reported by Jebb et al. and 2.1 kg in our trial. Patients in our trial could simultane-

ously or sequentially follow other lifestyle programmes, most likely resulting in a lower attendance rate to the WW programme.

The weight loss programme was offered on top of a high level of usual care, which included cardiac rehabilitation. Previous studies have shown that cardiac rehabilitation alone is insufficient to achieve clinically meaningful weight loss, with a number of studies reporting mean weight gain in patients completing cardiac rehabilitation ranging from +0.5kg to +1.8kg.21 Studies adding a weight loss intervention on top of cardiac rehabilitation showed better results, with weight loss ranging from -6.0 kg to -9.1 kg.22 23 Balancing between single versus multiple interventions with the risk of losing focus, our trial offered a dedicated smoking cessation counselling programme and a physical activity programme in addition to a weight loss intervention. After 12 months we found a weight loss of 2.4 kg (SD ±7.1) in the intervention group, which is less than a stand alone weight loss intervention, but significantly more than only following a cardiac rehabilitation programme. Another positive result from our main trial was that the number of patients who improved two or three lifestyle-related risk factors was significantly higher in the intervention group compared to the control group (intervention 13%, controls 6%, $p<0.001$).6

Attending the WW programme was the most important predictor of achieving weight loss, with univariate and multivariate logistic regression. The programme was well attended, (65% of patients). Also the number of attended meetings was linearly associated with weight loss, consistent with the literature.23 24 A recent meta-analysis demonstrated that marital status has a positive effect on CVD risk.25 In this secondary analysis, partner participation in the WW programme was associated with more successful weight loss in a univariable analysis (OR 2.97 95% C.I. 1.62-5.46). However, upon adjustment for other predictors, this significant association with successful weight loss was lost (OR 1.44 95% C.I. 0.82-3.91).

Strengths and limitations

There are several strengths to our study. First, the RESPONSE2 trial used existing community-based lifestyle programmes, without modifications in the programmes, which facilitates implementation of these programmes into daily practice. Second, the dropout rate as reflected by the number of patients not attending the 1 year follow-up visit (12%), 9% intervention vs 15% control) was considerably lower than those shown in other obesity intervention / weight loss trials.5 26 27

Some aspects of our study merit consideration. First, the follow-up period of our trial was 12 months and to evaluate a long-term impact on prognosis, a longer follow up period would be necessary. However, in a review on the efficacy of commercial weight-loss programmes, including the weight loss programme used in the RESPONSE-2 trial, consistent evidence was found supporting the long-term efficacy of this weight loss

programme.28 Second, we excluded patients with depressive symptoms, comorbidity (NYHA III or IV), a language barrier, or without internet access. Potentially, the excluded individuals represent patients with a lower socioeconomic status, who particularly need optimal secondary prevention.29 As shown in our results, even in non-depressive, highly motivated and educated patients, still 36% to 41% of the patients gain weight, and patient-tailored programmes, based on individual needs and capabilities of the patients, need to be further explored.

Conclusion

Weight loss in patients with CAD can be achieved through referral to a commercial weight loss programme, as part of a comprehensive lifestyle strategy. Patients referred to such programmes lose significantly more weight than those not referred. As the weight loss programme is widely available, it can easily be implemented into daily clinical practice in a large variety of settings and countries. Weight gain was highly prevalent, and prevention of weight gain may be as important as attempts at weight loss.

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APPENDIX 1

Characteristics of patient in the intervention group divided by successful weight reduction

	Total	Successful	Unsuccessful	p value
	n=280	n=90	n=190	
Lifestyle programs				
Participation in WW	182/280 (65%)	76/90 (84%)	106/190 (56%)	<0.001
Participation LS	30/279 (11%)	4/89 (4%)	26/190 (14%)	0.02
Participation DL	159/280 (57%)	52/90 (58%)	107/190 (56%)	0.90
Participation in WW + LS	15/280 (5%)	3/90 (3%)	12/190 (6%)	0.40
Participation in WW + DL	110/280 (39%)	44/90 (49%)	66/190 (35%)	0.03
No program participation	40/280 (14%)	5/90 (6%)	35/190 (18%)	0.00
Partner participation	120/280 (43%)	49/90 (54%)	71/190 (37%)	0.01
Partner participation in WW	81/190 (43%)	42/71 (59%)	39/119 (33%)	0.01
Attendance to lifestyle programs				
Weight reduction program				
Median meetings (min-max)	12 (0-50)	30 (0-50)	7 (0-50)	
0 meetings	5/181 (3%)	2/76 (3%)	3/105 (3%)	
1-9 meetings	70/181 (39%)	16/76 (21%)	54/105 (51%)	
10-19 meetings	29/181 (16%)	7/76 (9%)	22/105 (21%)	
20-29 meetings	27/181 (15%)	12/76 (16%)	15/105 (14%)	
30-39 meetings	18/181 (10%)	13/76 (17%)	5/105 (5%)	
≥ 40 meetings	32/181 (18%)	26/76 (34%)	6/105 (6%)	
Physical activity program				
≥ 12 weeks participation (completed)	133/159 (84%)	47/52 (90%)	86/107 (80%)	0.31
Smoking cessation counselling				
Program completed	26/30 (87%)	3/4 (75%)	23/26 (88%)	0.02
Information documented during visits				
Previous weight loss attempt	186/280 (66%)	67/90 (74%)	119/190 (63%)	0.05
Motivated for WW	206/268 (77%)	77/84 (92%)	129/184 (70%)	0.00
Motivated to start < 1 months	208/267 (78%)	77/84 (92%)	131/184 (72%)	0.00
Patient referred in visit 1 to WW	178/208 (86%)	69/77 (90%)	109/131 (83%)	0.20
Started with WW after first visit	132/174 (76%)	61/65 (94%)	71/109 (64%)	< 0.001

WW: Weight Watchers, DL: DirectLife, LS: Luchtsignaal