

ONLINE APPENDIX

Community-based commercial lifestyle programmes*Weight loss programme*

The weight reduction programme offered by Weight Watchers™ (www.weightwatchers.com) promotes a healthy diet using the ProPoints system, which addresses the total energy value in each product, healthy behaviour and regular physical activity, and utilizes group motivation. Patients were encouraged to attend weekly workshops and could use digital tools to monitor food intake, physical activity and weight change. A free subscription was provided for one year.

Physical activity programme

Philips DirectLife™ (www.philips.nl/c-m-pe/actieve-levensstijl/directlife/nieuwste#availability=all) is an internet-based health programme that encourages stepwise increases in levels of physical activity by promoting awareness of all daily exercise, independent of its intensity or type of activity. The programme uses a personal accelerometer to monitor daily physical activities, provide feedback and offer personalised internet-based coaching. After three months of active coaching, participants could continue to use the accelerometer and online portal to monitor their physical activity.

Smoking cessation counselling

Luchtsignaal™ (www.luchtsignaal.nl) is an existing national smoking cessation programme in The Netherlands, offering up to seven personalised telephone-based 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. If necessary, nicotine replacement therapy or varenicline could be prescribed.

Statistical methods to identify determinants of successful weight loss and weight gain

Determinants of successful weight loss ($\geq 5\%$) or weight gain (≥ 1 kg) compared with baseline were identified using individual patient data from intervention group patients with a BMI ≥ 27 kg/m² from the RESPONSE-2 trial. For both weight loss and weight gain, a set of candidate predictors assumed to influence weight change based on current literature and expert knowledge was selected a priori and are listed below. Because several candidate predictors were not available for control patients, we included only patients from the intervention group in the analyses.

We used stepwise multivariable logistic regression analysis with backward elimination and with successful weight loss ($\geq 5\%$) or weight gain (≥ 1 kg) as dependent variables. In the backward elimination procedure, variables with the largest p-value were removed sequentially and the logistic regression analysis was repeated until all p-values were smaller than <0.157 , corresponding with an all-subset approach with selection based on Aikake's information criterion (15).

We estimated the models in 20 imputed datasets and regression coefficients and p-values were pooled using Rubin's rule. Non-normal distributed continuous variables were log-transformed before imputation. In the final models, continuous variables were assessed for linearity by visual plots and model performance based on the R², C-statistic and Aikake Information Criterion and were categorised or transformed with restricted cubic splines if indicated.

Finally, we internally validated the models in 250 bootstrap samples drawn from the original data with missing values and missing values filled in by multiple imputation ($m=20$) in each bootstrap sample (Heymans M. Psfmi package. Available at: <https://mwheymans.github.io/psfmi/index.html>). We report pooled regression coefficients without shrinkage and AUCs and R² after shrinkage. We used the mice and psfmi packages in R-studio (version 3.6.1.) for these analyses.

Determinants of successful weight loss

Determinant	Data type	Missing data
1. Age	Continuous	-
2. Sex	Binary	-
3. Level of education	Binary	-
4. Having a partner at baseline	Binary	-
5. Never smoking or quit >6 months before hospitalisation	Binary	-
6. Baseline BMI	Continuous	-
7. Physical inactivity at baseline	Binary	-
8. Only overweight as risk factor at baseline	Binary	-
9. Participation in the weight loss programme	Binary	-
10. Participation in the smoking cessation programme	Binary	-
11. Participation in the physical activity programme	Binary	-
12. Partner participation in the weight loss programme *	Binary	125
13. Being motivated to lose weight	Binary	19
14. Being motivated to start weight loss directly after the baseline visit *	Binary	13
15. Referral to the weight loss programme directly after the baseline visit *	Binary	72

* Covariate not available in control patients

Determinants of weight gain

Determinant	Data type	Missing data
1. Age	Continuous	-
2. Sex	Binary	-
3. Ethnicity	Binary	-
4. Level of education	Binary	-
5. Having a partner	Binary	-
6. Smoking at baseline	Binary	-
7. Smoking cessation \leq 6 months before or during hospitalization	Binary	-
8. Established type-2 Diabetes	Binary	-
9. Baseline BMI	Continuous	-
10. Baseline physical inactivity	Binary	-
11. Participation in the weight loss programme	Binary	-
12. Participation in the smoking cessation programme	Binary	-
13. Participation in the physical activity programme	Binary	-
14. Partner participation in the weight loss programme *	Binary	125
15. Not motivated to lose weight	Binary	19

* Covariate not available in control patients

Analysis of loss to follow-up

We used univariable logistic regression analysis to evaluate associations between patients' baseline characteristics and the probability of being lost to follow-up at the 12 months follow-up (online appendix, table 1a, 'Overall LTFU') and whether or not the probability of being lost to follow-up was significantly interacted on by treatment allocation (online appendix, table 1a, 'Between-group LTFU'). Variables with a standardized mean difference (SMD) of ≥ 0.20 and/or a p-value < 0.05 were evaluated for their ability to identify patients lost to follow-up at the 12 months follow-up using the Receiver Operating Characteristic Area Under the Curve (AUC) and the Aikake's Information Criterion (AIC) (online appendix, table 1b). The loss to follow-up mechanism was defined as the model with the highest AUC and the lowest AIC.

Online appendix, table 1a: Analysis of patients lost to follow-up

	Intervention group		Control group		Overall LTFU *		Between-group LTFU *
	Attendees	Patients LTFU	Attendees	Patients LTFU	SMD	p-value	p-value
Randomization							
Treatment allocation	280 (91.2)	27 (8.8)	257 (85.1)	45 (14.9)	0.30	0.03	
Demographics							
Age (y)	58.6 ±9.0	57.3 ±9.0	59.7 ±9	55.6 ±9	0.33	0.01	0.53
Sex (Female)	65 (23)	6 (2.2)	57 (22)	14 (31)	0.12	0.42	0.29
Ethnicity (Caucasian)	264 (94)	25 (92.6)	238 (93)	41 (91)	0.07	0.74	0.30
Education (Higher) †	105 (38)	9 (33.3)	68 (27)	16 (36)	0.05	0.77	0.07
Partner	234 (84)	20 (74.1)	211 (82)	36 (80)	0.13	0.37	0.81
Index event					0.26	0.23	0.31
STEMI	114 (41)	15 (55.6)	98 (38)	22 (49)			
NSTEMI	103 (37)	7 (25.9)	88 (34)	14 (31)			
Unstable AP	26 (9)	1 (3.7)	26 (10)	6 (13)			
Stable angina revascularization	37 (13)	4 (14.8)	45 (18)	3 (7)			
Treatment					0.05	0.94	0.41
PCI	214 (76)	23 (85)	202 (79)	34 (76)			
CABG	29 (10)	1 (4)	30 (12)	6 (13)			
Medication only	37 (13)	3 (11)	25 (10)	5 (11)			
Previous CVD							
MI	58 (21)	9 (33)	65 (25)	6 (14)	0.04	0.85	0.27
PCI	45 (16)	8 (30)	44 (17)	7 (16)	0.12	0.43	1.00
CABG	15 (5)	0 (0)	10 (4)	4 (9)	0.04	0.95	0.99
Stroke	5 (2)	1 (4)	9 (4)	3 (7)	0.15	0.30	0.99
Peripheral artery disease	18 (6)	2 (7)	11 (4)	3 (7)	0.07	0.77	0.24
No known previous CVD	184 (66)	11 (41)	157 (61)	29 (66)	0.15	0.30	0.37
CVD risk factors							
Diabetes Mellitus	48 (17)	6 (22)	47 (18)	10 (22)	0.11	0.44	0.65
History of hypertension	108 (39)	8 (30)	115 (45)	23 (52)	0.04	0.83	0.68
History of dyslipidaemia	73 (26)	8 (30)	67 (26)	12 (27)	0.05	0.82	0.23
Smoking							
Smoking at baseline ‡	39 (14)	9 (33)	45 (18)	10 (22)	0.31	0.01	0.07
Pre-event smoking §	122 (44)	13 (48)	104 (41)	24 (53)	0.11	0.48	0.73
WHO physical activity norm **	108 (39)	7 (26)	101 (39)	14 (31)	0.21	0.14	0.94
Clinical data							

BMI, kg/m ²	31.7 ±3.6	32.3 ±4.5	31.2 ±3.5	31.6 ±3.6	0.12	0.33	0.34
Blood pressure, mmHg							
Systolic	134 ±18	137 ±19	135 ±18	140 ±16	0.23	0.08	0.57
Diastolic	79 ±10	83 ±11	79 ±10	83 ±12	0.36	<0.01	0.65
Cholesterol, mmol/L							
Total cholesterol	4.1 ±0.9	4.1 ±1.0	4.1 ±1.2	4.2 ±1.0	0.11	0.39	0.8
LDL-cholesterol	2.2 ±0.8	2.2 ±0.8	2.2 ±0.8	2.3 ±0.7	0.07	0.59	0.46
HDL-cholesterol	1.1 ±0.4	1.1 ±0.3	1.2 ±0.4	1.1 ±0.3	0.12	0.39	0.73
Triglycerides	1.5 [1.1–2.1]	1.6 [1.4–2.1]	1.5 [1.1–2.0]	1.5 [1.2–2.4]	0.19	0.12	0.79
Fasting plasma glucose, mmol/L	5.9 [5.4–6.7]	6.4 [5.3–8.0]	5.9 [5.4–6.6]	5.8 [5.4–6.5]	0.18	0.59	0.65
HbA1c, mmol/L	40.9 ±12.3	44.3 ±16.6	40.5 ±12.6	39.2 ±15.8	0.04	0.76	0.39
Medication							
Antiplatelet	278 (99)	27 (100)	250 (97)	43 (96)	0.08	0.85	1.00
β-Blockers	234 (84)	23 (85)	227 (88)	37 (82)	0.07	0.70	0.08
ACE inhibitor/ARB	220 (79)	16 (59)	185 (72)	37 (82)	0.04	0.85	0.07
Lipid lowering drugs	271 (97)	25 (93)	250 (97)	44 (99)	0.06	0.86	1.00

Continuous variables presented as mean ± standard deviation or median [inter quartile range] and dichotomous variables as counts (%); * P-values based on univariable logistic regression analysis (overall LTFU) and with treatment allocation as interaction (between group LTFU), † Higher education: universities of applied sciences and research universities, ‡ Baseline urine-cotinine level >200 ng/ml, § Patients who quit smoking ≤6 months before hospitalisation, ** Self-reported based on WHO recommendations; ACE: Angiotensin-converting enzyme, AP: Angina pectoris, ARB: Angiotensin II-receptor blocker, BMI: Body mass index, CABG: Coronary artery bypass grafting, CVD: cardiovascular disease, HDL-C: High density lipoprotein cholesterol, HbA1c: Glycated haemoglobin, LDL-C: Low density lipoprotein cholesterol, LTFU: loss/lost to follow-up, NSTEMI: Non ST-elevation myocardial infarction, PCI: Percutaneous coronary intervention, SMD: Standardized mean difference, STEMI: ST-elevation myocardial infarction.

Online appendix, table 1b: Coefficients and model performance from logistic regression models for the probability of patients being lost to follow-up at the 12 months assessment

Baseline variable	Models							
	1	2	3	4	5	6	7	8
Treatment allocation (Intervention group)	1.82 *							0.54 *
Age (y)		1.4 *						0.97 *
Index event								
STEMI			0.62					
NSTEMI			1.34					
Unstable AP			1.00					
Stable angina revascularization			1.67					
Smoking at baseline †				0.50 *				1.80 *
Inadequate physical activity ‡					1.55			
Systolic blood pressure, mmHg						0.99		
Diastolic blood pressure, mmHg							0.96 **	1.04 **
ROC-AUC	0.57	0.60	0.57	0.43	0.45	0.57	0.60	0.68
AIC	441	440	446	440	444	444	438	427

Regression coefficients presented as odds ratios; Significance codes: '***' <0.01, '**' <0.05, '*' <0.1; ROC-AUC: Receiver Operating Characteristic Area Under the Curve, AIC: Akaike's Information Criterion; † Baseline urine-cotinine level >200 ng/ml, ‡ Self-reported based on WHO recommendations.

Online appendix, table 2: Lifestyle programme participation in the intervention group stratified by successful weight loss ($\geq 5\%$ reduction of baseline weight in patients with baseline BMI ≥ 27 kg/m²)

	Total	Successful (n=90)	Unsuccessful (n=190)	p-value
Participation in lifestyle programs				
WW	182 / 280 (0.65)	76 / 90 (0.84)	106 / 190 (0.56)	≤ 0.001
Smoking cessation programme	30 / 280 (0.11)	4 / 90 (0.04)	26 / 190 (0.14)	≤ 0.05
Physical activity programme	159 / 280 (0.57)	52 / 90 (0.58)	107 / 190 (0.56)	0.82
WW and smoking cessation programmes	15 / 280 (0.05)	3 / 90 (0.03)	12 / 190 (0.06)	0.31
WW and physical activity programmes	110 / 280 (0.39)	44 / 90 (0.49)	66 / 190 (0.35)	≤ 0.05
None	40 / 280 (0.14)	5 / 90 (0.06)	35 / 190 (0.18)	≤ 0.01
Partner participation	120 / 227 (0.53)	49 / 81 (0.60)	71 / 146 (0.49)	0.09
Partner participation in WW	81 / 190 (0.43)	42 / 71 (0.59)	39 / 119 (0.33)	≤ 0.001
Attendance to lifestyle programmes *				
Weight loss programme				
Median meetings (range)	12 (0–50) 5 / 181	30 (0–50) 2 / 76	7 (0–50)	
0 meetings	(0.03)	(0.03)	3 / 105 (0.03)	
1-9 meetings	70 / 181 (0.39)	16 / 76 (0.21)	54 / 105 (0.51)	
10-19 meetings	29 / 181 (0.16)	7 / 76 (0.09)	22 / 105 (0.21)	
20-29 meetings	27 / 181 (0.15)	12 / 76 (0.16)	15 / 105 (0.14)	
30-39 meetings	18 / 181 (0.10)	13 / 76 (0.17)	5 / 105 (0.05)	
>40 meetings	32 / 181 (0.18)	26 / 76 (0.34)	6 / 105 (0.06)	
Physical activity programme				
12 weeks completed	133 / 159 (0.84)	47 / 52 (0.90)	86 / 107 (0.80)	0.12
Smoking cessation programme				
Full programme completed	26 / 30 (0.87)	3 / 4 (0.75)	23 / 26 (0.88)	0.47
Motivation characteristics				
Previous weight loss attempts	186 / 280 (0.66)	67 / 90 (0.74)	119 / 190 (0.63)	0.06
Motivated for WW	216 / 261 (0.83)	77 / 83 (0.93)	139 / 178 (0.78)	≤ 0.01
Motivated to start WW within 1 month	208 / 267 (0.78)	77 / 83 (0.93)	131 / 184 (0.71)	≤ 0.001
Referred to WW in 1st outpatient clinic visit	178 / 208 (0.86)	69 / 77 (0.90)	109 / 131 (0.83)	0.21
Started with WW after first outpatient clinic visit	132 / 174 (0.76)	61 / 65 (0.94)	71 / 109 (0.65)	≤ 0.001

Data on intervention group only; Values presented as counts (%); * Data on patients who agreed to participate in and were referred to a lifestyle programme: WW: weight loss programme.

Online appendix, table 3: Results from the sensitivity analysis; Adjusted outcome data at 12 months follow-up in patients with baseline BMI ≥ 27 kg/m²

	Baseline		Change at 12 months		Between group difference, mean (95% CI)	p-value	WW participants (n=182)	Missing data (interventions/controls)
	Intervention (n=280)	Control (n=257)	Intervention (n=280)	Control (n=257)				
Primary outcomes								
Body weight, kg	97.8 \pm 13.7	96.6 \pm 14.2	-2.4 \pm 7.1	-0.2 \pm 4.6	-2.4 (-3.4 – -1.4)	<0.001	-3.5 \pm 7.3	-
BMI, kg/m ²	31.65 \pm 3.6	31.18 \pm 3.5	-0.8 \pm 2.3	-0.1 \pm 1.5	-0.8 (-1.1 – -0.5)	<0.001	-1.1 \pm 2.4	-
Secondary outcomes								
Body fat percentage, %	33.5 \pm 8.5	32.3 \pm 8.7	-1.2 \pm 7.3	0.3 \pm 6.5	-1.6 (-2.9 – -0.3)	<0.05	-0.9 \pm 7.9	29/26
Waist circumference, cm	111.6 \pm 10.1	110 \pm 10.2	-3.7 \pm 6.8	-1.9 \pm 5.4	-2.2 (-3.3 – -1.2)	<0.001	-3.3 \pm 7.5	0 4
Blood pressure, mm Hg								
Systolic	134.2 \pm 18.4	134.9 \pm 17.5	-2.1 \pm 19.0	1.9 \pm 18.6	-4.2 (-7.2 – -1.3)	<0.01	4.2 \pm 21.6	0/1
Diastolic	79.2 \pm 9.6	79 \pm 10.3	-0.3 \pm 10.9	1.9 \pm 11.6	-2.2 (-3.8 – -0.6)	<0.01	-2.4 \pm 11.6	0/1
Cholesterol, mmol/L								
Total cholesterol	4.1 \pm 0.9	4.1 \pm 1.2	-0.03 \pm 0.94	-0.07 \pm 1.24	0.03 (-0.16 – 0.22)	0.73	0.06 \pm 1.32	9/7
LDL-C	2.2 \pm 0.8	2.2 \pm 0.8	0.01 \pm 0.85	-0.01 \pm 0.90	0.03 (-0.13 – 0.18)	0.74	0.04 \pm 1.07	11/7
HDL-C	1.1 \pm 0.4	1.2 \pm 0.4	0.06 \pm 0.34	0.04 \pm 0.33	0.01 (-0.04 – 0.07)	0.65	0.05 \pm 0.41	9/7
Triglycerides	1.5 [1.1–2.1]	1.5 [1.1–2.0]	-0.14 \pm 0.90	-0.05 \pm 1.14	-0.07 (-0.33 – 0.26)	0.45	-0.17 \pm 1.24	12/10
Glucose, mmol/L	5.9 [5.4–6.7]	5.9 [5.4–6.6]	-0.15 \pm 1.64	-0.17 \pm 1.43	-0.03 (-0.33 – 0.26)	0.82	-0.04 \pm 2.02	17/11
HbA1c, mmol/mol	40.9 \pm 12.3	40.5 \pm 12.5	0.41 \pm 10.10	1.66 \pm 11.31	-1.70 (-3.72 – 0.24)	0.08	-0.93 \pm 12.24	24/25

Values presented as mean \pm SD or median [inter quartile range]; BMI: body mass index, CI: Confidence interval, HDL-C: High density lipoprotein cholesterol, HbA1c: Glycated haemoglobin, LDL-C: Low density lipoprotein cholesterol, WW: Weight loss programme; Results are adjusted for covariates used to stratify the randomisation, covariates that were part of the loss to follow-up mechanism and level of education.

Online appendix, table 4: Achievement of lifestyle-related risk factor targets at 12 months follow-up in patients with baseline BMI ≥ 27 kg/m²

	Intervention group, No (%)	Control group, No (%)	Proportional difference, mean (95%CI)	Relative risk reduction (95%CI)	p-value
Lifestyle-related risk factor targets					
$\geq 5\%$ weight loss compared with baseline	90 / 280 (0.32)	40 / 257 (0.16)	0.17 (0.09 – 0.23)	2.07 (1.48 – 2.88)	<0.001
BMI ≤ 25 kg/m ²	10 / 280 (0.04)	0 / 257 (0.00)	0.04 (0.01 – 0.06)	Inf	<0.01
Non-smoking status					
Baseline smokers *	17 / 57 (0.30)	6 / 56 (0.11)	0.19 (0.04 – 0.33)	2.78 (1.18 – 6.54)	<0.05
Pre-event smokers †	48 / 65 (0.74)	42 / 48 (0.88)	-0.14 (-0.27 – 0.02)	0.84 (0.71 – 1.01)	0.10
$\geq 10\%$ increase in 6MWD compared with baseline ‡	79 / 164 (0.48)	64 / 154 (0.42)	0.07 (-0.04 – 0.17)	1.16 (0.91 – 1.48)	0.24
Absence of metabolic syndrome §	68 / 258 (0.26)	57 / 239 (0.24)	0.03 (-0.05 – 0.10)	1.11 (0.81 – 1.50)	0.54

6MWD: 6-minute walking distance; All patients had a baseline BMI ≥ 27 kg/m²; * In patients with a baseline urine-cotinine level >200 ng/ml, † In patients who quit smoking ≤ 6 months before hospitalisation, ‡ In patients with self-reported inadequate physical activity at baseline according to WHO recommendations, § According to American Heart Association guidelines.

Online appendix, table 5: Significant effect modification of determinant-outcome associations for successful weight loss and weight gain by treatment allocation

	Intervention group, No (%)	Control group, No (%)	Risk ratio (95%CI)	p-value	p-value interaction
≥5% weight loss compared with baseline					
Age					<0.01
≥65 years	39 / 75 (0.52)	13 / 88 (0.15)	3.52 (2.04 – 6.08)	<0.001	
<65 years	51 / 205 (0.25)	27 / 169 (0.16)	1.56 (1.02 – 2.37)	0.04	
Smoking history					0.01
Non-smoking status	69 / 158 (0.44)	25 / 153 (0.16)	2.67 (1.79 – 3.99)	<0.001	
Smoking *	21 / 122 (0.17)	15 / 104 (0.14)	1.19 (0.65 – 2.19)	0.59	
Motivated for weight loss †					<0.001
Motivated	77 / 216 (0.36)	25 / 189 (0.13)	2.70 (1.79 – 4.05)	<0.001	
Not motivated	6 / 45 (0.13)	12 / 49 (0.25)	0.54 (0.22 – 1.33)	0.20	
≥1.0 kg weight gain compared with baseline					
Smoking at baseline					<0.01
Smoking at baseline ‡	28 / 57 (0.49)	18 / 56 (0.32)	1.53 (0.96 – 2.43)	0.07	
Not smoking	68 / 223 (0.31)	85 / 201 (0.42)	0.72 (0.56 – 0.93)	0.01	

Values presented as counts, group size and percentage, * Patients with a baseline urine-cotinine level >200ng/ml or patients who quit smoking <6 months before hospitalization, † Patients who reported to be motivated for weight loss at the baseline visit, ‡ Patients with a baseline urine-cotinine level >200ng/ml.