

This is the peer reviewed version of the following article:

Galán, Iñaki; Ortiz, Cristina; Pérez-Ríos, Mónica; Ayuso-Álvarez, Ana; Rodríguez-Blázquez, Carmen; Damián, Javier; Fernández-Escobar, Carlos; García-Esquinas, Esther; López-Cuadrado, Teresa. **Light cigarette smoking and all-cause mortality in Spain. A national population-based cohort study.** *Ann Epidemiol.* 2023 Feb;78:9-12.

which has been published in final form at

<https://doi.org/10.1016/j.annepidem.2022.12.001>

## **Light cigarette smoking and all-cause mortality in Spain. A national population-based cohort study**

Iñaki Galán PhD<sup>1,2</sup>, Cristina Ortiz MSc<sup>1</sup>, Mónica Pérez-Ríos PhD<sup>3</sup>, Ana Ayuso-Álvarez MSc<sup>1</sup>, Carmen Rodríguez-Blázquez PhD<sup>1</sup>, Javier Damián PhD<sup>1</sup>, Carlos Fernández-Escobar MD<sup>4</sup>, Esther García-Esquinas PhD<sup>1,2,5</sup>, Teresa López-Cuadrado PhD<sup>1,2</sup>

<sup>1</sup>National Centre for Epidemiology, Institute of Health Carlos III, Madrid, Spain

<sup>2</sup>Department of Preventive Medicine and Public Health. Autonomous University of Madrid/IdiPAZ, Madrid, Spain

<sup>3</sup>Department of Preventive Medicine and Public Health. University of Santiago de Compostela, Santiago de Compostela, Spain

<sup>4</sup>Public Health and Epidemiology Research Group, School of Medicine and Health Sciences, Universidad de Alcalá, Alcalá de Henares, Madrid, Spain

<sup>5</sup> CIBERESP, Madrid, Spain.

### **Corresponding author:**

Iñaki Galán, MD, PhD.

National Centre for Epidemiology

Institute of Health Carlos III

Monforte de Lemos 5,

28029 Madrid (Spain)

Telephone: +34 918222679

Fax: +34 913877815

E-mail: [igalan@isciii.es](mailto:igalan@isciii.es)

## **Abstract**

**Purpose:** Regular light cigarette consumption (light smoking) is increasing in many countries; however, few studies have assessed its impact on mortality. The main aim of this study is to estimate the association between number of cigarettes consumed and all-cause mortality in Spain while focusing on light smoking.

**Methods:** Longitudinal study based on data from 42,902 individuals aged  $\geq 15$  years included in the 2011-2012 (Spanish) National Health Survey or the 2014 European Health Survey for Spain. Data were linked with the mortality registry up to December 2020. Multivariate Cox regression models were used to estimate hazard ratios (HR) adjusted for sociodemographic variables, lifestyle factors, and health status indicators.

**Results:** Compared to never smokers, the mortality HR for nondaily smokers was 1.30 (95%CI: 0.81-2.09), increasing to 2.23 (95%CI: 1.25-3.96) among those smoking 1-2 cigarettes/day, and to 1.54 (95%CI: 1.14-2.07) for consumers of 3-5 cigarettes/day. When individuals who reported trying to quit during the previous year were excluded, resulting HRs were 1.31 (95%CI: 0.81-2.10), 1.48 (95%CI: 0.69-3.19) and 1.64 (95%CI: 1.16-2.34), respectively.

**Conclusions:** Compared to never smokers, consumers of small quantities of tobacco, i.e., light smoking, had an increased mortality risk. In view of these results, we suggest the need for awareness-raising campaigns regarding how smoking even a small number of cigarettes a day causes serious harm to one's health.

**Keywords:** Smoking; light smoking; cigarettes; mortality; cohort study; Spain

**Abbreviations:** Cig/day, Cigarettes/day; CI, Confidence Interval; COPD, Chronic obstructive pulmonary disease; HR, Hazard Ratio; MEDAS, Mediterranean Diet Adherence Screener; NHIS, National Health Interview Survey.

## **Introduction**

The evolution of the global smoking epidemic is characterized by a substantial decrease in smoking prevalence, especially in the highly industrialized regions [1]. Concurrently, some countries report a reduction in the number of cigarettes consumed among smokers, thus, experiencing a lower prevalence of heavy smokers with a corresponding increase in light smokers [2]. From 1987 to 2020, the prevalence of smokers in Spain has decreased from 38.1% to 22.1%, while the proportion of smokers consuming fewer than 10 cigarettes a day increased from 23% to 37%. Daily consumers of small amounts of cigarettes represent 7.3% of the adult Spanish population in 2020 [3].

Individuals probably underestimate the risk of tobacco use. Occasional and/or low-frequency smoking is often considered relatively safe [4] in spite of evidence linking it to important health effects from both a clinical and public health perspective [5–7]. Unfortunately, very few studies have evaluated its association with mortality [8–11].

The aim of this study was to estimate the association between number of cigarettes consumed and all-cause mortality in Spain with a special focus on light smoking.

## **Materials and methods**

### *Design and Study Population*

Data came from a longitudinal prospective cohort study of 43,849 individuals aged 15 and over who participated in the 2011-2012 (Spanish) National Health Survey or in the 2014 European Health Survey for Spain. Both surveys used the same sample design and standardized questionnaires administered face-to-face using a Computer-Assisted Personal Interview (CAPI). Response rate was 71% of all selected households. Data were linked to mortality records through December 31, 2020 (Linking Mortality Data to

the Spanish Health Surveys, MESES study) by the (Spanish) National Statistics Institute using the national identification document number.

### *Variables*

The main independent variable was tobacco consumption, with individuals grouped as never smokers, ex-smokers, nondaily consumers, and daily consumers of 1-2, 3-5, 6-10, 11-20, 21-30 and >30 cigarettes/day (cig/day). We excluded people who smoked other type of tobacco products besides cigarettes. Sociodemographic covariates included sex, age (categorized into seven groups), educational attainment (no schooling/primary studies, secondary studies-first stage, secondary studies-second stage, and college), and place of birth (Spain native-born, foreign-born). Regarding lifestyle and health status variables, self-reported information was collected on sedentary leisure time (no exercise, almost completely sedentary leisure time); body mass index (BMI, kg/m<sup>2</sup>); daily alcohol intake (no consumption, low-risk [ $\leq 20$  g/d for men and  $\leq 10$  g/d for women], and high-risk [ $>20$ g/d for men and  $>10$ g/d for women] consumption); any binge drinking in the past month (consumption of  $\geq 6$  alcoholic drinks for men or  $\geq 5$  for women within a 4 to 6-hour interval); diet quality based on the index Mediterranean Diet Adherence Screener (MEDAS) [12,13]. Based on the MEDAS score ranging from 0 (lowest diet quality) to 10 (highest diet quality), participants were classified as having either low, medium, or high adherence. Respondents also reported their self-rated health (very good, good, neither good nor poor, poor, or very poor) and their history of physician-diagnosed chronic diseases (the number of the following health problems: heart attack, other heart diseases, stroke, chronic obstructive pulmonary disease (COPD), diabetes, stomach ulcer, cirrhosis/liver disease, and malignant tumours).

### *Data Analyses*

From the initial 43,849 individuals, we excluded those with missing values in potential confounders leading to a final sample size of 42,902 participants aged 15 and over. We performed multivariate Cox regression analyses to calculate hazard ratios (HR) and their corresponding 95% Confidence Intervals (CI).

We created four models as follows: 1) Model adjusted by sociodemographic and lifestyle variables (model 1); 2) Model 1 plus adjustment for health status variables (model 2); 3) Model 1 excluding individuals rating their health as “very bad” (model 3); 4) Model 1 excluding individuals reporting quitting attempts in the previous year (smoke-free for at least 24h) (model 4).

All estimates were weighted using sampling weights to reestablish proportionality. Due to the complex sampling design, we used appropriate methods to account for the effect of stratification and clustering on standard errors. All analyses were run with the Stata statistical software v.17 (StataCorp, College Station, Texas, U.S.).

## **Results**

Table 1 describes study participants’ characteristics. Smokers of 5 or fewer cig/day, compared with more-frequent smokers, were more likely to be women, to be younger, to report a higher level of education, to be foreign-born, and to report healthier lifestyles.

Table 2 shows the results of the different models estimating the association between smoking frequency and mortality, always compared to never smokers. Nondaily smokers have an HR of 1.30 (95%CI: 0.81-2.09) (Model 1); the HR increases to 2.23 (95%CI: 1.25-3.96) in smokers of 1-2 cig/day, and to 1.54 (95%CI: 1.14-2.07) in smokers of 3-5 cig/day. For consumers of 11 cig/day or more the risk kept increasing up to an HR of 2.96 (95%CI: 1.94-4.51) for smokers of >30 cig/day. These associations

were slightly reduced when adjusting for possible confounders such as health status measures (model 2). However, the magnitude of the associations increased when the analyses excluded individuals reporting "very poor" health (model 3). The greatest reduction in the association among smokers of 1-2 cig/day was observed when individuals who had attempted to quit smoking in the previous year were excluded (HR 1.48 (95% CI: 0.69-3.19) (model 4). Compared to never smokers, the HR for ex-smokers was 1.29 (95% CI: 1.17-1.43) (model 1) which did not vary substantially with further adjustments in following models.

## **Discussion**

Light smoking was associated with an increased mortality risk. The results were quite stable across models. Model 2 included self-rated health and history of chronic diseases, both likely mediators of the associations under examination. Thus, a reduction in the effect size of smoking on mortality was not unexpected. In model 3 we attempted to control for reverse causality since people with a very deteriorated health status may have modified their smoking frequency [14]. Finally, model 4 tried to assess whether the group of smokers trying to quit smoking may impact the association of interest. These individuals are likely to have decreased consumption which would place them in the light smoking categories [15]. Our results show that this group mainly impacts the mortality risk of smokers of 1-2 cigarettes/day with an HR going from 2.23 to 1.48, a risk magnitude very likely to approach that of lifetime low cigarette smoking.

Several studies report associations between nondaily tobacco consumption and mortality, although results vary greatly. Some authors report elevated risks with HRs ranging from 1.72 to 1.99 [9,16,17]; whereas others [18] find associations similar in magnitude to those reported here, and others fail to detect an association [10]. Placing



our results in the context of the existing literature is complex due to the lack of a standard definition for light smoking. Further, there are scarce studies reporting results for detailed categories, especially as low as 1-2 cigarettes/day [19]. In a study designed very similarly to ours, Qin and colleagues linked National Health Interview Survey (NHIS) data with mortality data with a median 8.2 year follow-up. They reported an HR of 1.94 for those consuming 1-2 cigarettes/day, 1.99 for a consumption of 3-5 cigarettes/day, and 1.34 for ex-smokers, all compared to never smokers [8]. In a recent pooled analysis of prospective cohort studies in Japan, was found lower estimates with HRs of 1.27/1.28 (men/women) for 1-2 cigarettes/day, and 1.45/1.49 (men/women) for 3-5 cigarettes/day [20]. Our findings very much support these results.

The main strength of our study is its population-based design with a large cohort representative of all regions of Spain. Second, mortality records were linked to our database using the national identification document, thus reducing record matching errors. Third, the adjustment for other lifestyle factors reduces the risk of residual confounding. The main limitation, not uncommon, is that our analyses are based on self-reported smoking data. Furthermore, we have no information on previous smoking history or any way of accounting for changes in smoking behavior that may have occurred during follow-up. It is possible that current low-intensity smokers may have smoked more heavily in the past.

## **Conclusions**

Smoking, even in quantities as small as  $\leq 5$  cigarettes/day, is consistently associated with an elevated risk of mortality, compared to never smoking. These results indicate the need for designing and implementing public campaigns to raise awareness about

smoking and how even a small number of cigarettes a day causes serious harm to one's health.

## **Contribution statement**

Iñaki Galán: Conceptualization, study design, methodology, writing the first draft and editing. Cristina Ortiz and Teresa López-Cuadrado: Methodology, data curation, data analysis, writing review and editing. Mónica Pérez-Ríos, Ana Ayuso-Álvarez, Carmen Rodríguez-Blázquez, Javier Damián, Carlos Fernández-Escobar and Esther García-Esquinas: Interpretation of the findings, critically revised the manuscript and editing.

All authors have given final approval of the submitted version.

## **Funding**

This work was supported by the Institute of Health Carlos III, Ministry of Science and Innovation [grant number PI19CIII/00021, FI17CIII/00003].

## **Declaration of interests**

None declared.

## **Ethics approval**

This study was approved by the Carlos III Institute of Health Ethical Research Committee, Number: CEI PI 28\_2019.

## **Disclaimer**

This article presents independent research. The views expressed are those of the authors and not necessarily those of the Institute of Health Carlos III.

## References

- [1] Dai X, Gakidou E, Lopez AD. Evolution of the global smoking epidemic over the past half century: strengthening the evidence base for policy action. *Tob Control* 2022;31:129–37. <https://doi.org/10.1136/tobaccocontrol-2021-056535>.
- [2] Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco Product Use Among Adults - United States, 2020. *MMWR Morb Mortal Wkly Rep* 2022;71:397–405. <https://doi.org/10.15585/mmwr.mm7111a1>.
- [3] Spanish Ministry of Health. National Health Interview Survey. <https://www.sanidad.gob.es/estadEstudios/estadisticas/encuestaNacional/>
- [4] Amrock SM, Weitzman M. Adolescents' Perceptions of Light and Intermittent Smoking in the United States. *Pediatrics* 2015;135:246–54. <https://doi.org/10.1542/peds.2014-2502>.
- [5] Schane RE, Ling PM, Glantz SA. Health effects of light and intermittent smoking: a review. *Circulation* 2010;121:1518–22. <https://doi.org/10.1161/CIRCULATIONAHA.109.904235>.
- [6] Hackshaw A, Morris JK, Boniface S, Tang J-L, Milenković D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. *BMJ* 2018;360:j5855. <https://doi.org/10.1136/bmj.j5855>.
- [7] Inoue-Choi M, Hartge P, Liao LM, Caporaso N, Freedman ND. Association between long-term low-intensity cigarette smoking and incidence of smoking-related cancer in the national institutes of health-AARP cohort. *Int J Cancer* 2018;142:271–80. <https://doi.org/10.1002/ijc.31059>.
- [8] Qin W, Magnussen CG, Li S, Steffen LM, Xi B, Zhao M. Light Cigarette Smoking Increases Risk of All-Cause and Cause-Specific Mortality: Findings from the NHIS Cohort Study. *Int J Environ Res Public Health* 2020;17:E5122. <https://doi.org/10.3390/ijerph17145122>.
- [9] Inoue-Choi M, Liao LM, Reyes-Guzman C, Hartge P, Caporaso N, Freedman ND. Association of Long-term, Low-Intensity Smoking With All-Cause and Cause-Specific Mortality in the National Institutes of Health-AARP Diet and Health Study. *JAMA Intern Med* 2017;177:87–95. <https://doi.org/10.1001/jamainternmed.2016.7511>.
- [10] Thomson B, Tapia-Conyer R, Lacey B, Lewington S, Ramirez-Reyes R, Aguilar-Ramirez D, et al. Low-intensity daily smoking and cause-specific mortality in Mexico: prospective study of 150 000 adults. *Int J Epidemiol* 2021;50:955–64. <https://doi.org/10.1093/ije/dyab013>.
- [11] Yang JJ, Yu D, Shu X-O, Freedman ND, Wen W, Rahman S, et al. Quantifying the association of low-intensity and late initiation of tobacco smoking with total and cause-specific mortality in Asia. *Tob Control* 2021;30:328–35. <https://doi.org/10.1136/tobaccocontrol-2019-055412>.
- [12] Schröder H, Fitó M, Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, et al. A Short screener is valid for assessing mediterranean diet adherence among older spanish men and women. *J Nutr* 2011;141:1140–5. <https://doi.org/10.3945/jn.110.135566>.
- [13] Ortiz C, López-Cuadrado T, Rodríguez-Blázquez C, Pastor-Barriuso R, Galán I. Clustering of unhealthy lifestyle behaviors, self-rated health and disability. *Prev Med* 2022;155:106911. <https://doi.org/10.1016/j.ypmed.2021.106911>.
- [14] Sattar N, Preiss D. Reverse Causality in Cardiovascular Epidemiological Research: More Common Than Imagined? *Circulation* 2017;135:2369–72. <https://doi.org/10.1161/CIRCULATIONAHA.117.028307>.
- [15] Owen N, Kent P, Wakefield M, Roberts L. Low-rate smokers. *Prev Med* 1995;24:80–4. <https://doi.org/10.1006/pmed.1995.1011>.
- [16] Inoue-Choi M, McNeel TS, Hartge P, Caporaso NE, Graubard BI, Freedman ND. Non-Daily Cigarette Smokers: Mortality Risks in the U.S. *Am J Prev Med* 2019;56:27–37. <https://doi.org/10.1016/j.amepre.2018.06.025>.
- [17] Inoue-Choi M, Christensen CH, Rostron BL, Cosgrove CM, Reyes-Guzman C, Apelberg B, et al. Dose-Response Association of Low-Intensity and Nondaily Smoking With

- Mortality in the United States. *JAMA Netw Open* 2020;3:e206436. <https://doi.org/10.1001/jamanetworkopen.2020.6436>.
- [18] Løchen M-L, Gram IT, Mannsverk J, Mathiesen EB, Njølstad I, Schirmer H, et al. Association of occasional smoking with total mortality in the population-based Tromsø study, 2001–2015. *BMJ Open* 2017;7:e019107. <https://doi.org/10.1136/bmjopen-2017-019107>.
- [19] Husten CG. How should we define light or intermittent smoking? Does it matter? *Nicotine Tob Res* 2009;11:111–21. <https://doi.org/10.1093/ntr/ntp010>.
- [20] Inoue-Choi M, Freedman ND, Saito E, Tanaka S, Hirabayashi M, Sawada N, et al. Low-intensity cigarette smoking and mortality risks: a pooled analysis of prospective cohort studies in Japan. *Int J Epidemiol* 2022;51:1276–90. <https://doi.org/10.1093/ije/dyab224>.

Table 1. Sample distribution according to smoking characteristics. Spanish population  $\geq 15$  years of age.

	Tobacco Consumption										P value
	Total	Number of daily cigarettes									
		Never smoker	Ex smoker	Nondaily smoker	1-2	3-5	6-10	11-20	21-30	>30	
<b>N<sup>a</sup></b>	42,902	22,415	10,156	1027	339	1374	2916	3936	482	257	
<b>Age, mean<sup>b</sup></b>	47.5	47.8	53.1	39.1	40.2	39.4	40.3	43.7	47.5	48.2	<0.001
<b>Sex, %<sup>b</sup></b>											<0.001
Women	51.5	62.3	36.5	42.2	47.0	54.0	48.9	38.4	29.4	19.6	
<b>Education level, %<sup>b</sup></b>											<0.001
College degree	17.3	17.8	19.5	20.6	20.7	18.1	14.8	10.7	12.1	9.2	
Secondary studies-2 <sup>nd</sup> stage	28.0	26.1	27.5	35.1	39.1	35.9	33.7	30.1	25.3	23.9	
Secondary studies-1 <sup>st</sup> stage	28.1	25.4	25.6	30.0	21.7	31.7	36.0	39.9	38.2	36.9	
$\leq$ primary studies	26.6	30.7	27.4	14.3	18.5	14.3	15.5	19.2	24.4	30.0	
<b>Spain-born, %<sup>b</sup></b>											<0.001
Yes	86.2	84.3	90.2	79.7	80.4	86.4	87.7	87.2	91.4	91.5	
<b>High-risk daily alcohol intake, %<sup>b</sup></b>											<0.001
Yes	8.6	4.6	11.2	14.4	11.3	11.9	11.4	15.6	23.6	31.7	
<b>Binge drinking previous month, %<sup>b</sup></b>											<0.001
Yes	6.8	4.0	7.1	12.8	13.6	11.5	11.0	12.1	14.5	22.6	
<b>Leisure-time sedentarism, %<sup>b</sup></b>											<0.001
Yes	40.6	39.5	36.6	33.1	34.4	38.1	43.4	52.9	61.7	65.3	
<b>Mediterranean diet, %<sup>b</sup></b>											<0.001
Low adherence	46.3	44.7	39.9	49.9	52.3	56.1	55.1	56.3	53.4	59.6	
Medium adherence	27.1	27.5	28.5	29.0	22.2	25.1	24.9	24.0	25.5	27.5	
High adherence	26.6	27.8	31.6	21.1	25.5	18.8	20.0	19.7	21.1	12.9	
<b>Body Mass Index, %<sup>b</sup></b>											<0.001
Underweight	2.3	2.4	1.2	3.1	4.5	3.8	3.4	2.7	1.5	2.2	
Normal weight	43.1	43.7	35.5	49.4	57.1	55.1	52.5	45.6	33.8	29.4	
Overweight	33.6	31.7	40.5	29.9	25.1	26.9	30.0	33.7	38.6	33.1	
Obesity	15.5	15.1	19.2	13.9	9.5	10.3	10.2	14.5	19.3	30.3	
Not available	5.5	7.1	3.6	3.7	3.8	3.9	4.0	3.4	6.8	5	
<b>Mortality, %<sup>c</sup></b>	7.6	8.0	10.2	2.8	5.2	3.5	3.1	4.9	7.1	12.2	<0.001

<sup>a</sup> Unweighted sample size; <sup>b</sup> weighted % or weighted mean; <sup>c</sup> weighted cumulative mortality

Table 2. Association between tobacco consumption amounts and overall mortality. Spanish population  $\geq 15$  years of age.

	Model 1 N=42,902		Model 2 N=42,902		Model 3 N=41,945		Model 4 N=40,044	
	HR*	95%CI	HR*	95%CI	HR*	95%CI	HR*	95%CI
<b>Tobacco Consumption</b>								
<b>Never smoker</b>	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
<b>Ex smoker</b>	1.29	1.17-1.43	1.14	1.03-1.27	1.33	1.20-1.48	1.29	1.17-1.43
<b>Nondaily smoker</b>	1.30	0.81-2.09	1.29	0.80-2.07	1.33	0.81-2.20	1.31	0.81-2.10
<b>1-2 cigarettes/day</b>	2.23	1.25-3.96	2.19	1.24-3.86	2.48	1.39-4.43	1.48	0.69-3.19
<b>3-5 cigarettes/day</b>	1.54	1.14-2.07	1.40	1.03-1.91	1.65	1.22-2.23	1.64	1.16-2.34
<b>6-10 cigarettes/day</b>	1.49	1.18-1.88	1.44	1.13-1.84	1.53	1.20-1.94	1.59	1.21-2.09
<b>11-20 cigarettes/day</b>	1.79	1.50-2.15	1.70	1.41-2.04	1.88	1.56-2.26	1.73	1.39-2.14
<b>21-30 cigarettes/day</b>	2.20	1.47-3.30	1.97	1.30-2.98	2.39	1.59-3.60	2.20	1.39-3.50
<b>&gt;30 cigarettes/day</b>	2.96	1.94-4.51	2.60	1.73-3.89	3.27	2.11-5.07	2.87	1.72-4.79

\* Hazard ratios estimated using Cox regression analysis

Model 1: Adjusted for age, sex, education level, native/foreign born, alcohol consumption, sedentary leisure time, balanced diet, and body mass index.

Model 2: Model 1 plus self-rated health and chronic diseases history

Model 3: Model 1 excluding individuals reporting very poor self-rated health

Model 4: Model 1 excluding individuals reporting any quit attempts (smoke-free for at least 24 hours) in the previous year