American Journal of
Preventive Medicine

RESEARCH ARTICLE

Long-Term Effectiveness of a Lifestyle Intervention: A Pragmatic Community Trial to Prevent Metabolic Syndrome

Davood Khalili, MD, MPH, PhD,[1,2] Samaneh Asgari, MSc,[1,2] Mojtaba Lotfaliany, MD,[3] Neda Zafari, MD, MPH,[1] Farzad Hadaegh, MD,[1] Amir-Abbas Momenan, MD, MPH,[1] Armin Nowroozpoor, MD,[1] Firoozeh Hosseini-Esfahani, PhD,[4] Parvin Mirmiran, PhD,[4,5] Parisa Amiri, PhD,[6] Fereidoun Azizi, MD[7]

Introduction: The purpose of this study is to evaluate the long-term effectiveness of a community-based lifestyle education on primary prevention of metabolic syndrome in a middle-income country.

Study design: This study followed 3,180 individuals free of metabolic syndrome who were under the coverage of three health centers in Tehran from 1999 until 2015. They were undergoing triennial examinations resulting in four re-exams. People in one of three areas received interventions consisting of family-, school-, and community-based educational programs, including a face-to-face educational session at baseline. Data were analyzed considering the incidence of metabolic syndrome at each re-exam and also repeated-measure analysis including all re-exams together. Weighting was considered to correct selection bias because of loss to follow-up. Data were analyzed in 2017.

Results: After 3 years, 149 of 852 participants in the intervention and 471 of 2,328 people in control area developed metabolic syndrome at first re-exam resulting in a RR of 0.78 (95% CI=0.67, 0.92). The difference between groups remained unchanged up to the 6-year follow-up (RR=0.79, 95% CI=0.66, 0.93, at second re-exam), but disappeared during the third and fourth re-exams (RR=1.04, 95% CI=0.91, 1.18 and RR=1.03, 95% CI=0.91, 1.16, respectively). Marginal models for longitudinal data showed a significant interaction between intervention and time of re-exams. Further analyses showed that the effect of the intervention might have been rooted in improvement of lipid profile and glucose level.

Conclusions: In a middle-income country, face-to-face educational sessions followed by a long-term maintenance community-level educational program could reduce the risk of metabolic syndrome for up to 6 years. A booster face-to-face session is recommended to retain this preventive effect.

Trial registration: This study is registered at Iran Registry for Clinical Trials (http://irct.ir) IRCT138705301058N1.

Am J Prev Med 2019;56(3):437−446.

From the [1]Prevention of Metabolic Disorders Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [2]Department of Biostatistics and Epidemiology, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [3]Non-Communicable Disease Control, School of Population and Global Health, University of Melbourne, Parkville, Victoria, Australia; [4]Nutrition and Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [5]Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [6]Research Center for Social Determinants of Health, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; and [7]Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Address correspondence to: Fereidoun Azizi, MD, Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, P.O. Box 19395-4763, Tehran, Iran. E-mail: azizi@endocrine.ac.ir.

0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2018.10.029

INTRODUCTION

Noncommunicable diseases (NCDs) are a huge burden worldwide, making them a major challenge for health policymakers and healthcare professionals.[1,2] The majority of people with NCDs live in low- and middle-income countries.[3] Iran, a low- and middle-income country itself, is confronting the high burden of NCDs and related mortalities[4−6]; therefore, there is an urgent need for pragmatic and effective interventions for the prevention of NCDs.

Four behaviors play a significant role in the development of most NCDs: tobacco use, physical inactivity, unhealthy diet, and alcohol consumption, which in turn cause four key metabolic changes: overweight/obesity, high blood glucose, high cholesterol, and high blood pressure.[7] Metabolic syndrome (MetS) was introduced as a cluster of NCD risk factors including obesity, dyslipidemia, dysglycemia, and high blood pressure, which occur together often.[8,9] Studies have shown that lifestyle interventions at the community level can reduce NCD risk factors and MetS.[10−13] However, the majority of the studies were conducted in high-income countries. The question remains whether realistic lifestyle interventions tailored for resource-constrained settings like Iran could reduce the risk factors of NCDs, especially in the long term.[10−13]

The Tehran Lipid and Glucose Study (TLGS) is a long-term pragmatic community-based lifestyle intervention program to prevent NCDs and their risk factors.[14] After 3.6 years of follow-up, the lifestyle intervention in the TLGS study reduced the NCD risk factors including obesity, dyslipidemia, and dysglycemia.[15] The current study evaluates the long-term effectiveness of the TLGS intervention on the primary prevention of MetS.

METHODS

The TLGS was designed with two main junctures: Phase I, a cross-sectional study of the prevalence of NCDs and their risk factors, implemented from 1999 to 2001; and Phase II, a prospective follow-up study along with lifestyle interventions and triennial data recollection. Four follow-up re-exams have been carried out from 2002 until 2015. Detailed descriptions of the TLGS have been reported elsewhere.[5,14]

Study Population

Three medical health centers in Tehran's district 13 were selected and 15,005 residents aged ≥3 years were recruited. An educational intervention was performed in one medical center that was part of the TLGS lifestyle intervention and included residents in the area; residents under the coverage of two other medical centers were used as the control. The rationale for choosing district 13 in Tehran was: (1) access to the documented data of >90% of the families, (2) stability of its population, and (3) appropriate distance between intervention and control areas to prevent cross-contamination. Moreover, this population was representative of the overall population of Tehran by age distribution and middle SES.[5] A total of 5,630 participants (from 15,005 all recruited residents) lived in the intervention area.[14] For the present study, 10,368 participants aged ≥20 years were selected from the baseline examination. Excluding those with MetS at baseline (n=3,617), those with missing data (n=535), and those who did not participate in follow-up re-exams (n=1,251, others had at least one re-exam), 4,965 participants remained for intention-to-treat (ITT) analysis. For per-protocol analysis, those who moved to or from the intervention area during follow-up years (n=1,785) were not considered for analysis, leaving 3,180 subjects (n=852 in intervention, and n=2,328 in control area; Figure 1).

The study was approved by the Ethical Committee of Research Institute for Endocrine Sciences and the National Research Council of the Islamic Republic of Iran. Informed consent was obtained from each participant. The TLGS is registered at Iran Registry for Clinical Trials, a WHO primary registry (http://irct.ir; IRCTID: IRCT138705301058N1).

Measures

Trained physicians obtained medical histories including smoking habits and physical activity and performed brief physical examinations. Physical activity was assessed with the Lipid Research Clinic questionnaire in the first exam and the Modifiable Activity Questionnaire in the re-exams.[14] Dietary data were collected from a subsample of the TLGS population in the second, third, and fourth re-exams, using a validated semi-quantitative food frequency questionnaire (FFQ) with 168 food items, developed for the TLGS. The validity and reliability of the FFQ for food group intake were assessed and were acceptable.[16,17]

A detailed description of anthropometric, blood pressure, and laboratory measurements including plasma glucose, 2-hour plasma glucose, total cholesterol, triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C) in the TLGS have been reported previously.[14] All physical examinations and laboratory measurements were carried out using the same protocols in all exams and for all participants, both in intervention and control areas. There was no blindness for assessing the outcomes.

From the Joint Interim Statement,[8,9] those who met at least three of the following five criteria were considered to have MetS: (1) waist circumference ≥95 cm for both sexes (based on national studies[18]); (2) TGs ≥150 mg/dL (1.7 mmol/L; or medication for elevated TGs); (3) HDL-C <40 mg/dL (1.0 mmol/L) in males, <50 mg/dL (1.3 mmol/L) in females (or medication for HDL-C); (4) systolic blood pressure ≥130 mmHg or diastolic ≥85 mmHg (or antihypertensive medication); and (5) fasting plasma glucose ≥100 mg/dL (5.5 mmol/L, or medication for elevated glucose).

Daily smoker was defined as someone who smoked any type of tobacco at least once a day, and occasional smoker was one who smoked, but not every day; both were considered current smokers and others as nonsmokers.

In the first phase of the TLGS using the Lipid Research Clinic questionnaire, an individual with <3 days of performing sports or heavy physical activity per week, was considered to have low physical activity. For other exams, low physical activity was defined as <600 METs per week, using the Modifiable Activity Questionnaire.[19]

The design of the TLGS for lifestyle interventions has been described previously.[14,15] Briefly, the intervention was adopted

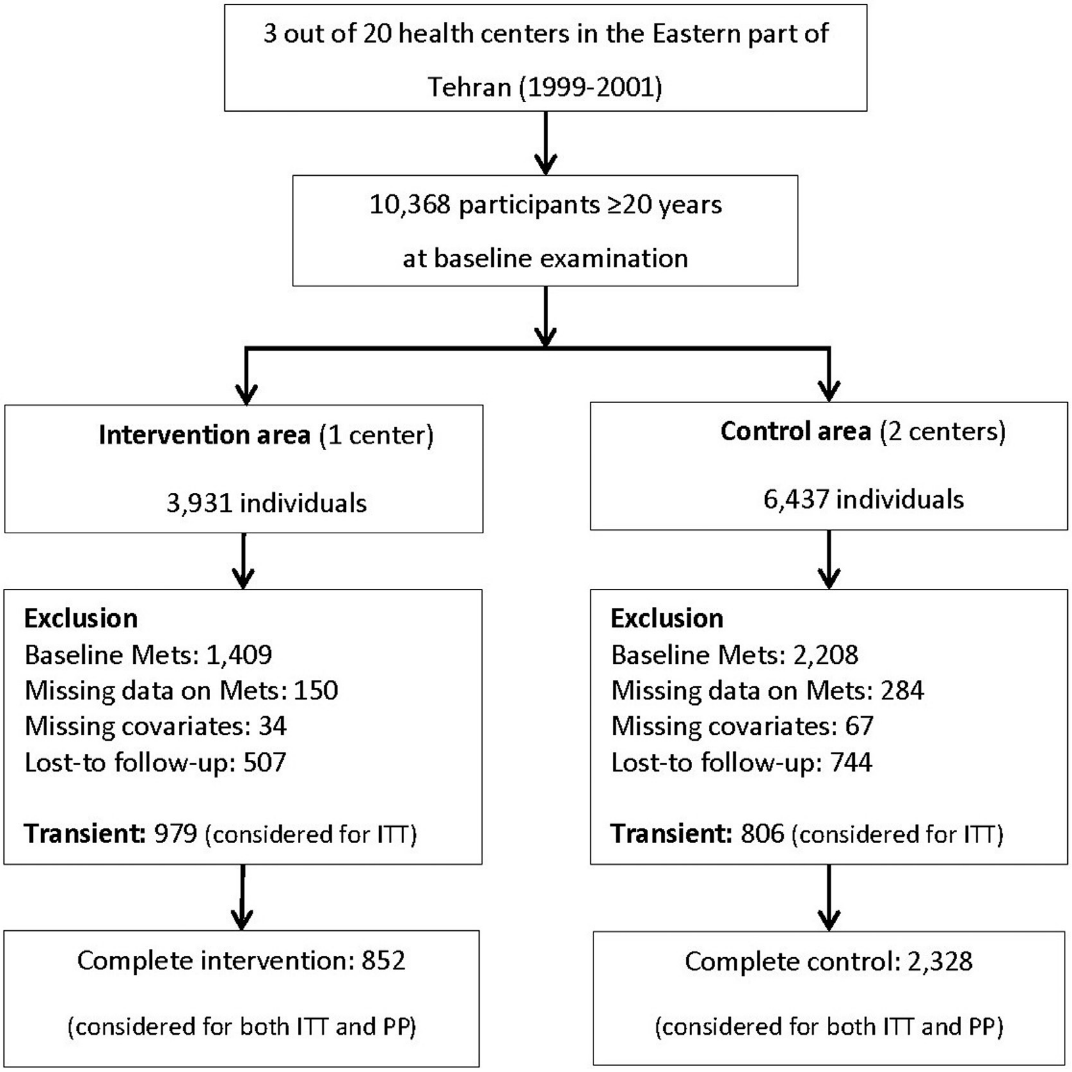

Figure 1. Flowchart of the study participants.
Mets, metabolic syndrome; ITT, intention to treat analysis; PP, per-protocol analysis.

from the American Heart Association guidelines, North Karelia project, and Knowledge, Attitude and Practice (KAP) study in the TLGS population.[20–22] All participants of the intervention area received a multicomponent lifestyle intervention. The goals of the intervention were to improve diet, increase physical activity, and encourage smoking cessation. In the intervention area, medical health centers benefited from a network of experienced health volunteers called health liaisons. They played a critical role in recruiting people and distributing educational materials to families, local tradespeople, schools, and mosques. These health liaison volunteers were trained by a professional team in the TLGS, and their activities in the community were supervised by the health center of the intervention area. The interventions had three components: family-based, school-based, and community-based interventions. The control group received routine health care delivered by the health centers, which were mainly some limited secondary prevention programs for diabetes and hypertension.

Family-based interventions were delivered by inviting families for group sessions (for >2 hours) between baseline and first re-exam. A total of 12–20 adults participated in every session, which summed up to 50% of the intervention population and nearly 70% of them were female. Methods of education included face-to-face consultation, family consultation, and slide and video presentations regarding healthy food preparation, benefits of physical activity, and harms of smoking. Training instructions were developed according to the applicable guidelines (following the American Heart Association and North Karelia project), baseline data, and the KAP study, which included questions related to weight change and dietary patterns. The KAP study provided some clues on requirements and points to be considered for healthy nutritional practice and what needs to be changed.[22] All smokers were invited to take part in a motivational consultation and then referred to a cessation clinic.

Families in the intervention area received health newsletters named "Courier of Health" every 3 months, which contained health topics (i.e., the food pyramid guide, weight management, health hazards of smoking, smoking-cessation techniques, the importance of daily walking and regular physical activity, and specific exercise recommendations). Occasionally, these newsletters contained some results of the TLGS, including the prevalence and the effect of risk factors in their area. Pamphlets or booklets on specific topics in lifestyle management were distributed two to four times per year to all families in the intervention area. These included food groups, recommended portions for each age group, types of fats, guidelines to reduce the fat content of foods, preparing healthy meals, smoking cessation benefits, and coping with stress. The health liaisons played a critical role in distributing educational materials to families. Telephone surveys showed that 50% of households had received and paid attention to the educational pamphlets and health newsletters. Only 7.5% of people were illiterate and were aged >50 years and could not read and understand the materials. Most participants in other households received the educational materials but did not pay attention to them and did not read them or did not remember the subjects.

Community-based interventions included public education in community gatherings, including social events and religious ceremonies, particularly at mosques in the holy month of Ramadan (two to four events annually). Public events on occasions, such as the World No Tobacco Day and the World Diabetes Day, were also held. In addition, public conferences were held in one of the largest local amphitheaters in the intervention area to deliver the key messages regarding lifestyle modifications (two to four conferences annually). More than 80% of the households participated in at least one of the public gatherings for national or religious holidays between every two examinations. Health promotion advertisements (billboards) were occasionally considered in the intervention area.

The school-based intervention directly addressed the entire school component, including students, parents, teachers, staff, and school environment.[23] All activities including classroom teachings, peer teachings, establishing the school health team, involving the families, and developing policy modifications, aimed to promote healthy nutritional habits, physical activity, and avoiding smoking. The monitoring process showed that nearly 60%−70% of the planned lifestyle interventions in school settings were successfully implemented during the follow-ups. Activities related to classroom teachings and peer teachings were completely implemented in all schools in the intervention area, but some families did not attend the school health team and some policy modifications, like red labeling for unhealthy snacks and green labeling for healthy foods in school buffets, were not completely successful.

All smokers were invited to take part in a motivational consultation and then referred to a cessation clinic.

Statistical Analysis

A post hoc sample size calculation showed that a sample size of 650 in the intervention group and 1,300 in the control group achieves 80% power to detect a RR of 0.8 when a 12-year cumulative incidence is 0.3 and a two-sided significance level is 0.05.

Baseline characteristics are described for followed and non-followed participants and mean and SD values for continuous variables are also reported for the intervention and control groups, and frequencies (%) are reported for categorical variables; the variables were compared between groups using appropriate statistical tests.

To find the effect of the intervention on the incidence of MetS at each re-exam, a log-binomial model was used to compute an adjusted RR.[24] A method described by Wacholder was applied to modify the convergence by truncating estimated risks to values slightly >0 and <1; this method is implemented in Stata's "binreg" command.[25] The incidence at each re-exam was calculated irrespective of the other re-exams. The data were also reanalyzed using marginal models for longitudinal data, so the subjects were repeatedly considered over time in triennial periods for four re-exams adjusted for baseline covariates. Generalized estimating equations were carried out with logit link function to estimate adjusted marginal means for the prevalence of MetS components over time by intervention status. The covariance matrix was structured by autoregessive correlation matrix.

To consider the differences between control and intervention groups and also the differences between followed and non-followed subjects, two propensity scores were calculated for each subject. One for the probability of allocating to the intervention or control group and the other one for the probability of being lost to follow-up, considering baseline covariates including sex, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, 2-hour-postprandial glucose, TC, TG, HDL-C, current smoking, low physical activity, antihypertensive drugs, lipid-lowering drugs, and diabetes drugs. The inverse of the two propensity scores was used as the sampling weight in the analysis.[26]

Three models were designed in the multivariable analysis. Model 1 included intervention group, sex, and age; Model 2 was further adjusted for baseline behavioral covariates including current smoking, education, and physical activity at baseline; and Model 3 was weighted for the inverse probability of the two propensity scores (i.e., inverse of their multiplication). In generalized estimating equations models, further adjustments were made for time and interaction of time X intervention in all three models. To avoid the effect of contamination between the intervention and control areas on the results, the authors preferred the per-protocol analysis; however, the results are reported based on ITT analysis as well.

Additionally, the prevalence of current smoking, low physical activity, and energy intake in each re-exam were plotted by intervention status. The results were adjusted for sex, age at each re-exam, and each variable itself at baseline.

Data were analyzed using Stata, version 14/SE, and considered two-tailed p-value <0.05 as statistically significant. Data were analyzed in 2017.

RESULTS

Baseline characteristics of both followed and non-followed subjects are depicted in Appendix Table 1 (available online). There was no significant difference between the two groups, except for the percentage of current smokers, which tended to be higher in non-followed individuals.

Comparison of baseline characteristics in control and intervention groups showed that those in the control group were younger, more educated, and had a higher percentage of current smoking than those in the intervention group. There was no significant difference between the two groups in other characteristics (e.g., anthropometric indices, glucose profile, and medications; Table 1).

Table 1. Baseline Characteristics of the Participants in Control, Intervention, and Transient Groups (TLGS, 1999–2015)

Characteristics	Control group (*n*=2,328)	Intervention group (*n*=852)	*p*-value[a]	Transient group (*n*=1,785)
Age (years), M (SD)	38.4 (13.6)	40.1 (14.8)	0.003	37.7 (12.1)
Female sex, n (%)	1,326 (57.0)	497 (58.3)	0.49	1,062 (59.5)
Waist circumference (cm), M (SD)	82.7 (10.3)	83.1 (10.6)	0.42	83.1 (9.9)
BMI, M (SD)	25.2 (4.1)	25.2 (4.1)	0.82	25.3 (3.9)
Systolic BP (mmHg), M (SD)	113 (14.4)	114 (15.4)	0.057	112.7 (13.5)
Diastolic BP (mmHg), M (SD)	74 (9.1)	74 (9.1)	0.23	74.2 (9.0)
TC (mmol/L), M (SD)	5.1 (1.1)	5.2 (1.1)	0.47	5.05 (1.0)
TG[b] (mmol/L), median (IQR)	1.28 (0.79)	1.22 (0.80)	0.07	1.26 (0.81)
HDL-C (mmol/L), M (SD)	1.15 (0.28)	1.17 (0.30)	0.04	1.14 (0.29)
Fasting plasma glucose (mmol/L), M (SD)	4.95 (0.93)	5.0 (1.21)	0.44	4.9 (0.84)
2-hour post challenge plasma glucose (mmol/L), M (SD)	5.66 (1.88)	5.73 (1.87)	0.4	5.7 (1.80)
Current smokers, n (%)	340 (14.6)	100 (11.7)	0.04	256 (14.3)
Low physical activity, n (%)	608 (26.1)	209 (24.5)	0.36	432 (24.2)
Education, n (%)			<0.001	
<6 years	568 (24.4)	269 (31.6)		429 (24.0)
6 to <12 years	1,426 (61.3)	490 (57.7)		1,080 (60.5)
≥12 years	334 (14.3)	93 (10.9)		276 (15.5)
Medication use, n (%)				
Anti-hypertensive drugs	54 (2.3)	19 (2.2)	0.88	41 (2.3)
Lipid lowering drugs	12 (0.5)	4 (0.5)	0.87	12 (0.7)
Anti-diabetes drugs	18 (0.8)	11 (1.3)	0.17	16 (0.9)

Note: Values are M (SD) for continuous variables and *p*-values were calculated by using *t*-test. Values are *n* (%) for categorical variables and *p*-value according to χ^2 or Fisher's exact test, as appropriate.
[a]The *p*-value is for comparison between intervention and control groups.
[b]TG values are median (IQR) and *p*-value according to Mann-Whitney *U* test.
BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; TC, total cholesterol; TG, triglyceride; TLGS, Tehran Lipid and Glucose Study.

From a total of 2,328 participants in the control and 852 in the intervention group, 471 (20.2%) and 149 (17.5%) developed MetS at first re-exam, respectively. Age- and sex-adjustment resulted in an RR of 0.81 (95% CI=0.69, 0.95) at the first re-exam, which did not change with further adjustments. This protective RR lasted for the second re-exam but not for the third and the fourth and, based on the ITT analysis, the results did not change dramatically (Table 2). Considering all re-exams together in a longitudinal manner showed the same results and revealed a significant interaction between intervention X time (p<0.05); the intervention reduced the odds of the presence of MetS for about 25% up to 6 years and the effect diminished afterward (Appendix Table 2, available online). The possible interaction of intervention with age, sex, and BMI was checked by including interaction terms in regression analyses. There were no important and significant interactions (all p-values >0.1), therefore, the authors did not perform subgroup analysis.

Table 2 also shows the risk difference (absolute risk reduction) between intervention and control areas. According to the final model, 6% (95% CI=2%, 9%) risk reduction was observed in the intervention compared with the control area (this amount decreased to 3% to 5% based on ITT). The reciprocal of this absolute risk reductions (1/0.06) is translated to a number needed to prevent of 17 (i.e., the number needed to intervene to prevent one new case of MetS).

Figure 2 depicts the differences between groups regarding MetS and its components through re-examinations. Prevalence of high waist circumference and blood pressure was the same in both intervention and control groups. Dyslipidemia, including low HDL and high TGs, was lower in the intervention group for up to 6 years; and the prevalence of high fasting plasma glucose was lower through the first 3 years.

Adjusted prevalence of low physical activity was the same in the control and intervention groups during follow-ups. Regarding the mean of energy intake, the two groups were not significantly different at the last three re-exams. However, the prevalence of current smoking was lower in the intervention group at all re-exams (Appendix Figure 1, available online). Comparing the characteristics of the intervention and control groups after 12 years

Table 2. Effect of Intervention on Incidence of Metabolic Syndrome at Each Follow-up Re-examination (TLGS 1999–2015)

Model[a]	Re-exam 1 after 3 years	Re-exam 2 after 6 years	Re-exam 3 after 9 years	Re-exam 4 after 12 years
Per-protocol analysis				
Model 1				
RR (95% CI)	0.81 (0.69, 0.95)	0.80 (0.68, 0.95)	1.03 (0.90, 1.16)	1.02 (0.90, 1.15)
p-value	0.009	0.010	0.693	0.751
Risk difference (95% CI)	−0.04 (−0.07, −0.01)	−0.04 (−0.07, −0.01)	0.01 (−0.02, 0.05)	0.00 (−0.03, 0.04)
p-value	0.012	0.009	0.442	0.830
Model 2				
RR (95% CI)	0.80 (0.68, 0.94)	0.79 (0.67, 0.94)	1.02 (0.90, 1.16)	1.02 (0.90, 1.15)
p-value	0.006	0.008	0.741	0.730
Risk difference (95% CI)	−0.04 (−0.07, −0.01)	−0.04 (−0.06, −0.01)	0.01 (−0.03, 0.05)	0.00 (−0.04, 0.04)
p-value	0.009	0.009	0.592	0.910
Model 3				
RR (95% CI)	0.78 (0.67, 0.92)	0.79 (0.66, 0.93)	1.04 (0.91, 1.18)	1.03 (0.91, 1.16)
p-value	0.003	0.006	0.579	0.669
Risk difference (95% CI)	−0.06 (−0.10, −0.02)	−0.06 (−0.09, −0.02)	0.01 (−0.03, 0.05)	0.01 (−0.03, 0.05)
p-value	0.002	0.004	0.581	0.671
ITT analysis				
Model 1				
RR (95% CI)	0.81 (0.71, 0.92)	0.90 (0.79, 1.02)	1.04 (0.94, 1.14)	0.96 (0.88, 1.05)
p-value	0.002	0.095	0.461	0.426
Risk difference (95% CI)	−0.04 (−0.07, −0.02)	−0.01 (−0.04, 0.01)	0.02 (−0.01, 0.04)	−0.01 (−0.04, 0.01)
p-value	0.001	0.312	0.219	0.317
Model 2				
RR (95% CI)	0.81 (0.71, 0.92)	0.90 (0.79, 1.02)	1.04 (0.94, 1.14)	0.97 (0.88, 1.06)
p-value	0.001	0.093	0.435	0.456
Risk difference (95% CI)	−0.04 (−0.07, −0.02)	−0.01 (−0.04, 0.01)	0.02 (−0.01, 0.04)	−0.02 (−0.04, 0.01)
p-value	0.001	0.221	0.243	0.291
Model 3				
RR (95% CI)	0.78 (0.68, 0.89)	0.89 (0.78, 1.01)	1.05 (0.95, 1.16)	0.95 (0.86, 1.04)
p-value	0.001	0.067	0.368	0.326
Risk difference (95% CI)	−0.05 (−0.08, −0.03)	−0.03 (−0.05, 0.00)	0.01 (−0.02, 0.04)	−0.02 (−0.05, 0.02)
p-value	0.001	0.062	0.370	0.323

Note: Model 1: intervention + sex + age; Model 2: intervention + sex + age + education, smoking, and physical activity at baseline; Model 3: intervention weighted by inverse probability of propensity score to adjust for baseline differences between Control and Intervention groups and also for differences between Followed and Non-followed subjects.

[a]Generalized linear models with extension to the binomial family and using log link to report risk ratios.

ITT, Intention to treat; TLGS, Tehran Lipid and Glucose Study.

showed that the pattern was the same as that at the beginning of the study (Appendix Table 3, available online).

DISCUSSION

The TLGS is the first long-term, integrated, community-based intervention aimed to address the NCD epidemic in Iran. The lifestyle intervention was designed to be pragmatic, low-intensity, and suitable to be scaled-up to the national level, considering the limitations in low- and middle-income countries. This study found that a face-to-face education session, followed by a long-term maintenance community-level education program could reduce the risk of MetS for up to 6 years. However, this effect disappeared afterward. This effect could be rooted in reductions in smoking, plasma TGs, and plasma glucose, and increasing HDL-C.

This investigation showed that the lifestyle intervention decreased the risk of developing MetS by about 20% up to 6 years. It is in line with other community interventions in Iran showing a reduction in the main NCD risk factors.[27,28] Similarly, in other community-based programs, such as the North Karelia Project, the intervention effectively reduced the cardiovascular disease risk factors during the first 5 years.[29] In the current study, the effect of lifestyle intervention on prevention of MetS did not

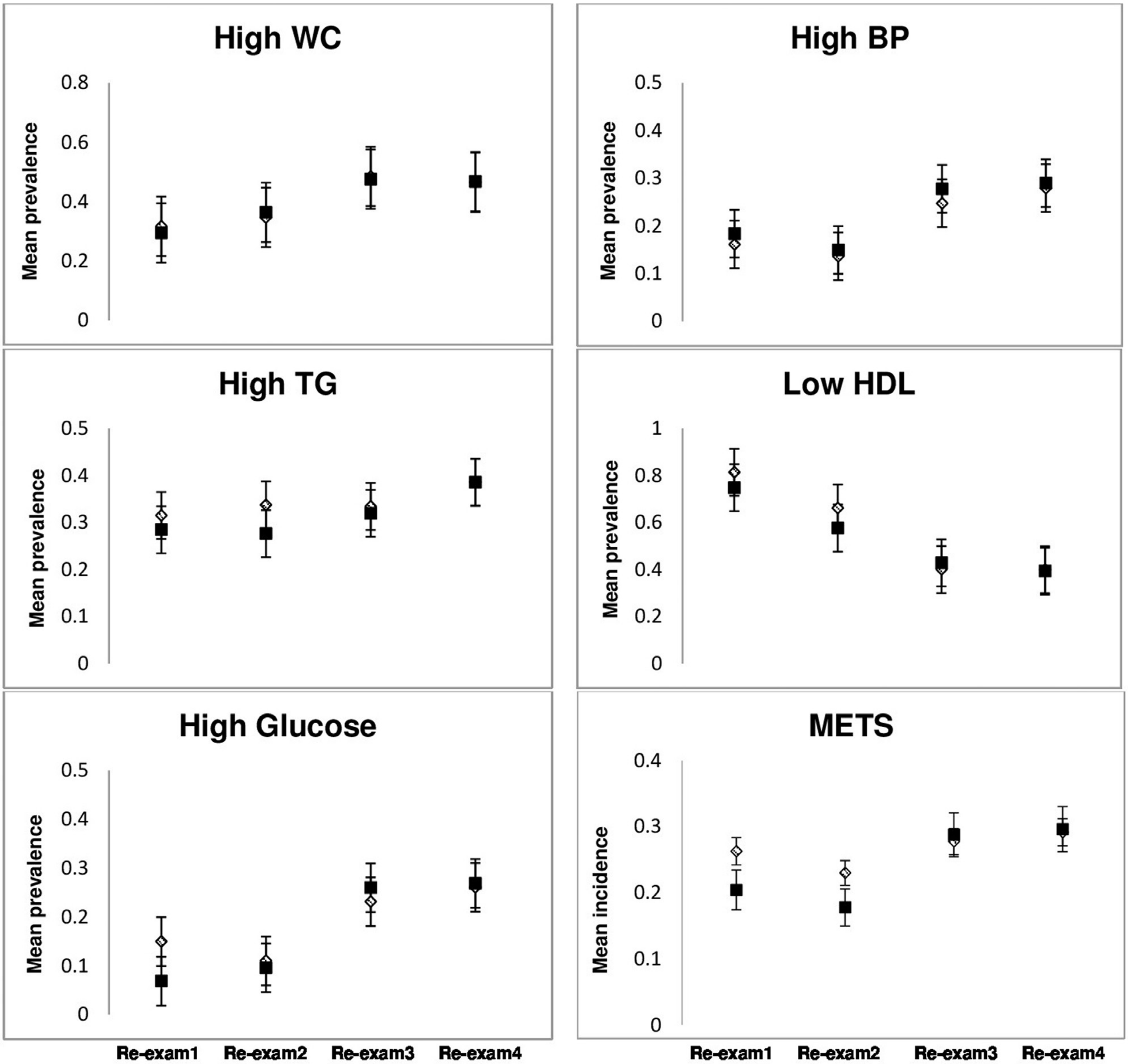

Figure 2. Incidence of METS and prevalence of its components in control and intervention groups at each follow-up re-examination (Tehran Lipid and Glucose Study, 1999–2015).

Note: Prevalence of high WC, high TG, low HDL cholesterol, high glucose, and high BP in each follow-up re-examination adjusted for age, sex, and the corresponding values of each variable at baseline; defined as marginal mean of the prevalence. Nobody had METS at baseline, so the graph shows the incidence of METS after 3, 6, 9, and 12 years regardless of the previous exam. Solid squares represent the intervention group. Striped rhombuses represent the control group.

BP, blood pressure; HDL, high-density lipoprotein; METS, metabolic syndrome; WC, waist circumference; TG, high triglycerides.

continue more than 6 years after the face-to-face education. Similarly, the effect of community-based education on reducing cardiovascular disease risk factors gained limited support from Pawtucket Heart Health Program with 10 years of follow-up.[30] Moreover, there are field trials that have failed to display a significant effect of the intervention on a large population scale.[30,31]

Smoking was the only behavioral risk factor that was significantly lower in the intervention group compared with the control group in the long term. Moreover, among MetS components, a positive association between lifestyle intervention and lower prevalence of high TGs, low HDL-C, and high fasting plasma glucose was observed. There are some potential explanations for these findings. First, this intervention focused on smoking prevention and cessation more than other risk factors, as there were multiple antismoking programs, including referring smokers to smoking-cessation clinics. Some of the effects of the lifestyle intervention to prevent MetS might have been through reducing smoking, which has been shown to be associated with MetS and related conditions.[32] Additionally, a meta-analysis showed that HDL-C level increased significantly after smoking cessation.[33] A large study in the U.S. on the National Health and Nutrition Examination Surveys concluded that smoking is associated with adverse lipid profiles among the U.S. adult population.[34] Second, the intervention might have improved the quality of participants' diet. This may be inferred by the improvement of lipid and glucose profiles of the participants. On the other hand, the measures to assess physical activity and eating might have been insensitive enough to see the differences between groups, and the missing data for FFQs at baseline did not allow the authors to perform an adequate analysis.

There was not enough evidence in this study to conclude that there is a significant difference between groups regarding physical inactivity, central obesity, and high blood pressure. First, this might be because the lifestyle intervention was not effective enough to convince participants to reduce their salt intake. Second, the intervention may not lead to improvement in the physical activity of a population without ample amount of leisure time, facilities, and empowerment. More investigations are needed to find the barriers that must be overcome to have a more physically active population. The current findings are in contrast with some trials that showed a noticeable improvement in obesity and blood pressure status related to lifestyle interventions.[35,36]

One third of Iranian adults have MetS,[9] therefore, a relatively low-cost and effective intervention is important for preventing MetS and, in turn, cardiovascular disease and other related NCDs in the population. The lifestyle intervention was associated with an absolute risk reduction of around 5%, which can potentially be translated to the prevention of one new case of MetS per 20 adults (i.e., number needed to prevent) if the lifestyle intervention was implemented for all people nationally. Moreover, the RR of around 0.80 is equal to decreasing the incidence of MetS by 20% (i.e., RR reduction of 20%). This effect can last up to 3−6 years, but not longer.

Future research is needed to investigate the possible strategies for improving the effects of the intervention over longer time spans. This can be achieved by reducing the barriers and improving the facilitators. From the results of previous studies in the TLGS, the most important barriers to healthy nutrition were interpersonal/cultural effects, lack of access to healthy foods, food preferences, and media advertisements.[37,38] Moreover, a booster face-to-face educational session (every 3−6 years) might help to keep the positive effect of education on preventing/delaying MetS incidence even for a longer time. Of note, the cost and feasibility of conducting the face-to-face educational sessions in the mass population should be assessed.

Limitations

Some limitations of this study should be noted. First, study participants were not randomly assigned to the intervention and control groups. Moreover, any moving from intervention to control area, and vice versa, may result in reducing the effect of the intervention during that time. For this reason, the effect of intervention in ITT was less than that in per-protocol analysis. On the other hand, any talk about healthy lifestyle between individuals from intervention and control areas may mask the effect of lifestyle education. The number of participants who were lost to follow-up or crossed between groups was relatively high (about 45% of eligible individuals). To address these issues, the authors performed both ITT and per-protocol analysis and calculated propensity scores for allocation to groups and for being lost to follow-up and performed inverse probability weighting. Finally, because it is a wide community trial, it is not possible to determine the effect of each part of the intervention separately. Nevertheless, the authors tried to specify the percentage of participants who received the family- and community-based interventions and the percentage of the planned school-based interventions successfully implemented.

Second, physical activity was measured using two different questionnaires at baseline and follow-ups. Third, measurements of dietary intake based on the FFQ were not available for all participants at the baseline and about 50% of participants through re-exams. Moreover, in free-living people, total calorie and nutrient intake vary on a day-to-day and seasonal basis.[39,40] The major strengths of this study are its long-term follow-up, as well as the large size of the study population. Furthermore, participants with MetS at baseline were excluded to investigate the preventive effect of the intervention on healthier individuals. Because of the nature of MetS, which could be resolved between re-exams, the analysis was performed for each re-exam both alone and with respect to other re-exams.

CONCLUSIONS

This study showed that MetS can be prevented by a pragmatic lifestyle intervention in the short term (6 years) but not after that. The effect is mainly rooted in improving smoking status as well as the lipid and glucose profile. For long-term maintenance, reducing the barriers and improving the facilitators of the lifestyle intervention program as well as booster face-to-face educational sessions are recommended.

ACKNOWLEDGMENTS

This study has been approved and funded by the National Research Council of the Islamic Republic of Iran by No. 121.

FA, DK, FH, AAM, and PM contributed to the study conception and design. DK, SA, and ML performed the statistical analysis. DK, SA, ML, NZ, and AN wrote the first draft. DK, FA, FH, ML, and AAM interpreted the data. FH, PM, PA, NZ, and AN critically revised the manuscript. FA and DK supervised the study. All authors read and approved the final version.

This study is registered at Iran Registry for Clinical Trials, a WHO primary registry (http://irct.ir). The registration date is 2008-10-29 and the Iran Registry for Clinical Trials IRCTID: IRCT138705301058N1.

No financial disclosures were reported by the authors.

SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2018.10.029.

REFERENCES

1. Beaglehole R, Bonita R, Horton R, et al. Priority actions for the noncommunicable disease crisis. *Lancet.* 2011;377(9775):1438–1447. https://doi.org/10.1016/S0140-6736(11)60393-0.
2. Daar AS, Singer PA, Persad DL, et al. Grand challenges in chronic noncommunicable diseases. *Nature.* 2007;450(7169):494–496. https://doi.org/10.1038/450494a.
3. WHO. Global status report on noncommunicable diseases 2014: attaining the nine global noncommunicable diseases targets; a shared responsibility. http://apps.who.int/iris/bitstream/handle/10665/148114/9789241564854_eng.pdf;jsessionid=918F3C9021-F32EF5F4A93944D94B9F91?sequence=1. Published 2014. Accessed December 31, 2018.
4. Hadaegh F, Hasheminia M, Lotfaliany M, Mohebi R, Azizi F, Tohidi M. Incidence of metabolic syndrome over 9 years follow-up; the importance of sex differences in the role of insulin resistance and other risk factors. *PLoS One.* 2013;8(9):e76304. https://doi.org/10.1371/journal.pone.0076304.
5. Azizi F, Rahmani M, Emami H, et al. Cardiovascular risk factors in an Iranian urban population: Tehran Lipid and Glucose Study (phase 1). *Soz Praventivmed.* 2002;47(6):408–426. https://doi.org/10.1007/s000380200008.
6. Sardarinia M, Akbarpour S, Lotfaliany M, et al. Risk factors for incidence of cardiovascular diseases and all-cause mortality in a middle eastern population over a decade follow-up: Tehran Lipid and Glucose Study. *PLoS One.* 2016;11(12):e0167623. https://doi.org/10.1371/journal.pone.0167623.
7. WHO. Risk factors. Global Health Observatory (GHO) data. www.who.int/gho/ncd/risk_factors/en/. Published 2017. Accessed July 4, 2018.
8. Alberti K, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation.* 2009;120(16):1640–1645. https://doi.org/10.1161/CIRCULATIONAHA.109.192644.
9. Azizi F, Hadaegh F, Khalili D, et al. Appropriate definition of metabolic syndrome among Iranian adults: report of the Iranian National Committee of Obesity. *Arch Iran Med.* 2010;13(5):426.
10. Álvarez-Bueno C, Cavero-Redondo I, Martínez-Andrés M, Arias-Palencia N, Ramos-Blanes R, Salcedo-Aguilar F. Effectiveness of multifactorial interventions in primary health care settings for primary prevention of cardiovascular disease: a systematic review of systematic reviews. *Prev Med.* 2015;76(suppl):S68–S75. https://doi.org/10.1016/j.ypmed.2014.11.028.
11. Ebrahim S, Taylor F, Ward K, Beswick A, Burke M, Davey Smith G. Multiple risk factor interventions for primary prevention of coronary heart disease. *Cochrane Database Syst Rev.* 2011(1):CD001561. https://doi.org/10.1002/14651858.CD001561.pub3.
12. Fleming P, Godwin M. Lifestyle interventions in primary care: systematic review of randomized controlled trials. *Can Fam Physician.* 2008;54(12):1706–1713.
13. Pennant M, Davenport C, Bayliss S, Greenheld W, Marshall T, Hyde C. Community programs for the prevention of cardiovascular disease: a systematic review. *Am J Epidemiol.* 2010;172(5):500–516. https://doi.org/10.1093/aje/kwq171.
14. Azizi F, Ghanbarian A, Momenan AA, et al. Prevention of non-communicable disease in a population in nutrition transition: Tehran Lipid and Glucose Study phase II. *Trials.* 2009;10:5. https://doi.org/10.1186/1745-6215-10-5.
15. Harati H, Hadaegh F, Momenan AA, et al. Reduction in incidence of type 2 diabetes by lifestyle intervention in a middle eastern community. *Am J Prev Med.* 2010;38(6):628–636. https://doi.org/10.1016/j.amepre.2010.03.003.
16. Hosseini Esfahani F, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. *J Epidemiol.* 2010;20(2):150–158. https://doi.org/10.2188/jea.JE20090083.
17. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran Lipid and Glucose Study. *Public Health Nutr.* 2010;13(5):654–662. https://doi.org/10.1017/S1368980009991698.
18. Azizi F, Khalili D, Aghajani H, et al. Appropriate waist circumference cut-off points among Iranian adults: the first report of the Iranian National Committee of Obesity. *Arch Iran Med.* 2010;13(3):243.
19. Momenan AA, Delshad M, Mirmiran P, Ghanbarian A, Azizi F. Leisure time physical activity and its determinants among adults in Tehran: Tehran Lipid and Glucose Study. *Int J Prev Med.* 2011;2(4).
20. McAlister A, Puska P, Salonen JT, Tuomilehto J, Koskela K. Theory and action for health promotion illustrations from the North Karelia Project. *Am J Public Health.* 1982;72(1):43–50. https://doi.org/10.2105/AJPH.72.1.43.
21. Krauss RM, Eckel RH, Howard B, et al. AHA Dietary Guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *Circulation.* 2000;102(18):2284–2299. https://doi.org/10.1161/01.CIR.102.18.2284.
22. Mirmiran P, Mohammadi-Nasrabadi F, Omidvar N, et al. Nutritional knowledge, attitude and practice of Tehranian adults and their relation to serum lipid and lipoproteins: Tehran Lipid and Glucose Study. *Ann Nutr Metab.* 2010;56(3):233–240. https://doi.org/10.1159/000288313.
23. Amiri P, Jalali-Farahani S, Akbar HM, et al. The effects of a community-based lifestyle intervention on metabolic syndrome and its components in adolescents: findings of a decade follow-up. *Metab Syndr Relat Disord.* 2018;16(5):215–223. https://doi.org/10.1089/met.2017.0055.
24. McNutt L-A, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol.* 2003;157(10):940–943. https://doi.org/10.1093/aje/kwg074.

25. Cummings P. Methods for estimating adjusted risk ratios. *Stata J.* 2009;9(2):175.
26. Mansournia MA, Altman DG. Inverse probability weighting. *BMJ.* 2016;352:i189. https://doi.org/10.1136/bmj.i189.
27. Sarrafzadegan N, Baghaei A, Sadri G, et al. Isfahan healthy heart program: evaluation of comprehensive, community-based interventions for non-communicable disease prevention. *Prev Control.* 2006;2(2):73–84. https://doi.org/10.1016/j.precon.2006.10.003.
28. Khosravi A, Mehr GK, Kelishadi R, et al. The impact of a 6-year comprehensive community trial on the awareness, treatment and control rates of hypertension in Iran: experiences from the Isfahan healthy heart program. *BMC Cardiovasc Disord.* 2010;10(1):61. https://doi.org/10.1186/1471-2261-10-61.
29. Puska P. From Framingham to North Karelia: from descriptive epidemiology to public health action. *Prog Cardiovasc Dis.* 2010;53(1):15–20. https://doi.org/10.1016/j.pcad.2010.01.003.
30. Carleton RA, Lasater TM, Assaf AR, Feldman HA, McKinlay S. The Pawtucket Heart Health Program: community changes in cardiovascular risk factors and projected disease risk. *Am J Public Health.* 1995;85(6):777–785. https://doi.org/10.2105/AJPH.85.6.777.
31. Luepker RV, Murray DM, Jacobs DR Jr., et al. Community education for cardiovascular disease prevention: risk factor changes in the Minnesota Heart Health Program. *Am J Public Health.* 1994;84(9):1383–1393. https://doi.org/10.2105/AJPH.84.9.1383.
32. Sun K, Liu J, Ning G. Active smoking and risk of metabolic syndrome: a meta-analysis of prospective studies. *PLoS One.* 2012;7(10):e47791. https://doi.org/10.1371/journal.pone.0047791.
33. Maeda K, Noguchi Y, Fukui T. The effects of cessation from cigarette smoking on the lipid and lipoprotein profiles: a meta-analysis. *Prev Med.* 2003;37(4):283–290. https://doi.org/10.1016/S0091-7435(03)00110-5.
34. Jain RB, Ducatman A. Associations between smoking and lipid/lipoprotein concentrations among U.S. adults aged ≥20 years. *J Circ Biomark.* 2018;7:1–10. https://doi.org/10.1177/1849454418779310.
35. Jafar TH, Hatcher J, Poulter N, et al. Community-based interventions to promote blood pressure control in a developing country: a cluster randomized trial. *Ann Intern Med.* 2009;151(9):593–601. https://doi.org/10.7326/0003-4819-151-9-200911030-00004.
36. McQuigg M, Brown J, Broom J, et al. Empowering primary care to tackle the obesity epidemic: the Counterweight Programme. *Eur J Clin Nutr.* 2005;59 (suppl): 1:S93–S100; discussion S101.
37. Farahmand M, Tehrani FR, Amiri P, Azizi F. Barriers to healthy nutrition: perceptions and experiences of Iranian women. *BMC Public Health.* 2012;12(1):1064. https://doi.org/10.1186/1471-2458-12-1064.
38. Farahmand M, Amiri P, Tehrani FR, Momenan AA, Mirmiran P, Azizi F. What are the main barriers to healthy eating among families? A qualitative exploration of perceptions and experiences of Tehranian men. *Appetite.* 2015;89:291–297. https://doi.org/10.1016/j.appet.2015.02.025.
39. Hebert J, Gupta P, Mehta H, Ebbeling C, Bhonsle R, Varghese F. Sources of variability in dietary intake in two distinct regions of rural India: implications for nutrition study design and interpretation. *Eur J Clin Nutr.* 2000;54(6):479–486. https://doi.org/10.1038/sj.ejcn.1601042.
40. Cai H, Shu X-O, Hebert JR, et al. Variation in nutrient intakes among women in Shanghai, China. *Eur J Clin Nutr.* 2004;58(12):1604–1611. https://doi.org/10.1038/sj.ejcn.1602013.