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The role of lifestyle behaviour on the risk of hypertension in the SUN cohort: The hypertension preventive score

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ABSTRACT

Lifestyles may influence the risk of hypertension. Our objective was to assess the association between a healthy-lifestyle score and the incidence of hypertension. The SUN Project is a dynamic, prospective cohort of Spanish university graduates (1999–2014). Among 14,057 participants initially free of hypertension, we assessed the influence of lifestyle-related factors based on a 10-item score that we previously reported to be associated with lower risk of major cardiovascular events. However, we focused on factors related to hypertension risk according to previous scientific evidence and international clinical guidelines and constructed a 6-item score including: no smoking, moderate-to-high physical activity, Mediterranean diet adherence, healthy body mass index, moderate alcohol intake and no binge drinking. We fitted Cox regression models to adjust for potential confounders. During a median follow-up of 10.2 years, we identified 1406 incident cases of medically diagnosed hypertension. The risk of developing hypertension was linearly reduced as participants better adhered to a healthy lifestyle pattern built by summing up these 6 factors (p for trend < 0.001). The highest category (5–6 factors) exhibited a significant 46% relative reduction in the risk of developing hypertension compared to the lowest category (0–1 factors) (multivariable-adjusted hazard ratio = 0.54; 95% CI: 0.42–0.68). Among the components of the score, BMI was apparently the main factor driving the association between the HLS and lower risk of hypertension. A healthy-lifestyle score including six simple healthy habits was longitudinally and linearly associated with a substantially reduced risk of hypertension. This index may be a useful tool for hypertension prevention.

1. Introduction

According to the 2017 ACC/AHA guidelines (hypertension defined as a systolic pressure ≥130 mmHg and diastolic pressure ≥ 80 mmHg) (Whelton et al., 2017), nearly 50% of United States adults (> 100 million) are now classified as hypertensive (Muntner et al., 2018). In Spain, according to a national population-based survey carried out between 2009 and 2010, the age-adjusted prevalence of hypertension was 43% in the adult population, (50% in men and 37% in women) (Menéndez et al., 2016). Moreover, hypertension is not only important because of its high prevalence, but also because it is a major modifiable risk factor that continues to be the greatest single contributor to the global burden of disease and to global mortality, leading to 9.4 million deaths each year in the world (Lim et al., 2012).

Appropriate and improved strategies for the primary prevention of high BP are urgently needed. Lifestyle and environmental factors are associated with the risk of hypertension. The most relevant risk factors associated with an increasing risk of hypertension are physical inactivity, obesity, high alcohol consumption, smoking, and unhealthy dietary patterns (Ezzati and Riboli, 2013). Moreover, current guidelines for the primary prevention of hypertension target these modifiable risk behaviours (Whelton et al., 2017). In the present study, we have also focused on these lifestyle-related factors.

However, the advances in technology and a much expensive medication-based preventive medicine often take excessive precedence over simpler, more sensible approaches to modify lifestyles (Carlos et al.,

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2014).

Beyond the traditional healthcare model, further progress is needed to implement healthy lifestyles initiatives. Supplementary education of healthcare professionals and the general population, intensified support for those attempting to change their lifestyles, and policies aimed at reducing the burden in complying with the recommendations for non-pharmacological reductions in BP are essential elements for hypertension prevention (Whelton et al., 2002).

The objective of our study was to assess the influence of lifestyle-related factors and the association between a simple and multi-dimensional healthy-lifestyle score (HLS) and the risk of hypertension in a Spanish cohort during a long follow-up period.

2. Methods

2.1. Study population

SUN (Seguimiento Universidad de Navarra) is a prospective, dynamic, and multipurpose cohort of Spanish university graduates. Information is updated biennially since December 1999. Its design has already been detailed (Seguí-Gómez et al., 2006). In total, 22,275 participants had been recruited up to March 2014. The following individuals were excluded: those with prevalent hypertension (n = 4379), those with prevalent chronic diseases (type 2 diabetes, cardiovascular disease (myocardial infarction or stroke) and cancer; n = 753), those who had total energy intake outside predefined limits (Willett, 1998) (n = 1721), and those lost to follow-up (n = 1365, retention = 91%). Finally, 14,057 participants remained in this study (Fig. 1).

The Institutional Review Board of the University of Navarra approved the study protocol. Participants were informed of the study characteristics, and voluntary completion of the first questionnaire was considered to imply informed consent.

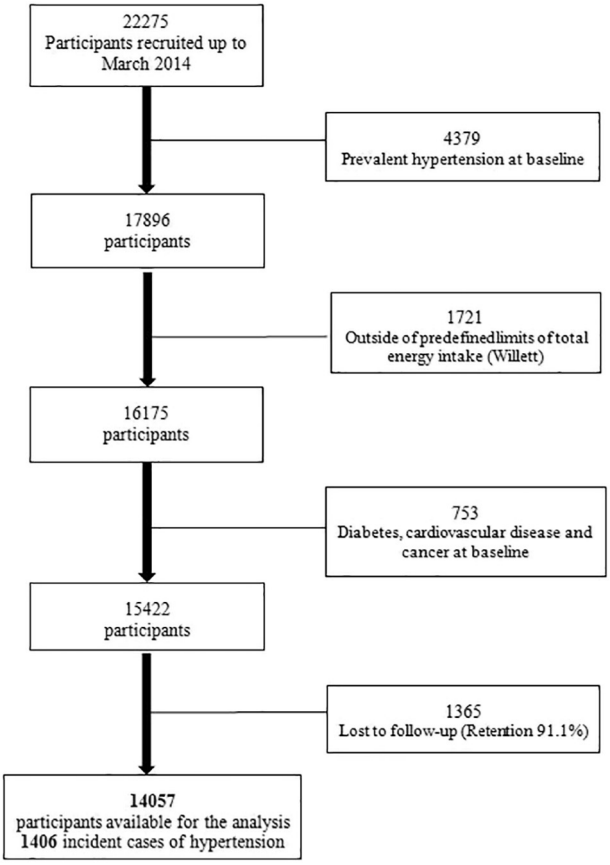

Fig. 1. Flow chart for the selection of participants. The SUN Project 1999–2014.

2.2. Main exposure variables

The baseline questionnaire collected information on socio-demographic, medical history, lifestyle aspects and anthropometric variables. The reproducibility and validity of the reported anthropometric (Bes-Rastrollo et al., 2005) and physical activity (Martínez-González et al., 2005) data were evaluated in cohort subgroups. A previously validated (Martin-Moreno et al., 1993) 136-question semi-quantitative food-frequency questionnaire was applied. Alcohol consumption was recorded via this questionnaire and other questions related to alcohol consumption habits were included in the baseline questionnaire. Adherence to the Mediterranean diet was estimated with the score (0–8 points) developed by Trichopoulou et al. (2003) although alcohol was excluded.

A previous study in our cohort (Díaz-Gutiérrez et al., 2018) associated lifestyle-related factors with lower risk of cardiovascular disease including the following 10 habits: never smoking, moderate-to-high physical activity (> 20 MET-h/week), Mediterranean diet adherence (≥4/8 points), body mass index (BMI) ≤22 kg/m^2, moderate alcohol consumption (women, 0.1–5.0 g/d; men, 0.1–10.0 g/d; abstainers excluded), low television exposure (< 2 h/d), no binge drinking (≤5 alcoholic drinks at any time), taking a short afternoon nap (≤30 min/d), meeting up with friends > 1 h/d, and working at least 40 h/week. In this study, we assessed the individual contribution of each item and the combined effect of the 10-point HLS with hypertension risk. However, we focused on those factors related to hypertension risk based on international clinical guidelines (Whelton et al., 2017; Piepoli et al., 2016) and solid scientific evidence (Chomistek et al., 2015; Chiuve et al., 2014). Therefore, we constructed a 0 to 6 point HLS (Table 1). According to the score, participants were categorized into 5 groups to ensure an adequate sample distribution with enough participants in each group.

Table 1
The hypertension preventive score. The SUN Project 1999–2014.

	Points in the score	N
Smoking		
Never smoker	1	6945
Smoker (current or former smoker)	0	7112
Physical activity (METs-h/week)		
Physically active (> 20 METs-h/week)	1	7144
Not physically active (≤20 METs-h/week)	0	6913
Mediterranean dietary pattern (modified Trichopoulou score)[a]		
High adherence (≥4/8 points)	1	8598
Low adherence (< 4/8 points)	0	5459
Body mass index (kg/m^2)		
≤22	1	6040
> 22	0	8017
Alcohol intake (g per day)		
Moderate alcohol intake (women 0.1–5 g/d; men 0.1–10 g/d)	1	6955
Abstainer or high alcohol intake (women > 5 g/d; men > 10 g/d)	0	7102
Binge drinking (alcoholic drinks on any occasion)		
Never binge drinking (≤5 alcoholic drinks on any occasion)	1	9707
Binge drinking (> 5 alcoholic drinks on any occasion)	0	4350

[a] Trichopoulou's score (from 0 to 8, higher scores indicate greater adherence, alcohol consumption was excluded).

2.3. Outcome assessment

The study outcome was incident self-reported hypertension. Cases of hypertension were recorded at baseline and in every follow-up questionnaire.

Participants were considered to have prevalent hypertension if they reported a medical diagnosis of hypertension at baseline, a systolic BP ≥130 mmHg, a diastolic BP ≥80 mmHg, or use of any antihypertensive drug (Whelton et al., 2017). New cases of hypertension were defined as those participants who did not have hypertension at baseline and reported a new medical diagnosis of hypertension during follow-up. The validity of self-reported hypertension has been previously assessed in a subsample of the cohort (Alonso et al., 2005). This validation study showed an adequate validity of the self-reported diagnosis of hypertension: among those participants who reported a diagnosis of hypertension, 82.3% (95% CI: 72.8–92.8) were confirmed through a conventional measurement of BP, and among those who did not report a diagnosis of hypertension, 85.4% (95% CI: 72.4–89.1) were confirmed as non-hypertensive. Moreover, we have validated each component of the metabolic syndrome (including high BP) (Fernández-Montero et al., 2011). We found adequate intra-class correlation coefficients for high systolic BP (0.47 [0.36–0.57]) and high diastolic BP (0.46 [0.34–0.56]), using direct assessments by an experienced physician as the gold standard.

2.4. Assessment of covariates

We evaluated the prevalence of family history of hypertension, type 2 diabetes, cancer, hypercholesterolemia, hypertriglyceridemia, sodium and potassium intake, aspirin and non-aspirin analgesics, and previous history of non-atherosclerotic cardiovascular disease.

2.5. Statistical analysis

Cox models were fitted (with age as the underlying time scale) to assess the risk of incident hypertension during follow-up according to HLS (5 categories). Hazard Ratios (HR) and their 95% confidence intervals (CI) were calculated by reference to the lowest scores (0–1 points). Person-years follow-up was calculated for each participant, from the date of baseline questionnaire completion until the date of final questionnaire completion, the date of diagnosis of hypertension, or date of death, whichever occurred first. We performed linear trend tests considering the HLS as a continuous variable.

Moreover, we assessed the relative importance of each one of the components of the HLS on hypertension risk. We have adopted the approach previously used by Trichopoulou et al. (2009). In this way, we subtracted alternately one component at a time from the score (accordingly reducing the 6-point score to 5-point score) and estimated the HRs associated with categories of highest vs. lowest adherence to the HLS removing each of the 6 components, one by one. To ensure proper comparability, we multiplied the logarithm of the estimated HRs by 5/6 before exponentiating them.

We tested a predefined multiplicative interaction between categories of BMI and the HLS via a likelihood ratio test. Moreover, we stratified the analysis by sex.

To control for possible confounding factors, a multivariable model was stratified by deciles of age and according to the entry date in the cohort, because of the dynamic design of the SUN cohort. In addition, the multivariable model was adjusted for the following possible additional confounding factors: sex, previous history of non-atherosclerotic cardiovascular disease (atrial fibrillation, paroxysmal tachycardia, heart failure, aortic aneurism, pulmonary embolism or peripheral venous thrombosis), hypercholesterolemia, hypertriglyceridemia, family history of hypertension, regular use of aspirin and non-aspirin analgesics, and energy-adjusted sodium and potassium intake. We additionally adjusted the multivariable model for baseline BMI (as a continuous variable).

Taking into account the 10-item HLS previously published, we also evaluated the combined effect and the individual impact of each specific healthy-lifestyle factor on hypertension risk, Cox models were fitted for each of the 10 lifestyle habits adjusting for the other healthy-lifestyle factors.

We conducted sensitivity analysis to assess the robustness of our results: (1) excluding early cases of incident hypertension (diagnosed during the first 2 follow-up years); (2) changing the cut-off point of incident hypertension (≥140, ≥90 mmHg) and excluding from the analysis participants in the high normal BP range (130–139, 80–89 mmHg); (3) excluding those participants with a weight gain ≥5 kg in the last 5 years before answering the baseline questionnaire; (4) additionally adjusting for employment status (unemployed or working); (6) additionally adjusting for years of university education; (6) changing the criteria of exclusion in energy limits (p5–95); (7) excluding pregnant women at baseline; (8) varying BMI cut-off points by sex (≤22 kg/m^2 for women; ≤25 kg/m^2 for men).

Analyses were performed using STATA/SE version 15.0. All p values presented are two-sided and were considered statistically significant at < 0.05.

3. Results

The baseline characteristics of participants by HLS are described in Table 2. Participants with more healthy lifestyle factors were slightly younger, more likely to be female, tended to have a lower BMI, lower alcohol intake, lower percentage of binge drinking, higher levels of physical activity and a greater adherence to the Mediterranean dietary pattern. Moreover, they had a lower proportion of cardiovascular risk factors (dyslipidaemia and smoking), lower sodium intake, lower analgesic consumption and higher potassium intake.

3.1. Hypertension cases

Among 14,057 participants who were free of hypertension at baseline, we identified 1406 incident hypertension cases after a median follow-up of 10.2 years (interquartile range: 6.2–13.0 years). In unadjusted and adjusted longitudinal models, a greater number of healthy lifestyle factors was monotonically associated with a lower risk of incident hypertension (p for trend < 0.001). Compared with the lowest category of healthy lifestyle (0–1 points), participants with the best score (5–6 points), exhibited a 46% relative reduction in the risk of developing hypertension (HR: 0.54; 95% CI: 0.42–0.68) (Table 3).

The relative importance of each one of the components of the HLS on hypertension risk was assessed by subtracting alternately one component at a time from the score. This evaluation is presented in Fig. 2. The observed changes in the HRs with the alternate exclusion of each of the 6 components of the score, suggested that BMI was the main factor driving the association between the HLS and lower risk of hypertension. Nevertheless, the 5-item score that excluded BMI still showed a significant inverse association with hypertension risk.

In the stratified by sex analysis, we found a significant inverse association between the HLS (lowest vs. highest scores) and the risk of hypertension similarly in both men and women (Fig. 3).

Despite the fact that dichotomized BMI was already included in the score, additional adjustment for BMI as a continuous variable showed similar results (HR: 0.71; 95% CI: 0.56–0.91; p for trend < 0.001). Moreover, the association between the number of healthy lifestyle factors and the risk of developing hypertension did not vary according to categories of baseline BMI (BMI < 30 and ≥30) (p interaction = 0.460).

The HLS as a continuous variable was significantly and inversely associated with the risk of hypertension (HR: 0.86; 95% CI: 0.83–0.90) per unit increase in the score.

We also assessed the 10-point HLS previously associated with major

Table 2
Baseline characteristics of the participants according to the number of healthy lifestyle factors. The SUN Project 1999–2014.

Number of healthy-lifestyle factors	0–1	2	3	4	5–6
Subjects (n)	1272	2721	4123	3661	2280
Women (%)	48.4	59.9	65.6	72.0	80.4
Age (years)	35.7 ± 10.0	36.5 ± 11.1	35.8 ± 10.8	35.2 ± 10.7	32.7 ± 9.9
Body mass index (kg/m^2)	24.8 ± 3.0	24.0 ± 3.2	23.3 ± 3.2	22.4 ± 3.0	21.1 ± 2.4
Categories of SBP[a] (%)					
< 100 mmHg	10.9	10.6	12.6	16.0	18.7
101–110 mmHg	25.0	29.2	30.4	31.7	35.4
111–120 mmHg	41.2	41.9	40.2	38.5	35.4
121–130 mmHg	22.9	18.4	16.8	13.9	10.3
Categories of DBP[b] (%)					
< 60 mmHg	12.2	13.5	14.6	16.9	18.6
61–70 mmHg	44.1	46.7	48.4	49.1	52.0
71–80 mmHg	43.8	39.8	37.0	34.0	29.5
Any health check-up (%)	72.6	74.8	74.3	74.2	75.9
Prevalent cardiovascular disease[c] (%)	0.79	1.14	1.04	1.20	0.75
Family history of hypertension (%)	38.1	38.8	40.1	41.4	37.8
Hypercholesterolemia (%)	15.0	14.4	13.6	13.3	10.4
Hypertriglyceridemia (%)	7.2	6.1	4.5	3.2	2.2
Smoking (%)					
Never smoker	6.4	24.9	44.1	64.4	88.1
Former smoker	32.9	30.9	26.1	16.3	6.1
Current smoker	58.2	40.1	26.9	17.2	5.2
Sodium intake (mg/day)	4248 ± 1872	4105 ± 2634	3929 ± 1896	3878 ± 1942	3706 ± 2070
Potassium intake (mg/day)	4097 ± 994	4452 ± 1130	4725 ± 1225	4916 ± 1253	5243 ± 1379
Analgesic intake (%)	11.8	11.9	10.8	10.5	8.7
Physical activity (MET-h/week)	14.5 ± 14.4	20.3 ± 19.7	24.8 ± 22.8	30.4 ± 24.1	38.8 ± 25.6
Mediterranean dietary pattern[d]	2.9 ± 1.4	3.5 ± 1.7	4.0 ± 1.7	4.4 ± 1.7	5.0 ± 1.4
Alcohol intake (g/day)	13.3 ± 15.2	8.4 ± 10.4	5.6 ± 7.5	3.7 ± 5.3	2.7 ± 3.0
TV watching (h/day)	1.7 ± 1.1	1.7 ± 1.2	1.6 ± 1.2	1.6 ± 1.2	1.5 ± 1.2
% binge drinking[e]	79.3	50.9	30.6	15.7	5.4
Sleeping mid-day nap (minutes/day)	19.2 ± 24	17.4 ± 18	15.6 ± 18	14.4 ± 18	13.2 ± 18
Time spent with friends (h/day)	1.44 ± 1.0	1.36 ± 1.0	1.34 ± 0.9	1.31 ± 0.9	1.41 ± 0.9
Working ≥40 h per week (%)	58.2	54.2	52.5	50.2	47.8

Data represent n (%) or means ± standard deviation (SD).
[a] Systolic blood pressure (SBP).
[b] Diastolic blood pressure (DBP).
[c] Atrial fibrillation, paroxysmal tachycardia, heart failure, aortic aneurism, pulmonary embolism or peripheral venous thrombosis.
[d] Trichopoulou's score (from 0 to 8, higher scores indicate greater adherence, alcohol consumption was excluded).
[e] Drinking > 5 alcoholic drinks at any time.

cardiovascular events. Similarly, a greater number of healthy-lifestyle factors were associated with a lower risk of hypertension. The HR for the highest category of adherence to the HLS was 0.69 (CI: 0.57–0.83).

When all of the lifestyle-related factors were analysed individually, we found inverse significant associations for physical activity (> 20 METs-h/week) (HR: 0.82; 95% CI: 0.74–0.91), BMI (≤22 kg/m^2) (HR: 0.60; 95% CI: 0.52–0.70) and avoidance of binge drinking (HR: 0.80; 95% CI: 0.71–0.91) with hypertension risk (Table 4).

Due to the non-significant association with never smoking, we additionally assessed the effect of pack-years of cigarette smoking on hypertension. Smokers of > 40 pack-year showed significant increases in the risk of developing hypertension as compared with those who never smoked (adjusted HR: 1.60; 95% CI: 1.20–2.14).

Moreover, we subtracted alternately one component at a time from the 10-point score model to evaluate the relative importance of each one of the components of the score. This analysis suggested that BMI was the main component driving the association between a higher HLS and lower risk of hypertension. However, the inverse association of the 9-item score with hypertension also remained statistically significant after excluding BMI (HR: 0.83; 95% CI: 0.70–0.98). On the other hand, we observed a slightly stronger inverse association between the HLS and hypertension risk after the exclusion of the following factors: working ≥40 h/week (0.61; 95% CI: 0.51–0.71) and moderate alcohol consumption (0.63; 95% CI: 0.53–0.76) from the score (Supplemental Fig. 1).

We performed several sensitivity analyses to test the association between the HLS and the risk of developing hypertension (Table 5). The calculated estimates were maintained in the same direction as the

Table 3
HR and 95% CI of incident hypertension according to the number healthy lifestyle factors. The SUN Project 1999–2014.

Number of healthy-lifestyle factors (0–6 points)[a]	0–1	2	3	4	5–6	p for trend
Subjects (n)	1272	2721	4123	3661	2280	
Cases/person-years	176/12426	343/25816	455/40001	307/35482	125/21636	
Sex and age adjusted	1 (ref.)	0.90 (0.75–1.09)	0.82 (0.69–0.98)	0.65 (0.54–0.79)	0.53 (0.42–0.66)	< 0.001
Multivariate adjusted[a]	1 (ref.)	0.92 (0.76–1.10)	0.83 (0.69–0.99)	0.67 (0.55–0.81)	0.54 (0.42–0.68)	< 0.001

[a] Adjusted for sex, age, year of completion of the questionnaire, regular use of aspirin and non-aspirin analgesics, CVD (atrial fibrillation, paroxysmal tachycardia, heart failure, aortic aneurism, pulmonary embolism or peripheral venous thrombosis), family history of hypertension, hypercholesterolemia, hypertriglyceridemia and energy-adjusted sodium and potassium intake.

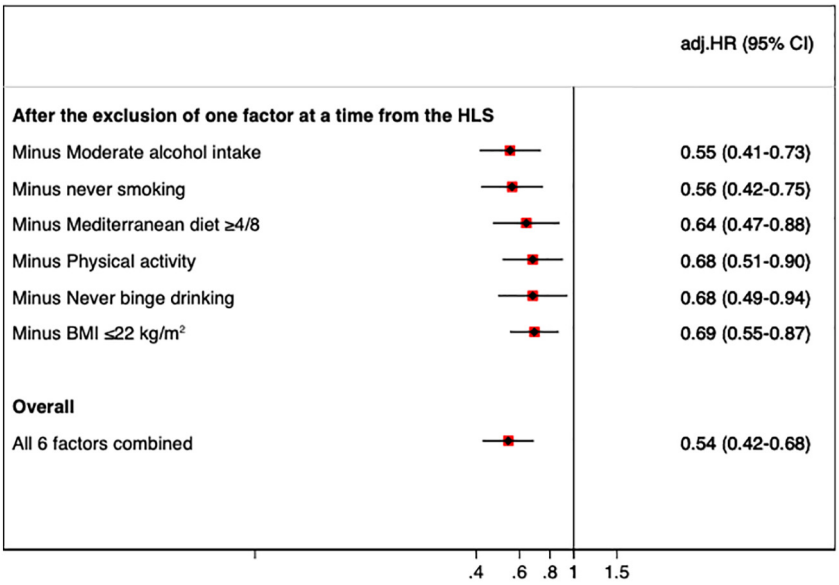

Fig. 2. HR associated with extreme categories (> 4 points vs. < 2 points) of the 5-item HLS after subtraction of one factor at a time. Originally estimated logarithms of hazard ratios were multiplied by 5/6 and then exponentiated to correct for a 5-point scale. The SUN Project 1999–2014.

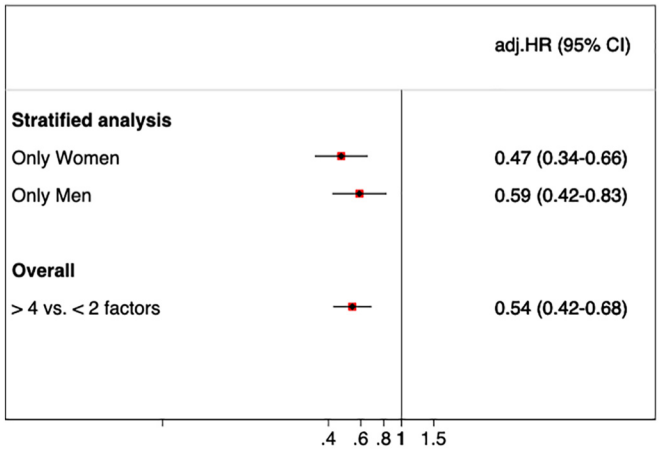

Fig. 3. Stratified by sex analysis of the association between the 6-point HLS and the risk of incident hypertension. The SUN Project 1999–2014.

estimates obtained in the main analysis. Furthermore, the analysis showed similar association between the HLS and the risk of hypertension with a different cut-off point of BMI (< 25 kg/m^2) in the score.

4. Discussion

In this study within the SUN cohort, the combination of never smoking, physical activity (> 20 METs-h/week), Mediterranean diet adherence (≥ 4/8 points), low body mass index ≤ 22 kg/m^2, moderate alcohol intake (women 0.1–5 g/d, men 0.1–10 g/d), and avoidance of binge drinking (never > 5 drinks on any occasion) was longitudinally associated with almost a 50% relative reduction in hypertension risk.

Several cohort studies have reported a positive impact of adopting a healthy lifestyle on hypertension risk (Thawornchaisit et al., 2013; Larsson et al., 2017). As expected, our results are in accordance with the existing evidence. However, despite differences between men and women regarding hypertension, in the stratified by sex analysis, we found a significant inverse association between the HLS and the risk of hypertension similarly in both men and women.

Most of the current guidelines for the primary prevention of hypertension target modifiable risk behaviours such as weight loss, healthy diet, increased physical activity and a reduction in alcohol consumption (Whelton et al., 2017).

Regarding healthy diet in relation with hypertension, the most analysed pattern is the DASH (Dietary Approach to Stop Hypertension) diet. In this score, we adopted a modified Mediterranean dietary index based on the traditional Mediterranean diet (Trichopoulou et al., 2003), excluding alcohol consumption. We considered separately alcohol consumption as another of the individual lifestyle factors included in the score. We found a significant inverse association when we analysed Mediterranean diet individually, in accordance with previous studies that showed a reduction in the risk of major cardiovascular events and an inverse and significant association of the Mediterranean diet with BP (Nissensohn et al., 2016).

Cardiovascular benefits of moderate alcohol consumption have been consistently reported (Ronksley et al., 2011). Moreover, better adherence to an overall healthy alcohol-drinking pattern was previously reported to be associated with reduced mortality in this cohort (Gea et al., 2014). In accordance with these findings, moderate alcohol consumption, showed an inverse though non-significant association with hypertension in our study, when this factor was analysed individually.

However, we admit that the role of moderate alcohol intake as a potentially beneficial factor for cardiovascular health in a young population has been in constant debate. The notion that potentially preventive effects of moderate-alcohol consumption are confined only to middle-aged or older individuals may be also related to the limited statistical power and different etiology of cardiovascular disease in younger populations.

In fact, a pooled analysis of 8 prospective cohorts from North America and Europe including 192,067 women and 74,919 men, specifically assessed whether moderate alcohol consumption was associated with a decreased risk of cardiovascular disease in younger adults (Hvidtfeldt et al., 2010). They reported an inverse association among younger subjects, with even stronger effects on the relative scale (hazard ratios) for younger (39 to 50 years) than for older subjects (60 years) when comparing moderate alcohol intake (5 to 29.9 g/d) with abstention. However, we do not imply that abstainers of any age should start drinking because of the existing evidence of a dose-dependent relationship between alcohol consumption and a higher average blood pressure (Fan et al., 2013).

On the other hand, avoidance of binge drinking clearly exhibited an

Table 4
HR and 95% CI of incident hypertension according to healthy lifestyle habits. The SUN Project 1999–2014.

	n	Cases/person-years	Sex and age adjusted	Multivariate adjusted[a]
Factors included in the 0 to 6 score				
Never smoking				
No (current and former smoker)	7112	838/68988	1 (ref.)	1 (ref.)
Yes (never smoker)	6945	568/66373	0.94 (0.84–1.05)	0.95 (0.85–1.06)
Physical activity (> 20 METs-h/week)				
No	6913	742/66255	1 (ref.)	1 (ref.)
Yes	7144	664/69106	0.81 (0.73–0.90)	0.82 (0.74–0.91)
Mediterranean dietary pattern[b] (score ≥ 4/8 points)				
No	5459	521/54564	1 (ref.)	1 (ref.)
Yes	8598	885/80797	0.90 (0.81–1.01)	0.89 (0.79–1.00)
BMI (≤22 kg/m^2)				
No	8017	1099/75524	1 (ref.)	1 (ref.)
Yes	6040	307/59837	0.58 (0.50–0.66)	0.60 (0.52–0.70)
Moderate alcohol intake (women 0.1–5 g/d; men 0.1–10 g/d)				
No	7102	730/68421	1 (ref.)	1 (ref.)
Yes	6955	676/66940	0.96 (0.87–1.07)	0.97 (0.87–1.08)
Avoidance of binge drinking[c]				
Any binge drinking	4350	435/41848	1 (ref.)	1 (ref.)
Never binge drinking	9707	971/93513	0.80 (0.71–0.90)	0.80 (0.71–0.91)
Factors excluded from the 0 to 6 score				
Reduced TV watching				
≥2 h/d	4088	400/40036	1 (ref.)	1 (ref.)
< 2 h/d	9969	1006/95325	0.99 (0.88–1.11)	1.01 (0.90–1.13)
Sleeping short mid-day nap (≤30 min/d)				
No sleeping mid-day nap or longer mid-day nap	6077	578/59919	1 (ref.)	1 (ref.)
Yes	7980	828/75442	1.04 (0.94–1.16)	1.04 (0.94–1.16)
Time spent with friends (> 1 h/d)				
No	5054	698/48815	1 (ref.)	1 (ref.)
Yes	9003	708/86546	1.05 (0.94–1.18)	1.05 (0.94–1.18)
Time working (h/week)				
< 40 h/week	6748	589/64863	1 (ref.)	1 (ref.)
≥40 h/week	7309	817/70498	1.08 (0.97–1.21)	1.07 (0.96–1.20)

[a] Adjusted for sex, age, year of completion of the questionnaire, regular use of aspirin and non-aspirin analgesics, CVD (atrial fibrillation, paroxysmal tachycardia, heart failure, aortic aneurism, pulmonary embolism or peripheral venous thrombosis), family history of hypertension, hypercholesterolemia, hypertriglyceridemia and energy-adjusted sodium, potassium intake and all the variables shown in table.
[b] Trichopoulou score (range of scores, 0 to 8, with higher scores indicating greater adherence, excluding alcohol intake).
[c] Drinking > 5 alcoholic drinks at any time.

important and significant inverse association in agreement with previous studies that supports the concept that a high intake of alcohol consumption causes harmful increases in BP (Fernández-Solà, 2015).

Regarding smoking, cessation of the habit is not always included as a part of lifestyle modifications or recommendations for the prevention and treatment of hypertension (Whelton et al., 2017). Our study showed an inverse although non-significant association between never smoking, and the risk of developing hypertension when it was analysed individually. Additionally, we compared former and current smokers versus never smokers. We found a slightly higher risk among current

Table 5
Sensitivity analyses and 95% CI of incident hypertension according to healthy lifestyle habits. The SUN Project 1999–2014.

	Number of healthy lifestyle factors					
Variable	0–1	2	3	4	5–6	p for trend
Overall	1 (ref.)	0.92 (0.76–1.10)	0.83 (0.69–0.99)	0.67 (0.55–0.81)	0.54 (0.42–0.68)	< 0.001
Excluding early cases[a]	1 (ref.)	0.86 (0.69–1.07)	0.81 (0.66–1.00)	0.63 (0.51–0.79)	0.53 (0.40–0.69)	< 0.001
Changing the cut-off point of incident hypertension[b]	1(ref.)	0.93 (0.80–1.09)	0.87 (0.74–1.00)	0.69 (0.58–0.81)	0.61 (0.50–0.74)	< 0.001
Excluding those with a weight gain[c]	1 (ref.)	0.94 (0.76–1.16)	0.86 (0.70–1.05)	0.69 (0.55–0.85)	0.58 (0.45–0.74)	< 0.001
Changing the criteria of energy limits[d]	1 (ref.)	0.95 (0.78–1.15)	0.87 (0.72–1.05)	0.69 (0.57–0.84)	0.59 (0.46–0.74)	< 0.001
Additional adjusting for the employment situation[e]	1 (ref.)	0.91 (0.76–1.10)	0.82 (0.69–0.99)	0.67 (0.55–0.81)	0.53 (0.42–0.68)	< 0.001
Additional adjusting for years of education	1 (ref.)	0.92 (0.77–1.11)	0.83 (0.70–0.99)	0.67 (0.55–0.81)	0.55 (0.43–0.69)	< 0.001
Substituting the cut-off point of BMI (< 25 kg/m^2) in the score	1 (ref.)	0.85 (0.68–1.05)	0.68 (0.55–0.84)	0.61 (0.49–0.75)	0.46 (0.36–0.58)	< 0.001
Excluding pregnant women at baseline	1 (ref.)	0.89 (0.73–1.07)	0.81 (0.67–0.98)	0.62 (0.51–0.76)	0.54 (0.42–0.69)	< 0.001
Varying BMI cut-off points by sex[f]						
Men (≤25 kg/m^2)	1 (ref.)	0.85 (0.66–1.10)	0.64 (0.50–0.83)	0.60 (0.46–0.78)	0.45 (0.34–0.61)	< 0.001
Women (≤22 kg/m^2)	1 (ref.)	0.82 (0.60–1.11)	0.77 (0.58–1.02)	0.61 (0.45–0.82)	0.47 (0.34–0.66)	< 0.001

[a] Incident hypertension before the first 2 years of follow-up.
[b] Incident hypertension diagnosis = 140/90 mmHg.
[c] Weight gain of 5 kg or more in the last 5 years before answering the baseline questionnaire.
[d] Changing the criteria of exclusion in energy limits (p5–95).
[e] Unemployed or working.
[f] BMI cut-off point: (≤22 kg/m^2 for women; ≤25 kg/m^2 for men).

smokers, yet it was non-significant. This could be due to a biased evaluation of the effect of smoking. Smoking has a long-term, cumulative effect on health and the recovery of the damage caused by smoking is slow (Gao et al., 2017). Indeed, when we assessed the effect of pack-years of cigarette smoking on hypertension we found that smokers of > 40 pack-years showed significant increases in the risk of developing hypertension as compared with those who never smoked.

Body-mass index $\leq 22\,kg/m^2$ was another factor included in our score. In fact, it was the factor with the greatest impact when it was analysed individually. Despite the fact that most of the risk scores related to cardiovascular disease and hypertension are based on a cut-off point of BMI ≥ 25 and ≥ 30 (Chiuve et al., 2014), there is evidence that a lower cut-off point should be considered. In a previous analysis of our cohort, the incidence of metabolic risk factors was already increased at levels as low as BMI of $22\,kg/m^2$ (Toledo et al., 2009). Moreover, a BMI ≥ 23.0 was associated with a higher risk of type 2 diabetes (Hu et al., 2001) and with a significant association with hypertension in an Asian population (An et al., 2013). Also, the recent global burden of disease study of obesity and mortality, showed that the increased mortality risk associated with high BMI starts at levels as low as $22\,kg/m^2$ (The GBD Obesity Collaborators, 2017).

In relation with physical activity, the most recent guidelines recommended moderate-to-vigorous physical activity above the range of 7.5–15 METs-h/week to obtain health benefits (Piercy and Troiano, 2018). Therefore, the cut-off point of ≥20METs-h/week of physical activity represents an appropriate goal in order to achieve an optimal benefit. Prospective cohort studies have shown that physical activity is an independent predictor of incident hypertension in women (Barlow et al., 2006) and men (Chase et al., 2009). Our results confirm these previous findings. A significant inverse association with the risk of incident hypertension was found when physical activity was analysed individually.

The association of each individual factor was not significant for all of the components of the score. The magnitude of the effect of each item varied as well. For instance, BMI showed similar strength of association than the other 5 factors together. However, the total risk reduction was still greater in the combined analysis than in the analysis considering only BMI as an individual factor.

In fact, when we subtracted one component at a time from the 6-item HLS, the results suggested, as expected, that BMI was the main contributor to the association between the HLS and the risk of hypertension. Nevertheless, the 5-item score that excluded BMI still showed a significant inverse association with hypertension risk, demonstrating that the other factors add also valuable information to the score.

We interpreted that the differences of the individual effects against the combined effect of several factors might be that the whole of the score probably makes more than the sum of its individual parts. Furthermore, an overall score better reflects the complexity of lifestyle influence on hypertension and it is better suited to enable the appreciation of the combined effects of a variety of individual lifestyle-related factors.

4.1. Limitations

Limitations of our study should of course be recognized. First, the SUN project is a relatively young cohort and it is restricted to university graduates. In consequence, it is not representative of the general Spanish population. Nonetheless, generalization of results in epidemiology should be based on biological mechanisms rather than on statistical representativeness (Rothman et al., 2013). Because the prevalence of hypertension is higher in the general population than in our cohort, the magnitude of the expected population impact of this hypertension prevention score would probably be even greater. Second, information on the variables included in the analyses was mainly self-reported. Therefore, some degree of misclassification bias is possible. However, physical activity (Martínez-González et al., 2005) and BMI (Bes-Rastrollo et al., 2005) were previously validated and dietary information was based on a previously validated food frequency questionnaire (Martin-Moreno et al., 1993). Third, the highly educated participants in this cohort might be more aware of the recommended healthy lifestyle habits and some of them could overestimate their healthy habits. Nevertheless, the presence of the misclassification bias is expected to be non-differential, and that would more likely lead the associations towards the null value. Fourth, the results were adjusted for several major potential confounders, but we cannot eliminate the presence of residual confounding factors that could partly explain our results.

In spite of these limitations, we consider that we have a solid study, and in that sense, we would like to highlight its main strengths. The SUN project is a relatively large cohort in a Mediterranean country, with a prospective longitudinal design with an extended follow up period and a high retention rate. Moreover, the restriction to university graduates of this study could be a factor that increases the quality of the self-reported data and reduces the misclassification bias. Additionally, the homogeneity of the participants minimizes the potential residual confounding and improves the internal validity of our results. Furthermore, another strong point is the robustness of our results along multiple sensitivity analysis.

5. Conclusion

A 6-point combined HLS based on a model previously related with lower risk of hard cardiovascular events, also showed an important inverse association with incident hypertension in a Spanish cohort of university graduates. A greater number of healthy lifestyle factors were monotonically associated with a substantial lower risk of hypertension events. Among the components of the score, BMI appeared to offer the greatest benefit to prevent hypertension, however, the other factors also contributed. This score could be a simple and useful tool for health care professionals to promote the prevention of hypertension through lifestyle modification, and could also empower patients and give them some independence from laboratory values. Further studies with longitudinal design and intervention studies would be needed to analyse participants from other socioeconomic status, different educational levels and participants with high cardiovascular risk.

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Disclosure

Conflicts of interest: none.

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Authors' contributions

MAMG, MBR and JMMM contributed to the conception or design of the work. JDG, LRE, MBR, MRC, MAMG contributed to the acquisition, analysis, or interpretation of data for the work. LRE drafted the manuscript. JDG, LRE, MBR, MRC, JMMM and MAMG critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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