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The risk of incident depression when assessed with the Lifestyle and Well-Being Index

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ABSTRACT

Objectives: Novel findings indicate links between unhealthy lifestyles and depression based on active inflammatory processes. Thus, identifying participants with poor habits could reveal differences in trends of incident depression. This study aimed to examine the association between an objective lifestyle assessment, as measured by the Lifestyle and Well-Being Index (LWB-I), and incident depression in healthy participants of a Spanish cohort.

Study design: This was a longitudinal analysis of a subsample of 10,063 participants from the *Seguimiento Universidad de Navarra* cohort study.

Methods: Group comparisons and Cox proportional hazard models were conducted using the LWB-I, which categorizes the sample into groups with healthy and unhealthy lifestyles and well-being. The main outcome was incident depression as well as secondary outcomes.

Results: Those classified to the transition category of LWB-I were associated with a hazard ratio of 0.67 (95% confidence interval: 0.52–0.87), and those in the excellent category showed a hazard ratio of 0.44 (95% confidence interval: 0.33–0.58), which in both groups reflects a significantly lower risk of incident depression compared with the group including those classified in the poor LWB-I level. Moreover, the available sensitivity analyses concerning time of depression diagnosis or antidepressant treatment further supported the role of nutrition and physical activity on incident depression. Interestingly, throughout the follow-up, incident depression was inversely related to healthier daily habits as measured by the LWB-I.

Conclusions: A global assessment of lifestyles such as the LWB-I provides valuable insight into the complex relationship between lifestyle factors and their link to depression risk.

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Introduction

Depression is a complex disease with diverse risk factors that are only partially uncovered.[1] A recent summary of evidence highlights the links between these risk factors and proinflammatory phenomena occurring in various organs within and beyond the central nervous system.[2] Similar chronic low-grade inflammation processes are present in cardiovascular diseases (CVDs)[3] and are known to be related to nutrition and physical activity (PA) among other lifestyle habits.[4] For CVD, healthy lifestyles form the basis of its prevention, and now these risk factors could serve the same purpose for depression as an important noncommunicable disease.[5,6]

To this day, no single biological mechanism is known to completely explain the features observed in patients with depression.[7] However, within the most accepted hypothesis of disease, signs of active inflammatory processes have been found.[8] The main features in patients with depression are monoamine neurotransmitter dysfunction, alterations of the brain-derived neurotrophic factor (BDNF), and an improper response to stress.[2,7] Monoamines are primarily derived from B-complex vitamins; thus, it has been proposed that ensuring adequate levels of these nutrients could also promote adequate neurotransmitter activity.[9,10] These patients also present an inability to establish new neuronal synapses because of low BDNF levels.[11,12] In this regard, vitamin A, vitamin B12, and an active lifestyle have been related to improved BDNF release and activity and provide a basis for the role of daily habits in this disease.[11,12] Finally, chronic stress is common in patients with depression and is known to alter sleep patterns and promote the formation of inflammatory molecules in the gut.[2] These molecules are short-chain fatty acids and are produced by specific strains of bacteria in the gut that flourish in patients with sedentary habits and unhealthy diets.[13] Under these conditions, short-chain fatty acids flow into the bloodstream and have inflammatory qualities in the brain as well as the peripheral nervous system.[2,7] In summary, inflammation is highly relevant for depression and thus could signal to early pathological disturbances in patients with poor lifestyles.

Given the potential implications of lifestyles in depression, a precision medicine framework that can characterize an individual's risk behaviors could help identify those at risk of developing depression.[5,14,15] In this regard, the Lifestyle and Well-Being Index (LWB-I) was recently conceptualized to stratify individuals into three health and well-being groups based on socio-economic, anthropometric, history of diseases, and, more importantly, lifestyle habits.[16] By quantitatively pondering 12 items, which include diet, PA, smoking, and sleep, among others, the LWB-I allocates individuals to three different states of increasingly better lifestyles and well-being. Thus, an assessment of lifestyle and well-being features may be linked to depression incidence stemming from the previously mentioned inflammatory mechanisms.[16]

The aim of this investigation was to longitudinally evaluate this LWB-I in association with incident depression in a subsample of the *Seguimiento Universidad de Navarra* (SUN) study.

Methods

Study population

This was a longitudinal analysis of a subsample of the SUN cohort study, which is a prospective, multipurpose, dynamic cohort, that began recruitment in 1999 with the purpose of establishing associations between lifestyles and chronic conditions.[17] Briefly, university graduates are sent an invitation letter with a description of the cohort, a baseline questionnaire, and a prepaid return package for participants to submit their completed questionnaire. Furthermore, data collection is obtained through subsequent standardized questionnaires every 2 years. The submission of the baseline questionnaire through national post is considered informed consent. These methods and the study protocol were approved by the Ethics Committee of the University of Navarra (code 2001/30) in accordance with the Declaration of Helsinki.

Selected participants were observed starting at baseline, which was defined as the fourth year of follow-up until the occurrence of the outcome or until the participant was censored due to causes other than the outcome. From the SUN cohort participants ($n = 22{,}894$), the following selection criteria were applied to ensure complete records on the exposure and outcome. Participants were required to provide complete information on the 12 items of the LWB-I at baseline ($n = 7819$ exclusions). Prevalent cases of depression (including cases occurring before the first year after baseline), prevalent use antidepressant therapy or hypnotics ($n = 2960$), and prevalent CVD (including coronary heart disease, stroke, and thromboembolic events), diabetes, and cancer ($n = 846$) were excluded. As dietary intake represented a critical component of the LWB-I, implausible energy intakes or intakes in the top 99th and bottom first percentile for their corresponding sex were excluded ($n = 268$). Finally, participants who did not provide follow-up information 2 years and 9 months after baseline ($n = 938$) were excluded. Thus, these analyses were conducted on a total of 10,063 participants (retention rate of 91.5%).

The LWB-I

Based on 12 anthropometric, sociodemographic, and lifestyle items, the LWB-I[12] estimates the quality of individual habits to calculate a single continuous score ranging from 0 (unhealthy lifestyle and well-being) to 100 (excellent lifestyles and well-being). The items and coding are (1) sex (male, female), (2) age (years), (3) body mass index (in kg/m^2 categorized as underweight <18.5 kg/m^2, normal weight 18.5–24.9 kg/m^2, overweight 25.0–29.9 kg/m^2, and obesity >30.0 kg/m^2), (4) family history of diseases for either parent (identifying the presence of obesity, diabetes, cancer, or CVD in one or both of the participants' parents ranging from 0 to 2), (5) pre-existing medical conditions (identifying the presence of diabetes, hypertension, or hypercholesterolemia; ranging from 0 to 3), (6) smoking habits (describing never, current, and former smokers of at least 100 cigarettes), (7) presence of insomnia (identifying participants without insomnia and currently experiencing insomnia or having at some point experienced insomnia), (8) leisure-time PA (categorized as exerting <2.5 h/wk of moderate intensity activities, exerting the recommended 2.5–5 h/wk of moderate/vigorous intensity according to the World Health Organization, and those exceeding the 5 h/wk of leisure-time PA), (9) fruits and vegetable consumption (continuous variable presented as servings/day), (10) sugary products (consisting of sodas, including "low calorie," sugar, marmalade, and honey; categorized as null consumption, <1 servings/day, and those consuming one or more serving daily), finally (11) an item evaluating the presence of sadness or diminished mood in the prior 4 weeks "*Have you felt downhearted and blue?*" and (12) an item evaluating tiredness in the previous four weeks "*Did you feel tired?*" (both coded in the categories of "*All of the time*," "*Most of the time*," "*A good bit of the time*," "*Some of the time*," "*A little bit of the time*," or "*None of the time*"). Weighting of variables was done using the coefficients of the prior publication, which are added to a constant of 98.1 points. In addition, the authors described a categorization method based on two systematically defined cut-points; participants with scores <80 were categorized as having *poor* LWB, from

80 to 86 (including these integers) participants were *transitioning* LWB, and those scoring >86 points were in the *excellent* LWB group.[12]

Outcome assessment

Within the SUN cohort, validation of self-reported incident depression was conducted in a separate study relying on a psychiatric evaluation.[14] For the present study, three definitions of increasing stringency for incident depression were used: (1) a newly diagnosed report of depression, (2) initiation of antidepressant therapy even if depression was not reported by participants, and (3) a self-reported diagnosis of depression accompanied by antidepressant therapy (earliest time were criteria 1 and 2 were fulfilled).

Statistical analyses

The description measures were means and standard deviations for normally distributed data, using analysis of variance, and percentages for categorical data, analyzed using Chi-squared distributions. Cox proportional hazard models were performed with time zero defined as year 4 of follow-up, until the occurrence of the outcomes or censorship. Models were adjusted for working hours-day, cigarette packs-year, alcohol consumption (excluding wine), total daily energy intake in model 1, and model 2 was additionally adjusted for supplement intake, competitiveness, psychological tension, and dependence. Nelson–Allen curves of incident cases were obtained and adjusted for the list of confounders of model 2 using the inverse probability of the treatment weighting method. Sensitivity analyses included narrowing the diagnostic window further to include only those diagnosed between the 6th and 10th year of follow-up; previously excluded participants with non-communicable diseases were reintroduced into the sample; and participants who had prevalent consumption of antidepressant drugs were reintroduced into the analyses. The analyses were performed with the STATA statistical software package version 16 (College Station, TX, USA; Stata Corp LLC). All *P*-values presented are two tailed, and the statistical significance was set at 0.05.

Results

The final sample (n = 10,063 participants, 60% females, mean age 37.5 years [SD 11.3]) is shown in Fig. 1. When comparing categories of poor and excellent LWB-I, participants with poor LWB were prominently female (69.1%) and had a greater prevalence of obesity (6.5% compared with 3.2%) and family members who experienced non-communicable diseases more often (20.8% compared with 16.4%; Table 1). In comparison, participants in the excellent LWB had healthier habits and fewer reports of diminished well-being; more than half of the participants did not smoke (55.2% compared with 48.6%) nor experienced insomnia (52.3% compared with 26.6%) and performed higher amounts of PA overall (25.0 [5.7] METs-h/wk compared with 18.5 [3.6] METs-h/wk; Table 1).

After an average follow-up of 9 years, a total of 319 participants reported a case of incident depression, 283 cases of antidepressant initiation, and 106 cases reported incident depression in combination with the use of antidepressants. The crude Cox proportional hazards models, using as a reference the category of poor LWB, revealed crude estimations for participants with transitioning LWB experienced a hazard ratio (HR) of 0.62 (95% confidence interval [CI]: 0.48-0.80) and for those in the category of excellent LWB experienced an HR of 0.38 (95% CI:0.29-0.51). Fully adjusted models remained significant, revealing an HR of 0.67 (95% CI: 0.52-0.87) and HR of 0.44 (95% CI: 0.33-0.58) for the transitioning and excellent LWB groups, respectively. These models also revealed a significant linear trend $P < 0.001$. As for the alternative definitions of the outcome, participants incident in the group of excellent LWB compared with poor, an HR of 0.32 (95% CI: 0.24-0.45) was found for the outcome of antidepressant therapy initiation. Finally, the strict criteria of incident depression and initiation of antidepressant drugs (Table 2), those in the category of excellent LWB an HR of 0.26 (95% CI: 0.15–0.44) was found; *P* for trend <0.001.

The sensitivity analyses revealed that these estimates remained highly significant when the diagnostic window was narrowed: fully adjusted HR of 0.51 (95% CI: 0.36-0.71) with only 106 cases of incident depression (Table 3). Finally, the Nelson–Allen curves further identified distinct differences in trends of incident depression across groups (Fig. 2). While the poor LWB group observed a constant cumulative incidence of cases, the transitioning and excellent LWB groups revealed less prominent slopes during the follow-up.

Discussion

In this longitudinal study evaluating the 12 items of the LWB-I, which included anthropometric, dietary, PA, and sleep, participants classified into the groups of transitioning or excellent lifestyles and well-being were less likely to report incident depression, initiate an antidepressant therapy, or report incident depression that required treatment with antidepressants. In contrast, the group of poor lifestyles and well-being had higher cases of depression, which could be attributed to a higher prevalence of obesity, hypertension, or dyslipidemia, but also lower PA levels and experiencing insomnia. These results add to the discussion of the biological links between lifestyles and depression, which involve inflammatory mechanisms and biomarkers. With tools such as the LWB-I, it is plausible to identify subgroups of the population at higher risk of this and other non-communicable diseases.

Clinical trials intervening on diet and PA (along with standard care) are known to improve depressive symptomatology; however, there is limited evidence of these interventions on incident depression.[19,20] In practice, healthful diets have yet to demonstrate a preventive effect depression incidence.[21,22] Despite this fact, benefits to patients' well-being have been reported and novel trials have set out to determine the size of these effects of dietary interventions such as a Mediterranean diet or through intermittent fasting.[23,24] In contrast, there are concrete examples of PA interventions and their ability to reduce the risk of incident depression in a Brazilian population.[25] These benefits have also been extended to patients with anxiety.[26] Adding to this evidence, a recent review and meta-analysis also concluded that aside from PA, reducing alcohol intake, improving insomnia, and smoking cessation are also effective in controlling depressive symptoms.[27] For these reasons, the simultaneous assessment of key determinants provided by the LWB-I questionnaire[16] could facilitate the identification of subjects at higher susceptibility to depression and the prescription of tailored recommendations to improve their mental health.[8]

Assessment of the items contained in the LWB-I, but more importantly, the weighted contributions of each factor, provides (1) an integral assessment of lifestyle determinants and (2) an objective understanding of the contributions of each item to the index.[28] Although these were observational analyses, sequence of events was accounted for in our primary and sensitivity analyses and in agreement with current literature.[4,28] Previous studies, including

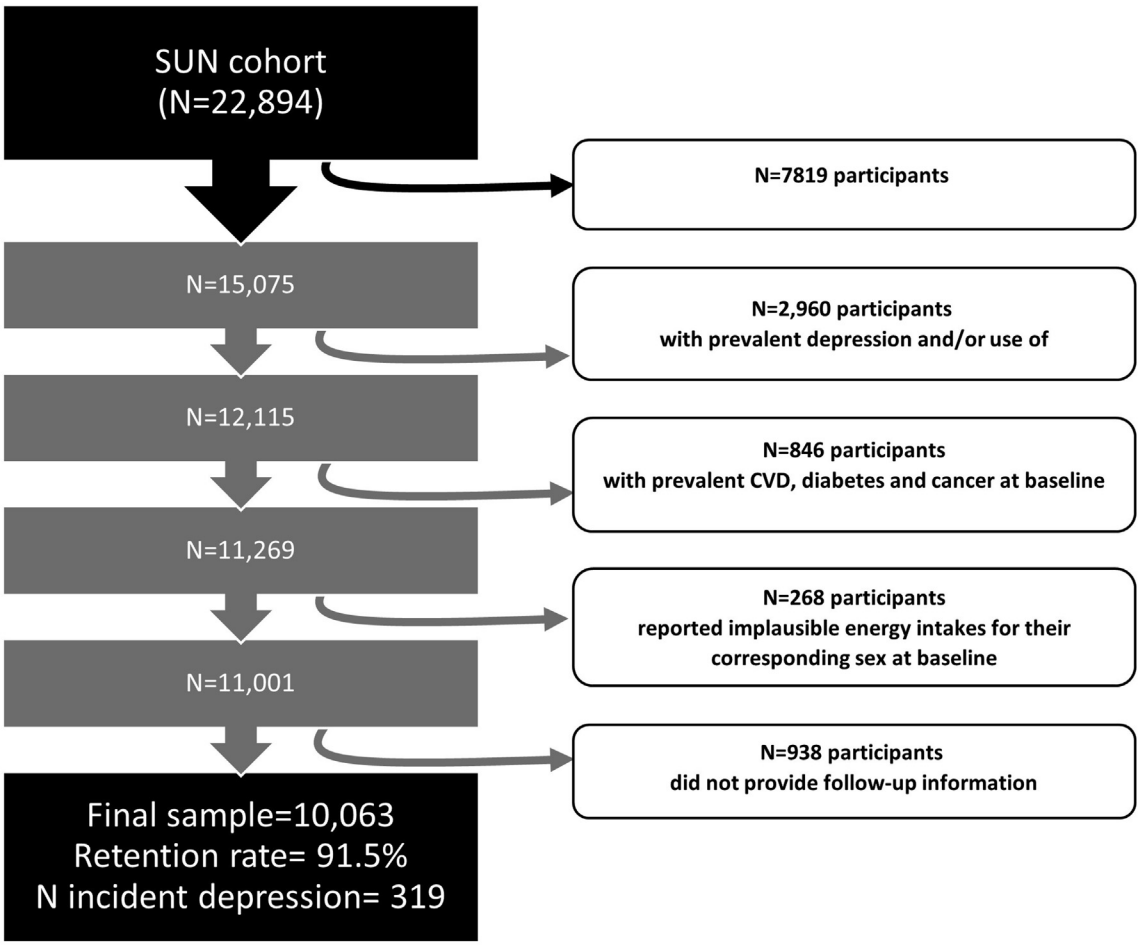

Fig. 1. Flowchart of inclusion criteria and final sample selection.

clinical trials, indicate that adherence to healthy lifestyles reduce the risk for CVD, diabetes, and premature death primarily through the reduction of inflammatory markers, and similar mechanisms are theorized to occur in depression.[4] Thus, questionnaires evaluating stress, sleep quality, comprehensive health status, dietary habits, obesity, smoking status, as well as age and gender can contribute to a personalized disease management through daily modifiable factors.[29]

The present analysis is not without some limitations. The characteristics of the sample, highly educated individuals with low prevalence of mood disorders, limit our ability to make assumptions of these associations in other economic groups and yet ensure minimal differences in well-being and life satisfaction across the sample. In addition, the cohort relies on self-reported data and outcomes prone to measurement error; however, these measures have been extensively validated.[18] The LWB-I, on the other hand, was designed as a general measure of health and not specifically for incident depression. However, the utilization of this tool is founded on the previously described biological mechanisms and thus valid under this assumption. Regarding its items, it has been suggested that weight perception and the measures of well-being lead participants to report poor life satisfaction in the absence of inflammatory markers.[30,31] This would entail a misclassification of individuals to the poor LWB group and drive our results to the null. In this regard, we cannot be certain of the degree of misclassification; however, the differences between the poor and transitioning groups would be expected to increase. Our sensitivity analyses targeted matters of inverse causality as well as long follow-up periods, ensuring a link between exposure and outcome. Replicating this study, using the LWB-I in different samples could provide external validation of this measure and give insights into the robustness of the tool; however, these require a thorough description of these described associations. The strengths of our study include the longitudinal and prospective design that reduces the risk of bias due to reverse causality. We have conducted a wide array of sensitivity analyses to test the robustness of our results and the LWB-I to shed light around alternative explanations for the association between unhealthy lifestyles and increased risk of incident depression.

Overall, multicomponent lifestyle interventions could potentially help manage depressive symptoms; for this purpose, a personalized assessment of lifestyle measures is required to potentially reduce the risk of incident depression.[14,19,23] With the LWB-I, a quantitative assessment of lifestyles, we observed a lower relative risk of incident depression in participants assigned to the transition and excellent LWB groups. Both were characterized by lower magnitudes of CVD and metabolic risk factors (two proinflammatory conditions), suggesting that habits and perceived health status measured by the LWB-I are also associated with depression risk.

Table 1
Description of the sample according to the LWB-I items and categories at baseline ($N = 10,063$).

Characteristics	Poor LWB (<80 points)	Transition LWB (80–86 points)	Excellent LWB (>86 points)	*P* value[a]
n (%)	2631 (26.2)	3173 (31.5)	4259 (42.3)	
Sex, female (%)	69.1	62.0	52.9	<0.001
Age (years)	36.9 (10.8)	38.1 (11.6)	37.4 (11.4)	<0.001
BMI (kg/m^2)	23.4 (3.6)	23.3 (3.4)	23.3 (3.1)	0.540
Underweight (<18.5; %)	3.2	3.2	3.0	<0.001
Normal weight (18.5–24.9; %)	63.6	63.9	66.8	
Overweight (25.0–29.9; %)	26.7	27.6	27.0	
Obesity (>30.0; %)	6.5	5.3	3.2	
Family history of diseases[b] (%)				<0.001
None	35.0	36.9	39.4	
1	44.2	43.1	44.2	
2	20.8	20.0	16.4	
Pre-existing diseases[b] (%)				<0.001
None	68.6	68.6	75.2	
1	24.2	25.0	21.7	
2	7.2	6.4	3.1	
Smoking status (%)				<0.001
Never	48.6	47.0	55.2	
Current	28.2	26.9	21.5	
Former	23.2	26.1	23.3	
Insomnia (%)				<0.001
Never	26.6	31.5	53.2	
Rarely	51.0	52.5	42.2	
Yes	22.4	16.0	4.6	
Physical activity (METs-h/week)	18.5 (3.6)	20.8 (21.1)	25.0 (5.7)	<0.001
Fruits + vegetables (servings/day)	4.8 (2.9)	4.7 (2.8)	5.0 (3.3)	<0.001
Added sugars[c] (total servings)	2.0 (1.9)	2.0 (1.8)	1.9 (1.7)	0.007
None	3.8	4.0	4.7	<0.001
<1/day	92.1	92.2	92.8	
>1/day	4.1	3.8	2.5	

BMI, body mass index; LWB-I, Lifestyle and Well-Being Index.
Data are presented as unadjusted means (SD) or percentages for categorical data.
Units of measurement are presented along with each variable.
Prior assessment of data distribution of continuous variables was analyzed using tests for normality and graphical means.
[a] P-values were obtained using Chi-squared distribution for categorical variables and one-way analyses of variance for continuous variables.
[b] Identifies the number of diseases present for each subject. Diseases include diabetes, hypertension, and hypercholesterolemia.
[c] Pooled analysis of standard servings of sodas including products labeled as "low calorie" (200 cc), sugar (10 g), and marmalade (10 g), and honey were included.

Table 2
Relative risk of incident depression, antidepressant therapy initiation, and incident depression accompanied by antidepressant therapy (hazard ratios and 95% CI) according to the categories of the LWB-Index among participants of the SUN cohort.

	LWB-Index categories[a]			*P* trend[b]
Outcomes	Poor LWB	Transition LWB	Excellent LWB	
Incident depression (*N*)	2631	3173	4259	
Number of cases	133	101	85	
Person-years	23,950	29,561	40,154	
Crude model	1.00 (Ref)	0.62 (0.48–0.80)	0.38 (0.29–0.51)	<0.001
Multivariate model 1[c]	1.00 (Ref)	0.64 (0.49–0.83)	0.40 (0.30–0.52)	<0.001
Multivariate model 2[d]	1.00 (Ref)	0.67 (0.52–0.87)	0.44 (0.33–0.58)	<0.001
Antidepressant therapy				
Total cases ($n = 283$)				
Crude model	1.00 (Ref)	0.53 (0.41–0.70)	0.28 (0.20–0.37)	<0.001
Multivariate model 1[c]	1.00 (Ref)	0.54 (0.42–0.71)	0.33 (0.24–0.45)	<0.001
Multivariate model 2[d]	1.00 (Ref)	0.58 (0.45–0.77)	0.32 (0.24–0.45)	<0.001
Incident depression and antidepressant therapy				
Total cases ($n = 106$)				
Crude model	1.00 (Ref)	0.56 (0.37–0.87)	0.21 (0.12–0.35)	<0.001
Multivariate model 1[c]	1.00 (Ref)	0.58 (0.38–0.90)	0.22 (0.13–0.38)	<0.001
Multivariate model 2[d]	1.00 (Ref)	0.63 (0.41–0.93)	0.26 (0.15–0.44)	2<0.001

CI, confidence interval; HR, hazard ratio; LWB-I, Lifestyle and Well-Being Index.
[a] LWB-I scores (0–100 points) categorized as poor LWB (<80 points), transition LWB (80–86 points), and excellent LWB (>86 points).
[b] Test for lineal trend calculated for the three categories of LWB-I.
[c] Adjusted for working hours-day, cigarette packs-year, alcohol consumption (excluding wine), and total daily energy intake.
[d] Same adjustments as model 1 and additionally: supplement intake, level of competitiveness, psychological tension, and dependence.

Table 3
Sensitivity analyses: relative risk of incident depression (hazard ratios and 95% CI) according to the categories of the LWB-Index among participants using alternative exclusions and follow-up times.

Sensitivity Analysis	Total cases	Person-years[a]	LWB-Index categories[b]			*P* trend[c]
			Poor LWB	Transition LWB	Excellent LWB	
N			2631	3173	4259	
1. Narrowed diagnostic window (between 6th and 10th year of FU)[d]	214	83,810	1.00 (Ref)	0.73 (0.53–1.00)	0.51 (0.36–0.71)	<0.001
2. Including participants with prevalent chronic diseases[d]	344	99,389	1.00 (Ref)	0.66 (0.51–0.84)	0.44 (0.34–0.57)	<0.001
3. Including participants with prevalent use of antidepressants[d]	331	95,756	1.00 (Ref)	0.68 (0.52–0.87)	0.46 (0.35–0.60)	<0.001

CI, confidence interval; FU, follow-up; HR, hazard ratio; LWB-I, Lifestyle and Well-Being Index.
[a] Person-years for the entire sample.
[b] LWB-I scores (0–100 points) categorized as poor LWB (<80 points), transition LWB (80–86 points), and excellent LWB (>86 points).
[c] Test for lineal trend calculated for the three categories of LWB-I.
[d] Estimates are adjusted for working hours-day, cigarette packs-year, alcohol consumption (excluding wine), total daily energy intake, supplement intake, level of competitiveness, psychological tension, and dependence.

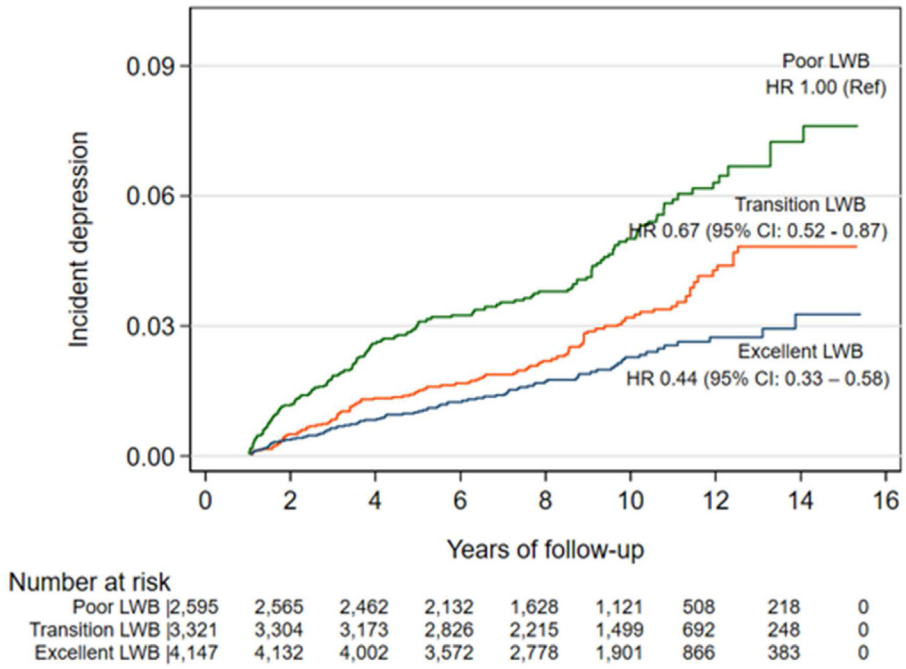

Fig. 2. Nelson–Allen curves for incident depression (percentage) and the LWB-I. Adjusted with inverse probability weighting method.

Conclusion

In a sample of Spanish university graduates, good health and well-being based on an assessment of lifestyles—according to the LWB-I—was significantly and inversely associated with the risk of subsequent depression. Using this index, individuals who were categorized into the "excellent" and "transitioning" LWB-I groups showed lower rates of incident depression and lower rates of antidepressant initiation, all compared with their unhealthy counterparts.

Author statements

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Ethical approval

The study design, methods, and informed consent were approved by the Research Ethics Committee of the University of Navarra (2001/03) in line with the principles of the Declaration of Helsinki. Each participant voluntarily submitted their completed

baseline questionnaire in a prepaid package through the national post; this was considered as an informed consent to participate in the study.

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Competing interests

The authors declare no competing interests of any kind.

Author contributions

O.P., C.S.O., and J.A.M. contributed to the conception and design of the study. C.S.O., M.B.R., and J.A.M. were involved in the acquisition of data. O.P., M.S.H., and C.S.O. conducted the data analysis, in addition to J.A.M. and V.O. with whom data were interpreted. O.P., C.S.O., V.O., and J.A.M. drafted the first article, and all authors contributed equally to the revision of the article and intellectual content. Final approval of the version to be submitted was given by O.P., M.S.H., C.S.O., V.O., C.F.L., M.B.R., A.S.V., and J.A.M.

Research data (data sharing and collaboration)

Data are not readily available. Requests for data will be reviewed by the team.

References

1. Bueno-Antequera J, Munguia-Izquierdo D. Exercise and depressive disorder. *Adv Exp Med Biol* 2020;**1228**:271–87. https://doi.org/10.1007/978-981-15-1792-1_18.
2. Pano O, Martinez-Lapiscina EH, Sayon-Orea C, Martinez-Gonzalez MA, Martinez JA, Sanchez-Villegas A. Healthy diet, depression and quality of life: a narrative review of biological mechanisms and primary prevention opportunities. *World J Psychiatr* 2021;**11**:997–1016. https://doi.org/10.5498/wjp.v11.i11.997.
3. Tsai MC, Yeh TL, Hsu HY, Hsu LY, Lee CC, Tseng PJ, et al. Comparison of four healthy lifestyle scores for predicting cardiovascular events in a national cohort study. *Sci Rep* 2021;**11**:22146. https://doi.org/10.1038/s41598-021-01213-6.
4. Ventriglio A, Sancassiani F, Contu MP, Latorre M, Di Slavatore M, Fornaro M, et al. Mediterranean diet and its benefits on health and mental health: a literature review. *Clin Pract Epidemiol Ment Health* 2020;**16**:156–64. https://doi.org/10.2174/1745017902016010156.
5. Li Y, Pan A, Wang DD, Liu X, Dhana K, Franco OH, et al. Impact of healthy lifestyle factors on life expectancies in the US population. *Circulation* 2018;**138**:345–55. https://doi.org/10.1161/CIRCULATIONAHA.117.032047.
6. Sanchez-Villegas A, Cabrera-Suarez B, Molero P, Gonzalez-Pinto A, Chiclana-Actis C, Cabrera C, et al. Preventing the recurrence of depression with a Mediterranean diet supplemented with extra-virgin olive oil. The PREDI-DEP trial: study protocol. *BMC Psychiatr* 2019;**19**:63. https://doi.org/10.1186/s12888-019-2036-4.
7. Otte C, Gold SM, Penninx BW, Pariante CM, Etkin A, Fava M, et al. *Major depressive disorder*. Nature Publishing Group; 2016. p. 1–20.
8. Mörkl S, Wagner-Skacel J, Lahousen T, Lackner S, Holasek SJ, Bengesser SA, et al. The role of nutrition and the gut-brain Axis in psychiatry: a review of the literature. *Neuropsychobiology* 2018:1–9. https://doi.org/10.1159/000492834.
9. Trautmann C, Bock A, Urbach A, Hubner CA, Engmann O. Acute vitamin B12 supplementation evokes antidepressant response and alters Ntrk-2. *Neuropharmacology* 2020;**171**:108112. https://doi.org/10.1016/j.neuropharm.2020.108112.
10. Almeida OP, Ford AH, Hirani V, Singh V, vanBockxmeer FM, McCaul K, et al. B vitamins to enhance treatment response to antidepressants in middle-aged and older adults: results from the B-VITAGE randomised, double-blind, placebo-controlled trial. *Br J Psychiatry* 2014;**205**:450–7. https://doi.org/10.1192/bjp.bp.114.145177.
11. Murawska-Ciałowicz E, Wiatr M, Ciałowicz M, Gomes de Assis G, Borowicz W, Rocha-Rodrigues S, et al. BDNF impact on biological markers of depression-role of physical exercise and training. *Int J Environ Res Publ Health* 2021;**18**. https://doi.org/10.3390/ijerph18147553.
12. Marx W, Lane M, Hockey M, Aslam H, Berk M, Walder K, et al. *Diet and depression: exploring the biological mechanisms of action*. Springer Nature; 2021. p. 134–50.
13. Kelly JR, Kennedy PJ, Cryan JF, Dinan TG, Clarke G, Hyland NP. *Breaking down the barriers: the gut microbiome, intestinal permeability and stress-related psychiatric disorders*. Frontiers Media S.A.; 2015. p. 392.
14. Wong VW, Ho FY, Shi NK, Sarris J, Chung KF, Yeung WF. Lifestyle medicine for depression: a meta-analysis of randomized controlled trials. *J Affect Disord* 2021;**284**:203–16. https://doi.org/10.1016/j.jad.2021.02.012.
15. Konig IR, Fuchs O, Hansen G, von Mutius E, Kopp MV. What is precision medicine? *Eur Respir J* 2017;**50**:1700391. https://doi.org/10.1183/13993003.00391-2017.
16. Pano O, Sayon-Orea C, Hershey MS, Bes-Rastrollo M, Martinez-Gonzalez MA, Martinez JA. Development of a general health score based on 12 objective metabolic and lifestyle items: the lifestyle and well-being index. *Health Care* 2022;**10**:1088. https://doi.org/10.3390/healthcare10061088.
17. Carlos S, De La Fuente-Arrillaga C, Bes-Rastrollo M, Razquin C, Rico-Campà A, Martínez-González MA, et al. Mediterranean diet and health outcomes in the SUN cohort. *Nutrients* 2018;**10**:439.
18. Sanchez-Villegas A, Schlatter J, Ortuno F, Lahortiga F, Pla J, Benito S, et al. Validity of a self-reported diagnosis of depression among participants in a cohort study using the Structured Clinical Interview for DSM-IV (SCID-I). *BMC Psychiatr* 2008;**8**:43. https://doi.org/10.1186/1471-244X-8-43.
19. Lassale C, Batty GD, Baghdadli A, Jacka F, Sanchez-Villegas A, Kivimaki M, et al. Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies. *Mol Psychiatr* 2019;**24**:965–86. https://doi.org/10.1038/s41380-018-0237-8.
20. Wang J, Zhou Y, Chen K, Jing Y, He J, Sun H, et al. *Dietary inflammatory index and depression: a meta-analysis*. Cambridge University Press; 2019. p. 654–60.
21. Ein N, Armstrong B, Vickers K. The effect of a very low calorie diet on subjective depressive symptoms and anxiety: meta-analysis and systematic review. *Int J Obes* 2019;**43**:1444–55. https://doi.org/10.1038/s41366-018-0245-4.
22. Firth J, Marx W, Dash S, Carney R, Teasdale SB, Solmi M, et al. The effects of dietary improvement on symptoms of depression and anxiety: a meta-analysis of randomized controlled trials. *Psychosom Med* 2019;**81**:265–80. https://doi.org/10.1097/PSY.0000000000000673.
23. Sánchez-Villegas A, Martínez-González MA, Estruch R, Salas-Salvadó J, Corella D, Covas MI, et al. Mediterranean dietary pattern and depression: the PREDIMED randomized trial. *BMC Med* 2013;**11**:208. https://doi.org/10.1186/1741-7015-11-208.
24. Jeitler M, Lauche R, Hohmann C, Choi KA, Schneider N, Steckhan N, et al. A randomized controlled trial of fasting and lifestyle modification in patients with metabolic syndrome: effects on patient-reported outcomes. *Nutrients* 2022;**14**. https://doi.org/10.3390/nu14173559.
25. Feter N, Caputo EL, Leite JS, Delpino FM, Cassuriaga J, Huckembeck CM, et al. Physical activity and the incidence of depression during the COVID-19 pandemic in Brazil: findings from the PAMPA cohort. *Ment Health Phys Act* 2022;**23**:100468. https://doi.org/10.1016/j.mhpa.2022.100468.
26. Rees-Punia E, Newton CC, Westmaas JL, Chantaprasopsuk S, Patel AV, Leach CR. Prospective COVID-19 related changes in physical activity and sedentary time and associations with symptoms of depression and anxiety. *Ment Health Phys Act* 2021;**21**:100425. https://doi.org/10.1016/j.mhpa.2021.100425.
27. Young CL, Trapani K, Dawson S, O'Neil A, Kay-Lambkin F, Berk M, et al. Efficacy of online lifestyle interventions targeting lifestyle behaviour change in depressed populations: a systematic review. *Aust N Z J Psychiatr* 2018;**52**:834–46. https://doi.org/10.1177/0004867418788659.
28. Sayón-Orea C, Razquin C, Bulló M, Corella D, Fitó M, Romaguera D, et al. Effect of a nutritional and behavioral intervention on energy-reduced mediterranean diet adherence among patients with metabolic syndrome: interim analysis of the PREDIMED-plus randomized clinical trial. *JAMA* 2019;**322**:1486–99. https://doi.org/10.1001/jama.2019.14630.
29. Tousen Y, Mizushima R, Koitaya N, Kurotani K, Nishihira J, Maeda-Yamamoto M, et al. [A literature review on the relationship between questionnaires for assessing minor health complaints and health status indices among Japanese people]. *Nihon Koshu Eisei Zasshi* 2022;**69**:368–82. https://doi.org/10.11236/jph.21-099.
30. Hadwen BB, He JB, Funk C, McKinney K, Wilk P. Association between accuracy of weight perception and life satisfaction among adults with and without anxiety and mood disorders: a cross-sectional study of the 2015-2018 Canadian Community Health Survey. *J Public Health* 2022. https://doi.org/10.1093/pubmed/fdac047.
31. Rogante E, Sarubbi S, Lamis DA, Canzonetta V, Sparagna A, De Angelis V, et al. Illness perception and job satisfaction in patients suffering from migraine headaches: trait anxiety and depressive symptoms as potential mediators. *Headache* 2019;**59**:46–55. https://doi.org/10.1111/head.13461.