Chapter 9

A lifestyle intervention in obese women with infertility improved body composition among those who experienced childhood adversity

L. van Dammen[1,2], N.R. Bush[3], S.R. de Rooij[4], C. van de Beek[5], B.W.J. Mol[6], M.A.Q. Mutsaerts[7], A.M. van Oers[1,8], H. Groen[2], A. Hoek[1] and T.J. Roseboom[4,5]

[1] Department of Obstetrics and Gynaecology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
[2] Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
[3] Departments of Psychiatry and Pediatrics, Center for Health and Community, Division of Developmental Medicine, University of California San Francisco, San Francisco, California, USA
[4] Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Amsterdam UMC at the University of Amsterdam, Amsterdam, The Netherlands
[5] Department of Obstetrics and Gynaecology, Amsterdam UMC at the University of Amsterdam, Amsterdam, The Netherlands
[6] Department of Obstetrics and Gynaecology, Monash University, Clayton, Victoria, Australia
[7] Department of General Practice, University Medical Centre Utrecht, University of Utrecht, Utrecht, the Netherlands
[8] Department of Obstetrics and Gynaecology, Medisch Spectrum Twente, Enschede, the Netherlands.

In preparation

Abstract

Importance: Childhood adversity has been linked with higher receptivity to behavioral change interventions in childhood and adolescence, although it is not clear if this higher receptivity is enduring until adulthood.

Objective: We assessed whether the effects of a preconception lifestyle intervention in obese infertile women depended on women's exposure to childhood adversity.
Design, Setting and Participants: Follow-up of a preconception lifestyle intervention RCT (the LIFEstyle study) conducted in the Netherlands. RCT participants were 577 infertile women between 18 and 39 years of age with a body mass index (BMI) ≥ 29 kg/m^2 at time of randomization. The participation at follow-up (median=6 years after randomization) was n=110 (19%).

Intervention: A six-month lifestyle intervention aimed at improving diet and increasing physical activity.

Main outcomes and measures: Body composition and blood pressure was assessed at 0, 6 and 72 months after randomization. During a physical examination 72 months post randomization, we assessed weight, waist and hip circumference, body fat percentage, and blood pressure. Childhood adversity was assessed with the LEC-5 questionnaire. Regression models tested the interaction between childhood adversity and lifestyle intervention randomization group in the prediction of change in body composition and blood pressure.

Results: Among the 110 women in our follow up study, n=65 reported no childhood adverse events, n=28 reported 1 type of childhood adverse events and n=17 reported ≥ 2 types of childhood adverse events. Among women who experienced childhood adversity, after six years the intervention had significantly reduced weight (-10.0 (95% CI -18.5 to -1.5) kg, p = 0.02), BMI (-3.2 (-6.1 to -0.2) kg/m2, p = 0.04) and body fat percentage (-4.5 (95% CI -7.2 to -1.9) p < 0.01). Among women without childhood adversity, the intervention did not affect these outcomes (2.7 (-3.9 to 9.4) kg, p = 0.42), (0.9 (-1.4 to 3.3) kg/m2, p = 0.42) and (1.7 (95% CI -0.3 to 3.7) p = 0.10), respectively).

Conclusion: In obese infertile women, the effect of a life style intervention on body composition after 6-years was modified by childhood adversity. Childhood adversity seems to be an important predictor of long term intervention effectiveness.

Introduction

Obesity is an increasing worldwide problem, with serious negative health effects (1). The first step in the treatment of obesity is lifestyle modification through behavioral change. Lifestyle interventions have shown moderate results in terms of weight loss in short and long term, and explanations for these results are currently lacking (2, 3).

The timing of the lifestyle intervention seems to play an important role in the effectiveness and weight loss results (4). Women are especially receptive to lifestyle advice in the preconception period. For example, smoking cessation rates are almost eight times higher in women with the wish to conceive, compared to women who are not planning a pregnancy (5). The LIFEstyle study examined the effect of a preconception lifestyle intervention in obese infertile women on uncomplicated live birth rates and cardiometabolic health. While no beneficial effect was seen on the primary outcome term vaginal delivery, the lifestyle intervention proved to be successful in reducing body weight and blood pressure and led to an improved metabolic profile six months after the start of the intervention (6).

Besides the importance of timing of the intervention, individual characteristics may also be important in intervention effectiveness. Research suggests that the lack of consistent effects of behavioral interventions on behavior change might be partially explained by a difference in history of childhood adversity between participants, such that childhood adversity may render individuals more susceptible to the environment (7-9). Individuals exposed to childhood adversity may possess internal strengths and coping skills making them more receptive to interventions aiming at behavior change in childhood and adolescence (10). However, the role of childhood adversity in lifestyle intervention effectiveness in reducing weight has not been studied yet.

We hypothesized that women who had experienced childhood adversity lost more weight in response to a lifestyle intervention, compared to those without exposure to childhood adversity.

Methods

LIFEstyle study

The LIFEstyle study, a randomized controlled trial (RCT) was carried out in 23 hospitals throughout the Netherlands from 2009 to 2012. A detailed description of the lifestyle intervention and the primary and secondary outcomes can be found in the study protocol (11). Participants were infertile women between 18 and 39 years of age with a body mass index (BMI) ≥ 29 kg/m2. Women with premature ovarian insufficiency, endocrinopathy, severe endometriosis, untreated preexisting hypertension, or women with a history of hypertension related pregnancy complications were not eligible for participation. In total 577 women provided written informed consent, of whom 290 were assigned to a six-month lifestyle intervention aimed at improving diet and physical activity. The control group did not receive a lifestyle intervention and could start with infertility treatment as indicated. Participants were approximately 30 years old at time of randomization, and had a mean BMI of 36 kg/m^2 (range = 29-51). Participants in the lifestyle intervention group were coached by trained nurses through six face-to-face sessions and four telephone calls. The intervention aimed at 5-10% weight loss or a BMI ≤ 29 kg/m^2. An individualized behavioral modification plan was made. Intervention coaches counselled patients about lifestyle leading to overweight and infertility, and formulated a 'patient contract', together with the patient, describing her individual goals. If the participant reached 5-10% weight loss or BMI ≤ 29 kg/m^2 or after the six month intervention period, she could start with infertility treatment as indicated.

In non-pregnant participants body weight (kg), height (cm), waist- and hip circumference (cm), and blood pressure (mmHg, in seated position) was measured by research nurses six months post randomization. Fasting blood samples were collected and levels of glucose, triglycerides and high-density lipoprotein cholesterol (HDL-C) were obtained from biochemical analyses performed in the laboratory from the University Medical Center Groningen. Polycystic ovary syndrome was diagnosed at baseline according to Rotterdam 2003 criteria (12).

The primary outcome of the LIFEstyle study was the vaginal birth of a healthy singleton after ≥ 37 weeks of gestation, of which the results were published in 2016, showing similar rates in the intervention and control group (13). The effects of the lifestyle intervention on weight loss and cardiometabolic health were published in 2018 (6). In the short-term (six months after randomization), the lifestyle intervention led to a significant lower body weight, decreased waist- and hip circumference, blood pressure, a lower prevalence of metabolic syndrome and improved physical quality of life (6).

Follow-up visit

A follow-up visit of the LIFEstyle study was conducted after a median of 6.0 years (IQR 5.2 to 6.7) after randomization (14). In total 564 women were eligible for participation in this follow-up study, and of 550 women the latest contact information could be determined. These women were asked if they were willing to fill out questionnaires and participate in physical measurements.

Questionnaire

The 17-item Life Events Checklist for DSM-5 (LEC-5) was used to evaluate adverse events during childhood and adolescence. This questionnaire is characterized by adequate psychometric properties, based on previous research (15). In order to establish childhood adversity (between birth and 18 years of age), this questionnaire was modified slightly. For events that a person experienced or witnessed, the year in which the event took place was asked. This year was later used to calculate age at exposure. A total score was calculated with all items summed (if a woman reported any type of event occurring once or more before the age of 19, she received a score of one for experiencing that type of event during childhood). The scores were categorized in two different ways. For the first score, *the dichotomous childhood adversity score*, women who did not experience any childhood adversity were coded as zero, and women who experienced one or more types of childhood adverse events received a score of one. The second score, *the childhood adversity groups score*, divided women into three categories: a group that did not experience any type of event; a group that experienced one type of event; and a group that experienced two or more types of events. The second score provides additional information regarding exposure to several types of events, as a measure of severity of exposure.

Physical measurements

All women were examined in a mobile research vehicle, parked near the participant's house, as part of the follow-up. Weight, height, waist- and hip-circumference were measured twice, and a third time if there was a difference of either > 0.5 kg or > 0.5 cm for weight and height respectively, or > 1 cm for waist- and hip-circumference. Seated blood pressure was measured three times, after a five-minute resting period. Mean values were calculated based on all available measurements. Body fat percentage was measured with arm-to-leg bioelectrical impedance analysis using the Bodystat 1500 (Bodystat Ltd, Isle of Man, UK). Fasting blood samples were collected by trained nurses. Levels of glucose, triglycerides and HDL-C were obtained through biochemical analyses at the AMC Clinical Chemistry Laboratory.

The presence of metabolic syndrome six months and six years post randomization was assessed with cut-off values for obesity, and cut-off values or medication use for hyperglycemia, dyslipidemia and hypertension, based on the US National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) criteria (16).

Statistical analyses

Participant characteristics were analyzed with ANOVA tests, *t*-tests, chi-square tests and Kruskal-Wallis tests, as appropriate. Baseline differences of participants and non-participants in the follow-up analyses were assessed with *t*-tests, Fisher-Freeman-Halton tests and chi-square tests. The change in weight, BMI, waist- and hip-circumference and blood pressure was calculated, and an interaction term was calculated as the product of randomization group and the dichotomous childhood adversity score. The difference between the intervention and control group in changes in body composition and blood pressure were assessed with univariate regression models, with adjustment for baseline levels. Univariate regression models were used to assess the effect of the interaction between randomization group (intervention and control group) and dichotomous childhood adversity score (no adversity versus any adversity), covarying for the baseline measurement of that outcome. The regression analyses were also carried out separately for the intervention and control group and dichotomous childhood adversity groups, for each outcome, to assess the main effects. These univariate regression models were repeated with childhood adversity categorized in three groups (no adversity, 1 type of event and ≥ 2 types of events).

Results

The baseline differences between participants and those who did not participate in the follow-up analyses are described in Table 1. Results showed that participants were more often Caucasian, compared to non-participants, no other differences were observed. A total of 121 women provided written informed consent; of these, six women declined to participate and, five women had no physical examination, thus complete data was available for 110 women (Supplementary Figure 1). In total, n=65 women (n=34 intervention group, n=31 control group) reported no childhood adverse events, n=28 (n=10 intervention group, n=18 control group) reported 1 type of adverse event, and n=17 (n=6 intervention group, n=11 control group) reported 2 or more types of adverse events during childhood. The most common adverse event was a transportation accident (n=18) including car, boat, train and plane accidents. Physical assault (n=11) was the second most common reported event, followed by sexual assault (n=8), unwanted sexual experiences (n=8), life threatening illness/injury (n=7), severe illness/injury (n=6) and sudden unexpected death of someone close (n=6). Table 2 shows the participant characteristics, first divided into childhood adversity exposure groups, and then divided by randomization group. Women with a history of childhood adversity were significantly younger compared to women without childhood adversity. No differences were observed in ethnicity and education level, smoking status, baseline polycystic ovary syndrome diagnosis, number of women who do not have a child and BMI between childhood adversity groups or randomization groups.

Intervention effects six months after randomization and childhood adversity

Among the women who participated in the follow-up, weight change between baseline and six months after randomization was not different between the intervention and control group (-1.78 (95% CI -4.83 to 1.26) p = 0.24). Similarly, no differences were observed between the groups for BMI, waist- and hip circumference, systolic and diastolic blood pressure (-0.53 (95% CI -1.61 to 0.56) p = 0.33), (-1.13 (95% CI -5.85 to 3.58) p = 0.63), (0.86 (95% CI -5.12 to 6.84) p = 0.77), (-3.71 (95% CI -9.59 to 2.17) p = 0.21) and (-0.50 (95% CI -5.75 to 4.75) p = 0.85), respectively. The prevalence of metabolic syndrome was similar for the intervention and control group six months post randomization (OR=1.16 (95% CI 0.19 to 8.36) p = 0.81). The univariate regression models showed that the intervention effect on body composition outcomes six months after randomization differed for women with and without childhood adversity (Table 3). Women exposed to childhood adversity had no significantly different BMI, waist- and hip circumference,

systolic blood pressure or odds for metabolic syndrome than women not exposed to childhood adversity, although the mean values were consistently lower.

Intervention effects six years after randomization

Weight change between baseline and six years after randomization across the entire group that participated in the follow-up, was not different between the intervention and control group (-1.79 (95% CI -3.36 to 6.95) $p = 0.49$), there was also no difference between groups in change from baseline to six years after randomization in BMI (-0.60 (95% CI -1.22 to 2.42) $p = 0.51$). Change from baseline to six years after randomization in waist- and hip circumference was not different between the intervention and control group, (-0.78 (95% CI -3.43 to 4.98) $p = 0.72$) and -0.51 (95% CI -3.00 to 4.03) $p = 0.77$ respectively). Similarly, change in systolic- and diastolic blood pressure was not different between the intervention and control group, (-0.20 (95% CI -5.46 to 5.05) p = 0.94) and -0.54 (95% CI -4.03 to 2.97) $p = 0.76$, respectively). Body fat percentage six years after randomization was not different between the intervention and control group (-0.73 (95% CI -2.38 to 0.92) $p = 0.38$), nor was the prevalence of metabolic syndrome six years after randomization (OR=0.41 (95% CI 0.13 to 1.27) $p = 0.12$).

Intervention effects six years after randomization and childhood adversity

The univariate regression models showed that the intervention effect six years after randomization on body composition outcomes differed significantly for women with and without childhood adversity. The intervention led to weight loss six years post randomization among women who experienced childhood adversity (-10.0 (95% CI -18.5 to -1.5) kg, $p = 0.02$), but not among those without childhood adversity (2.7 (95% CI -3.9 to 9.4) kg, $p = 0.42$), (interaction effect adversity*group coefficient for weight change: (95% CI): -12.7 (-23.3 to -2.1) kg, $p = 0.02$). The intervention led to a significantly lowered BMI six years post randomization among women who experienced childhood adversity (-3.2 (95% CI -6.1 to -0.2) kg/m^2, $p = 0.04$), but not among those without childhood adversity (0.9 (95% CI -1.4 to 3.3) kg/m^2, $p = 0.42$) (interaction effect adversity*group coefficient for BMI change: (95% CI): -4.3 (-8.1 to -0.6) kg/m^2, $p = 0.02$). The intervention significantly lowered waist circumference six years post randomization among women who experienced childhood adversity (-7.9 (95% CI -15.1 to -0.7) cm, $p = 0.03$), but not among those without childhood adversity (1.7 (95% CI -3.7 to 7.1) cm, $p = 0.53$) (interaction effect adversity*group coefficient for waist circumference change: (95% CI): -7.7 (-16.5 to 1.1) cm, $p = 0.09$). Similar results were observed for lowered hip circumference in women with childhood adversity (-6.8 (95% CI -12.6 to -1.0) cm, $p = 0.02$), but not among women without childhood

adversity (2.7 (95% CI -1.8 to 7.2) cm, p = 0.23) (interaction effect adversity*group coefficient for hip circumference change: (95% CI): -9.3 (-16.5 to -2.1) cm, p = 0.01), and lower body fat percentage among women with childhood adversity (-4.5 (95% CI -7.2 to -1.9) $p < 0.01$), compared to women without childhood adversity (1.7 (95% CI -0.3 to 3.7) p = 0.10) (interaction effect adversity*group coefficient for body fat percentage: (95%): -6.2 (-9.4 to -2.9) $p < 0.01$). In Figures 1-3 the results of the interaction analyses are shown with childhood adversity groups (no adversity, 1 type of event and ≥ 2 type of events), with similar results as described above, with childhood adversity as a dichotomous exposure variable.

There was no interaction effect between childhood adversity and randomization group on systolic and diastolic blood pressure, and metabolic syndrome six years post randomization (all p's ≥ 0.05). All analyses were adjusted for age, since women with childhood adversity exposure were younger compared to women without childhood adversity exposure. The adjustment did not alter the results (data not shown).

Discussion

In this study, we found that a lifestyle intervention was more effective in improving body composition six years after randomization in women who experienced childhood adversity, compared to women without childhood adversity. No differences in body composition changes were observed between the intervention and control group, without taking childhood adversity into account. This suggests childhood adversity may be an important factor in lifestyle intervention success.

To our knowledge, this is the first study in which a lifestyle intervention in women was found to be more effective in improving body composition among those who experienced childhood adversity. Previous research suggests childhood adversity may be seen as a toughening experience(17), and has often been linked to resilience (10, 18). There are several other factors that have been linked to lifestyle intervention success in reducing weight, including high socioeconomic status, high motivation to change lifestyle and not having received previous dietetic support (19, 20). Our results indicate childhood adversity may also play a role in intervention effectiveness in improving body composition. Childhood adversity is associated with impaired mental and physical health (21), including obesity (22). In order to reduce the risk of cardiovascular disease associated with both childhood adversity and obesity (21, 23), lifestyle interventions to reduce weight are important, and may be especially effective for those who are receptive to interventions.

Although the lifestyle intervention improved body composition among women who were exposed to childhood adversity, no effects were observed for blood pressure or metabolic syndrome six years after randomization. The small sample size in these analyses led to low statistical power, reducing the certainty of the observed results. Further follow-up could shed light on the potential long-term effects of improved body composition after lifestyle intervention on cardiovascular risk in women exposed to childhood adversity.

The analyses with *the dichotomous childhood adversity score* and the childhood adversity groups score showed the same results regarding body composition. These results indicate that a lifestyle intervention is effective in improving body composition in women exposed to childhood adversity, and even in those exposed to several types of childhood adverse events, suggesting these intervention effects are not only present for women with moderate childhood adversity exposure.

A limitation to the findings reported here was attrition. Roughly 20% of the women who were randomized participated in the follow-up, which reduced statistical power. Furthermore, there was selective participation of Caucasian women, which

may have influenced the results, and limit the generalizability of our results to other ethnicities. Furthermore, childhood adversity was assessed six years after randomization, and recall bias may have led to an overestimation or underestimation of childhood adversity, which has been suggested by previous research (24). However, reports of childhood adversity have shown to be relatively stable over time and reliable in adulthood (25). Another limitation concerns our inability to explore potential pathways through which childhood adversity was related to intervention effectiveness. Because of the small sample size, mediation analyses to unravel potential mechanisms through which childhood adversity affected intervention effectiveness were not possible. Such mechanisms could be resilience, improved diet or increased physical activity as a result of the lifestyle intervention. The small sample size and subsequent reduced power in these analyses assessing the effect of the intervention on body composition six months after the start of the intervention should be taken into account when interpreting these results. No statistically significant differences were observed on body composition outcomes six months after the start of the intervention between women who were exposed to childhood adversity and those who were not exposed to childhood adversity. The direction of the non-significant differences was in line with the statistically significant differences observed six years post randomization, suggesting lifestyle intervention in women exposed to childhood adversity may also be effective in improving body composition in the shorter term. Further research is necessary to confirm our findings.

Our results show that women who were exposed to childhood adversity improved their body composition six years after a lifestyle intervention, whereas women who were not exposed to childhood adversity did not improve their body composition. Future research should consider childhood adversity as a possible determinant of intervention effectiveness.

Acknowledgements

We thank all women who participated in the LIFEstyle study and the follow-up visit. We thank all students, PhD students, research nurses, and other research personnel involved in the LIFEstyle study and follow-up visit.

Source of Funding and Conflicts of Interest: This research was supported by The Netherlands Organization for Health Research and Development (50-50110-96-518), the Dutch Heart Foundation (Grant number: 2013T085), and the European Commission (Horizon2020 project 'DynaHealth', 633595). The department of obstetrics and gynaecology from the UMCG receives an unrestricted educational grant from Ferring Pharmaceutical BV the Netherlands, unrelated to the present study. The authors report no conflicts of interest.

References

1. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766-81.
2. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation. 2010;121(4):586-613.
3. Wu T, Gao X, Chen M, van Dam RM. Long-term effectiveness of diet-plus-exercise interventions vs. diet-only interventions for weight loss: a meta-analysis. Obes Rev. 2009;10(3):313-23.
4. Messina J, Campbell S, Morris R, Eyles E, Sanders C. A narrative systematic review of factors affecting diabetes prevention in primary care settings. PLOS ONE. 2017;12(5):e0177699.
5. McBride CM, Emmons KM, Lipkus IM. Understanding the potential of teachable moments: the case of smoking cessation. Health Educ Res. 2003;18(2):156-70.
6. van Dammen L, Wekker V, van Oers AM, et al. Effect of a lifestyle intervention in obese infertile women on cardiometabolic health and quality of life: A randomized controlled trial. PLOS ONE. 2018;13(1):e0190662.
7. Belsky J, van Ijzendoorn MH. What works for whom? Genetic moderation of intervention efficacy. Dev Psychopathol. 2015;27(1):1-6.
8. Obradovic J, Bush NR, Stamperdahl J, Adler NE, Boyce WT. Biological sensitivity to context: the interactive effects of stress reactivity and family adversity on socioemotional behavior and school readiness. Child Dev. 2010;81(1):270-89.
9. Boyce NRBWT. Differential Sensitivity to Context: Implications for Developmental Psychopathology. Developmental Psychopathology2016.
10. Soleimanpour S, Geierstanger S, Brindis CD. Adverse Childhood Experiences and Resilience: Addressing the Unique Needs of Adolescents. Academic Pediatrics. 2017;17(7, Supplement):S108-S14.
11. Mutsaerts MAQ, Groen H, ter Bogt NCW, et al. The LIFESTYLE study: costs and effects of a structured lifestyle program in overweight and obese subfertile women to reduce the need for fertility treatment and improve reproductive outcome. A randomised controlled trial. BMC Women's Health. 2010;10(1):22.
12. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertility and Sterility. 2004;81(1):19-25.
13. Mutsaerts MAQ, van Oers AM, Groen H, et al. Randomized Trial of a Lifestyle Program in Obese Infertile Women. New England Journal of Medicine. 2016;374(20):1942-53.
14. van de Beek C, Hoek A, Painter RC, et al. Women, their Offspring and iMproving lifestyle for Better cardiovascular health of both (WOMB project): a protocol of the follow-up of a multicentre randomised controlled trial. BMJ Open. 2018;8(1).
15. Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric properties of the life events checklist. Assessment. 2004;11(4):330-41.
16. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and Management of the Metabolic Syndrome. An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. 2005;112(17):2735-52.
17. Dienstbier RA. Mutual impacts of toughening on crises and losses. Life crises and experiences of loss in adulthood. Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc; 1992. p. 367-84.
18. Masten AS, Best KM, Garmezy N. Resilience and development: Contributions from the study of children who overcome adversity. Development and Psychopathology. 1990;2(4):425-44.

19. Govil SR, Weidner G, Merritt-Worden T, Ornish D. Socioeconomic status and improvements in lifestyle, coronary risk factors, and quality of life: the Multisite Cardiac Lifestyle Intervention Program. Am J Public Health. 2009;99(7):1263-70.

20. Karsten MDA, van Oers AM, Groen H, et al. Determinants of successful lifestyle change during a 6-month preconception lifestyle intervention in women with obesity and infertility. European Journal of Nutrition. 2018.

21. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the Adverse Childhood Experiences (ACE) study. Am J Prev Med. 1998;14.

22. Greenfield EA, Marks NF. Violence from parents in childhood and obesity in adulthood: Using food in response to stress as a mediator of risk. Social Science & Medicine. 2009;68(5):791-8.

23. Burke GL, Bertoni AG, Shea S, et al. The Impact of Obesity on Cardiovascular Disease Risk Factors and Subclinical Vascular Disease: The Multi-Ethnic Study of Atherosclerosis. Archives of internal medicine. 2008;168(9):928-35.

24. Colman I, Kingsbury M, Garad Y, et al. Consistency in adult reporting of adverse childhood experiences. Psychol Med. 2016;46(3):543-9.

25. Yancura LA, Aldwin CM. Stability and change in retrospective reports of childhood experiences over a 5-year period: findings from the Davis Longitudinal Study. Psychol Aging. 2009;24(3):715-21.

Table 1. Baseline characteristics participants and non-participants in the analyses.

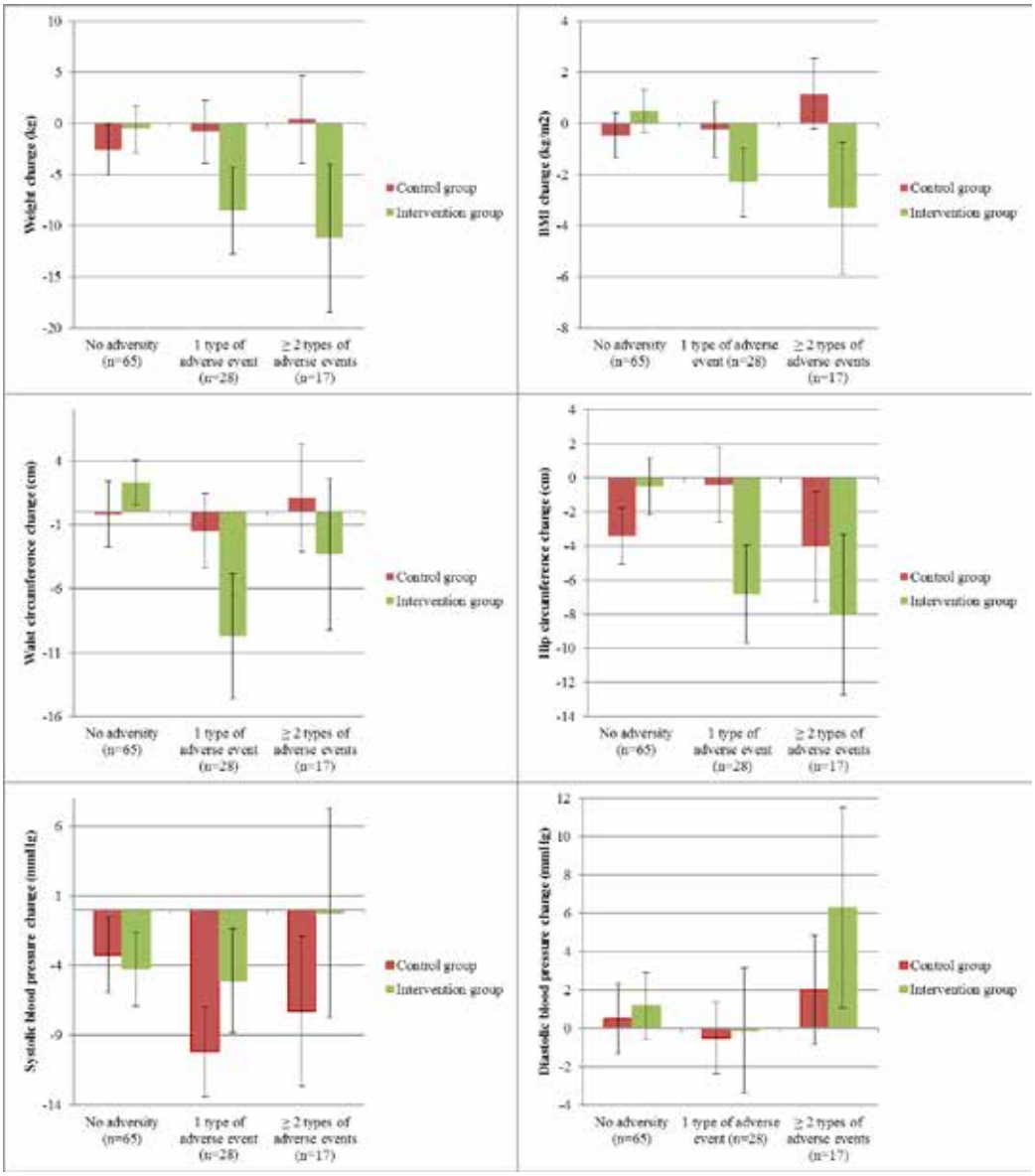
	Participants (n=110)	**Non-participants in the analyses (n=464)**	***p* value**
Age (mean (SD))	30.3 (4.1)	29.6 (4.7)	0.10
Race (Caucasian, n (%))	104 (94.5)	398 (85.8)	0.01
Current smoker (n (%))	25 (22.9)	111 (24.1)	0.79
Education level (n (%))			0.30
- Primary school	1 (1.0)	26 (5.9)	
- Secondary education	25 (23.8)	106 (23.9)	
- Intermediate vocational education	52 (49.5)	214 (48.2)	
- Advanced vocational education or university	27 (25.7)	98 (22.1)	
Polycystic ovary syndrome (n (%))	43 (39.1)	158 (34.2)	0.33
Weight in kg (mean(SD))	103.3 (12.1)	103.2 (13.3)	0.94
BMI kg/m2 (mean(SD))	35.7 (3.0)	36.1 (3.5)	0.23
Waist circumference in cm (mean(SD))	106.7 (10.1)	108.3 (9.2)	0.10
Hip circumference in cm (mean(SD))	124.0 (8.3)	125.3 (8.9)	0.16
Systolic blood pressure in mmHg (mean(SD))	125.4 (12.4)	126.6 (14.3)	0.42
Diastolic blood pressure in mmHg (mean(SD))	80.6 (7.6)	79.6 (9.4)	0.29

Table 2. Characteristics participants (N=110).

	No childhood adversity (n=65)	Childhood adversity (n=45)	p value	Intervention group (n=50)	Control group (n=60)	p value
Age (mean (SD))	36.7 (4.3)	34.7 (4.1)	0.02	35.8 (4.5)	35.9 (4.2)	0.89
Race (Caucasian, n (%))*	59 (91)	45 (100)	0.08	48 (96)	56 (93)	0.54
Current smoker (n (%)	7 (11.9)	9 (20.9)	0.42	7 (12.7)	9 (19.1)	0.66
Education level (n (%))			0.35			0.47
- Primary school	0 (0)	2 (4.7)		0 (0)	2 (3.6)	
- Secondary education	11 (18.6)	10 (23.3)		12 (25.5)	9 (16.4)	
- Intermediate vocational education	30 (50.8)	20 (46.5)		23 (48.9)	27 (49.1)	
- Advanced vocational education or university	18 (30.5)	11 (25.6)		12 (25.5)	17 (30.9)	
Polycystic ovary syndrome (n (%))*	26 (40.0)	17 (37.8)	0.81	20 (40.0)	23 (38.3)	0.86
No child (n(%))	12 (21.1)	8 (18.6)	0.76	12 (26.7)	8 (14.5)	0.13
Body Mass Index in kg/m² (mean (SD))*	35.6 (3.1)	35.9 (2.9)	0.61	35.5 (2.9)	35.9 (3.2)	0.57

* Measured at baseline.

Figure 1. Regression results of the association between weight, BMI, waist- and hip circumference and systolic- and diastolic blood pressure change from baseline to six years post randomization and childhood adversity for the control and intervention group, adjusted for baseline weight or BMI, waist- or hip circumference or systolic- and diastolic blood pressure.



Supplementary Figure 1. Flowchart participants in the LIFEstyle study and follow-up

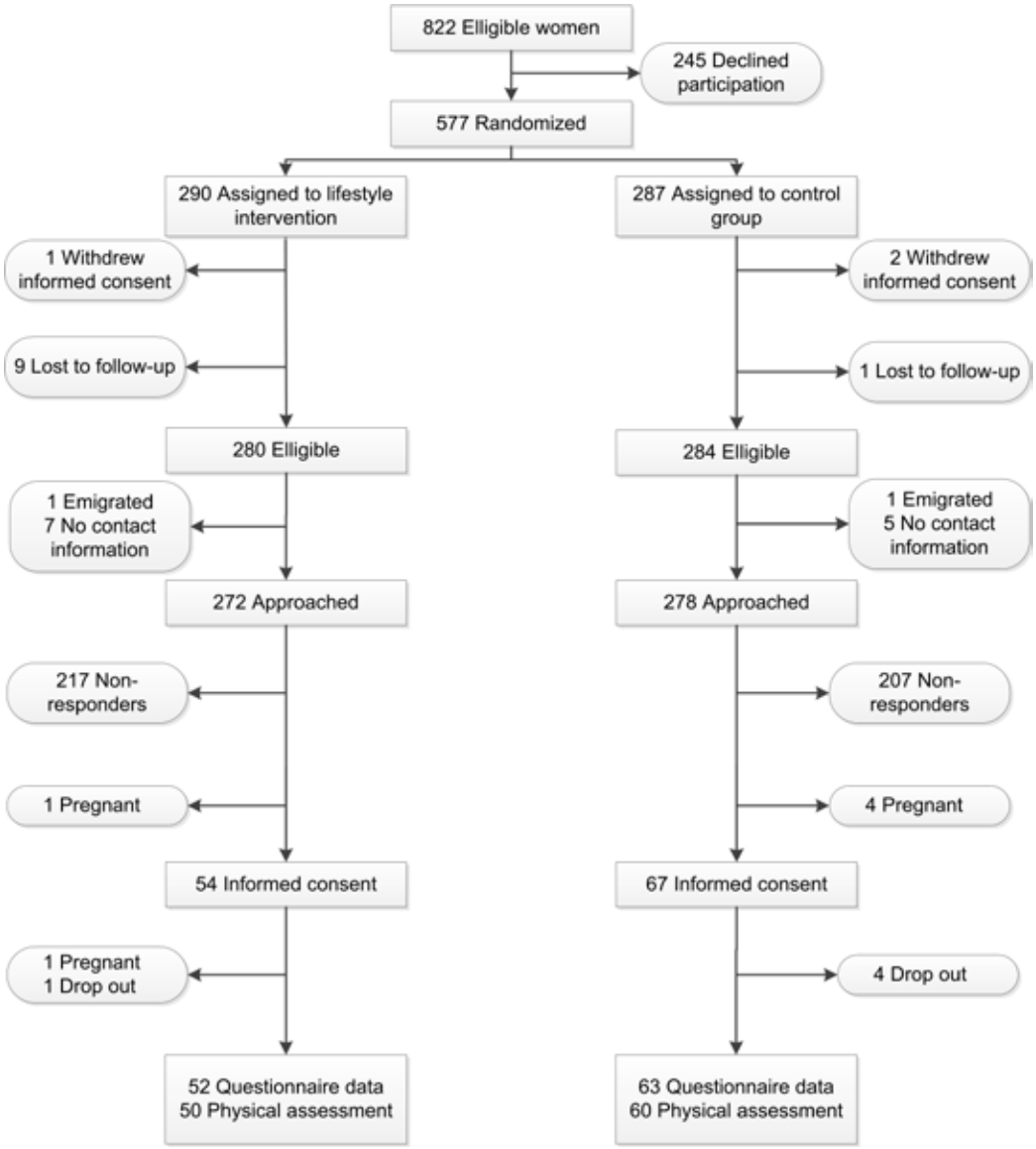


Table 3. Differences between childhood adversity exposure groups in body-composition and blood pressure change from baseline to 6-months post randomization.

	Intervention group			Control group		
	No childhood adversity (n=16)	**Childhood adversity (n=5)**	***p* value**	**No childhood adversity (n=18)**	**Childhood adversity (n=13)**	***p* value**
Δ weight baseline-six months	-4.1 (7.7)	-4.0 (5.9)	0.96	-1.3 (3.5)	-3.3 (3.4)	0.16
Δ BMI baseline-six months	-1.0 (2.7)	-1.8 (2.3)	0.66	-0.4 (1.2)	-1.1 (1.1)	0.09
Δ waist-circumference baseline-six months	-2.1 (8.4)	-4.0 (10.8)	0.71	-0.9 (9.4)	-1.0 (4.3)	0.96
Δ hip-circumference baseline-six months	-17.6 (12.1)	-20.5 (11.4)	0.75	-17.9 (7.6)	-20.8 (11.5)	0.61
Δ SBP baseline-six months	-2.5 (11.3)	-7.8 (14.3)	0.49	-4.0 (13.2)	-2.1 (11.0)	0.25
Δ DBP baseline-six months	-2.7 (6.9)	0.2 (8.7)	0.48	-1.9 (9.5)	-1.0 (8.7)	0.83
Odds ratio metabolic syndrome*	0.51 (95% CI 0.02 to 15.03)		0.70	3.40 (95% CI 0.31 to 36.91)		0.32

*Odds ratio six months post randomization adjusted for baseline prevalence.