PROTOCOL

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Effectiveness of an intensive intervention to improve lifestyles in people with intermediate cardiovascular risk (DATE study): Study protocol for a randomized controlled trial

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Abstract

Aim: The aim of this study was to evaluate the effectiveness of an intensive intervention led by primary care nurses for lifestyle modification among people with intermediate cardiovascular risk.

Background: Cardiovascular diseases may be prevented by adopting healthy lifestyles. Interventions focused on populations at risk are more efficient than those aimed at the general population. More than 50 per cent of cardiovascular events occur in people with intermediate cardiovascular risk, but only a few studies have targeted this population.

Design: A randomized controlled trial approved in January 2017.

Methods: We will recruit 208 participants aged 35–74 years who have intermediate cardiovascular risk. They will be selected by consecutive sampling and will be randomized into a control group or intervention group. Individual standardized brief counselling on healthy lifestyles will be provided to both groups. Additionally, individuals from the intervention group will receive four weekly group sessions focusing on cardiovascular risk, healthy diet, moderation in alcohol consumption, daily physical activity, stress management and smoking cessation and two motivational follow-up calls. The primary outcome will be the lifestyle modification measured by total steps recorded by a pedometer, total score on the Mediterranean Diet Adherence Screener and percentage of current smokers.

Discussion: This study will allow us to investigate whether an intensive intervention based on a multifactorial group approach is more effective in lifestyle modification than individual standardized brief counseling among adults with intermediate

cardiovascular risk. Our results could lead to the establishment of new strategies for cardiovascular risk management.

1 | INTRODUCTION

Vascular diseases are implicated in 30% of all deaths worldwide, with 17.3 million fatalities each year (Mendis, Puska, & Norrving, 2011). In Spain, these diseases are a leading public health concern, having caused 124,197 deaths in 2015 (29.4% of all fatalities) (Deaths according to Cause of Death Year 2015, 2017). Vascular diseases have also been associated with the development of other disorders that can affect patient quality of life, such as cognitive impairment and dementia (Corriveau et al., 2016).

1.1 | Background

The World Health Organisation (WHO) estimates that around 80% of all cardiovascular diseases could be avoided through health-promoting behaviours (The World Health Report-Reducing risks, promoting healthy life, 2002). These observations have led to many studies designed to evaluate the efficacy and effectiveness of different interventions aimed at improving cardiovascular health. In this regard, the European cardiovascular prevention guidelines (Graham et al., 2007) consider that it is more efficient to act on the population without established disease but with a high risk of developing such disorders than on the general or low-risk population.

Likewise, a Cochrane Review (Ebrahim et al., 2011) indicated that interventions designed to reduce cardiovascular risk based on changes in lifestyle have not been effective in reducing morbidity–mortality in the general population, but they could prove effective when targeting high-risk populations and when combined with drug treatment strategies. However, although 56% of all cardiovascular events occur in individuals classified as having intermediate risk (Marti et al., 2011), few studies have focused on this particular population. We, therefore, consider that it is necessary to establish the efficiency of interventions targeting this risk group.

Eating habit interventions involving more frequent orientation or reinforcement sessions are more effective (Maderuelo-Fernandez et al., 2015). In our setting, the Mediterranean diet is considered as the most healthy form of diet, but until the PREDIMED (Prevention with Mediterranean Diet) study (Estruch et al., 2006), no clinical trials had been carried out to determine whether its effects are greater than those of a low-fat diet in the primary prevention of cardiovascular disorders. In the first phase, this study recorded an average increment of 1.8 points on a 14-point scale assessing adherence to the Mediterranean diet in the study groups versus a

> **Why is this research needed?**
>
> - This study will be the first to investigate the effects of a nurse-led intensive intervention based on a multifactorial group approach towards lifestyle modification aimed at the primary prevention of cardiovascular diseases in people with intermediate cardiovascular risk.
> - The results from this study could provide the necessary information to establish new strategies for the health education and treatment for patients with intermediate cardiovascular risk.

0.3-point increment in the control group (Salas-Salvado et al., 2008). After 4 years of follow-up, the results indicated a 30% reduction in the incidence of major cardiovascular events in the intervention groups versus the control group (Estruch, Ros, & Martinez-Gonzalez, 2013).

A recent meta-analysis of trials in primary care has shown that promoting physical activity among sedentary individuals increases the proportion of individuals who become physically active after 12 months (odds ratio [OR]: 1.42; 95% confidence interval [95%CI]: 1.17–1.73), although this effect has not been confirmed over the long term (Hobbs et al., 2013; Orrow, Kinmonth, Sanderson, & Sutton, 2012). The PEPAF (Experimental Programme for the Promotion of Physical Activity) study (Grandes et al., 2009) found that counselling on physical activity offered only minor results, while the prescription of a physical activity plan yielded considerably more relevant outcomes. The study intervention achieved an increment in physical activity of 18 min/week (95% CI: 6–31) compared with the control group, with an increase in 1.3 METS/hour/week (95% CI: 0.4–2.2). Furthermore, the number of patients who reached the minimum recommended physical activity levels was 3.9% higher in the intervention group (95% CI: 1.2–6.9) than in the control group.

The percentage smoking cessation was observed to increase with the intensity of the intervention, the time dedicated and the number and diversity of contacts, including follow-up visits (Lemmens, Oenema, Knut, & Brug, 2008). Isolated minimum counselling for smoking cessation targeted to the general population results in an average cessation rate of 5% after 1 year (Russell, Wilson, Taylor, & Baker, 1979), while interventions involving intensive follow-up can reach percentages of over 20% (Lemmens et al., 2008; Stead, Bergson, & Lancaster, 2008).

A systematic review has found that brief counselling offers only moderate efficacy in reducing intake among non-alcoholics (Alvarez-Bueno, Rodriguez-Martin, Garcia-Ortiz, Gomez-Marcos, & Martinez-Vizcaino, 2015). There is scientific evidence of the effectiveness of simultaneous interventions targeting multiple risk factors, particularly in individuals with a high risk of disease (Alvarez-Bueno et al., 2015; Goldstein, Whitlock, & DePue, 2004; Sweet & Fortier, 2010). Group interventions may offer benefits from social support and could be more cost effective (Bayley et al., 2015), but the impact on cardiovascular risk from multifactorial group interventions is unclear. Goyer et al. (Goyer et al., 2013) tested an interdisciplinary multifaceted intervention with weekly group sessions in adults with multiple cardiovascular risk factors. The intervention was superior to programmes in a specialized clinic or in usual care family practice in reducing cardiovascular risk and improving health behaviours after 2 years of follow-up. A combination of educational training on lifestyle modification and a peer group intervention also had benefits on cardiovascular risk factors over a 1-year period among adults at risk of cardiovascular disease (Gomez-Pardo et al., 2016). Similar results have been reported by studies which implemented nurse-led education programmes based on lifestyle group counselling in primary healthcare settings (Gilis-Januszewska et al., 2017; Jarl, Tolentino, James, Clark, & Ryan, 2014; Laatikainen et al., 2007).

The presence of cardiovascular risk factors in adult life may be related to an increased risk of cognitive decline in old age (Anstey, Sargent-Cox, Garde, Cherbuin, & Butterworth, 2014). Likewise, there may be a relationship between lifestyle and cognitive decline, with healthy habits being associated with a lower risk of cognitive decline (Crichton, Elias, Dore, & Robbins, 2012; Grodstein, 2007). Recent studies have suggested that a multidisciplinary approach to cardiovascular risk factors could reduce the risk of cognitive impairment (Richard et al., 2016).

There is a close relationship between cardiovascular diseases and quality of life (Wannamethee & Shaper, 1991). Epidemiological studies have demonstrated the influence on self-perceived health of different factors such as smoking or obesity (Corica et al., 2008; Guiterrez-Bedmar, Segui-Gomez, Gomez-Gracia, Bes-Rastrollo, & Martinez-Gonzalez, 2009). Likewise, there is evidence of an association between quality of life and healthy lifestyles (Koltyn, 2001; Munoz, Fito, Marrugat, Covas, & Schroder, 2009; Stephens, 1988). This is supported by our earlier study where perceived quality of life was associated with food habits and physical activity in a large sample of adults with intermediate cardiovascular risk (Sanchez-Aguadero et al., 2016).

2 | THE STUDY

2.1 | Aims

The goal of this study is to quantify the short- and long-term effects of an intensive intervention led by primary care nurse practitioners in terms of changes in lifestyle in a sample that comprises Spanish

men and women aged between 35–74 years classified as having intermediate cardiovascular risk.

2.1.1 | Objectives

The general objectives of this study are:

- To design an intensive intervention to effectively modify lifestyles, physical activity, adherence to the Mediterranean diet and smoking among people with intermediate cardiovascular risk.
- To evaluate the effectiveness of the designed intervention on lifestyle modification, cardiovascular risk factor control, cardiovascular risk reduction, quality of life and cognitive performance improvement in people with intermediate cardiovascular risk.

2.1.2 | Hypotheses

- The intervention will increase physical activity, enhance the adherence to the Mediterranean diet and decrease the percentage of current smokers.
- The experimental group will have improved cardiovascular risk factors, quality of life and cognitive performance.

2.2 | Design/methodology

2.2.1 | Design and setting

This study is a randomized controlled trial. As illustrated in Figure 1, three evaluation visits are scheduled (at baseline and at 3 and 12 months after randomization).

Study setting

The study will be conducted in the Primary Care Health Area of Salamanca, Spain, in the Miguel Armijo Health Centre, San Juan Health Centre and La Alamedilla Primary Care Research Unit, which are part of the Biomedical Research Institute of Salamanca.

2.2.2 | Study population

A total of 208 patients will be selected by consecutive sampling at the primary care centres. Then, they will be randomized into an intervention group (IG) and control group (CG) using the Epidat 4.0 software package.

Inclusion criteria

The study will include adults aged 35–74 years who have intermediate cardiovascular risk, which is defined as coronary risk at 10 years >10% and <20% according to the Framingham risk equation, Grundy version (Grundy, Pasternak, Greenland, Smith, & Fuster, 1999).
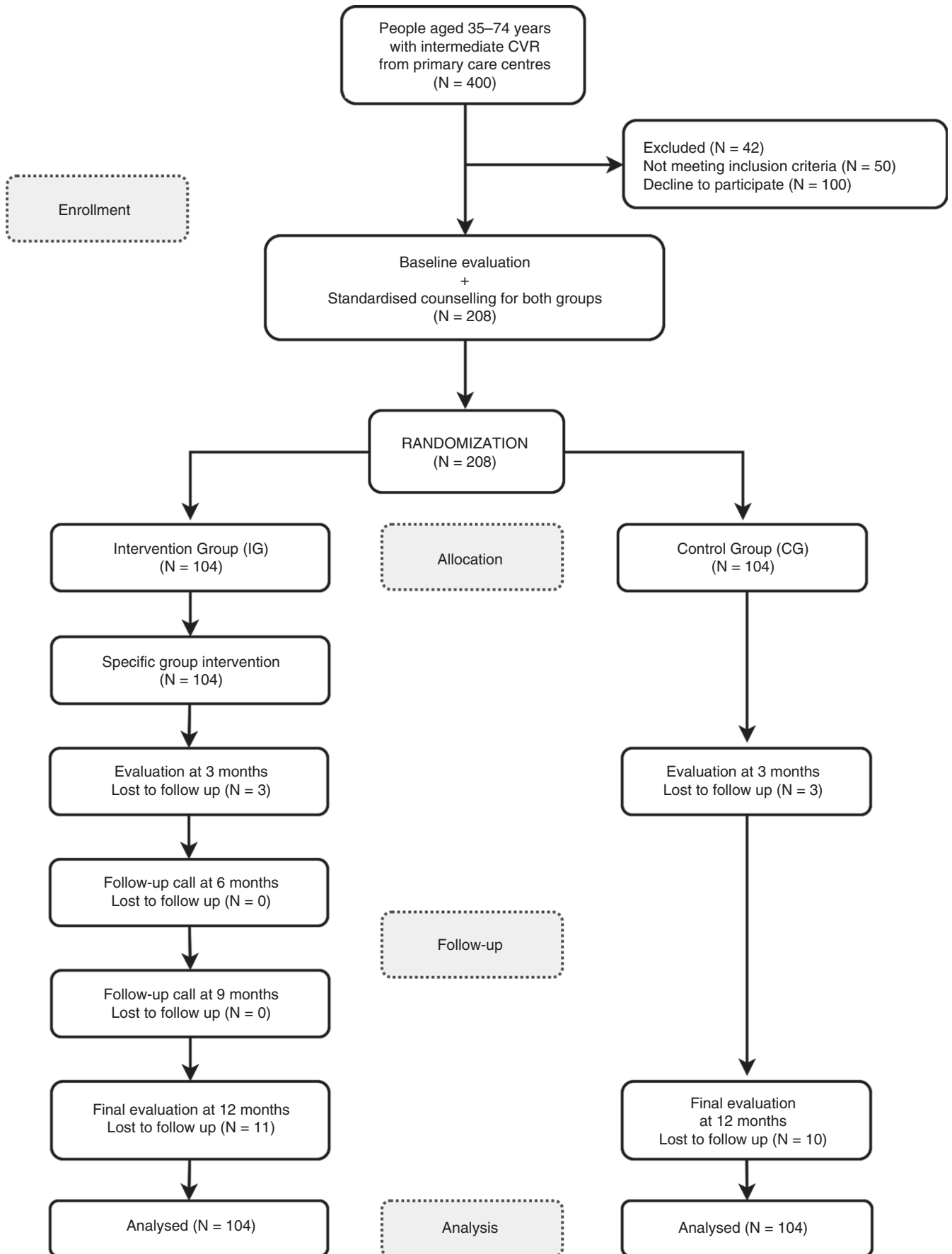
People aged 35–74 years
with intermediate CVR
from primary care centres
(N = 400)

Excluded (N = 42)
Not meeting inclusion criteria (N = 50)
Decline to participate (N = 100)

Enrollment

Baseline evaluation
+
Standardised counselling for both groups
(N = 208)

RANDOMIZATION
(N = 208)

Intervention Group (IG)
(N = 104)

Allocation

Control Group (CG)
(N = 104)

Specific group intervention
(N = 104)

Evaluation at 3 months
Lost to follow up (N = 3)

Evaluation at 3 months
Lost to follow up (N = 3)

Follow-up call at 6 months
Lost to follow up (N = 0)

Follow-up

Follow-up call at 9 months
Lost to follow up (N = 0)

Final evaluation at 12 months
Lost to follow up (N = 11)

Final evaluation
at 12 months
Lost to follow up (N = 10)

Analysed (N = 104)

Analysis

Analysed (N = 104)

FIGURE 1 Flow-chart of DATE study; (CVR: Cardiovascular Risk).

Exclusion criteria

The study will exclude people who are unable to perform exercise or to follow the Mediterranean diet and institutionalized patients and those with a personal history of atherosclerotic disease, terminal illness, or mental disorders that limit compliance with the intervention.

2.2.3 | Sample size

Sample size estimation has been carried out for the primary study variables. Regarding physical activity, we would need 208 participants (104 per group) to detect an increment of 1850 steps/day in the IG versus CG with an alpha risk of 0.05, beta risk of 0.20 and a standard deviation (SD) of 4500 steps per day. For the Mediterranean diet (MD), 208 participants (104 per group) would be required to detect an increase in 0.82 points in the MD questionnaire in the IG versus CG, assuming an alpha risk of 0.05, beta risk of 0.20 and an SD of 2 points. A follow-up loss of 10% is expected.

2.2.4 | Primary and secondary outcomes

The primary outcome will be lifestyle modification measured by the total steps recorded by a pedometer, the total score on the Mediterranean Diet Adherence Screener and the percentage of current smokers. Secondary outcomes will include cardiovascular risk factors measured by the lipid profile, peripheral blood pressure, glycaemia and glycosylated haemoglobin. In addition, quality of life and cognitive performance will also be measured and treated as second outcomes. All outcomes will be measured at 3 and 12 months after randomization.

2.2.5 | Variables and measurement instruments

Sociodemographic and clinical variables

Data on age, sex, marital status, educational level and occupation will be recorded. Family and personal history of cardiovascular diseases will be documented. We will collect the data of diagnosis of hypertension, diabetes, dyslipidaemia or atrial fibrillation and information on prescribed drugs (antiplatelet and anticoagulant agents, oral contraceptives, hormonal therapy, lipid-lowering, antihypertensive and antidiabetic agents).

Peripheral blood pressure

Systolic (SBP) and diastolic (DBP) blood pressures will be measured with a validated Omron M10-IT model sphygmomanometer (Omron Healthcare, Kyoto, Japan) on the participant's dominant arm with a cuff of appropriate size as determined by the upper arm circumference. Three measurements will be performed with the subject in a seated position after at least 5 min of rest following the recommendations of the European Society of Hypertension (2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of

Arterial Hypertension, 2013). The average of the last two measurements will be recorded.

Anthropometric measurements

Body weight will be determined in duplicate with the subject barefoot and wearing light clothing using a homologated electronic balance (Scale 7830; Soehnle Professional GmbH & Co, Backnang, Germany) after proper calibration (precision ± 0.1 kg). Height will be measured with the subject standing and barefoot to record the average of two readings rounded to the nearest centimetre using a portable system (Seca 222; Medical scale and measurement system, Birmingham, UK). Following the recommendations of the Spanish Society for the Study of Obesity (SEEDO) (Salas-Salvado, Rubio, Barbany, & Moreno, 2007), the waist circumference will be measured twice using a flexible tape parallel to the floor at the level of the midpoint between the last rib and the iliac crest. The measurements will be taken without clothing in a standing position after inspiration. Hip circumference will be similarly determined at the level of the trochanters. Body mass index (BMI) will be calculated as the weight (kg) divided by height squared (m^2).

Body composition

Body composition will be determined using an Inbody 230 analyser (Karelis, Chamberland, Aubertin-Leheudre, & Duval, 2013). The analyser estimates total body water, dry lean mass, body fat mass, skeletal muscle mass, percentage body fat, the distribution of lean body mass, the ratio of segmental lean mass and the impedance of each body segment.

Arterial stiffness evaluation

A Vasera VS-2000 device (Fukuda Denshi) will be used to determine the cardio-ankle vascular index (CAVI), brachial–ankle pulse wave velocity (ba-PWV) and ankle–brachial index (ABI) at rest. CAVI ≥ 9, ba-PWV ≥ 17.5 and ABI ≤ 0.9 will be considered abnormal.

Laboratory variables

Spot morning urine sampling will be performed to determine the albumin–creatinine ratio. Venous blood samples will be collected between 08:00 am and 9:00 am after participants have fasted and abstained from smoking, alcohol and caffeinated beverages for 12 hr. Plasma glucose, creatinine, serum total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and triglyceride concentrations will be determined using standard enzymatic automated methods. Glycosylated haemoglobin, high sensitivity C-reactive protein levels and fibrinogen values will be measured with an immune-turbidimetric assay. The analysis will be performed at a hospital in a city participating in external quality assurance programmes of the Spanish Society of Clinical Chemistry and Molecular Pathology.

Cardiovascular risk estimation

The risk of cardiovascular morbidity and mortality will be estimated using the risk equation based on the Framingham study (Grundy

et al., 1999). The equation includes age, sex, total cholesterol, HDL cholesterol, glycaemia and SBP as quantitative variables and smoking as a dichotomous variable.

Lifestyle-related variables

Smoking Smoking will be assessed using a questionnaire on smoking history and tobacco consumption patterns. The carbon monoxide concentration will be measured by a MicroCO co-oximeter (MicroMedical Ltd, Kent, UK) after asking participants about when the last time they smoked a cigarette.

Alcohol consumption Alcohol consumption will be determined using a questionnaire on alcohol consumption in the past 7 days specifying drinks and their volumes.

Diet Adherence to the Mediterranean diet will be assessed using a 14-point Mediterranean Diet Adherence Screener that has previously been validated in Spain (Schroder et al., 2011). The screener explores the compliance with various aspects considered the characteristic of the Mediterranean diet. Total scores greater than or equal to nine points will be considered as indicating adequate adherence.

The participants' dietary habits will be evaluated using a validated semiquantitative food frequency questionnaire (Fernandez-Ballart et al., 2010). The estimated frequency corresponds to the previous year at the time of the interview and is divided into nine intake categories ranging from never to more than six servings per day, which are multiplied by the typical portion sizes for each food. This will be used to estimate daily energy intake, macronutrients and micronutrients.

Physical activity Physical activity will be measured using a digital pedometer (Omron HJ-321 Tri-Axial) (Huang, Xu, Yu, & Shull, 2016). The pedometer will be fastened to the right side of the subject's waist for seven consecutive days during habitual physical activities (except bathing, performing activities in the water and sleeping). The pedometer records calories burned, distance walked, total steps and aerobic steps (counted separately when walking more than 60 steps per minute and more than 10 min continuously).

The short version of the International Physical Activity Questionnaire (IPAQ) will also be used (Roman Vinas, Ribas Barba, Ngo, & Serra Majem, 2013). The questionnaire evaluates sitting and activity time in the past 7 days, differentiating between walking, moderate-intensity and vigorous-intensity activities according to the energy expenditure estimated for each of them (3.3, 4 and 8 metabolic equivalents of task [MET], respectively). It allows for the calculation of MET-minutes/week and the classification of participants into three activity levels (low, intermediate and high).

Cognitive performance

Attention and executive functions The Trail Making Test A will be used to evaluate attention and the Trail Making Test B will be used for executive functions and processing speed (Trail Making Test:

Reitan, 1992). Sustained and selective attention, executive functions and processing speed will be assessed with the Stroop test (Golden, 2005).

Verbal memory A list of 15 different words from the Rey Auditory Verbal Learning Test (Rey, 1964) will be used to evaluate the immediate verbal memory via immediate recall over three attempts. Delayed verbal memory will be assessed by the free recall of words learned in the first part of the evaluation after 10 min.

Working memory Working memory will be explored with the WAIS Digit Span Backward test (Wechsler, 1987).

Phonological fluency Phonological fluency will be evaluated by asking the participants to enumerate as many words as possible starting with different letters for one minute (Valencia et al., 2000).

Quality of life

Quality of life will be assessed using the Spanish version of the Short Form-12 (SF-12) questionnaire (Gandek et al., 1998). The questionnaire explores eight dimensions of quality of life (physical functioning, physical role, body pain, general health, vitality, emotional role, social functioning and mental health), which can be aggregated into two summary measures (physical and mental composite scores). Higher the scores indicate better quality of life.

Motivation to change

At each interview, the participants' motivation stage will be classified according to the Prochaska and Diclemente model (pre-contemplation, contemplation, determination, action, maintenance and relapse) (Prochaska & Velicer, 1997).

2.2.6 | Intervention

Common to both groups

All participants will receive individual standardized counselling on healthy diet, daily physical activity, stress management, smoking cessation and moderation in alcohol consumption for 5 min.

Specific to the intervention group

Individuals allocated to the IG will attend group sessions for four consecutive weeks, which will be held in health centres. Each session will last 60–90 min and will be led by two trained nurse practitioners. Ten participants will attend each group. During each session, attendance will be recorded and printed educational materials related to the topic addressed will be distributed:

1. First group session—why is lifestyle important?: A guided discussion session will be held to explain the concept and relevance of cardiovascular risk, the most important cardiovascular risk factors and ways to modify them and the main cardiovascular diseases, their causes and preventive measures.

2. Second group session—bites of knowledge: A heart-healthy cooking workshop will be held to explain how to purchase the healthiest foods from the supermarket, distribute them adequately in the regular diet and cook them in a healthy way. The workshop will also underscore the importance of moderating alcohol intake. With this idea in mind, brief initial considerations will be made for healthy eating habits, the Mediterranean diet and moderate alcohol consumption, followed by participant preparation of three heart-healthy dishes (first, second and dessert courses).

3. Third group session—each step counts: A physical activity and relaxation workshop will inform about the benefits of regular physical activity and stress reduction, with training on how to cope with stress and comply with the current recommendations for physical activity. A brief initial consideration will be made for the importance of physical activity and stress control, followed by the implementation of a physical activity programme with the control of heart rate, which is divided into five stages (warm-up, muscle resistance exercise with an elastic band, heart-healthy walking, stretching and relaxation exercises).

4. Fourth group session—myths and facts about smoking: A guided discussion session will be held for smokers, which is designed to clarify the benefits of smoking cessation, inform of the difficulties that can be met and prepare participants to achieve and maintain smoking cessation. With this idea in mind, a series of myths and facts about smoking will be discussed with the use of audiovisual material to evoke reflection (cinematographic scenes, publicity advertisements, etc.).

Furthermore, participants from the IG will receive two follow-up calls at 6 and 9 months after randomization, with focus on reinforcing lifestyle modification and recording the barriers to behaviour change that they encountered.

2.2.7 | Statistical analysis

Data will be provided as the $M \pm SD$ for quantitative variables or using the frequency distribution for qualitative variables. The results will be analysed made on an intent-to-treat (ITT) basis. The Kolmogorov–Smirnov test will be used to verify statistical normality. The association between independent qualitative variables will be analysed with the Chi-squared test along with the McNemar test for paired samples. A student t test will be applied for comparison of the means between two groups and a paired t test will be used to assess changes in the same group. The relationship between quantitative variables will be analysed using Pearson's or Spearman's correlation coefficients as appropriate. Multivariate linear regression analysis will be used to examine the variables that are the greatest determinants for changes in physical activity and eating habits. To analyse the effect of the intervention, the changes observed in the control group (CG) and the intervention group (IG) will be compared with the estimation of the Cohen d statistic, adjusting for variables that may influence the results. Logistic regression will be used to analyse the odds ratio (OR) for achieving the objectives of diet and exercise compliance. Gender will be considered in the analysis to assess differences between males and females in the short and long-term results. The impact of the intervention could be modified by age, gender, cultural and socioeconomic background, body mass index and certain disease conditions (diabetes, dyslipidaemia, etc.) and baseline lifestyles, which will be controlled in the analysis. The contrasting of hypotheses will be established using an alpha risk of 0.05 as the limit of statistical significance. The data will be analysed using IBM's SPSS Statistics for Windows version 23.0 (IBM Corporation, Armonk, NY, USA).

2.3 | Ethical considerations

The study was approved by the Clinical Research Ethics Committee of the Health Area of Salamanca ("CREC of Health Area of Salamanca") in January 2017. The trial has been registered at ClinicalTrials.gov with identifier NCT03164499.

2.3.1 | Informed consent

Participants must sign an informed consent form before inclusion in the study in accordance with the Declaration of Helsinki. They will be informed about the objectives of the study and the risks and benefits of the examinations that they will undergo, including the sample collection. None of the testing can result in life-threatening risks for the participants. Subject confidentiality will be ensured at all times in accordance with current laws and regulations on personal data protection (LOPD 15/1999 of 13 December) and the conditions described in Act 14/2007 on biomedical research.

2.4 | Validity and reliability/rigour

Valid and reliable instruments will be used to collect data. In addition, randomization will ensure a lack of systematic bias in the data. The study follows all the Consolidated Standards of Reporting Trials (CONSORT) recommendations (Schulz, Altman, & Moher, 2010), but participants cannot be blinded because of the nature of the intervention. Nevertheless, the investigator who analyses the data will be blinded to participant allocation and researchers performing randomization and specific intervention will be different from those conducting the evaluation and common intervention.

3 | DISCUSSION

Primary prevention is one of the most effective strategies for reducing the impact of cardiovascular diseases and it is more efficient to focus such strategies on individuals without established disease who are at risk of developing such disorders (Ebrahim et al., 2011; Graham et al., 2007). Many interventions have been developed to improve cardiovascular health in different populations. However, to the best of our knowledge, no previous study has conducted a

nurse-led intensive intervention simultaneously targeting several different lifestyle factors in particularly susceptible individuals with intermediate cardiovascular risk.

There is limited evidence on the efficacy of interventions designed to simultaneously address multiple risk behaviours in a primary care setting. It seems that multifactorial interventions produce small changes in lifestyle and if maintained over time, they could lead to a significant improvement in cardiovascular risk, quality of life and cognitive decline (Goldstein et al., 2004; Richard et al., 2016; Sweet & Fortier, 2010). However, it is still not clear whether it is more effective to use group or individual interventions in simultaneously addressing various risk factors (Bayley et al., 2015). Our results might contribute further evidence in this sense.

In a randomized controlled trial conducted with 185 adults with at least two modifiable cardiovascular risk factors, an interdisciplinary multifaceted programme was carried out with 12 weekly group sessions focusing on nutrition, physical activity and stress management/motivation. The intervention resulted in multiple lifestyle modifications, cardiovascular risk reduction and psychological improvement throughout the 2-year study duration. These findings are in accordance with our hypotheses. In this study, we hope to demonstrate that the designed intervention strategy contributes to improving lifestyle, cardiovascular risk factors, cardiovascular risk, cognitive performance and quality of life among individuals at intermediate cardiovascular risk.

The results of this study could lead to the creation of a new treatment tool based on lifestyle modification through a nurse-led intensive multifactorial intervention with group sessions and follow-up calls. This would allow for more efficient management of cardiovascular risk factors in a primary care setting. It could also contribute to preventing complications such as target organ damage, cardiovascular and cerebrovascular events and cognitive decline. Furthermore, such an intervention could improve patient quality of life and lessen the need for drug therapies among individuals with intermediate cardiovascular risk.

3.1 | Limitations

The analysis of the results related to lifestyle modifications and quality of life will be based on self-reported data, although validated tools will be used. However, objective data will be available in the case of physical activity (from pedometers), cardiovascular risk factors, cardiovascular risk estimation and cognitive performance, which may serve as quality control. Counselling based on healthy lifestyles provided to the control group might underestimate the intervention effect. Nonetheless, we have considered that the inclusion of control participants without any intervention would not be ethical.

4 | CONCLUSION

This study has the potential to improve lifestyles in people with intermediate cardiovascular risk via a nurse-led multifactorial

intervention based on educational group sessions and motivational follow-up calls.

CONFLICT OF INTEREST

No conflict of interest has been declared by the authors.

AUTHOR CONTRIBUTIONS

All authors have agreed on the final version and meet at least one of the following criteria [recommended by the ICMJE (http://www.icmje.org/recommendations/)]:

- substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
- drafting the article or revising it critically for important intellectual content.

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REFERENCES

Alvarez-Bueno, C., Cavero-Redondo, I., Martinez-Andres, M., Arias-Palencia, N., Ramos-Blanes, R., & Salcedo-Aguilar, F. (2015). Effectiveness of multifactorial interventions in primary health care settings for primary prevention of cardiovascular disease: A systematic review of systematic reviews. *Preventive Medicine*, *76*(Suppl), S68–S75. https://doi.org/10.1016/j.ypmed.2014.11.028

Alvarez-Bueno, C., Rodriguez-Martin, B., Garcia-Ortiz, L., Gomez-Marcos, M. A., & Martinez-Vizcaino, V. (2015). Effectiveness of brief interventions in primary health care settings to decrease alcohol consumption by adult non-dependent drinkers: A systematic review of systematic reviews. *Preventive Medicine*, *76*(Suppl), S33–S38. https://doi.org/10.1016/j.ypmed.2014.12.010

Anstey, K. J., Sargent-Cox, K., Garde, E., Cherbuin, N., & Butterworth, P. (2014). Cognitive development over 8 years in midlife and its association with cardiovascular risk factors. *Neuropsychology*, *28*(4), 653–665. https://doi.org/10.1037/neu0000044

Bayley, A., de Zoysa, N., Cook, D. G., Whincup, P. H., Stahl, D., Twist, K., & Ismail, K. (2015). Comparing the effectiveness of an enhanced MOtiVational intErviewing InTervention (MOVE IT) with usual care for reducing cardiovascular risk in high risk subjects: Study protocol for a randomised controlled trial. *Trials*, 16, 112. https://doi.org/10.1186/s13063-015-0593-5

Corica, F., Corsonello, A., Apolone, G., Mannucci, E., Lucchetti, M., Bonfiglio, C., & Marchesini, G. (2008). Metabolic syndrome, psychological status and quality of life in obesity: The QUOVADIS Study. *International Journal of Obesity (London)*, 32(1), 185–191. https://doi.org/10.1038/sj.ijo.0803687

Corriveau, R. A., Bosetti, F., Emr, M., Gladman, J. T., Koenig, J. I., Moy, C. S., & Koroshetz, W. (2016). The science of vascular contributions to cognitive impairment and dementia (VCID): A framework for advancing research priorities in the cerebrovascular biology of cognitive decline. *Cellular and Molecular Neurobiology*, 36(2), 281–288. https://doi.org/10.1007/s10571-016-0334-7

Crichton, G. E., Elias, M. F., Dore, G. A., & Robbins, M. A. (2012). Relation between dairy food intake and cognitive function: The maine-syracuse longitudinal study. *International Dairy Journal*, 22(1), 15–23. https://doi.org/10.1016/j.idairyj.2011.08.001

Deaths according to Cause of Death. Year 2015. (2017). Spanish Statistical Office [Press release]

Ebrahim, S., Taylor, F., Ward, K., Beswick, A., Burke, M., & Davey Smith, G. (2011). Multiple risk factor interventions for primary prevention of coronary heart disease. *The Cochrane Database of Systematic Reviews*, 1, Cd001561. https://doi.org/10.1002/14651858.cd001561.pub3

ESH/ESC Task Force for the Management of Arterial Hypertension. (2013). 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC). *Journal of Hypertens*, 31(10), 1925–1938. https://doi.org/10.1097/hjh.0b013e328364ca4c

Estruch, R., Martinez-Gonzalez, M. A., Corella, D., Salas-Salvado, J., Ruiz-Gutierrez, V., Covas, M. I., & Ros, E. (2006). Effects of a Mediterranean-style diet on cardiovascular risk factors: A randomized trial. *Annals of Internal Medicine*, 145(1), 1–11. https://doi.org/10.7326/0003-4819-145-1-200607040-00004

Estruch, R., Ros, E., & Martinez-Gonzalez, M. A. (2013). Mediterranean diet for primary prevention of cardiovascular disease. *The New England Journal of Medicine*, 369(7), 676–677. https://doi.org/10.1056/NEJMc1306659

Fernandez-Ballart, J. D., Pinol, J. L., Zazpe, I., Corella, D., Carrasco, P., Toledo, E., & Martin-Moreno, J. M. (2010). Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. *British Journal of Nutrition*, 103(12), 1808–1816. https://doi.org/10.1017/s0007114509993837

Gandek, B., Ware, J. E., Aaronson, N. K., Apolone, G., Bjorner, J. B., Brazier, J. E., & Sullivan, M. (1998). Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: Results from the IQOLA Project. International quality of life assessment. *Journal of Clinical Epidemiology*, 51(11), 1171–1178. https://doi.org/10.1016/S0895-4356(98)00109-7

Gilis-Januszewska, A., Lindstrom, J., Tuomilehto, J., Piwonska-Solska, B., Topor-Madry, R., Szybinski, Z., & Hubalewska-Dydejczyk, A. (2017). Sustained diabetes risk reduction after real life and primary health care setting implementation of the diabetes in Europe prevention using lifestyle, physical activity and nutritional intervention (DE-PLAN) project. *BMC Public Health*, 17(1), 198. https://doi.org/10.1186/s12889-017-4104-3

Golden, C. J. (2005). *Stroop: Test de colores y palabras*. Madrid: TEA Ediciones.

Goldstein, M. G., Whitlock, E. P., & DePue, J. (2004). Multiple behavioral risk factor interventions in primary care. Summary of research evidence. *American Journal of Preventive Medicine*, 27(2 Suppl), 61–79. https://doi.org/10.1016/j.amepre.2004.04.023

Gomez-Pardo, E., Fernandez-Alvira, J. M., Vilanova, M., Haro, D., Martinez, R., Carvajal, I., & Fuster, V. (2016). A comprehensive lifestyle peer group-based intervention on cardiovascular risk factors: The randomized controlled fifty-fifty program. *Journal of the American College of Cardiology*, 67(5), 476–485. https://doi.org/10.1016/j.jacc.2015.10.033

Goyer, L., Dufour, R., Janelle, C., Blais, C., L'Abbe, C., Raymond, E., & Larochelle, P. (2013). Randomized controlled trial on the long-term efficacy of a multifaceted, interdisciplinary lifestyle intervention in reducing cardiovascular risk and improving lifestyle in patients at risk of cardiovascular disease. *Journal of Behavioral Medicine*, 36(2), 212–224. https://doi.org/10.1007/s10865-012-9407-3

Graham, I., Atar, D., Borch-Johnsen, K., Boysen, G., Burell, G., Cifkova, R., & Dudina, A. (2007). European guidelines on cardiovascular disease prevention in clinical practice: Executive summary: Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (Constituted by representatives of nine societies and by invited experts). *European Heart Journal*, 28(19), 2375–2414. https://doi.org/10.1093/eurheartj/ehm316

Grandes, G., Sanchez, A., Sanchez-Pinilla, R. O., Torcal, J., Montoya, I., Lizarraga, K., & Serra, J. (2009). Effectiveness of physical activity advice and prescription by physicians in routine primary care: A cluster randomized trial. *Archives of Internal Medicine*, 169(7), 694–701. https://doi.org/10.1001/archinternmed.2009.23

Grodstein, F. (2007). Cardiovascular risk factors and cognitive function. *Alzheimer's & Dementia*, 3(2 Suppl), S16–S22. https://doi.org/10.1016/j.jalz.2007.01.001

Grundy, S. M., Pasternak, R., Greenland, P., Smith, S. Jr, & Fuster, V. (1999). Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: A statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*, 100(13), 1481–1492. https://doi.org/10.1161/01.CIR.100.13.1481

Guiterrez-Bedmar, M., Segui-Gomez, M., Gomez-Gracia, E., Bes-Rastrollo, M., & Martinez-Gonzalez, M. A. (2009). Smoking status, changes in smoking status and health-related quality of life: Findings from the SUN ("Seguimiento Universidad de Navarra") cohort. *International Journal of Environmental Research and Public Health*, 6(1), 310–320. https://doi.org/10.3390/ijerph6010310

Hobbs, N., Godfrey, A., Lara, J., Errington, L., Meyer, T. D., Rochester, L., & Sniehotta, F. F. (2013). Are behavioral interventions effective in increasing physical activity at 12 to 36 months in adults aged 55 to 70 years? A systematic review and meta-analysis. *BMC Medicine*, 11, 75. https://doi.org/10.1186/1741-7015-11-75

Huang, Y., Xu, J., Yu, B., & Shull, P. B. (2016). Validity of FitBit, Jawbone UP, Nike+ and other wearable devices for level and stair walking. *Gait & Posture*, 48, 36–41. https://doi.org/10.1016/j.gaitpost.2016.04.025

Jarl, J., Tolentino, J. C., James, K., Clark, M. J., & Ryan, M. (2014). Supporting cardiovascular risk reduction in overweight and obese hypertensive patients through DASH diet and lifestyle education by primary care nurse practitioners. *Journal of the American Association of Nurse Practitioners*, 26(9), 498–503. https://doi.org/10.1002/2327-6924.12124

Karelis, A. D., Chamberland, G., Aubertin-Leheudre, M., & Duval, C. (2013). Validation of a portable bioelectrical impedance analyzer for the assessment of body composition. *Applied Physiology, Nutrition, and Metabolism*, 38(1), 27–32. https://doi.org/10.1139/apnm-2012-0129

Koltyn, K. F. (2001). The association between physical activity and quality of life in older women. *Womens Health Issues*, 11(6), 471–480. https://doi.org/10.1016/S1049-3867(01)00128-1

Laatikainen, T., Dunbar, J. A., Chapman, A., Kilkkinen, A., Vartiainen, E., Heistaro, S., & Janus, E. D. (2007). Prevention of type 2 diabetes by

lifestyle intervention in an Australian primary health care setting: Greater Green Triangle (GGT) Diabetes Prevention Project. *BMC Public Health*, 7, 249. https://doi.org/10.1186/1471-2458-7-249

Lemmens, V., Oenema, A., Knut, I. K., & Brug, J. (2008). Effectiveness of smoking cessation interventions among adults: A systematic review of reviews. *European Journal of Cancer Prevention*, 17(6), 535–544. https://doi.org/10.1097/CEJ.0b013e3282f75e48

Maderuelo-Fernandez, J. A., Recio-Rodriguez, J. I., Patino-Alonso, M. C., Perez-Arechaederra, D., Rodriguez-Sanchez, E., Gomez-Marcos, M. A., & Garcia-Ortiz, L. (2015). Effectiveness of interventions applicable to primary health care settings to promote Mediterranean diet or healthy eating adherence in adults: A systematic review. *Preventive Medicine*, 76(Suppl), S39–S55. https://doi.org/10.1016/j.ypmed.2014.12.011

Marti, R., Parramon, D., Garcia-Ortiz, L., Rigo, F., Gomez-Marcos, M. A., Sempere, I., & Ramos, R. (2011). Improving interMediate risk management, MARK study. *BMC Cardiovascular Disorders*, 11, 61. https://doi.org/10.1186/1471-2261-11-61

Mendis, S., Puska, P., & Norrving, B. (2011). *Global atlas on cardiovascular disease prevention and control*. W. H. Organization, W. H. Federation & W. S. Organization (Eds.), Retrieved from http://www.who.int/cardiovascular_diseases/publications/atlas_cvd/en/

Munoz, M. A., Fito, M., Marrugat, J., Covas, M. I., & Schroder, H. (2009). Adherence to the Mediterranean diet is associated with better mental and physical health. *British Journal of Nutrition*, 101(12), 1821–1827. https://doi.org/10.1017/s0007114508143598

Orrow, G., Kinmonth, A. L., Sanderson, S., & Sutton, S. (2012). Effectiveness of physical activity promotion based in primary care: Systematic review and meta-analysis of randomised controlled trials. *BMJ*, 344, e1389. https://doi.org/10.1136/bmj.e1389

Prochaska, J. O., & Velicer, W. F. (1997). The transtheoretical model of health behavior change. *American Journal of Health Promotion*, 12(1), 38–48. https://doi.org/10.4278/0890-1171-12.1.38

Reitan, R. M. (1992). *Trail making test: Manual for a administration and scoring*. Tucson, AZ: Reitan Neuropsychology Laboratory.

Rey, A. (1964). *L'Examen clinique en psychologie*. Paris: Press Universitaire de France.

Richard, E., Jongstra, S., Soininen, H., Brayne, C., Moll van Charante, E. P., Meiller, Y., & Andrieu, S. (2016). Healthy ageing through internet counselling in the elderly: The HATICE randomised controlled trial for the prevention of cardiovascular disease and cognitive impairment. *British Medical Journal Open*, 6(6), e010806. https://doi.org/10.1136/bmjopen-2015-010806

Roman Vinas, B., Ribas Barba, L., Ngo, J., & Serra Majem, L. (2013). Validity of the international physical activity questionnaire in the Catalan population (Spain). *Gaceta Sanitaria*, 27(3), 254–257. https://doi.org/10.1016/j.gaceta.2012.05.013

Russell, M. A., Wilson, C., Taylor, C., & Baker, C. D. (1979). Effect of general practitioners' advice against smoking. *British Medical Journal*, 2 (6184), 231–235. https://doi.org/10.1136/bmj.2.6184.231

Salas-Salvado, J., Fernandez-Ballart, J., Ros, E., Martinez-Gonzalez, M. A., Fito, M., Estruch, R., & Covas, M. I. (2008). Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: One-year results of the PREDIMED randomized trial. *Archives of Internal Medicine*, 168(22), 2449–2458. https://doi.org/10.1001/archinte.168.22.2449

Salas-Salvado, J., Rubio, M. A., Barbany, M., & Moreno, B. (2007). SEEDO 2007 Consensus for the evaluation of overweight and obesity and the establishment of therapeutic intervention criteria. *Medicina Clinica*, 128(5), 184–196. https://doi.org/10.1016/S0025-7753(07)72531-9

Sanchez-Aguadero, N., Alonso-Dominguez, R., Garcia-Ortiz, L., Agudo-Conde, C., Rodriguez-Martin, C., de Cabo-Laso, A., & Recio-Rodriguez, J. I. (2016). Diet and physical activity in people with intermediate cardiovascular risk and their relationship with the health-related quality of life: Results from the MARK study. *Health and Quality of Life Outcomes*, 14(1), 169. https://doi.org/10.1186/s12955-016-0572-x

Schroder, H., Fito, M., Estruch, R., Martinez-Gonzalez, M. A., Corella, D., Salas-Salvado, J., & Covas, M. I. (2011). A short screener is valid for assessing Mediterranean diet adherence among older Spanish men and women. *Journal of Nutrition*, 141(6), 1140–1145. https://doi.org/10.3945/jn.110.135566

Schulz, K. F., Altman, D. G., & Moher, D. (2010). CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *PLoS Medicine*, 7(3), e1000251. https://doi.org/10.1371/journal.pmed.1000251

Stead, L. F., Bergson, G., & Lancaster, T. (2008). Physician advice for smoking cessation. *The Cochrane Database of Systematic Reviews*, 2, Cd000165. https://doi.org/10.1002/14651858.cd000165.pub3

Stephens, T. (1988). Physical activity and mental health in the United States and Canada: Evidence from four population surveys. *Preventive Medicine*, 17(1), 35–47. https://doi.org/10.1016/0091-7435(88)90070-9

Sweet, S. N., & Fortier, M. S. (2010). Improving physical activity and dietary behaviours with single or multiple health behaviour interventions? A synthesis of meta-analyses and reviews. *International Journal of Environmental Research and Public Health*, 7(4), 1720–1743. https://doi.org/10.3390/ijerph7041720

The World Health Report-Reducing risks (2002). *Promoting healthy life*. Geneva: World Health Organization.

Valencia, N. J., Laserna, J. A., Pérez-García, M., Orozco, C., Miñán, M., Garrido, C., & Morente, G. (2000). Influencia de la escolaridad y el sexo sobre la ejecución en el FAS, nombrar animales y nombrar frutas. *Psicología Conductual*, 8(2), 283–295.

Wannamethee, G., & Shaper, A. G. (1991). Self-assessment of health status and mortality in middle-aged British men. *International Journal of Epidemiology*, 20(1), 239–245. https://doi.org/10.1093/ije/20.1.239

Wechsler, D. (1987). *Wechsler memory scale – Revised manual*. San Antonio, TX: Psychological Corporation.