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Feasibility and effectiveness of a lifestyle intervention after complicated pregnancies to improve risk factors for future cardiometabolic disease

D. Berks[a], M. Hoedjes[b], H. Raat[b], A. Franx[c], C.W.N. Looman[b], M.F. Van Oostwaard[a], D.N.M. Papatsonis[d], J.J. Duvekot[a,*], E.A.P. Steegers[a]

[a] Erasmus MC, Department of Obstetrics and Gynaecology, Division of Obstetrics and Prenatal Medicine, Rotterdam, The Netherlands
[b] Erasmus MC, Department of Public Health, Rotterdam, The Netherlands
[c] University Medical Centre Utrecht, Division Woman and Baby, Utrecht, The Netherlands
[d] Amphia Hospital, Department of Obstetrics and Gynaecology, Breda, The Netherlands

A B S T R A C T

Objectives: To evaluate the feasibility and effectiveness of a postpartum lifestyle intervention after pregnancies complicated by preeclampsia, fetal growth restriction (FGR) and/or gestational diabetes mellitus (GDM) to improve maternal risk factors for future cardiometabolic disease.

Methods: Women following a complicated pregnancy were included six months postpartum in this specific pre-post controlled designed study. It has been conducted in one tertiary and three secondary care hospitals (intervention group) and one secondary care hospital (control group). The program consisted of a computer-tailored health education program combined with three individual counselling sessions during seven months. Primary outcome measures were the proportion of eligible women and weight change during the intervention.

Results: Two hundred and six women were willing to participate. The proportion of eligible women who complied with the intervention was 23%. Major barrier was lack of time.

Adjusted weight change attributed to lifestyle intervention was −1.9 kg (95%-CI −4.3 to −0.3). Further changes were BMI (-0.9 kg/m^2 (95%-CI −1.4 to −0.3)), waist-to-hip ratio (−0.04 cm/cm (95%-CI −0.06 to −0.03)), blood pressure medication use (19% (95%-CI 9% to 28%)), HOMA2-score (59 %S (95%-CI 18 to 99)) and total fat intake (−2.9 gr (95%-CI −4.6 to −1.2)).

Conclusions: The results support feasibility and effectiveness of a lifestyle intervention after complicated pregnancies to improve maternal cardiometabolic risk factors. Further randomized controlled studies are needed with longer follow-up to evaluate durability. In the meantime, we suggest health care professionals to offer lifestyle interventions to women after complicated pregnancies.

1. Introduction

After pregnancies complicated by preeclampsia, fetal growth restriction and/or gestational diabetes mellitus, women are at an increased risk to develop cardiometabolic disease in later life. Women with a history of preeclampsia suffer from a two-fold increased risk of ischemic heart disease and stroke [1]. This increased risk may be due to shared risk factors, or an independent association between preeclampsia and cardiometabolic disease in later life [1]. Women with foetal growth restriction have an up to three-fold increased risk of future cardiovascular disease if it was the only pregnancy complication and an up to seven-fold increased risk in combination with preeclampsia [2–5]. Women with a history of gestational diabetes mellitus have a 20–60% risk of developing diabetes mellitus 5 to 10 years later [6].

Based on these observations pregnancy could be interpreted as a stress-test for cardiometabolic health [7]. As stress-test, pregnancy could identify young women with a high risk of future cardiovascular disease. So far, the scientific focus has been to examine differences in cardiometabolic risk factors between women with a history of complicated pregnancies and those with uncomplicated pregnancies [8].

As a stress-test for cardiometabolic health, a complicated pregnancy could identify 'high-risk' women at a young age. This provides opportunities to prevent future cardiometabolic disease. In addition, the complicated pregnancy might boost a woman's motivation to prevent future disease, thus providing a window of opportunity for starting a lifestyle intervention program [9].

Focus group studies have confirmed that women are willing to participate in a lifestyle intervention after pregnancy complications [10–13]. Just communicating the cardiovascular risk does not seem to be effective to achieve lifestyle changes [14]. More intensive lifestyle interventions programs after pregnancies complicated by preeclampsia

* Corresponding author at: Erasmus MC, Department of Obstetrics and Gynecology, Division of Obstetrics and Prenatal Medicine, Dr. Molewaterplein 50, 3015 GE Rotterdam, The Netherlands.
E-mail address: j.j.duvekot@erasmusmc.nl (J.J. Duvekot).

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or fetal growth restriction have not been evaluated yet [15].

The primary aim of this study is to evaluate the feasibility of a lifestyle intervention program after complicated pregnancies associated with an increased risk of future cardiometabolic disease by comparing the proportion of eligible women who completed the intervention to other lifestyle intervention programs. Secondary aim is to test effectiveness of this intervention in improving maternal cardiometabolic risk factors by analyzing change in weight and other cardiometabolic risk factors before and after the intervention.

2. Methods

The Postpartum Rotterdam Appraisal of Cardiometabolic health and Tailored Intervention (PRo-ACTIve) study is a feasibility study to develop and evaluate a postpartum lifestyle intervention program. It was designed as a multicenter, specific pre-post controlled study [16] to develop and evaluate the lifestyle intervention. During the first year of the study a control cohort was considered to be a vital part of the effect evaluation of the intervention.

Women with pregnancies complicated by preeclampsia, fetal growth restriction and/or gestational diabetes mellitus were included between February 2007 and September 2010. Final data collection was at November 2011. Preeclampsia was defined according to ISSHP-criteria [17]: blood pressure of 140/90 mmHg or higher and proteinuria of at least 300 mg/day after a gestational age of at least 20 weeks. Severe preeclampsia was defined according to ACOG-criteria [18]: a blood pressure of 160 mmHg systolic or higher or 110 mmHg diastolic or higher; proteinuria of 5 g or more in a 24-hour urine specimen or dipstick urinalysis of 3+ or greater in two random urine samples collected at least 4 h apart; cerebral or visual disturbances; elevated liver enzymes; thrombocytopenia; fetal growth restriction. Fetal growth restriction was defined according to ACOG-criteria [19]: fetal abdominal circumference < 5th percentile and umbilical artery Doppler with a pulsatility index ≥95th percentile and/or absent or reversed end-diastolic flow on last ultrasonic examination before delivery. Gestational diabetes mellitus was defined according to the 2003 report of the international expert committee of the American Diabetes Association on the diagnosis and classification of diabetes mellitus [20]: a fasting glucose > 6.1 mmol/L or a 2-hour glucose > 7.8 mmol/L after a 75-grams oral glucose tolerance test. Other inclusion criteria were age ≥18 years at time of inclusion, Dutch, Turkish or Moroccan ethnicity and mastery of the Dutch language. Women with pre-pregnancy cardiovascular and/or metabolic conditions, like renal insufficiency, pre-existent hypertension or diabetes mellitus were excluded. Cases of fetal growth restriction due to intra-uterine infection, congenital anomalies or abnormal fetal karyotype were also excluded.

At the Erasmus University Medical Center in Rotterdam (tertiary care hospital) and three secondary care hospitals (Sint Franciscus Hospital, Rotterdam, Maasstad Hospital, Rotterdam and Sint Elisabeth Hospital, Tilburg) women were screened for eligibility and asked to participate in the lifestyle intervention program. At the Amphia Hospital, Breda (secondary care hospital) women were screened for eligibility and subsequently served as the control group. At 5 months postpartum all eligible women were given or sent information about the study together with a letter of invitation to participate. If no response was received within two weeks, women were called on different weekdays. If twice unanswered, women were registered as unable-to-contact. Interested women were invited for a first visit six months postpartum. If during this visit informed consent was obtained, they were registered as participants.

2.1. Study planning

The time-schedule of the study is shown in Fig. 1. The first visit was scheduled at six months postpartum, because we aimed for minimal changes in the measured variables due to ongoing recovery after pregnancy [21], and to minimize the chance that the women were going to be pregnant again during the study period. During the first visit, participants were extensively screened for cardiometabolic risk factors. Anthropometric measures included weight, height, waist- and hip circumference, blood pressure and heart rate. Weight was measured on a digital weighting scale in tenths of kilograms. Blood pressure and heart rate were measured according to the guideline of the British Hypertension Society (2004-BHS IV) [22]. Biochemical measures included high density lipoprotein (HDL) (HDL_Cholesterol plus 3rd generation (HDLC3), Cobas®, Roche Diagnostics), low density lipoprotein (LDL) (LDL-Cholesterol plus 2nd generation (LDL_C), Cobas®, Roche Diagnostics) and total cholesterol (Cholesterol Gen.2 (CHOL2), Cobas®, Roche Diagnostics), HDL/total cholesterol ratio, triglycerides (Triglycerides (TRIGL), Cobas®, Roche Diagnostics), fasting glucose (Glucose HK Gen.3 (GLUC3), Cobas®, Roche Diagnostics), fasting insulin (Insulin, Cobas®, Roche Diagnostics), the Homeostasis Model Assessment (HOMA)2-score [23] as measure of insulin sensitivity and high-sensitive C-reactive protein (CRP) (C-Reactive Protein Gen.3 (CRPL3), Cobas®, Roche Diagnostics). Lifestyle was evaluated by three questionnaires, i.e. for saturated fat-intake the Maastricht Fatlist [24], for physical activity the International Physical Activity Questionnaire (IPAQ) [25] and for smoking habits the short version of the questionnaire of STIVORO (the Dutch anti-smoking association, www.stivoro.nl).

For the participants in the intervention group but not for the controls, three subsequent sessions with a trained lifestyle counsellor (MH) were scheduled between 7 and 10 months postpartum. The intervention consisted of a combination of individual counselling sessions based on the technique of motivational interviewing [26] and the use of a computer-tailored Dutch health education program (www.gezondlevencheck.nl of the Dutch Heart Association). The counselling sessions were preferably face-to-face, but could be taken by telephone if the woman wanted. The computer-tailored health education program and the three questionnaires were completed by the participants before each counselling session. The program provided feedback on the individual scores on the questionnaires. Based on these scores, Individual tailored lifestyle advice was discussed during the sessions and used to set personal lifestyle goals. Progress on the individual goals was discussed, and if applicable adjusted, at each subsequent session.

During the visit at 10 months postpartum the complete screening for cardiometabolic risk factors was repeated with exclusion of the lifestyle questionnaires. Women were encouraged to maintain their lifestyle program.

The final visit of the study was scheduled 13 months postpartum. The complete screening for cardiometabolic risk factors was repeated again, including the lifestyle questionnaires. In addition, women who participated in the lifestyle intervention program but not the controls received questionnaires to evaluate the intervention program (eTable 1 to 3), including the Patient Satisfaction Questionnaire (PSQ-18) [27]. The questions were based on the motivators and barriers reported in previous focus group studies [12,13]. Additionally, a qualitative semi-structured interview was conducted among women in the intervention group but not the controls (eTable 4).

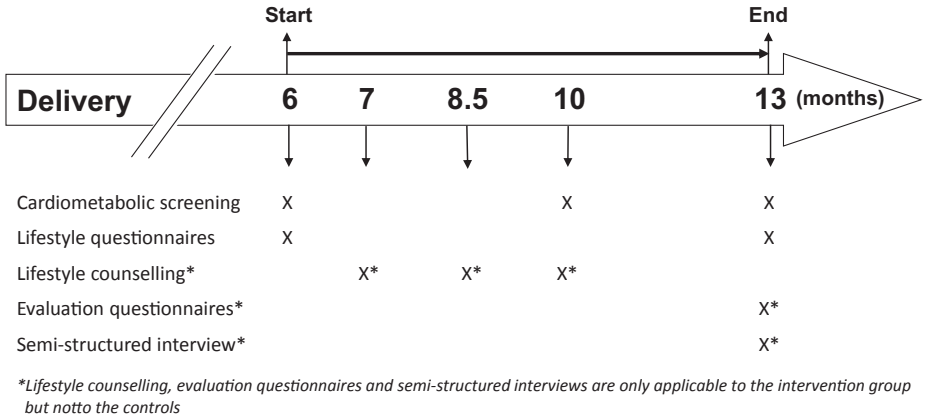

Fig. 1. Time-schedule of study in months after delivery.

2.2. Statistical analysis

Primary outcome of feasibility was the proportion of eligible women who completed the intervention. This best represents how many women who could receive lifestyle intervention were actually motivated to complete the intervention. The higher this proportion, the more feasible it would be to plan larger-scale studies to test effect of postpartum lifestyle intervention after complicated pregnancy and to offer lifestyle intervention – if effective - as usual care. The proportion of eligible women who completed the intervention was defined as:

$$\frac{n_{\text{Completed study}}}{n_{\text{Eligible}}} = Rate_{Participation} * Rate_{Adherence} = Rate_{Participation} * (1 - Rate_{Dropout})$$

Participation rate was defined by the number of women who agreed to participate in the study divided by the total of women who were eligible for participation. Based on other studies in primary lifestyle interventions [28,29], a participation rate of 15% was expected. Adherence was defined by the number of women who attended the 13 months visit divided by the number of women who agreed to participate in the study. Based on other studies in primary lifestyle interventions in fertile women [30] an adherence of 75% was expected. Based on these numbers, the lifestyle intervention was found to be feasible if the proportion of eligible women that completed the intervention was at least 11%.

The primary outcome measure for effectiveness was change in weight before and after the intervention. If the lifestyle intervention would be effective in improving diet and exercise, it would result in weight loss. Weight, as part of Body Mass Index (BMI) is a major risk factor of cardiometabolic disease. A weight loss of 2.7 kg, corresponding with a risk reduction of 50% for diabetes mellitus after 4 years, was considered clinically relevant [31,32]. With mean weight loss in the intervention group of 3.5 kg (SD 5.5), mean weight loss in the control group of 0.8 kg (SD 4.4) [31], α 0.05 (2-sided), β 0.80 and a cases-to-control ratio of 2:1 and an expected drop-out rate of 30% we calculated a sample size of 108 cases and 54 controls. Secondary outcome measures included the other anthropometrical, biochemical and lifestyle measurements.

Based on the intention-to-treat principle, women who became pregnant during the study period were considered as drop-out. Their pregnancy would have had considerable influence on the outcome measures. Women who dropped out for other reasons were approached for the final visit at 13 months postpartum.

Statistical analyses were performed using IBM SPSS Statistics, version 20, International Business Machines Corp©. The weight change between six months postpartum and the end of the study at 13 months postpartum was calculated for each participant in the intervention and control group. Using a linear regression model with weight change as outcome variable, we used the regression coefficient of the case group as effect of the intervention and thus adjusted for normal or 'background' change in the control group that would supposedly have occurred if lifestyle intervention had not been conducted (model 1). We also adjusted for known confounders (baseline weight measure at start at 6 months postpartum, duration of breastfeeding), and significantly different demographic variables between the case and control group (model 2). This analysis was repeated for all secondary outcome measures, where the baseline weight measure was replaced by the baseline measure of the dependent variable. Results are presented as mean change and 95% confidence interval.

During the study we experienced lower adherence in the control group than expected. To compensate, we multiple imputed the 13-month measures for participants who had attended the visits at 6 and 10 months postpartum. The imputation model was based on the mean and standard deviation of participants who attended all visits, with a random generated z-score. Sensitivity analysis was performed by comparing the findings with the analysis without imputation. Three random iterations of imputation were done. Significant findings were only reported, if all 3 iterations showed significant results.

The study was funded by a research grant of ZonMw (61200024). Ethical approval was granted by the institutional review board of the Erasmus University Medical Centre (2006-164) and the participating secondary care hospitals.

2.3. Patient involvement

No patients were involved in setting the research question or the outcome measurements. The Dutch HELLP-foundation participated in the advisory board that advised the research group during design and early recruitment to and conduct of the study. The Dutch HELLP-foundation is a patient advocacy organization, serving women after a hypertensive disorder of pregnancy. Preliminary results were presented at the yearly congress of the Dutch HELLP-foundation on November 2nd 2013. After publication of the study, a summary of the results will be published in the periodical of the HELLP-foundation.

3. Results

Table 1 summarizes the demographics and baseline measures at enrolment. Significant differences between the intervention and control group were observed for ethnicity, marital status, birth weight, frequency of preeclampsia and severe preeclampsia and gestational age at delivery. Furthermore, the groups significantly differed in weight, systolic blood pressure and diastolic blood pressure at baseline measurement.

Table 1
Baseline characteristics of the study participants (n = 206).

	Cases (n = 144)	Controls (n = 62)	p-value
Age (years)	31.6 ± 4.2	30.7 ± 8.8	0.31
Ethnicity			0.03
Dutch	94%(1 3 4)	97%(60)	
Turkish	3%(5)	–	
Moroccan	3%(5)	3%(2)	
Education			0.05
Primary school	8%(12)	2%(1)	
Secondary school	44%(63)	45%(28)	
Higher education	44%(64)	48%(30)	
Unknown	3%(5)	5%(3)	
Married	58%(84)	42%(26)	0.03
Primiparous	70%(1 0 1)	71%(44)	> 0.99
Twin pregnancy	8%(12)	5%(3)	0.56
Birth weight (grams)	2209 ± 1137	2947 ± 868	< 0.001
Breastfeeding (days)	42(0–421)	33(0–465)	0.88
Pregnancy complication			
Preeclampsia	83%(1 2 0)	68%(42)	0.02
Severe (% of preeclampsia)	76%(91)	57%(24)	0.03
IUGR	24%(35)	24%(15)	> 0.99
Gestation diabetes mellitus	15%(21)	26%(16)	0.07
Insulin (% of gestational diabetes mellitus)	52%(11)	31%(5)	0.32
Gestational age at delivery (days)	242 ± 31	263 ± 20	< 0.001
Baseline measures at start of study			
Weight (kg)	81 ± 20	75 ± 16	0.02
BMI (kg/m2)	28.3 ± 6.6	26.4 ± 5.4	0.05
WHR (cm/cm)	0.83 ± 0.06	0.82 ± 0.06	0.14
Systolic blood pressure (mmHg)	120 ± 12	112 ± 13	< 0.001
Diastolic blood pressure (mmHg)	77 ± 10	71 ± 9	0.001
Blood pressure medication	9%(13)	6%(4)	0.78

Numbers in Mean ± SD, Median(Range) or %(n), significance is calculated with ANOVA (means), Mann-Whitney-U(medians) or Chi-Square(%).

3.1. Feasibility

The proportion of eligible women that completed the intervention was 94/407 (23%). Fig. 2 shows the inclusion, participation and adherence to the study. Of the eligible women 41% declined participation (43% in the intervention group, 39% in the control group). The main reported reason for declining participation was lack of time. An additional 27% of the eligible women could not be contacted (21% in the intervention group, 37% in the controls).

Of the 144 women who participated in the intervention group, 28% dropped out between 6 and 10 months postpartum, compared to 18% in the controls. The main reason was again lack of time. An additional 7% drop-out in the intervention group was observed between 10 and 13 months postpartum compared to 31% in the controls. The main reason for drop-out at this time was a next pregnancy

Evaluation questionnaires were completed by 99% of the women who completed the intervention, but by none of the women who dropped out. Reported values are percentages of the responders. The questionnaires and their scores are shown in Appendices 1 to 3.

A strong motivator to participate in the lifestyle intervention was the experienced morbidity in the pregnancy (85%). Other motivators were the perceived increased risk of future disease (60%), risk of recurrence in a next pregnancy (58%) and the possibility to improve personal health (60%). A majority of the responders reported that feedback on their risk profile made them aware of their risk of future disease (80%) and empowered them to improve their lifestyle (84%).

Satisfaction with the lifestyle intervention was high (86%). A majority of the responders was satisfied with the counselling sessions (89%) and use of the computer-tailored health education program (61%). Perceived barriers to participate in the lifestyle intervention were travel distance (33%) and travel time (35%) to the hospital, although 76% thought the hospital to be a good setting for the counselling sessions. A total of 65% agreed that counselling sessions conducted by telephone were a good alternative for face-to-face counselling.

Preferred time between counselling sessions was eight weeks (range 4–16) and preferred average duration of the intervention program was 12 months (range 2–72). Preferred time to start with lifestyle intervention was at three months postpartum (range 0–26).

3.2. Effectiveness

Based on the differences in demographic and baseline measurements in Table 1, we introduced prevalence of preeclampsia and severe preeclampsia, as well as gestational age at delivery into the adjustment model for the effect analysis.

Table 2 shows the changes in the intervention group after lifestyle intervention. Weight was significantly decreased by 4 kg in the intervention group. After adjustment for the change in controls, baseline weight, duration of breastfeeding, preeclampsia and severity of preeclampsia and gestational age at delivery, a significant decrease of 1.9 kg (0.3–3.4) could still be attributed to the lifestyle intervention. BMI and waist-to-hip ratio also significantly decreased, which remained after adjustment. Total and LDL-cholesterol changed significantly in the intervention group. However, after adjustment for the mentioned confounders this change was no longer significant. The change in HOMA2-score in the intervention group became significant after adjustment for the mentioned confounders. Lifestyle habits all showed favorable trends in the intervention group after adjustment for the mentioned confounders except for total fat score, which decrease was significant.

Fig. 3 shows the unadjusted change over time in the intervention and the control groups. All anthropometrical measures (Fig. 3a) show a rebound effect in the intervention group between the 10 and 13 months visit after counselling visits were discontinued. An increase in the use of blood pressure medication was observed in the intervention group, compared to a decrease in the control group.

4. Discussion

We found a high proportion of eligible women who complied with the intervention, and women had a significant weight loss after the intervention, supporting feasibility and effectiveness of lifestyle intervention to improve maternal cardiometabolic risk factors.

4.1. Feasibility

The proportion of eligible women who complied with the intervention was 23%, twice the percentage we assumed (11%). Participation rate in the intervention group was 35%, which was higher than the expected 15%. On the other hand, adherence in the intervention group was 65%, which was lower than the expected 75%.

Participation rate in our study was twice as high as in other primary lifestyle interventions [28,29]. We showed that the pregnancy complication, the perceived increased risk of future disease and the risk of recurrence in a next pregnancy were strong motivators to comply with the study. This supports the idea that a complicated pregnancy opens a window of opportunity for lifestyle intervention. Adherence to the intervention (65%) was lower than expected. The main reason for drop-out was lack of time and was 4 times higher in the first half of the follow-up compared to the second half. Prior research showed that women generally prefer the location of the counselling close to home [11], suggesting that offering the lifestyle intervention in a primary health care setting might increase participation and adherence.

Only two recent studies on lifestyle interventions after metabolic complicated pregnancy reported participation and adherence rates. Both studies aimed to reduce the risk of type 2 diabetes mellitus in

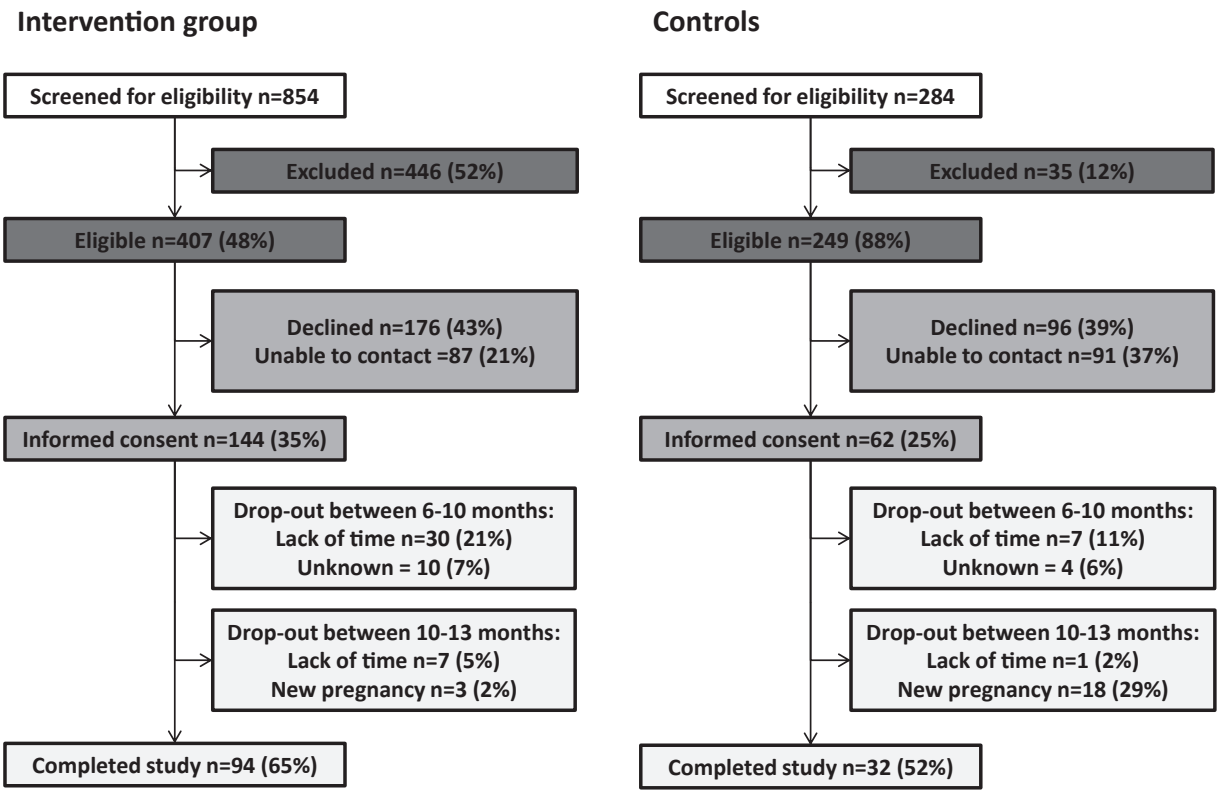

Fig. 2. Flowchart of inclusion, participation and compliance.

Table 2
Effect of lifestyle intervention program.

Parameter	Unit	Intervention group (n = 144)			Effect lifestyle intervention program at 13 months postpartum (95% CI)	
		6 months	13 months	p-value	Model 1*	Model 2#
Weight	kg	81 ± 20	77 ± 19	< 0.001	−1.8 (−3.2 to −0.3)	−1.9 (−3.4 to −0.3)
BMI	kg/m^2	28 ± 7	27 ± 6	< 0.001	−0.8 (−1.3 to −0.3)	−0.9 (−1.4 to −0.3)
Waist-to-hip ratio	cm/cm	0.83 ± 0.06	0.81 ± 0.07	< 0.001	−0.04 (−0.06 to −0.03)	−0.04 (−0.06 to −0.03)
Systolic blood pressure	mm Hg	120 ± 12	117 ± 12	0.09	1.4 (−2.2 to 4.9)	0.7 (−3.1 to 4.4)
Diastolic blood pressure	mm Hg	77 ± 10	75 ± 8	0.10	1.2 (−1.4 to 3.8)	0.8 (−1.9 to 3.6)
Blood pressure medication	%	9%	16%	0.02	15% (4% to 25%)	19% (9% to 28%)
Heart rate	bpm	75 ± 11	71 ± 8	< 0.01	−2.9 (−5.6 to 0.6)	−0.7(−4.1 to 2.7)
Total cholesterol	mmol/L	5.0 ± 0.9	4.6 ± 0.8	< 0.001	−0.2 (−0.4 to 0.1)	−0.2 (−0.4 to 0.1)
LDL-cholesterol	mmol/L	3.1 ± 0.8	2.9 ± 0.7	< 0.001	−0.1 (−0.3 to 0.1)	−0.1 (−0.3 to 0.2)
HDL-cholesterol	mmol/L	1.4 ± 0.3	1.3 ± 0.4	0.50	0.1 (−0.02 to 0.2)	0.1 (−0.02 to 0.2)
HDL/total cholesterol ratio	mol/mol	3.9 ± 1.2	3.7 ± 1.2	0.08	−0.1 (−0.3 to 0.1)	0.1 (−0.3 to 0.2)
Triglycerides	mmol/L	1.3 ± 0.9	1.2 ± 1.0	0.07	−0.04 (−0.2 to 0.1)	−0.02 (−0.2 to 0.2)
Fasting glucose	mmol/L	4.9 ± 0.6	4.9 ± 0.9	0.31	0.1 (−0.2 to 0.3)	0.01 (−0.3 to 0.4)
75 gr-OGTT 2-hour value	mmol/L	5.2 ± 1.2	5.0 ± 1.7	0.54	0.1 (−0.7 to 0.9)	0.1 (−0.9 to 1.0)
Abnormal glucose (DM-2)	%	14%	12%	0.45	−13% (−39% to 12%)	−22% (−45% to 1%)
HOMA2-score	%S	130 ± 106	144 ± 111	0.57	71 (−12 to 154)	59 (18 to 99)
CRP	mmol/L	5.7 ± 9.4	5.7 ± 8.1	0.76	0.2 (−2.6 to 2.9)	0.9 (−2.2 to 4.1)
Urinary protein/creatinine ratio	g/mol	12 ± 23	12 ± 23	0.40	2 (1 to 4)	2 (0.1 to 4)
Total protein in 24-hour urine	g/24 h	113 ± 207	116 ± 159	0.58	27 (−12 to 66)	29 (−3 to 60)
Smoking	%	15%	14%	0.74	−5% (−17% to 7%)	−5% (−16% to 7%)
Physical activity	MET	3672 ± 6554	3830 ± 4240	0.07	2251 (329 to 4174)	844 (−945 to 2634)
Physical activity	steps/day	8290 ± 2508	8658 ± 2099	0.47	452 (−695 to 1599)	302 (−1373 to 770)
Fat intake total	g/day	17.0 ± 5.1	15.1 ± 5.1	< 0.001	−2.9 (−4.8 to −1.0)	−2.9 (−4.6 to −1.2)
Fat intake snacks	g/day	6.2 ± 3.0	5.5 ± 3.0	< 0.01	−0.8 (−2 to −0.4)	−1.0 (−2.0 to 0.04)

* Model 1: adjusted for change in controls.
\# Model 2: adjusted for change in controls, measure at intake, duration of breastfeeding, preeclampsia and severity, gestational age at delivery.

women with a history of gestational diabetes mellitus. The proportions of eligible women that completed the intervention were 43% [33] (intervention was initiated at seven to eight weeks postpartum with a follow-up of 12 months) and 24% respectively (women were recruited within one to three years after their pregnancy with a follow-up of two years) [35]. This might indicate that the window of opportunity for lifestyle intervention after a complicated pregnancy is most present shortly after delivery and disappears over time. Offering lifestyle intervention six weeks after delivery might lead to a higher proportion of women complying to lifestyle intervention.

Of all eligible women in the intervention group, 21% could not be traced. Other postpartum lifestyle studies report similar percentages up

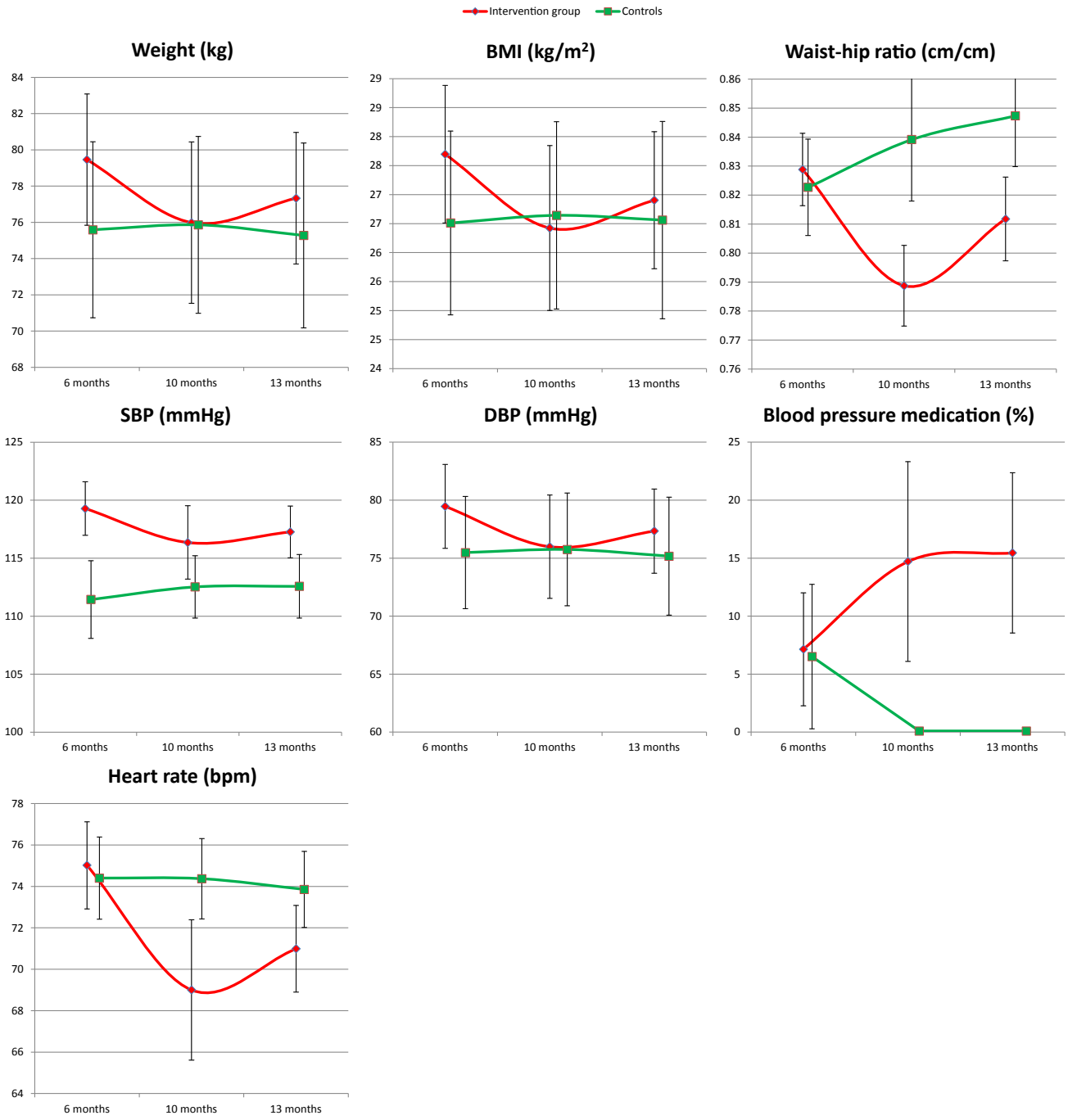

Fig. 3a. Anthropometric changes during the study period.

to 35% [35]. Traceability might be improved shortly after delivery, when women are still in contact with their gynecologist or midwife.

We used a health education program with tailored advice, already on-line available by the Dutch Heart Foundation. The women in our study liked the possibility to complete the computer-tailored health education online in their own time and found its advice easy to understand. It was, however, not specifically tailored to postpartum women and therefore the advice was not always readily applicable. During the counselling sessions, we tailored the advice to the personal situation. New developments like web-based tailored advice for postpartum women [34] as well as the use of new media like smartphones [36,37] are interesting new ways to challenge low participation and adherence in postpartum lifestyle interventions.

Tailoring the start of the intervention to the woman's need might increase participation and adherence rates. Some women who completed the study would in retrospect have preferred to start with the intervention several weeks postpartum. In our study, women were informed at a fixed moment (five months postpartum).

We used the proportion of eligible women who complied with the intervention as measure of feasibility. Other studies focus on dropout rate [30]. However, dropout rate is biased by the motivation of participants and thus by the process of inclusion. By comparing studies by the proportion of eligible women who complied with the intervention, this bias is eliminated.

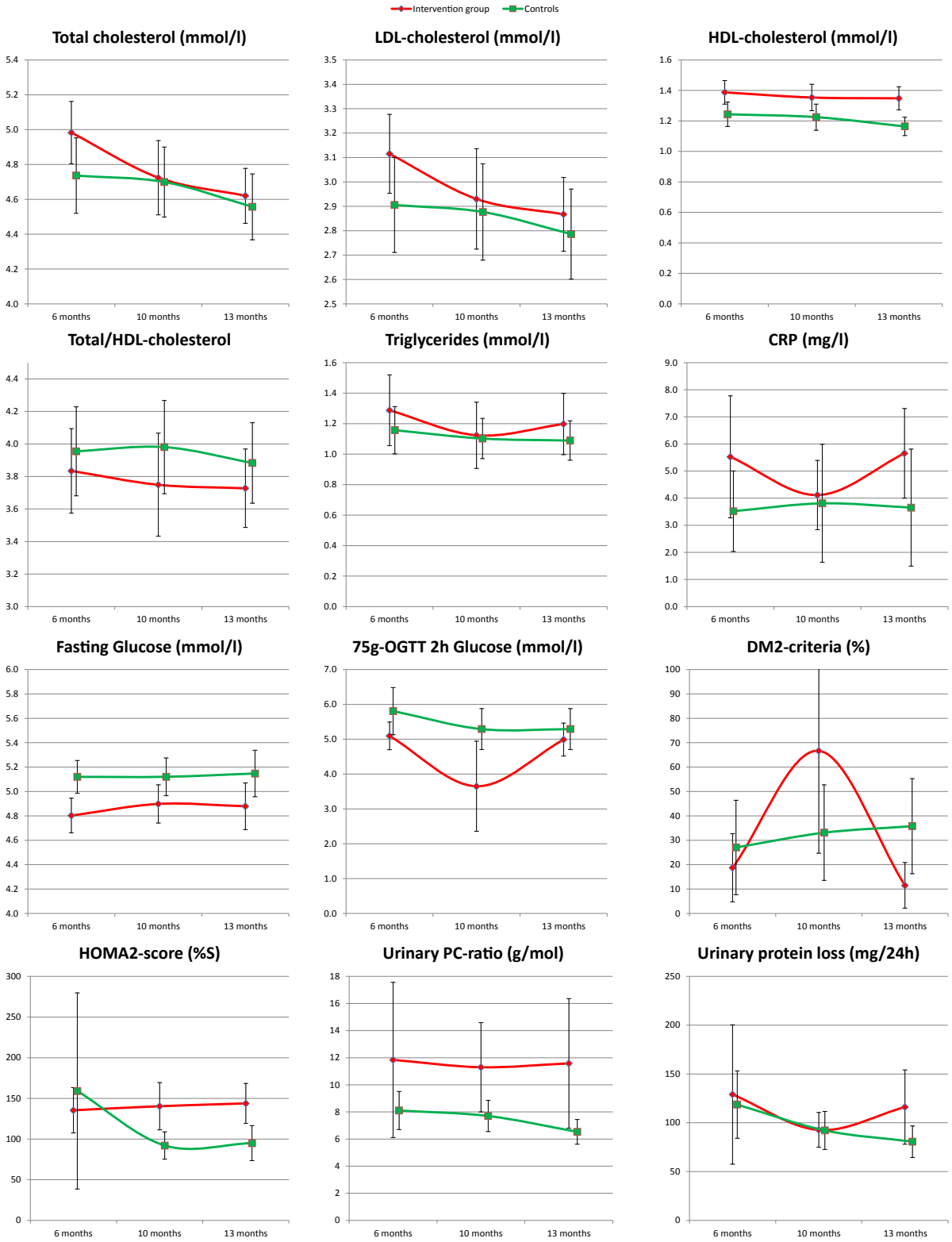

Fig. 3b. Biochemical changes during the study period.

4.2. *Effectiveness*

Women in the intervention group had a significant weight loss that could be attributed to the lifestyle intervention. Also the secondary outcomes BMI, waste-to-hip ratio, HOMA2-score and total fat score significantly improved.

Blood pressure medication was significantly more prescribed in the intervention group than in the control group. An explanation might be that the intervention group more often had preeclampsia and severe preeclampsia, leading to a longer recovery time and a longer need for blood pressure medication up to two years [21]. This was also expressed in a significantly higher baseline blood pressure in the

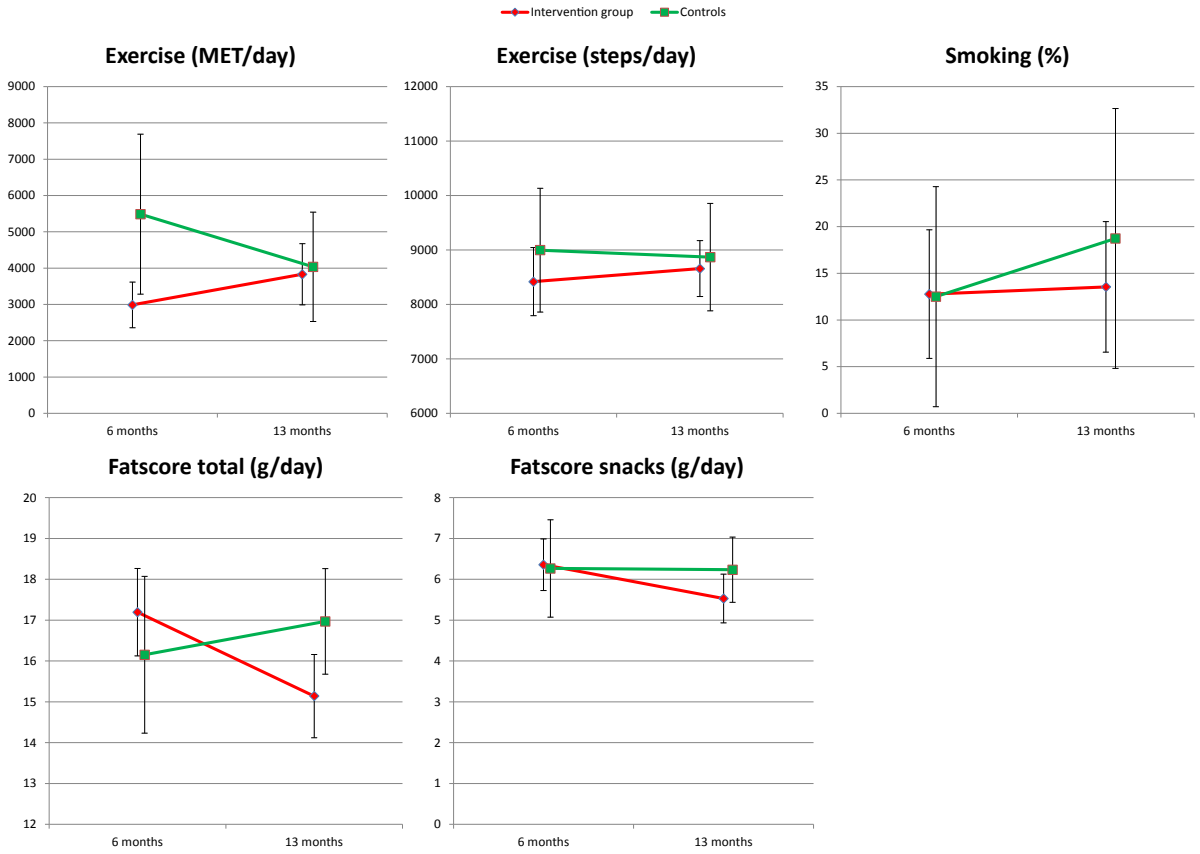

Fig. 3c. Lifestyle changes during the study period.

intervention group. However, after adjustment for these variables the difference remained significant.

The effect of improved cardiometabolic risk factors was achieved between 6 and 10 months. Between 10 and 13 months a loss of effect was observed. Similar rebound effects were observed in other lifestyle intervention studies [38]. There are currently no strategies that effectively address the challenge of promoting sustained long-term behavioral change [39]. Studies with longer follow-up and on-going counselling with promising new strategies [36,37] must show if and how the improved cardiometabolic risk status by postpartum lifestyle intervention can be sustained.

The potential reduction in risk of recurrence of the sustained pregnancy complication was an important motivator for the women participating in the intervention. Lifestyle interventions before or during pregnancy are known to be effective in improving obstetrical outcome [40,41]. If started shortly after a complicated pregnancy, lifestyle intervention might give a larger reduction of the risk of recurrence in the next pregnancy than starting at a next pregnancy or when a next pregnancy is intended. Further studies are needed to evaluate this hypothesis.

We used weight loss as proving effectiveness of lifestyle intervention to reduce cardiovascular risk. Although used by many other lifestyle intervention studies as primary outcome variable to test effectiveness, recently the Look AHEAD study showed that in obese adults with type 2 diabetes during the years after intervention weight was partly regained [42]. Moreover, although weight remained significantly lower in participants to the intervention compared to the controls, no reduction in the rate of cardiovascular events was observed [42]. This undermines the claim of effectiveness of weight reduction on cardiovascular risk and demands for lifestyle intervention studies with follow-up that is long enough to use cardiovascular events as end-point.

4.3. Strengths and weaknesses of the study

A major strength of this study is that it addresses a topic that is frequently being mentioned in preeclampsia research, but has never been studied before.

Another strength of this study is that we used validated questionnaires to evaluate lifestyle habits and tailored them to individual goals in the counselling sessions to make them easily applicable. Finally, we had a high participation rate as compared to other primary lifestyle studies, adding to the generalizability of our results. Although selection bias can never be totally eradicated in primary lifestyle intervention studies, our non-randomized study design and still low participation and adherence rates contributed to this bias.

Some other factors limit generalizability of our results. First we did not have information about the women who declined participation or could not be traced. Whether our results are applicable to these women, is unclear. Second, the majority of the women in the study were Dutch. Whether our results are applicable to other than Dutch women, is unclear.

The criteria we used for gestational diabetes mellitus were based on the 2003 report of the expert committee on the diagnosis and classification of diabetes mellitus [20]. In 2010 new criteria for gestational diabetes mellitus were presented after completion of the HAPO-study [43]. Compared to the inclusion criteria of our study, the fasting glucose threshold is lower (5.1 mmol/l) and the 2-h glucose threshold after a 75-grams oral glucose tolerance test is higher (8.4 mmol/l). This might limit generalizability of our results to women who have been diagnosed with gestational diabetes mellitus based on other criteria than the ones we used.

Current guidelines recommend lifestyle modification and early evaluation for the most high-risk women [44], the provision of

information to patients and primary care clinicians about increased risks in later life [45], assessment of traditional risk factors and to pursue a healthy lifestyle [46], counselling about beneficial effects of a healthy lifestyle and regular (1–5 yearly) cardiovascular assessments [47] or counselling for a healthy lifestyle and cardiovascular assessment at menopause [48]. Our study provides support to recommend the availability of postpartum lifestyle intervention in these guidelines.

5. Conclusion

This study supports the feasibility and effectiveness of a lifestyle intervention after complicated pregnancies. We suggest that clinicians should discuss the possible beneficial effects of lifestyle intervention with women who experienced a cardiometabolic complicated pregnancy at the regular visit 6 weeks postpartum. If women are willing to comply, lifestyle intervention programs should be made available, preferably close to home in a primary health care setting.

We suggest randomized controlled trials, to decrease selection bias, in varied populations with a follow-up period of several years to confirm efficacy and durability of postpartum lifestyle intervention after complicated pregnancies. A longer follow-up is needed to evaluate the effect and durability on cardiometabolic risk. The ideal primary outcome of these studies would be cardiometabolic events, although the low prevalence of these events needs large cohorts. To further decrease selection bias, more research is needed on motivators and barriers of women to increase participation and adherence to lifestyle intervention.

6. Disclosure of interests

None.

7. Contribution to authorship

DB, MH, HR, AF, ES and JD conceived and designed the study. DB, MH, DP and MO participated in recruitment of the women and collected the data. MH conducted the counselling sessions. DB, MH and CL conducted the statistical analyses. DB and MH wrote the manuscript. DB, MH, HR, AF, DP, MO, CL, ES and JD reviewed, edited and contributed to the manuscript. All authors read and approved the final manuscript.

8. Details of ethics approval

Ethical approval was granted on 22nd of August 2006 by the institutional review board of the Erasmus University Medical Centre (2006-164) and the participating secondary care hospitals.

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Appendix A. Supplementary data

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