

Long-term outcomes following completion of a structured nutrition and exercise lifestyle intervention program for patients with metabolic syndrome

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Introduction: Metabolic syndrome is associated with an increased risk of cardiovascular disease and multiple other chronic health conditions. Studies have demonstrated the effectiveness of structured diet and exercise programs to improve the components of metabolic syndrome. The durability of these benefits after program completion is unclear. The aim of this study was to evaluate trends in cardiovascular risk factors 12 months post completion of a 12- or 24-week structured lifestyle intervention program.

Methods: Individuals with metabolic syndrome were referred to the Metabolic Fitness program, a 12- or 24-week lifestyle intervention program consisting of weekly exercise and nutrition education sessions. Patients were assessed at baseline, 12 weeks, and 24 weeks for those in the 24-week program. Data collection included weight, body mass index, waist circumference, body composition percentage, sBP, dBP, fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol. Unstructured follow-up data were obtained by retrospective chart review for up to 12 months post program completion.

Results: Two-hundred twenty-five patients were enrolled in the 12-week program and 121 in the 24-week program. At the conclusion of the 12-week program, patients showed significant improvement in sBP and dBP. At the conclusion of the 24-week program, patients showed significant improvement in body mass index, weight, sBP, dBP, fasting blood glucose, total cholesterol, and triglycerides. However, 12 months after program completion, while the majority of parameters were still improved compared with baseline, only change in low-density lipoprotein cholesterol remained significantly improved compared with the end of 12-week program, and sBP had increased back above baseline in both programs.

Conclusion: Patients with metabolic syndrome participating in a structured lifestyle intervention program show significant improvement in their cardiovascular risk and metabolic profile at program completion. The durability of these improvements appears to wane over time, however, stressing the need for programs that can facilitate maintenance of long-term behavior change.

Keywords: metabolic syndrome, lifestyle interventions, obesity

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Introduction

As obesity has increased in the United States, metabolic syndrome is becoming an increasingly important issue in healthcare. The prevalence in the United States is estimated to be at least 30% of the general population and even higher in older and minority populations.¹⁻³ Metabolic syndrome is associated with an increased risk of cardiovascular disease, including hypertension, stroke, myocardial infarction, heart

failure, atrial fibrillation, and the need for coronary revascularization.⁴ While it has been established that lifestyle modifications and weight loss reduce this risk, weight loss is often difficult to achieve and maintain.^{5,6} Many studies have shown that structured lifestyle intervention programs involving dietary modifications and exercise, even as short as 3 months, result in improvements in the components of metabolic syndrome.^{7–10} However, it is unclear whether patients continue to maintain these improvements in the long term. Understanding whether patients continue to maintain their lifestyle modifications as well as the risk factor optimization they achieved will help define the key aspects of a successful lifestyle intervention program. As such, the aim of this study was to evaluate the trends in cardiovascular risk factors over the course of 12 months post completion of the 12- or 24-week structured lifestyle program.

Methods

Eligibility

Individuals with a diagnosis of metabolic syndrome were referred to the Metabolic Fitness Program (MetFit) at the discretion of their personal physician. To be included in this outcome study, metabolic syndrome was defined as having at least three of the five following clinical variables: waist circumference at least 40 inches (>102 cm) in men and 35 inches (>88 cm) in women, triglycerides ≥ 150 mg/dL (8.3 mmol/L) or treatment targeting triglycerides, high-density lipoprotein cholesterol (HDL-C) <40 mg/dL (2.2 mmol/L) in men and <50 mg/dL (2.8 mmol/L) in women, fasting glucose ≥ 100 mg/dL (5.6 mmol/L) or treated diabetes, and BP $\geq 130/85$ mmHg or on treatment for hypertension.¹¹ Written informed consent was obtained from all patients. Ethics approval was regulated by the University of Michigan Medical School Institutional Review Board (HUM0045929).

Program description

The original MetFit program began in 2005 and consisted of 90-minute weekly sessions for 12 weeks. The weekly sessions included 45-minute lectures regarding nutrition, exercise, and psychological distress and 45-minute exercise sessions. Participants were provided with free use of the cardiac rehabilitation fitness center for the duration of the program and were advised to engage in 150–300 minutes of exercise per week. Dietitians provided caloric adjustments needed in a Mediterranean diet to achieve a 3 months weight loss goal of 5% of current body weight. The 24-week program began in 2009. Patients were encouraged to enroll in the 24-week program with the option to enroll for 12 weeks and continue

at their discretion. Enrollees in the 24-week program were encouraged to set a weight loss goal of 10% of body weight. The out-of-pocket cost to the participants was \$350 for 12 weeks and \$700 for 24 weeks. Health insurance covered the baseline assessment by the nurse practitioner and lab studies, including glucose, total cholesterol, triglycerides, HDL-C, low-density lipoprotein cholesterol (LDL-C), hsCRP, insulin, and alanine aminotransferase. An initial diagnostic, symptom-limited exercise electrocardiogram was obtained when indicated. The aerobic exercise prescription was designed to target 60%–85% of heart rate reserve.

Data collection for follow-up

Baseline height, weight, body mass index (BMI), waist circumference, body composition percentage (assessed using bioelectrical impedance, Tanita Body Composition Analyzer Model TBF-310; Tanita, Arlington Heights, IL, USA), blood pressure (systolic and diastolic per AHA standard protocol), glucose, total cholesterol, triglycerides, HDL-C, and LDL-C were obtained after a 12-hour fast. The baseline assessment was repeated at 3 months and then again at 6 months if the participant elected to continue. Long-term follow-up data were obtained by chart review of the electronic medical record for any appointment within the Michigan Medicine Health System where primary or subspecialty care was provided near 3, 6, 9, and 12 months after program completion.

Statistical methods

Mean and SD are reported for continuous variables and percentages are reported for categorical variables. Chi-squared test of association is used for testing difference between groups for binary and categorical variables (eg, gender), and *t*-test is used for continuous variables (eg, age and weight). Generalized estimating equation approach is used to model repeated measurements of outcomes to evaluate changes after completing programs and to evaluate interactions of change with baseline variables.

Results

Baseline characteristics

There were 225 participants in the 12-week program and 121 participants in the 24-week program. Baseline characteristics of participants in the 12- and 24-week program are summarized in Table 1. There were no significant differences between the program groups, with the exception of patients in the 12-week program being slightly younger (51.1 vs 53.8, $P=0.03$) and having a slightly higher baseline LDL-C (6.2 vs 5.6, $P=0.01$).

Table 1 Baseline characteristics of patients in 12- and 24-Week Programs

Variables Mean (SD) or N (%)	12 weeks N=225	24 weeks N=121	P-value
Age	51.1	53.8	0.03
Gender	155 (68.9%)	72 (59.5%)	0.08
Race			
White	190 (84.4%)	111 (91.7%)	0.15
Black	13 (5.8%)	8 (3.3%)	
Other	22 (9.8%)	6 (5%)	
Education			
High School	19 (8.6%)	8 (6.6%)	0.51
Post High School	50 (22.7%)	21 (17.4%)	
College	66 (30%)	43 (35.5%)	
Post-graduate	85 (38.6%)	49 (40.5%)	
Diabetes	61 (27.1%)	35 (28.9%)	0.72
BMI	37.6 (7.1)	38.2 (6.39)	0.43
Systolic BP (mmHg)	119.8 (16.32)	119.4 (14.19)	0.82
Diastolic BP (mmHg)	72.5 (8.79)	71.2 (9.46)	0.20
LDL-C (mmol/L)	6.2 (1.9)	5.6 (2.0)	0.01
HDL-C (mmol/L)	2.6 (0.7)	2.5 (0.6)	0.34
Triglycerides (mmol/L)	10.2 (6.7)	11.5 (6.4)	0.07

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Results at program completion

The baseline, end of program, and longitudinal post-program follow-up results of participants who completed the 12-week program are displayed in Table 2. One hundred fifty-four of the initial 225 participants completed the 12-week program, which was defined as attending at least nine sessions and the program completion evaluation. By the end of the 12-week program, participants achieved significant improvements in dBp (-3.1 mmHg, $P \leq 0.001$) and sBP (-4.9 mmHg, $P=0.003$). With the exception of change in HDL-C, the remaining parameters of interest all had improved by the completion of the program, though not at a statistically significant level. The mean weight loss at the end of the 12-week program was 2.8 kg.

The results of the 24-week MetFit program are displayed in Table 3. One hundred two of the initial 121 participants completed the 24-week program. At 24 weeks, participants had obtained significant improvements in BMI (-2.78 kg/m², $P=0.0009$), weight (-8.0 kg, $P=0.0073$), dBp (-3.99 mmHg, $P=0.0013$), sBP (-5.2 mmHg, $P=0.0058$), glucose

(-0.9 mmol/L, $P=0.0022$), total cholesterol (-0.6 mmol/L, $P=0.0096$), and triglycerides (-2.5 mmol/L, $P=0.0018$).

At the beginning of both the 12-week and 24-week programs, 100% of participants fulfilled criteria for metabolic syndrome. Among those in the 12-week program, 73.1% met criteria for metabolic syndrome at program completion. Similar results were seen in the 24-week program after 12 weeks (72.3% met criteria for metabolic syndrome). However, by the end of the 24-week program, only 35.4% had criteria for metabolic syndrome.

End of program vs longitudinal follow-up results

Comparing results from program completion to longitudinal follow-up results, among participants who completed the 12-week program, there was a significant increase in sBP and dBp at 3, 6, 9, and 12 months. In addition, there was a statistically significant increase in glucose compared with end of program at 3 and 6 months, though not when evaluated further out (9 and 12 months). Notably, the statistically significant improvement in LDL-C persisted over long-term follow-up when assessed at 12 months post program completion. BMI, weight, and triglycerides had all increased back above end-of-program values over longitudinal follow-up. Total cholesterol remained improved compared with end-of-program values, though not at statistically significant values.

For patients who completed the 24-week program, compared with end-of-program values, there was a significant increase in sBP at all points over longitudinal follow-up. At 3 months after program completion, participants continued to show statistically significant improvements in total cholesterol and triglycerides, though over time these improvements waned. Weight and BMI improvements were not maintained compared with end of the 24-week program.

Baseline vs longitudinal follow-up results

When evaluating long-term outcomes compared with baseline values, participants in the 12-week program maintained improvements in BMI, weight, total cholesterol, and LDL-C but not at a statistically significant level. Of note, sBP was statistically significantly increased compared with baseline over all follow-up time points.

Compared with baseline values, participants in the 24-week program had a statistically significantly increased sBP over longitudinal follow-up. Participants' weight, total cholesterol, LDL-C, and triglycerides remained improved compared with baseline over total duration of follow-up,

Table 2 Long-term outcomes among patients in 12-week program^a

Variables (mean SD) N: number at each time point	During program Δ baseline, <i>P</i> -value δ end of program, <i>P</i> -value		Follow-up after end of program Δ baseline, <i>P</i> -value δ end of program, <i>P</i> -value			
	Baseline	12-weeks	3 months	6 months	9 months	12 months
BMI N: 225, 148, 108, 112,94, 105	37.6 (7.2)	36.5 (6.8) −1.1	37.1 (6.8) −0.4 0.67	37.0 (7.09) −0.56 0.54	36.8 (6.9) −0.72 0.38	37.5 (7.10) −0.11 0.99
Weight (kg) N: 225, 153, 109, 112,94, 108	106.91 (23.8)	104.1 (23.6) −2.8	106.87 (23.4) −0.04 2.8	105.1 (25.3) −1.8 2	106.1 (24.5) −0.8 2	106.0 (25.6) −0.9 1.9
Systolic BP (mmHg) N: 219, 145, 110, 114,93, 111	119.8 (16.3)	114.9 (13.7) −4.9, 0.003	126.5 (14.9) 6.7,< 0.001 11.6,< 0.001	126.1 (15.9) 6.3,< 0.001 11.2,< 0.001	127.2 (16.9) 7.4,< 0.001 12.3,< 0.001	129.3 (15.1) 9.5,< 0.001 14.4,< 0.001
Diastolic BP (mmHg) N: 219, 145, 110, 114,95, 111	72.5 (8.8)	69.4 (8.2) −3.1,< 0.001	74.2 (9.9) 1.6 4.7,< 0.001	73.6 (9.6) 1.1 4.1,< 0.001	72.6, (9.3) 0.11 3.2, 0.006	74.4 (10.1) 1.9 4.9,< 0.001
Fasting blood glucose (mmol/L) N: 225, 153, 67, 68,47, 53	6.4 (2.2)	6.1 (1.7) −0.3	6.7 (2.3) 0.3 0.6, 0.03	6.7 (2.3) 0.3 0.6, 0.02	6.7 (2.1) 0.3 0.6	6.5 (2.6) 0.1 0.4
Total cholesterol (mmol/L) N: 225, 154, 55, 63,45, 59	10.6 (2.4)	10.2 (2.6) −0.4	9.8 (2.4) −0.8, 0.02 −0.4	10.0 (2.2) −0.6 −0.2	10.0 (2.6) −0.6 −0.2	9.9 (2.8) −0.7 −0.3
HDL-C (mmol/L) N: 225, 154, 55, 63,45, 57	2.56 (0.7)	2.49 (0.7) −0.07	2.56 (0.7) 0 0.07	2.64 (0.9) 0.08 0.15	2.34 (0.7) −0.22, 0.05 −0.15	2.47 (0.6) −0.09 −0.02
LDL-C (mmol/L) N: 215, 147, 52, 62,44, 58	6.2 (1.9)	5.8 (2.0) −0.4	5.4 (1.8) −0.8, 0.004 −0.4	5.6 (2.0) −0.6, 0.03 −0.2	5.8 (2.0) −0.4 0	5.3 (1.7) −0.9, <0.001 −0.5, 0.04
Triglycerides (mmol/L) N: 225, 154, 55, 63,45, 58	10.2 (6.7)	9.4 (6.0) −0.8	9.8 (7.1) −0.4 0.4	9.0 (5.4) −1.2 −0.4	10.4 (6.9) 0.2 1.0	10.4 (6.8) 0.2 1.0

Notes: ^aBold values represent continued improvement for that outcome compared with either baseline or end-of-program value, respectively. *P*-values shown for variables that were statistically significant compared with either baseline or end-of-program values, respectively.

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

though not at statistically significant levels. Improvements in fasting glucose levels were not maintained over follow-up, however.

Interaction analyses

The interaction analyses showed that for participants with diabetes at baseline, their dBP increased at a significantly higher rate after completion of the 24-week program than participants without diabetes at baseline (slope 2.8 vs 1.1,

$P=0.05$). Triglycerides also increased at a higher rate after completion of the 24-week program in those with compared with those without diabetes (slope 14.8 vs -1.7 , $P=0.07$). Interestingly, there was no significant difference in outcomes after program completion based on gender. Finally, for participants of the 24-week program with a baseline BMI of ≤ 30 kg/m², their BMI increased at a significantly higher rate after program completion than participants with a BMI >30 kg/m² (slope 1.23 vs 0.3, $P=0.02$).

Table 3 Long-term outcomes among patients in 24-week program^a

Variables (mean SD) N=number at each time point	During program Δ baseline, <i>P</i> -value δ end of program, <i>P</i> -value		Follow-up after end of program Δ baseline, <i>P</i> -value δ end of program, <i>P</i> -value			
	Baseline	24 weeks	3 Months	6 Months	9 Months	12 Months
BMI N: 121, 102, 49, 46, 46, 45	38.2 (6.39)	35.4 (5.83) −2.78, <0.001	36.1 (6.6) −2.11, 0.05 0.67, 0.05	36.4 (6.1) −1.73 1.05	37.4 (6.6) −0.74 2.04	38.3 (6.0) 0.15 2.93
Weight (kg) N: 121, 102, 49, 46, 46, 45	110.7 (23.3)	102.7 (20.1) −8, 0.007	105.9 (21.3) −4.8 3.2	106.4 (19.8) −4.3 3.7	108.8 (21.2) −1.9 6.1	110.1 (19.1) −0.6 7.4
Systolic BP (mmHg) N: 118, 94, 52, 48, 42, 45	119.4 (14.1)	114.2 (12.6) −5.2, 0.005	124.8 (15.6) 5.4, 0.02 10.6, 0.02	126.0 (18.6) 6.6, 0.01 11.8, 0.01	129.0 (15.9) 9.6, <0.001 14.8, <0.001	130.8 (16.3) 11.4, <0.001 16.6, <0.001
Diastolic BP (mmHg) N: 118, 94, 53, 48, 42, 45	71.2 (9.4)	67.2 (8.1) −3.9, 0.001	72.9 (10.3) 1.7 5.7	73.6 (10.1) 2.4 6.4	74.2 (10.0) 2.9 6.9	73.1 (10.2) 1.9 5.9
Fasting blood glucose (mmol/L) N: 121, 102, 24, 21, 19, 27	6.9 (2.7)	6.0 (1.6) −0.9, 0.002	6.2 (1.5) −0.7 0.2	7.1 (3.4) 0.2 1.1	7.1 (2.5) 0.2 1.1	7.5 (2.4) 0.6 1.5
Total cholesterol (mmol/L) N: 121, 102, 16, 12, 12, 18	10.3 (2.4)	9.7 (2.2) −0.6, 0.009	(1.7) −1.5, 0.01 −0.9, 0.01	9.7 (2.4) −0.6 0	10.2 (1.8) −0.1 0.5	9.8 (2.2) −0.5 0.1
HDL-C (mmol/L) N: 121, 102, 16, 12, 12, 17	2.49 (0.6)	2.46 (0.6) −0.3	(0.5) −0.13 −0.10	(0.5) −0.06 −0.03	2.89 (0.8) 0.40, 0.03 0.43, 0.03	2.73 (1.3) 0.24 0.27
LDL-C (mmol/L) N: 111, 100, 16, 12, 13, 17	5.6 (2.0)	5.4 (1.7) −0.2	5.0 (1.4) −0.6 −0.4	5.5 (2.2) −0.1 0.1	5.4 (1.5) −0.2 0	5.3, (2.0) −0.3 −0.1
Triglycerides (mmol/L) N: 121, 103, 16, 12, 12, 17	11.5 (6.4)	9.1 (4.6) −2.5, 0.001	(3.5) −4.4, 0.007 −2.0, 0.007	10.5 (7.0) −1.0 1.4	8.3 (4.8) −3.2 −0.8	10.7 (7.1) −0.8 1.6

Notes: ^aBold values represent continued improvement for that outcome compared with either baseline or end-of-program value, respectively. *P*-values shown for variables that were statistically significant compared with either baseline or end-of-program values, respectively.

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Discussion

While increasing physical activity and improving nutrition in order to achieve weight loss help reduce cardiovascular risk factors, patients often have difficulty achieving and subsequently maintaining these improvements. Participants in both our 12- and 24-week lifestyle programs achieved significant improvements in multiple metabolic criteria and the program was effective for weight loss. For participants in the 12-week program, the most significant improvement was in BP control at program end. Among those in the 24-week program, there was a statistically significant improvement in weight, BMI, sBP and dBP, glucose, total cholesterol, and triglycerides at program conclusion. Our results mirror those summarized in

a recent systematic review and meta-analysis that highlighted resolution of components of the metabolic syndrome among individuals who completed structured lifestyle interventions.¹² In clinical practice, a significant challenge is the maintenance of weight loss over time.¹³ Herein, we demonstrate similar findings where only LDL-C remained significantly improved compared with end of program among those in the 12-week program and BP worsened to above baseline levels in both programs by 12 months post program completion. Over the 12-month follow-up, weight, BMI, total cholesterol, LDL-C, and triglycerides did remain improved compared with baseline values, however, in both the 12- and 24-week programs, though not at a statistically significant level.

While there is limited data regarding long-term outcomes after participating in a structured lifestyle intervention program, our findings are consistent with earlier studies where participants regain weight over time, but the majority are able to remain below program entry weight.¹⁴ Research has demonstrated that subsets of patients are successfully able to achieve and maintain weight loss after structured lifestyle programs, however. One of the largest studies that also had prolonged follow-up is the National Weight Control Registry, which noted that >87% of participants were still maintaining at least 10% weight loss at 5 and 10 years of follow-up.¹⁵ Several patient characteristics have been highlighted as being associated with maintenance of weight loss. These include increases in leisure-time physical activity, self-monitoring weight, and low-fat diets.¹⁶ There has also been extensive research investigating lifestyle program design features that promote maintenance of weight loss. Much of the data is supportive of extended care models post structured program completion via incorporation of follow-up touch points. These include face-to-face visits, telephone calls, or other eHealth modalities (internet based or mobile technology based).^{14,17–19} With the pervasiveness of technology in our daily living, eHealth-based maintenance programs represent a potentially low-cost, scalable mode to promote sustained weight loss, but additional investigations are needed to definitively establish their efficacy.²⁰

Evaluating our findings in further detail highlighted several results of note. First, of all the metabolic and cardiac outcomes of interest, the least durable element of improvement was that achieved in BP. Among both the 12- and 24-week programs, sBP quickly increased, and among those in the 12-week program, dBP also quickly rebounded at a statistically significant level shortly after program completion. This finding of rebound in blood pressure over a relatively short time frame associated with failure to maintain weight loss over has been well described.²¹ In this instance, there may also have been some contribution of changes in antihypertensive medications made in response to positive effects from the program that required further titration as the amount of weight loss diminished over longitudinal follow-up. Additionally, there may also have been difference in methods of BP readings as readings done as part of the program were strictly protocolized whereas those done as part of routine clinical care are less so. Among the other outcomes of interest, improvements in LDL-C appeared to be the most durable among those in the 12-week program whereas decrease in triglycerides was more readily maintained among those in the 24-week program. These trends may in part be impacted by medication use, particularly statins among this cohort, but are informative for

counseling patients regarding expected trend of cardiovascular risk factors and metabolic profile in relation to changes in weight over time.²² Finally, participation in the program for 24 weeks provided a clear benefit as the percentage of participants who fulfilled criteria for metabolic syndrome at program completion continued to decrease between 12 and 24 weeks.

There are several limitations to note related to this study. The most important is that follow-up was not uniform and varied in terms of completeness across participants given that this was a retrospective analysis. As a result, we were unable to assess follow-up of all parameters of interest over the 1-year post program completion timeline for all patients, and thus may have over- or underestimated the durability of improvements in cardiovascular risk factors in this overall cohort. These data represent real-world trends based on routine clinical care, however, and thus remain quite informative. Second, we are not able to definitively track how changes in medications over longitudinal follow-up may have impacted relevant outcomes, again due to the retrospective nature of the longitudinal follow-up data collection. Last, in this analysis we limited our follow-up time frame to 1 year post program completion which on the whole still speaks to a relatively short duration to assess maintenance of improvement in cardiovascular risk factors. Future studies with built-in follow-up assessments post program completion over longer durations are needed to characterize trends in more detail.

In conclusion, a 12- and 24-week structured lifestyle intervention program resulted in significant improvements in multiple components of the metabolic syndrome. The degree of benefit maintained over about 1 year post program completion diminished over time, particularly in terms of BP. Although improvements in outcomes were not maintained compared with end-of-program values, participants maintained improvements in cardiovascular and metabolic risk factors compared with baseline values with the exception of BP, though not at a statistically significant level. Continued efforts to identify lifestyle intervention designs that can facilitate long-term maintenance of weight loss are needed in order to optimize cardiovascular outcomes.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002;287(3):356–359.

2. Grundy SM, Brewer HB, Cleeman JI, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Arterioscler Thromb Vasc Biol.* 2004;24(2):e13–e18.
3. Mozumdar A, Liguori G. Persistent increase of prevalence of metabolic syndrome among U.S. adults: NHANES III to NHANES 1999–2006. *Diabetes Care.* 2011;34(1):216–219.
4. Malik S, Wong ND, Franklin SS, et al. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. *Circulation.* 2004;110(10):1245–1250.
5. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 2002;346(6):393–403.
6. Svetkey LP, Erlinger TP, Vollmer WM, et al. Effect of lifestyle modifications on blood pressure by race, sex, hypertension status, and age. *J Hum Hypertens.* 2005;19(1):21–31.
7. Dalzell C, Nigam A, Juneau M, et al. Intensive lifestyle intervention improves cardiometabolic and exercise parameters in metabolically healthy obese and metabolically unhealthy obese individuals. *Can J Cardiol.* 2014;30(4):434–440.
8. Pettman TL, Buckley JD, Misan GM, Coates AM, Howe PR. Health benefits of a 4-month group-based diet and lifestyle modification program for individuals with metabolic syndrome. *Obes Res Clin Pract.* 2009;3(4):221–235.
9. Rubenfire M, Mollo L, Krishnan S, et al. The metabolic fitness program: lifestyle modification for the metabolic syndrome using the resources of cardiac rehabilitation. *J Cardiopulm Rehabil Prev.* 2011;31(5):282–289.
10. Rodriguez-Escudero JP, Somers VK, Heath AL, et al. Effect of a lifestyle therapy program using cardiac rehabilitation resources on metabolic syndrome components. *J Cardiopulm Rehabil Prev.* 2013;33(6):360–370.
11. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001;285(19):2486–2497.
12. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. *BMC Med.* 2012;10:138.
13. Maclean PS, Wing RR, Davidson T, et al. NIH working group report: innovative research to improve maintenance of weight loss. *Obesity.* 2015;23(1):7–15.
14. Svetkey LP, Stevens VJ, Brantley PJ, et al. Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. *JAMA.* 2008;299(10):1139–1148.
15. Thomas JG, Bond DS, Phelan S, Hill JO, Wing RR. Weight-loss maintenance for 10 years in the National Weight Control Registry. *Am J Prev Med.* 2014;46(1):17–23.
16. McGuire MT, Wing RR, Klem ML, Hill JO. Behavioral strategies of individuals who have maintained long-term weight losses. *Obes Res.* 1999;7(4):334–341.
17. Wing RR, Tate DF, Gorin AA, Raynor HA, Fava JL. A self-regulation program for maintenance of weight loss. *N Engl J Med.* 2006;355(15):1563–1571.
18. Perri MG, Limacher MC, Durning PE, et al. Extended-care programs for weight management in rural communities: the treatment of obesity in underserved rural settings (TOURS) randomized trial. *Arch Intern Med.* 2008;168(21):2347–2354.
19. Montesi L, El Ghoch M, Brodosi L, Calugi S, Marchesini G, Dalle Grave R. Long-term weight loss maintenance for obesity: a multidisciplinary approach. *Diabetes Metab Syndr Obes.* 2016;9:37–46.
20. Hutcheson MJ, Rollo ME, Krukowski R, et al. eHealth interventions for the prevention and treatment of overweight and obesity in adults: a systematic review with meta-analysis. *Obes Rev.* 2015;16(5):376–392.
21. Stevens VJ, Obarzanek E, Cook NR, et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Ann Intern Med.* 2001;134(1):1–11.
22. Wing RR, Espeland MA, Clark JM, et al. Association of weight loss maintenance and weight regain on 4-year changes in CVD risk factors: the Action for Health in Diabetes (Look AHEAD) Clinical Trial. *Diabetes Care.* 2016;39(8):1345–1355.

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