AMERICAN JOURNAL OF
Preventive Medicine

RESEARCH ARTICLE

Exercise Intensity and Incidence of Metabolic Syndrome: The SUN Project

María Hidalgo-Santamaria, MD,[1] Alejandro Fernandez-Montero, MD, PhD,[2,3] Miguel A. Martinez-Gonzalez, MD, PhD, MPH,[3,4] Laura Moreno-Galarraga, MD, PhD,[3,5] Almudena Sanchez-Villegas, MD, PhD,[6] María T. Barrio-Lopez, MD, PhD,[7] Maira Bes-Rastrollo, PhD, MPH[3,4]

Introduction: Emerging evidence suggests that vigorous physical activity may be associated with higher cardioprotective benefits than moderate physical activity. This study aimed to assess the long-term relationship between the intensity of leisure time physical activity (LTPA) and the risk of developing metabolic syndrome (MS) in a prospective cohort study.

Methods: The *Seguimiento Universidad de Navarra* (SUN) Project comprises Spanish university graduates. Participants (n=10,145) initially free of MS were followed for a minimum of 6 years (2008–2014). Analysis was conducted in 2015. Physical activity was assessed though a validated questionnaire. The intensity of each physical activity was measured in METs. The intensity of LTPA was estimated by the ratio between total METs/week and total hours of LTPA/week, obtaining the mean METs/hour of LTPA. MS was defined according to the harmonizing definition. The association between the intensity of LTPA (METs/hour) and MS was assessed with logistic regression models adjusting for potential confounders.

Results: Among 10,145 participants initially free of any MS criteria, 412 new MS cases were observed. Vigorous LTPA was associated with a 37% relatively lower risk (AOR=0.63, 95% CI=0.44, 0.89) compared with light LTPA. For a given total energy expenditure, independent of the time spent on it, participants who performed vigorous LTPA exhibited a higher reduction in the risk of MS than those who performed light to moderate LTPA.

Conclusions: Vigorous LTPA was significantly associated with lower risk of developing MS after a 6-year follow-up period.

Am J Prev Med 2017;52(4):e95–e101.

INTRODUCTION

Metabolic syndrome (MS) is the combination of five metabolic abnormalities: central adiposity, dyslipidemia, insulin resistance, glucose intolerance, and hypertension.[1] It is strongly associated with atherosclerosis, cardiovascular disease, Type 2 diabetes, and all-cause mortality.[2,3] Early identification, treatment, and prevention of MS present major challenges for healthcare professionals.

There is evidence of the effectiveness of physical activity in primary and secondary prevention of several chronic diseases and premature death.[4–6] Leisure time physical activity (LTPA) refers to activity that is not

From the [1]Department of Internal Medicine, University of Navarra Clinic, Pamplona, Navarra, Spain; [2]Department of Occupational Medicine, University of Navarra Clinic, Pamplona, Navarra, Spain; [3]Instituto de Investigación Sanitaria de Navarra, Pamplona, Navarra, Spain; [4]Department of Preventive Medicine and Public Health, University of Navarra, Pamplona, Navarra, Spain; [5]Pediatrics Service, Complejo Hospital de Navarra, Servicio Navarro de Salud, Pamplona, Navarra, Spain; [6]Department of Clinical Sciences, University of Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; and [7]Department of Cardiac Electrofisiology and Clinic Arrhythmology, Monteprincipe Hospital, Boadilla de Monte, Madrid, Spain

Address correspondence to: María Hidalgo-Santamaría, MD, Department of Internal Medicine, University of Navarra Clinic, Av. Pio XII, 36. 31008. Pamplona, Navarra, Spain. E-mail: mhidalgos@unav.es.

0749-3797/$36.00
http://dx.doi.org/10.1016/j.amepre.2016.11.021

required as an essential activity of daily living (sports participation, exercise conditioning, and recreational activities).[7] The protective effect of LTPA on the incidence of MS has been established.[8–12]

Emerging evidence suggests that vigorous physical activity (VPA), rather than light or moderate activity, may be associated with higher cardioprotective benefits and superior reduction of mortality.[13] European recommendations state that additional benefits can be obtained by increasing the intensity of LTPA.[14] The American Heart Association proposes an average of 40 minutes of moderate to vigorous intensity activity three or four times/week.[15] Cross-sectional studies have suggested that VPA may provide an important benefit for cardiometabolic disease prevention.[16–19] There are also some longitudinal studies, but they did not take into account important dietary or lifestyle confounders.[20,21]

The aim of this study was to assess the relationship between levels of intensity in LTPA and the long-term risk of developing MS.

METHODS

The *Seguimiento Universidad de Navarra* (SUN) project is a prospective, multipurpose, dynamic cohort, formed by Spanish university graduates and started in December 1999.[22–24] Participant recruitment is open permanently. Follow-up is based on biennial questionnaires. (Further information and the cohort profile are available at: www.unav.edu/departamento/preventiva/sun.) The authors selected participants with a minimum of 6 years of follow-up. A total of 5,367 participants were excluded who had at least one MS component or BMI >30 (waist circumference was not measured at baseline). Also, 1,399 participants who had extremely low or high total energy intake and 841 participants who had not answered any of the follow-up questionnaires (retention rate, 93.6%) and 2,268 participants with missing information on MS at the 6-year follow-up were excluded. After exclusions, 10,145 participants entered the final analyses. Final data were from December 2014. Analysis was conducted in 2015.

The study was approved by the IRB of the University of Navarra. Voluntary completion of the first questionnaire was considered to imply informed consent.

Measures

Data for LTPA were gathered through a 17-item self-administered questionnaire. This questionnaire collects information about 17 different types of LTPA (walking, jogging, athletics, cycling, stationary cycling, swimming, tennis, soccer, basketball, dance, hiking, gymnastics, gardening, skiing, martial arts, and sailing) and about the time spent on each. This 17-item questionnaire was validated using triaxial accelerometers.[25] METs corresponding to each activity were established using the Compendium of Physical Activities.[26] Afterward, the number of METs for each activity was multiplied by the hours dedicated to it per week, obtaining the total METs/week for each activity. Total energy expenditure in LTPA was quantified by summing the total METs/week of all the activities performed by each participant. The intensity of LTPA was estimated by the ratio of total METs/week and total hours of LTPA/week, obtaining the mean METs/hour.

The covariables used in the analyses included: sociodemographic variables (sex, age, education level), health-related habits (smoking status, alcohol intake), medical history (prevalence of cancer and cardiovascular disease), lifestyle and dietary factors (adherence to the Mediterranean diet or any diet, total energy intake, fast food, french fries, snacking, sugar-sweetened soda intake, and time spent on TV watching, computer use, household chores, physical activity at work, sleeping hours, and nap minutes/day), anthropometric data (height, body weight, and BMI), and total energy expenditure in LTPA/week (METs/week). To measure nutritional variables, this study used a 136-item semi-quantitative food frequency questionnaire with demonstrated validity and reproducibility.[27–29] The validity of self-reported data on BMI and body weight has also been published in a specific report.[30]

This study defined MS according to the harmonizing definition of the International Diabetes Federation; American Heart Association; and National Heart, Lung, and Blood Institute.[1] The presence of any three of the following five risk factors constitutes a diagnosis of MS: elevated waist circumference (in Europeans: ≥94 cm or ≥80 cm, for men and women, respectively), elevated triglycerides (≥150 mg/dL) or drug treatment for elevated triglycerides, reduced high-density lipoprotein cholesterol (<40 mg/dL for men and <50 mg/dL for women) or drug treatment for reduced high-density lipoprotein cholesterol, elevated blood pressure (systolic ≥130 mmHg, diastolic ≥85 mmHg, or both) or antihypertensive drug treatment, and elevated fasting glucose (≥100 mg/dL) or drug treatment for elevated glucose.

Information was self-reported (questionnaires) and obtained by participants from their blood tests and medical checkups provided at no cost by the Spanish Public National Health System. A measuring tape was sent to all participants, including a detailed explanation of how to measure their own waist. Validation of these self-reported MS data has also been published.[31,32]

Statistical Analysis

The sample was divided into quartiles according to their mean METs/hour of LTPA. The first quartile (light LTPA) was considered the reference category and the fourth was considered the vigorous LTPA group. The authors compared the incidence of MS or any of its components between them after using logistic regression models. ORs were estimated and 95% CIs were calculated. The first model was built without any adjustment (crude), a second model adjusted for age and sex, and a third multivariable-adjusted model considered potential confounders.

Additional analyses were conducted by creating five new categories that combined time spent in LTPA (≤6.3 or >6.3 hours/week, median of total time/week spent in LTPA) and intensity of LTPA (light to moderate, <6 METs/hour; vigorous, ≥6 METs/hour). The authors compared the incidence of MS between these five joint categories, taking as the reference category those who did not perform any LTPA, in the multivariable-adjusted logistic regression model. All presented *p*-values are two-tailed. Analyses were performed using Stata, version 12.0.

RESULTS

The authors studied 10,145 participants initially free of any criteria for MS and observed 412 (4.1%) new

Table 1. Baseline Characteristics of Participants According to the Intensity of LTPA

Characteristic	Q1 (light)	Q2	Q3	Q4 (vigorous)
Mean METs/hour (range)	2.52–4.00	4.01–4.82	4.83–5.64	5.65–10.55
n	2,562	2,495	2,529	2,528
Age (years)	37.3 (10.8)	36.6 (10.6)	36.0 (10.3)	35.6 (9.7)
Sex, men (%)	23.5	26.6	33.5	49.0
BMI at baseline	22.7 (2.9)	22.6 (2.8)	22.7 (2.7)	22.9 (2.6)
Waist circumference (cm)[a]	83.0 (12.2)	82.1 (11.7)	82.8 (12.0)	83.7 (11.8)
Triglycerides (mg/dL)[a]	85.2 (47.3)	84.2 (46.8)	83.6 (44.6)	82.2 (42.9)
HDL-C (mg/dL)[a]	64.7 (20.9)	65.7 (21.1)	65.5 (20.1)	64.3 (20.8)
Systolic blood pressure (mmHg)[a]	113.2 (14.6)	112.9 (12.8)	113.8 (13.9)	114.0 (14.1)
Diastolic blood pressure (mmHg)[a]	68.8 (10.6)	68.9 (9.5)	69.4 (9.9)	(69.5 (10.1)
Plasma glucose (mg/dL)[a]	87.3 (12.6)	87.0 (11.9)	86.6 (11.7)	87.0 (13.4)
Energy intake (kcal/day)	2312 (598)	2340 (585)	2368 (599)	2431 (620)
Adherence to Mediterranean diet (0 [minimum]–9 [maximum] score)	3.6 (1.4)	3.7 (1.5)	3.7 (1.5)	3.6 (1.5)
Alcohol (g/day)	5.1 (8.2)	5.4 (7.9)	6.0 (8.8)	6.9 (8.5)
Educational level (%)				
College	29.0	26.4	23.6	19.4
Postgraduate	48.2	50.4	49.3	50.4
Master	6.0	6.8	7.4	9.6
Doctorate	7.5	8.3	10.4	11.6
TV watching (hours/week)	12.2 (9.5)	11.1 (8.5)	11.1 (8.9)	10.1 (8.5)
Following any special diet (%)	5.7	5.5	7.5	6.1
Fast food (g/day)	20.6 (19.0)	20.3 (18.7)	21.4 (19.9)	23.6 (22.2)
Computer use (hours/week)	13.1 (14.7)	13.8 (14.6)	15.0 (15.0)	16.6 (15.0)
House chores (hours/week)	13.4 (11.7)	12.4 (11.0)	11.2 (10.6)	10.0 (9.8)
Physical activity at work (minutes/day)	42 (84)	42 (90)	42 (84)	30 (66)
Total hours of LTPA per week (h/week)	4.8 (3.8)	7.2 (5.6)	9.4 (7.1)	11.8 (8.3)
Total METs of LTPA per week (METs/week)	17.3 (14.2)	32.0 (25.3)	49.4 (37.4)	76.0 (54.6)
Nap (minutes/day)	24 (54)	18 (48)	24 (60)	18 (42)
Sleep (hours/day)	7.3 (0.9)	7.2 (1.0)	7.2 (0.9)	7.2 (0.9)
Smoking status (%)				
Current smokers	26.6	21.8	20.3	20.5
Former smokers	25.7	25.4	28.1	25.0
Cardiovascular disease (%)	2.6	1.8	2.5	2.2
Cancer (%)	4.0	3.2	3.7	2.2

Note: Q1–Q4 are quartiles of mean METs per hour of LTPA. Values are expressed as means (SD), unless otherwise noted.
[a]Variables measured at 6-year follow-up.
HDL-C, high-density lipoprotein cholesterol; LTPA, leisure time physical activity; Q, quartile.

(incident) cases of MS after 6 years of follow-up (60.5% men). Participants who performed higher-intensity LTPA were more frequently men, with a higher educational level, and a higher amount of total energy expenditure in LTPA. When analyzing the type of exercise predominant in each quartile of intensity of LTPA, walking and stair climbing were the predominant aerobic exercises in the first quartile, whereas the predominant activities were anaerobic vigorous activities (soccer, skiing, and athletics), but also aerobic vigorous activities (jogging and hiking) in the fourth quartile. Table 1 shows baseline characteristics of participants.

As shown in Table 2, participants who performed more vigorous LTPA presented a lower risk of developing MS than those who performed light-intensity LTPA in an age- and sex-adjusted model and after adjusting for potential confounding factors (OR=0.63, 95% CI=0.44, 0.89). Incidence decreased also in the intermediate-intensity categories.

This study found interaction between sex and intensity of LTPA (p=0.015 for interaction). Stratified analyses showed an MS risk reduction associated with vigorous LTPA in men (multivariable AOR=0.40, 95% CI=0.24, 0.65) but not in women (OR=0.98, 95% CI=0.59, 1.65).

Table 2. MS Risk at 6-Year Follow-up, According to Intensity of LTPA

Variable	Q1 (light)	Q2	Q3	Q4 (vigorous)	*p* for trend
Mean METs/hour (range)	2.52–4.00	4.01–4.82	4.83–5.64	5.65–10.55	
n	2,562	2,495	2,529	2,528	
Cases, *n*	135	97	101	79	
Crude OR (95% CI)	1 (ref)	0.73 (0.56, 0.95)	0.75 (0.57, 0.97)	0.58 (0.44, 0.77)	**<0.001**
Sex, age-adjusted OR (95% CI)	1 (ref)	0.74 (0.56, 0.98)	0.76 (0.58, 1.01)	0.57 (0.42, 0.76)	**<0.001**
Multivariable-adjusted OR (95% CI)[a]	1 (ref)	0.79 (0.59, 1.06)	0.80 (0.59, 1.08)	0.63 (0.44, 0.89)	**0.015**

Note: Q1–Q4 are quartiles of mean METs/hour of LTPA. Boldface indicates statistical significance ($p < 0.05$).
[a]Adjusted for age, sex, smoking status, baseline BMI, total energy intake, adherence to the Mediterranean diet, following any special diet, snacking, sugar-sweetened soda consumption, alcohol intake, french fries consumption, fast-food consumption, educational level, computer use, TV watching, house chores, hours sleeping, napping, physical activity at work, prevalence of cardiovascular disease and cancer, and total energy expenditure in LTPA per week.
LTPA, leisure time physical activity; MS, metabolic syndrome.

Men performed more-vigorous physical activities and for a longer time. The mean intensity of LTPA for women was 4.74 (SD=1.01) METs/hour and for men it was 5.25 (SD=1.18) METs/hour.

A statistically significant interaction was also found between intensity of LTPA and age (≤55 years/>55 years). Stratified analyses showed an MS risk reduction associated with vigorous LTPA in older participants (multivariable AOR=0.10, 95% CI=0.03, 0.29) but not in younger ones (OR=0.76, 95% CI=0.55, 1.12). No interaction was found between intensity of LTPA and other specified factors.

Multivariable AORs of MS were calculated between extreme quartiles of time spent in LTPA (OR=0.76, 95% CI=0.46, 1.27, for highest versus lowest quartile) and total energy expenditure in LTPA (OR=0.78, 95% CI=0.57, 1.07, for highest versus lowest quartile). The risk of developing individual MS components associated with LTPA intensity is shown in Table 3. The patterns for MS components were similar to those observed for the overall MS, with an inverse association except for elevated glucose. However, only waist circumference was significant.

Additional analysis with the five new categories of the joint combination time and intensity of LTPA are shown in Figure 1. Participants who performed vigorous LTPA showed a lower risk of developing MS than those who performed light to moderate LTPA within the same time category.

DISCUSSION

The present study investigated the association between intensity of LTPA and MS. The results showed that vigorous LTPA was inversely associated with the long-term risk of developing MS in comparison with light LTPA, after controlling for total energy expenditure and a wide array of confounding factors.

The incidence of MS was low (4.1%). This was expected because this study comprised a young cohort

Table 3. MS Components Risk at 6-Year Follow-up, According to the Intensity of LTPA

Variable	Q1 (light)	Q2	Q3	Q4 (vigorous)	*p* for trend
Mean METs/hour (range)	2.52–4.00	4.01–4.82	4.83–5.64	5.65–10.55	
n	2,562	2,495	2,529	2,528	
Waist circumference[a]	1 (ref)	0.85 (0.74, 0.96)	0.86 (0.76, 0.99)	0.67 (0.58, 0.78)	0.004
Elevated triglycerides[b]	1 (ref)	0.92 (0.72, 1.19)	1.00 (0.78, 1.29)	0.80 (0.59, 1.07)	0.176
Reduced HDL-C[c]	1 (ref)	1.03 (0.80, 1.32)	0.81 (0.62, 1.07)	0.85 (0.62, 1.15)	0.241
Elevated blood pressure[d]	1 (ref)	0.90 (0.77, 1.06)	1.01 (0.86, 1.20)	0.94 (0.78, 1.13)	0.269
Elevated glucose[e]	1 (ref)	0.95 (0.77, 1.18)	0.87 (0.69, 1.08)	1.02 (0.80, 1.30)	0.671

Note: Values are OR (95% CI) unless otherwise noted. Q1–Q4 are quartiles of mean METs/hour of LTPA. Adjusted for age, sex, smoking status, baseline BMI, total energy intake, adherence to the Mediterranean Diet, following any special diet, snacking, sugar-sweetened soda consumption, alcohol intake, french fries consumption, fast-food consumption, educational level, computer use, TV watching, house chores, hours sleeping, napping, physical activity at work, cardiovascular disease, and total energy expenditure in LTPA per week.
[a]≥94 cm for men or ≥80 cm for women.
[b]≥150 mg/dL.
[c]<40 mg/dL for men and <50 mg/dL for women.
[d]Systolic ≥130 mmHg or diastolic ≥85 mmHg.
[e]≥100 mg/dL.
HDL-C, high-density lipoprotein cholesterol; LTPA, leisure time physical activity; MS, metabolic syndrome.

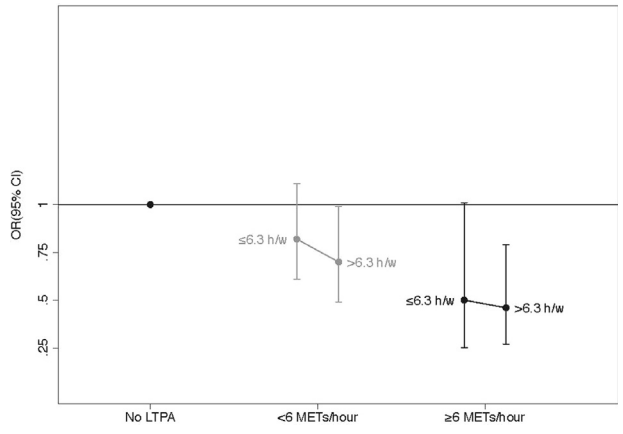

Figure 1. MS risk according to the intensity of LTPA and time spent in LTPA.

Note: Intensity was specified as light to moderate LTPA (<6 METs/hour) and vigorous LTPA (≥6 METs/hour). Time spent in LTPA was specified in two categories taking the median as cut off (≤6.3 hours per week and >6.3 hours per week). The reference group included those participants that were not engaged in any exercise. Data were adjusted by age, sex, smoking status, baseline BMI, total energy intake, adherence to the Mediterranean diet, following any special diet, snacking, sugar-sweetened soda consumption, alcohol intake, french fries consumption, fast-food consumption, educational level, computer use, TV watching, house chores, hours sleeping, napping, physical activity at work, prevalence of cardiovascular disease and cancer, and total energy expenditure in LTPA per week.

LTPA, leisure time physical activity; MS, metabolic syndrome.

from which participants with any MS component at baseline were excluded. The component of MS that exhibited the strongest association with VPA was waist circumference (Table 3). It is likely that exercise would have a greater impact on overweight adults than on subjects with normal weight, but the mean BMI for all groups in this cohort was <23. Despite this suboptimal setting, the study did find significant associations, but may have underestimated the potential benefits of VPA in this healthy cohort. The authors also estimated the multivariable AOR of MS within quartiles of total energy expenditure in LTPA and hours of LTPA, but found that even though they were in the direction of an inverse association, results were not significant.

A plausible biological pathway through which VPA may have a greater influence on MS than an equivalent energy expenditure of moderate physical activity is the reduction in abdominal obesity.[33] A clinical trial showed that men who performed moderate to vigorous intensity exercise experienced greater loss of overall and abdominal fat.[34] This could explain why the authors found that a significant inverse association was present only among men. Also, this could be due to the differences in the physical activity patterns. Men performed VPA more frequently and for a longer duration than women. Furthermore, the variability in the intensity of LTPA was lower among women. The association between sex and VPA could have influenced the results by bringing them toward the null among women, because, as it is well known, it is more difficult to find differences between ordered categories (quartiles) of an exposure when the variability in that exposure is lower. Vigorous LTPA was associated with the reduction of MS incidence in older participants (aged >55 years), probably owing to their higher susceptibility to develop MS, obesity, and diabetes.

The present findings are consistent with some previous cross-sectional studies that show the beneficial effects of VPA on reducing the incidence of MS,[16–18,35,36] but not many studies have examined the effects of different intensities of physical activity, independent of total energy expenditure, in a prospective way. A prospective cohort study, the Copenhagen City Heart Study, confirmed the role of physical activity in reducing MS risk and suggested that the intensity, more than the quantity of physical activity, was important. But potential differences in dietary habits, which may have a significant impact on the results, were not taken into account.[20] To the authors' knowledge, this is the first study to examine the association between intensity of LTPA and MS in a large prospective cohort, including lifestyle and dietary confounding factors.

The effects of VPA may vary, depending on the examined outcome. This study did not find any significant association between intensity of LTPA and high blood pressure, high triglycerides, low high-density lipoprotein cholesterol, or impaired glucose metabolism after 6 years of follow-up, even though all the non-significant estimates were in the direction of an inverse association, similar to the results of other studies.[37–39]

Current physical activity guidelines[7] imply that, at the same time, VPA consumes about twice as many calories as moderate physical activity, so health benefits of VPA are derived from the shorter timeframe needed to expend the appropriate amount of energy. These findings suggest that other benefits of VPA, independent of energy expenditure rates, should be considered. People should be advised to practice VPA, not only as a time-efficient approach, but also for achieving greater health benefits.

Limitations

This study has important strengths such as its large size, the long follow-up period, and the existence of previously published validation studies. One limitation of the study is that the sample was not representative; however, is not necessary for the sample to be representative, and the fact that all participants were university students adds validity to the high-quality information derived from their questionnaires.

CONCLUSIONS

In this cohort, vigorous LTPA prevented MS better than light and moderate LTPA, independent of total time and total energy spent in LTPA. Further studies should be conducted to confirm these results.

ACKNOWLEDGMENTS

We thank the other members of the *Seguimiento Universidad de Navarra* (SUN) Group: A Alonso, A Balaguer, MT Barrio López, FJ Basterra-Gortari, S Benito Corchón, JJ Beunza, S Carlos Chillerón, L Carmona, S Cervantes, J de Irala Estévez, C de la Fuente Arrillaga, PA de la Rosa, M Delgado Rodríguez, CL Donat Vargas, C Galbete Ciáurriz, M García López, A Gea Sánchez, E Goñi Ochandorena, F Guillén Grima, A Hernández, F Lahortiga, J Llorca, C López del Burgo, A Marí Sanchís, A Martí del Moral, N Martín Calvo, JA Martínez, JM Núñez-Córdoba, AM Pimenta, M RuizCanela, A Ruiz Zambrana, D Sánchez Adán, A Sánchez-Villegas, C Sayón-Orea, E Toledo, J Toledo, Z Vázquez Ruiz, and I Zazpe.

This work was supported by the Spanish Government-Instituto de Salud Carlos III, and the European Regional Development Fund (RD 06/0045, CIBERObn, grants PI10/02658, PI10/02293, PI13/00615, PI14/01668, PI14/01798, PI14/01764, and G03/140), the Navarra Regional Government (45/2011 and 122/2014), and the University of Navarra.

A Fernandez-Montero contributed to data research, extracted data, performed data analysis, and drafted the manuscript. M Bes-Rastrollo reviewed data analysis and contributed to discussion, revision, and intellectual revision of the manuscript. L Moreno-Galarraga, A Sanchez-Villegas, and MT Barrio-Lopez reviewed data analysis and contributed to discussion and revision of the manuscript. MA Martinez-Gonzalez contributed to the design, generation of the database, data analysis, and intellectual revision of the manuscript. All authors made substantial contributions to conception and design, acquisition of data, and approved the final version to be published.

No financial disclosures were reported by the authors of this paper.

REFERENCES

1. Alberti KG, 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*. 2009:1640–1645. http://dx.doi.org/10.1161/CIRCULATIONAHA.109.192644.
2. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol*. 2007;49(4):403–414. http://dx.doi.org/10.1016/j.jacc.2006.09.032.
3. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002;288(21):2709–2716.
4. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. *CMAJ*. 2006;174(6):801–809. http://dx.doi.org/10.1503/cmaj.051351.
5. Lee IM, Skerrett PJ. Physical activity and all-cause mortality: what is the dose—response relation. *Med Sci Sports Exerc*. 2001;33(suppl 6):S459–S471. http://dx.doi.org/10.1097/00005768-200106001-00016.
6. Leon AS, Connett J. Physical activity and 10.5 year mortality in the Multiple Risk Factor Intervention Trial (MRFIT). *Int J Epidemiol*. 1991;20(3):690–697. http://dx.doi.org/10.1093/ije/20.3.690.
7. WHO. *Global Recommendations on Physical Activity for Health*. Geneva; 2010.
8. Holme I, Tonstad S, Sogaard AJ, Larsen PG, Haheim LL. Leisure time physical activity in middle age predicts the metabolic syndrome in old age: results of a 28-year follow-up of men in the Oslo study. *BMC Public Health*. 2007;7:154. http://dx.doi.org/10.1186/1471-2458-7-154.
9. Huffman KM, Sun JL, Thomas L, et al. Impact of baseline physical activity and diet behavior on metabolic syndrome in a pharmaceutical trial: results from NAVIGATOR. *Metabolism*. 2014;63(4):554–561. http://dx.doi.org/10.1016/j.metabol.2014.01.002.
10. Yang X, Telama R, Hirvensalo M, et al. The longitudinal effects of physical activity history on metabolic syndrome. *Med Sci Sports Exerc*. 2008;40(8):1424–1431. http://dx.doi.org/10.1249/MSS.0b013e318172ced4.
11. Laaksonen DE, Lakka HM, Salonen JT, et al. Low levels of leisure-time physical activity and cardiorespiratory fitness predict development of the metabolic syndrome. *Diabetes Care*. 2002;25(9):1612–1618. http://dx.doi.org/10.2337/diacare.25.9.1612.
12. He D, Xi B, Xue J, et al. Association between leisure time physical activity and metabolic syndrome: a meta-analysis of prospective cohort studies. *Endocrine*. 2014;46(2):231–240. http://dx.doi.org/10.1007/s12020-013-0110-0.
13. Gebel K, Ding D, Chey T, et al. Effect of moderate to vigorous physical activity on all cause mortality in middle-aged and older Australians. *JAMA Intern Med*. 2015;175(6):970–977. http://dx.doi.org/10.1001/jamainternmed.2015.0541.
14. EU Physical Activity Guidelines. Recommended policy actions in support of health-enhancing physical activity. Brussels, October 10, 2008. http://www.ua.gov.tr/docs/default-source/gen%C3%A7lik-program%C4%B1/eu-physical-activity-guidelines-2008-(ab-beden-e%C4%9Fitimi-rehberi).pdf?sfvrsn=0. Accessed December 7, 2016.
15. Haskell WL, Lee I-M, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;116(9):1081–1093. http://dx.doi.org/10.1161/CIRCULATIONAHA.107.185649.
16. Janssen I, Ross R. Vigorous intensity physical activity is related to the metabolic syndrome independent of the physical activity dose. *Int J Epidemiol*. 2012;41(4):1132–1140. http://dx.doi.org/10.1093/ije/dys038.
17. Hu B, Liu X, Wang C, et al. Vigorous-intensity physical activity is associated with metabolic syndrome among the Chinese middle-aged population: a cross-sectional study. *Int J Sport Nutr Exerc Metab*. 2015;25(2):119–127. http://dx.doi.org/10.1123/ijsnem.2013-0231.
18. Greenwood EA, Noel MW, Kao CN, et al. Vigorous exercise is associated with superior metabolic profiles in polycystic ovary syndrome independent of total exercise expenditure. *Fertil Steril*. 2016;105(2):486–493. http://dx.doi.org/10.1016/j.fertnstert.2015.10.020.
19. Shuval K, Barlow CE, Finley CE, et al. Standing, obesity, and metabolic syndrome: findings from the Cooper Center Longitudinal Study. *Mayo Clin Proc*. 2015;90(11):1524–1532. http://dx.doi.org/10.1016/j.mayocp.2015.07.022.
20. Laursen AH, Kristiansen OP, Marott JL, Schnohr P, Prescott E. Intensity versus duration of physical activity: implications for the metabolic syndrome. A prospective cohort study. *BMJ Open*. 2012;2(5):e001711. http://dx.doi.org/10.1136/bmjopen-2012-001711.
21. Meng DJ, Chen JC, Huang JF, et al. Relationship between physical activity and the incidence of metabolic syndrome in Chinese adults: a prospective cohort study. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2013;47(4):312–317.

22. Seguí-Gómez M, de la Fuente C, Vázquez Z, et al. Cohort profile: the "Seguimiento Universidad de Navarra" (SUN) Study. *Int J Epidemiol*. 2006;35(6):1417–1422. http://dx.doi.org/10.1093/ije/dyl223.
23. Martínez-González MA, Sanchez-Villegas A, De Irala J, Marti A, Martínez JA. Mediterranean diet and stroke: objectives and design of the SUN project. Seguimiento Universidad de Navarra. *Nutr Neurosci*. 2002;5(1):65–73. http://dx.doi.org/10.1080/10284150290007047.
24. Martínez-González MA. The SUN cohort study (Seguimiento University of Navarra). *Public Health Nutr*. 2006;9(1a):127–131. http://dx.doi.org/10.1079/phn2005935.
25. Martinez-Gonzalez MA, López-Fontana C, Varo JJ, Sánchez-Villegas A, Martinez JA. Validation of the Spanish version of the physical activity questionnaire used in the Nurses 'Health Study and the Health Professionals' follow-up study. *Public Health Nutr*. 2005;8(7):920–927. http://dx.doi.org/10.1079/PHN2005745.
26. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of physical activities: a second update of codes and MET values. *Med Sci Sports Exerc*. 2011;43(8):1575–1581. http://dx.doi.org/10.1249/MSS.0b013e31821ece12.
27. Martın-Moreno JM, Boyle P, Gorgojo L, et al. Development and validation of a food frequency questionnaire in Spain. *Int J Epidemiol*. 1993;22(3):512–519. http://dx.doi.org/10.1093/ije/22.3.512.
28. Fernández-Ballart JD, Piñol JL, Zazpe I, et al. Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. *Br J Nutr*. 2010;103(12):1808–1816. http://dx.doi.org/10.1017/S0007114509993837.
29. de la Fuente-Arrillaga C, Ruiz ZV, Bes-Rastrollo M, Sampson L, Martinez-González MA. Reproducibility of an FFQ validated in Spain. *Public Health Nutr*. 2010;13(9):1364–1372. http://dx.doi.org/10.1017/S1368980009993065.
30. Bes-Rastrollo M, Pérez-Valdivieso JR, Sanchez-Villegas A, Alonso A, Martinez Gonzalez MA. Validación del peso e índice de masa corporal autodeclarados de los participantes de una cohorte de graduados universitarios. *Rev Esp Obes*. 2005;3:183–189.
31. Fernandez-Montero A, Beunza J, Bes Rastrollo M, et al. Validity of self-reported metabolic syndrome components in a cohort study. *Gac Sanit*. 2011;25:303–307.
32. Barrio Lopez M, Bes Rastrollo M, Beunza J, et al. Validation of metabolic syndrome using medical records in the SUN cohort. *BMC Public Health*. 2011;11:867. http://dx.doi.org/10.1186/1471-2458-11-867.
33. Trapp EG, Chisholm DJ, Freund J, Boutcher SH. The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *Int J Obes (Lond)*. 2008;32:684–691. http://dx.doi.org/10.1038/sj.ijo.0803781.
34. McTiernan A, Sorensen B, Irwin ML, et al. Exercise effect on weight and body fat in men and women. *Obesity (Silver Spring)*. 2007;15(6):1496–1512. http://dx.doi.org/10.1038/oby.2007.178.
35. Rennie KL, McCarthy N, Yazdgerdi S, Marmot M, Brunner E. Association of the metabolic syndrome with both vigorous and moderate physical activity. *Int J Epidemiol*. 2003;32(4):600–606. http://dx.doi.org/10.1093/ije/dyg179.
36. Mensink GB, Ziese T, Kok FJ. Benefits of leisure-time physical activity on the cardiovascular risk profile at older age. *Int J Epidemiol*. 1999;28(4):659–666. http://dx.doi.org/10.1093/ije/28.4.659.
37. Pavey TG, Peeters G, Bauman AE, Brown WJ. Does vigorous physical activity provide additional benefits beyond those of moderate? *Med Sci Sports Exerc*. 2013;45(10):1948–1955. http://dx.doi.org/10.1249/MSS.0b013e3182940b91.
38. Paffenbarger RS, Lee IM. Intensity of physical activity related to incidence of hypertension and all-cause mortality: an epidemiological view. *Blood Press Monit*. 1997;2(3):115–123.
39. Williams PT. Relationship of running intensity to hypertension, hypercholesterolemia, and diabetes. *Med Sci Sports Exerc*. 2008;40(10):1740–1748. http://dx.doi.org/10.1249/MSS.0b013e31817b8ed1.