Smoking-attributable mortality in Spain: A systematic review

Mortalidad atribuida al consumo de tabaco en España: Revisión sistemática

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Abstract

Smoking-attributable mortality (SAM) is an indicator that reflects the evolution of the tobacco epidemic at the population level. The objective of this study is to identify and to describe published studies that have estimated SAM in Spain. A search in PubMed and EMBASE databases was performed, limited to studies published until April 15th, 2021. Studies that estimated SAM in Spain or its constituent regions were included. Of the 146 studies identified, 22 met eligibility criteria. The first estimate of SAM in Spain dates from 1978 and the last from 2017. Twelve of the studies found estimated SAM at national level, 8 in regions, 1 in a province and 1 in a city. Most estimates were made for adults aged over 34, categorized as smokers, ex-smokers and never smokers. Observed mortality derived, in all studies, from official records, and relative risks mostly from Cancer Prevention Study II. In the period analyzed, a decrease in the burden of SAM was observed. In Spain, different SAM estimates are available globally, but they do not have regular periodicity, and such estimates are infrequently made by region. Due to variations in methodology and data sources, it is difficult to assess changes in SAM. Having global and regional periodic estimates would be necessary to correctly monitor the tobacco epidemic in Spain.

Key words: mortality/smoking, tobacco, Spain, mortality.

Resumen

La mortalidad atribuida (MA) al consumo de tabaco es un indicador que refleja la evolución de la epidemia tabáquica a nivel poblacional. El objetivo de este trabajo es identificar y describir los estudios publicados que hayan estimado MA al consumo de tabaco en España. Se realizó una búsqueda en las bases de datos de PubMed y EMBASE de los trabajos publicados hasta el 15/04/2021. Se incluyeron estudios que estimaron MA en España en su conjunto o en unidades territoriales. Se identificaron 146 estudios y 22 cumplieron los criterios de elegibilidad. La primera estimación de MA en España data de 1978 y la última de 2017. En 12 estudios se estimó la MA a nivel nacional, 8 en comunidades autónomas, 1 a nivel provincial y 1 en una ciudad. La mayoría de estimaciones se realizaron en adultos mayores de 34 años categorizados como fumadores, exfumadores y nunca fumadores. La mortalidad observada derivó en todos los estudios de registros oficiales y los riesgos relativos mayoritariamente del *Cancer Prevention Study II*. En el periodo analizado se observó una disminución en la carga de MA en relación con la mortalidad total. En España se dispone de estimaciones de MA a nivel global, pero no tienen periodicidad regular y es infrecuente que se realicen en unidades territoriales. Debido a variaciones en la metodología y en las fuentes de datos es difícil evaluar de forma precisa cambios en la MA. Sería necesario disponer de estimaciones periódicas globales y para monitorizar correctamente la epidemia tabáquica en España.

Palabras clave: mortalidad/fumar, tabaco, España, mortalidad.

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Smoking is the leading cause of preventable death worldwide due to its high prevalence and strength of association with different causes of death (U.S. Department of Health and Human Services, 2014). In Spain, 28.2% of men and 20.8% of women aged 16 and over were smokers in 2017 (Ministerio de Sanidad, Consumo y Bienestar, 2018). According to data from Spain's National Institute of Statistics (INE), diseases of the circulatory system, tumours and respiratory diseases were the main causes of death in Spain in 2018; these large groups of causes of death are all associated with smoking (Instituto Nacional de Estadística, 2018).

Against this background, the World Health Organization (WHO) has developed strategies such as MPOWER (Monitor, Protect, Offer, Warn, Enforce, Raise) and agreements such as the "WHO Framework Convention for tobacco control" for the purpose of building alliances between countries to develop policies, mobilize resources and plan interventions to reduce smoking. One of the strategies implemented in MPOWER is monitoring, understood as the observation of indicators that allow the development of the tobacco epidemic in the population to be described (World Health Organization, 2008).

The tobacco epidemic can be monitored using a variety of indicators. One of them is smoking-attributable mortality (SAM), which makes it possible to analyze the development of the tobacco epidemic and the impact it has on the health of populations in a simple and objective way through the application of different estimation methods (Pérez-Ríos & Montes, 2008). In addition, calculating SAM allows comparisons to be made of the impact of smoking across geographical areas, age groups or different smoking-attributable diseases.

Studies have been published in Spain that estimate the impact of smoking on population mortality. These studies vary in their geographic scope, publication date, and methodology. A review of all information available to date on the burden of smoking on mortality in Spain and/or its constituent regions is essential for a comprehensive view of its impact on the Spanish population and to understand how it has developed over time. The aim of this review is to identify and describe these studies.

Methods

The search methodology followed PRISMA guidelines (*Preferred Reporting Items for Systematic reviews and Meta-Analyses*) (Page et al., 2021; Rethlefsen et al., 2021).

Literature search

A search was carried out in the MEDLINE (PubMed) and EMBASE databases using the search strategy (((mortality) AND attribut*) AND (smok* OR tobacco)) AND (Spain OR name of the autonomous communities and cities). In the EMBASE database, the search was filtered by title, abstract, and keywords. Duplicates were removed manually. The search was completed with a manual check using metasearch engines such as Google Scholar and with a bibliography review of studies meeting the selection criteria.

The search was conducted on June 1, 2020, and updated on April 15, 2021. An alert was set in PubMed for weekly updates of new literature up to that date. The systematic review was registered in the PROSPERO database (Rey-Brandariz et al., 2021).

Inclusion criteria

All studies estimating SAM in Spain and published before April 15, 2021 were included, regardless of the estimation method used, whether covering the whole country or a smaller constituent area such as autonomous community (AC), province or city. Reports, conference contributions, simulation studies, studies not making estimates in the general population, joint estimates with other risk factors, re-analysis of SAM, studies exclusively estimating potential years of life lost (PYLL), analyzing morbidity or performing projections were not included. The search was not limited by language.

Study selection and information extraction

Two investigators (JRB and AGO) independently reviewed the titles and abstracts of the studies found. Those preselected by both were obtained and read in full. The information of the studies meeting inclusion criteria was extracted in a database designed for the purpose. The information extracted from each study was: year and journal of publication; regarding SAM: geographic scope (location for which the estimate was made), temporal scope (year/s of estimates), ages studied, age groups for which SAM was estimated and estimation method used; regarding smoking prevalence: data source, year of the study from which the prevalence was derived, categories of smoker included (smoker, ex-smoker, never smoker) and age groups; regarding relative risk (RR): data source; and regarding observed mortality (OM): data source, year of mortality and causes analyzed. Information was extracted on the percentages of attributable mortality (AM) versus OM in global, in men and in women; the cause of death group (tumours, cardiovascular/cardiometabolic and respiratory diseases) and the specific cause of death with the highest burden of SAM in both sexes, in men and in women. Differences in the data extracted by the two researchers (JRB and AGO) were resolved by consensus.

Results

Search results

Of the 146 studies found, 22 met the inclusion criteria. The EMBASE search provided 13 unidentified papers in

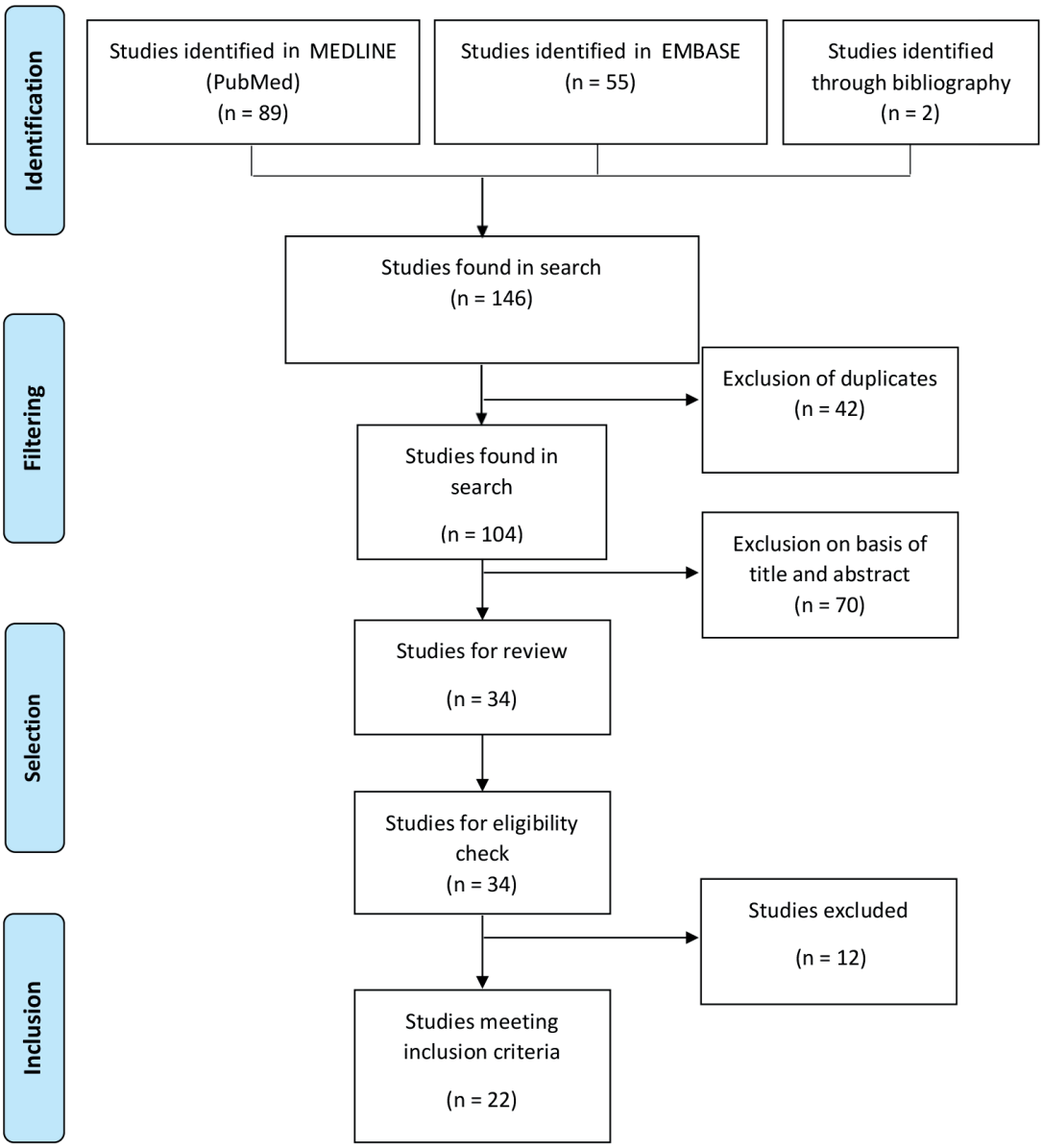

Figure 1. Flow chart of literature search.

the PubMed search, of which one met the inclusion criteria. The bibliography review of the studies included provided two further papers and the Google Scholar search did not return any studies on older adults. Thirty-four potentially relevant papers were identified and of these, 12 were excluded on reading the full text. The reasons for exclusion were that the estimates were made in a specific population (working-age population: 35-64 years) (Olivia-Moreno, Trapero-Bertran & Peña-Longobardo, 2019), the estimate was combined with other risk factors (Janssen, Trias-Llimós & Kunst, 2021), the study involved a reanalysis of SAM calculated in previous studies (Haeberer et al., 2020), did not attribute mortality (Gregoraci et al., 2017; Kulik et al., 2014; Long et al., 2021; Mackenbach et al., 2015, Rodríguez Tapioles, Pueyos Sánchez, Bueno Cavanillas, Delgado Rodríguez & Gálvez Vargas, 1994), estimated PYLL (García Benavides & Hernández Aguado, 1989), analyzed morbidity (González-Enríquez et al., 2002) or involved projections (Banegas Banegas et al., 1993; Sánchez et al., 2010). The study selection process is reflected in Figure 1, and Table 1 describes the main characteristics of the studies included.

Characteristics of the studies included

Regarding the studies included, 12 made estimates of SAM at the national level (Banegas et al., 2011; Banegas, Díez Gañán, González Enríquez, Villar Álvarez & Rodriguez-Artalejo, 2005; Banegas, Díez Gañán, Rodríguez-Artalejo, Pérez-Regadera & Villar Álvarez, 2001; Banegas, Rodríguez-Artalejo, Graciani, Billar & Herruzo, 2003; González Enríquez, Rodríguez Artalejo, Banegas Banegas & Villar Álvarez, 1989a; González Enríquez, Rodríguez Artalejo, Martín Moreno, Banegas Banegas & Villar Álvarez,

Table 1. *Main characteristics of studies estimating smoking-attributable mortality (SAM) in Spain (at national, autonomous community, province, city levels), 1978-2017.*

Author	Area	Year AM estimated	Population age	Age groups for estimation	Prevalence			Relative Risk	Observed mortality			
					Year	Smoker category	Age groups	Source	Year	Year SGϕ	Causes not included¶	Additional causes¶
NATIONAL												
González Enríquez et al., 1989a	Spain	1983	–	–	1970-1979	–	–	Various studies	1983	1984	–	Asthma
González Enríquez et al., 1989b	Spain	1984	–	–	–	–	–	Various studies	1984	1984	–	Asthma
González Enríquez et al., 1997	Spain	1978-1992	≥ 35 years	35-44 / 45-64 / ≥ 65	1978-1992	Smoker, ex-smoker, never smoker	35-44 / 45-64 / ≥ 65	CPS II	1978-1992	1989	Other vascular†	Hypertensive disease, pneumonia and influenza and asthma
Banegas et al., 2001	Spain	1998	≥ 35 years	Not specified	1997	Smoker, ex-smoker, never smoker	35-64 / ≥ 65	CPS II	1998	1989	–	Tuberculosis, pneumonia and influenza and asthma
Banegas et al., 2003	Spain	–	≥ 35 years	–	1987	–	–	CPS II	1995-1999	1989	–	Hypertensive disease, tuberculosis pneumonia, influenza, and asthma
Montes et al., 2004	Spain	2001	≥ 35 years	Not specified	2001	Smoker, ex-smoker, never smoker	35-64 / ≥ 65	CPS II	2001	1989	–	Hypertensive disease, pneumonia and influenza
Banegas et al., 2005	Spain	2001	≥ 35 years	35-64 / ≥ 65	2001	Smoker, ex-smoker, never smoker	35-64 / ≥ 65	CPS II	2001	2004	–	Various §
Hernández García et al., 2010	Spain	2006	≥ 35 years	Not specified	2006	Smoker, ex-smoker, never smoker	35-64 / ≥ 65	CPS II	2006	1989	–	Hypertensive disease, pneumonia, influenza, tuberculosis and asthma
Banegas et al., 2011	Spain	2006	≥ 35 years	35-64 / ≥ 65	2006	Smoker, ex-smoker, never smoker	35-64 / ≥ 66	CPS II	2006	1989	–	Various §
Gutiérrez Abejón et al., 2015	Spain	2012	≥ 18 years	Not specified	2012	Smoker, ex-smoker, never smoker	18-34 / 35-64 / ≥ 65	CPS II	2012	1989	–	Hypertensive disease, pneumonia, influenza, tuberculosis and asthma
Pérez Ríos et al., 2020	Spain	2016	≥ 35 years	35-54 / 55-64 / 65-74 / ≥ 75	2014 and 2016	Smoker, ex-smoker, never smoker	35-54 / 55-64 / 65-74 / ≥ 75	5 cohorts**	2016	2014	–	–
Rey et al., 2021	Spain/ 17 ACs	2017	≥ 35 years	35-54 / 55-64 / 65-74 / ≥ 75	2011,2014 and 2016	Smoker, ex-smoker, never smoker	35-54 /55-64 / 65-74 / ≥ 75	5 cohorts**	2017	2014	–	–
AUTONOMOUS COMMUNITY, PROVINCE, CITY												
Rodríguez Tapioles et al., 1997	Granada	1985	≥ 15 years	≤ 45 / 46-65 / 66-75 / ≥ 76	1990	–	–	Meta-analysis	1985	1989	Cervical cancer, rheumatic, cardiopulmonary diseases	–
Valero Juan et al., 1999	Extremadura	1993	≥ 15 years	–	1993	Smoker, ex-smoker, never smoker	–	Granada study (Rodríguez Tapioles et al., 1994)	1993	1989	Rheumatic, cardiopulmonary diseases, aortic aneurysm, atherosclerosis and other vascular†	–
Bello Luján et al., 2001	Canary Isles	1975-1994	≥ 35 years	Not specified	1975-1994	Smoker, ex-smoker, never smoker	35-44 / 45-64 / ≥ 65	CPS II	1975-1994	1989	–	Hypertensive disease, pneumonia, influenza, tuberculosis and asthma

Table 1. *(Cont.)*

Author	Area	Year AM estimated	Population age	Age groups for estimation	Prevalence			Relative Risk	Observed mortality			
					Year	Smoker category	Age groups	Source	Year	Year SGϕ	Causes not included¶	Additional causes¶
AUTONOMOUS COMMUNITY, PROVINCE, CITY												
Santana Armas et al., 1998	Canary Isles	1995	–	–	1995	–	–	CPS II	1995	1989	Rheumatic, cardiopulmonary diseases, aortic aneurysm, atherosclerosis and other vascular†	Hypertensive disease and asthma
Santos Zarza et al., 2001	Castilla y León	1995	≥ 15 years	–	1993	Smoker, ex-smoker, never smoker	–	Granada study (Rodríguez Tapioles et al., 1994)	1995	1989	Rheumatic, cardiopulmonary diseases, aortic aneurysm, atherosclerosis and other vascular†	–
Criado Álvarez et al., 2002	Castilla La Mancha	1987 and 1997	≥ 35 years	Not specified	1987and 1997	–	–	CPS II	1987 and 1997	1989	–	Hypertensive disease, pneumonia, influenza, tuberculosis and asthma
Jané et al., 2003	Barcelona	1983-1998	≥ 35 years	35-44 / 45-54 / 55-64 / 65-74 / ≥ 75	1983-1998	–	–	CPS II	1983-1998	1989	–	Hypertensive disease, pneumonia, influenza, and asthma
Zorrilla Torras et al., 2005	Madrid	1992-1998	≥ 35 years	35-64 / ≥ 65	1992-1998	Smoker, ex-smoker, never smoker	–	CPS II	–	1989	–	Hypertensive disease, pneumonia, influenza, tuberculosis and asthma
Pérez Ríos et al., 2009	Galicia	2001-2006	≥ 35 years	35-64 / ≥ 65	2001-2006	Smoker, ex-smoker, never smoker	35-64 / ≥ 65	CPS II	–	2004	–	–
Pérez Ríos et al., 2011	Galicia	1980-2007	≥ 35 years	35-64 / ≥ 65	Not applicable*	Not applicable*	Not applicable*	CPS II	1980-2007	2004	–	–

Note. CPS II: *Cancer Prevention Study II*, SG: *Surgeon General*.

ϕ Year of *Surgeon General's* report on which the study was based in terms of establishing causes of smoking related deaths.

¶ Included in relation to the causes established by the *Surgeon General*. Causes are deemed to be diseases with which a causal relationship has been established, and the latter correspond to individual nosological entities (e.g., stomach cancer) or code groups in the 10th International Classification of Diseases (ICD - 10) used by international convention (e.g., Lung refers to trachea, bronchi, and lung)

† "Other vascular" includes the following diseases according to ICD-10 codes: I72 (other types of aneurysm), I73 (other peripheral vascular diseases), I74 (embolism and arterial thrombosis), I75 (atheroembolism), I76 (septic arterial embolism), I77 (other disorders of arteries and arterioles), I78 (capillary disease).

§ Included by code CIE-10: C46.2, C45.7, C68, I10-I15, I52, I97-I98, R00.1, R00.8, R01.2, G45, G93.6, G93.8, G95.1, M30-M31, J20.9, J98.0, A15-A16, A48.1, B05.2, B90.9, J45-J46, J65

* Estimation method used: prevalence independent.

** The National Institutes of Health- American Association of Retired Persons Diet and Health Study, the American Cancer Society's CPS II Nutrition Cohort, the Women's Health Initiative, the Nurses' Health Study and the Health Professionals Follow-up Study.

1989b; González Enríquez, Villar Álvarez, Banegas Banegas, Rodríguez Artalejo & Martín Moreno, 1997; Gutiérrez-Abejón et al., 2015; Hernández-García, Sáenz-González & González-Celador, 2010; Montes, Pérez-Ríos & Gestal, 2004; Pérez-Ríos et al., 2020; Rey et al., 2021), eight in autonomous communities (Bello Luján, Lorenzo Ruano, Gil Muñoz, Saavedra Santana & Serra Majem, 2001; Criado-Álvarez, Morant Ginestar & De Lucas Veguillas, 2002; Pérez Ríos et al,. 2009; Pérez Ríos et al., 2011; Santana Armas, Orengo, Santana Armas, Lorenzo & Serra Majem, 1998; Santos Zarza, Valero Juan & Sáenz González, 2001; Valero Juan, Carrero Santos, Nelia Lubián & Sáenz González, 1999; Zorrilla-Torras, García-Marín, Galán-Labaca & Gandarillas-Grande, 2005), one in a province (Granada) (Rodríguez Tapioles et al., 1997) and one in a city (Barcelona) (Jané, Borrell, Nebot & Pasarín, 2003). At the national level, estimates were made for the period 1978-1992, for the years 1983, 1984, 1998, 2012, 2016 and 2017, and twice for 2001 and 2006. Galicia and the Canary Islands were the autonomous communities with the highest SAM estimates.

The prevalence-dependent method was used to estimate SAM in all studies, except for one study carried out in Galicia which used the prevalence-independent method. Regarding study population age, 15 analyses were carried out in adults aged 35 years and over, four in the population aged 15/18 years and over, and three studies failed to in-

dicate age. In 20 of the 21 studies using the prevalence-dependent method, prevalence data came from national or local surveys and 15 studies included three smoker categories: smokers, ex-smokers and never smokers. OM in all studies was taken from official registers, and in 16 of the 22 studies, RR was taken from Cancer Prevention Study II (CPS-II) (Table 1).

In 15 studies, AM was estimated for more causes of death than those causally linked to smoking by the Surgeon General's reference report for the year of estimation and in four, mortality was attributed to causes with an established causal relationship to smoking at the time of estimation (Table 1).

In all studies, the attribution of mortality focused on smoking, with the exception of two studies: one carried out in Barcelona (Jané et al., 2003) in which AM was also estimated for alcohol use and another at national level in which AM was also estimated for blood pressure, overweight/obesity and diabetes (Banegas et al, 2003).

Results of the estimation of smoking-attributable deaths

In 1978, it was estimated that 13.7% of the deaths observed at the national level were attributable to smoking (González Enríquez et al., 1997). This percentage rose to 16.0% in 1998 (Banegas et al., 2001), remained at approximately 15%-16% until 2012 (Gutiérrez Abejón et al., 2015) and fell to 13.7% in 2016 (Pérez Ríos et al., 2020). By AC, the proportion of AM versus OM was 9.4% in Castilla y León in 1995 (Santos Zarza et al., 2001) and 11.7% in Extremadura in 1993 (Valero Juan et al., 1999). In the estimate made in 2017, AM increased in both autonomous communities to 11.3% and 13.6%, respectively (Rey et al., 2021). In the Canary Islands, the percentage of AM reached 20.7% in 1975, fell to 15.3% in 1994 (Bello Luján et al., 2001) and remained stable in 2017 (15.3%) (Rey et al., 2021). The estimates for Castilla La Mancha were 18.7% in 1987 and 1997 (Criado Álvarez et al., 2002) and 12.4% in 2017 (Rey et al., 2021).

In men, it was estimated that SAM accounted for 20.3% of the total OM in 1983 (González Enríquez et al., 1989a), increased to 28.3% in 1998 (Banegas et al., 2001) and decreased after 2001 (Banegas et al., 2005), reaching 22.6% in 2012 (Gutiérrez Abejón et al., 2015). In women, the percentage of SAM compared to the total OM was 5.4% in 1983 (González Enríquez et al., 1989a), approximately 2%-3% between 1992-2001 (Banegas et al., 2001; Banegas et al., 2005; González Enríquez et al., 1997; Montes et al., 2004) and increased to 7.8% in 2006 (Hernández García et al., 2010). The ratio of AM in men compared to women decreased over the years; thus, in 1998 it was 92.5% (Banegas et al., 2001), i.e., 92.5% of SAM occurred in men, 91.0% in 2001 (Banegas et al., 2005; Montes et al., 2004); and 84%-85% in 2016 and 2017 (Pérez Ríos et al., 2020; Rey et al., 2021).

In 1978, the first study to estimate SAM in Spain established that 51.4% of SAM had been due to cardiovascular/cardiometabolic diseases, which placed them as the group of causes with the highest burden of AM (González Enríquez et al., 1997). This percentage decreased to 30%-35% in the estimates made between 2001 and 2006 (Hernández-García et al., 2010; Montes et al., 2004), and 27.5% in the estimate made in 2017 (Rey et al., 2021). As from the 1990s, tumours became the main group of causes of SAM, with 50% of SAM caused by tumours in the latest estimates (Pérez-Ríos et al., 2020; Rey et al., 2021). The burden of respiratory diseases in SAM has remained stable at around 20%-23% from estimates in 1992 and 1998 (Banegas et al., 2001; González Enríquez et al., 1997) up to the most recent ones (Pérez-Ríos et al., 2020; Rey et al., 2021).

In relation to specific causes, lung cancer took the place of ischemic heart disease as the main specific cause of SAM in Spanish men in 1992 (González Enríquez et al., 1997). In women, it is worth noting that ischemic heart disease was first replaced by chronic obstructive pulmonary disease (COPD) in 1992 (González Enríquez et al., 1997) and the latter by lung cancer in 2006 (Banegas et al., 2011). Table 2 offers a detailed summary of the main results of all studies included.

Discussion

This study shows that AM estimates are not made periodically in Spain and that no comparable information is available to assess the impact of smoking at more disaggregated regional levels such as the autonomous communities. Despite data pointing to variations in the development of the tobacco epidemic in terms of prevalence across different Spanish regions, studies that estimate AM at a more regional, i.e., autonomous community, province or city level are scarce and do not allow conclusions to be drawn regarding impact on mortality.

All studies estimating SAM in Spain use OM data taken from the cause of death statistics recorded by the INE; however, these do not always include all the pathologies with an established causal relationship with smoking at the time of estimation in the Surgeon General's reports. The Surgeon General has published four main reports assessing the status of causal links between smoking and mortality. The first, published in 1964, established a causal relationship with lung and laryngeal cancer in men and chronic bronchitis (U.S. Department of Health, Education and Welfare 1964). The second report, published in 1989, included causal relationships with various tumours (lung and larynx in both sexes, lip, oral cavity, pharynx, oesophagus, pancreas, cervix, bladder, kidney and renal pelvis); cardiovascular diseases (ischemic heart disease, cerebrovascular disease,

Table 2. *Percentages of smoking attributable mortality (SAM) over observed mortality and group of causes of death and specific cause of death with a higher burden of SAM. Data are presented in total (men and women), in men and in women.*

Author	Area	Year AM estimated	Percentage of AM			Group of cause of death with highest AM			Specific cause of death with highest AM		
			Total	Men	Women	Total	Men	Women	Total	Men	Women
NATIONAL											
González Enríquez et al., 1989a	Spain	1983	13.0%	20.3%	5.4%	CVD	CVD	CVD	Ischemic heart disease	Ischemic heart disease	Ischemic heart disease
González Enríquez et al., 1989b	Spain	1984	13.8%	–	–	CVD	CVD	CVD	Ischemic heart disease	Ischemic heart disease	Ischemic heart disease
González Enríquez et al., 1997	Spain	1978-1992	1978: 13.7% 1992: 14.7%	1992: 26.3%	1992: 2.0%	1978: CVD 1992: tumours	1978: CVD 1992: tumours	1978: CVD 1992: CVD	1978: ACV 1992: Lung cancer	1978: CVA 1992: Lung cancer	1978: CVA 1992: COPD
Banegas et al., 2001	Spain	1998	16.0%	28.3%	2.5%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	COPD
Banegas et al., 2003	Spain	–	16.0%	–	–	Tumours	Tumours	CVD	Lung cancer	Lung cancer	COPD
Montes et al., 2004	Spain	2001	–	24.5%	2.6%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	COPD
Banegas et al., 2005	Spain	2001	15.5%	27.1%	2.9%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	COPD
Hernández García et al., 2010	Spain	2006	16.2%	23.9%	7.8%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	Otras cardiopatías
Banegas et al., 2011	Spain	2006	14.7%	25.1%	3.4%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	Lung cancer
Gutiérrez Abejón et al., 2015	Spain	2012	15.2%	22.6%	7.6%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	Otras cardiopatías
Pérez Ríos et al., 2020	Spain	2016	13.7%	–	–	Tumours	Tumours	Tumours	Lung cancer	Lung cancer	Lung cancer
Rey et al., 2021	Spain/ 17 ACs	2017	12.9%	–	–	Tumours	Tumours	Tumours	Lung cancer	Lung cancer	Lung cancer
AUTONOMOUS COMMUNITY, PROVINCE, CITY											
Rodríguez Tapioles et al., 1997	Granada	1985	15.9%	21.2%	10.0%	CVD	CVD	CVD	Ischemic heart disease	COPD	Ischemic heart disease
Valero Juan et al., 1999	Extremadura	1993	11.7%	16.8%	6.3%	Tumours	Tumours	CVD	Lung cancer	Lung cancer	CVA
Bello Luján et al., 2001	Canary Isles	1975-1994	1975: 20.0% 1994: 15.3%	–	–	1975: CVD 1994: CVD	1975: ECV 1994: ECV	1975: CVD 1994: CVD	1975: ACV 1994: Ischemic heart disease	1975: CVA 1994: Lung cancer	1975: CVA 1994: Ischemic heart disease
Santana Armas et al., 1998	Canary Isles	1995	14.9%	20.2%	8.0%	Tumours	–	–	Lung cancer	Lung cancer	Lung cancer
Santos Zarza et al., 2001	Castilla y León	1995	9.4%	7.2%	2.3%	CVD	CVD	CVD	Lung cancer	Lung cancer	Ischemic heart disease
Criado Álvarez et al., 2002	Castilla La Mancha	1987and 1997	1987: 18.7% 1997: 18.7%	1987: 14.2% 1997: 15.0%	1987: 4.5% 1997: 3.8%	1987: ECV 1997: ECV	–	–	1987: ACV 1997: Lung cancer	1987: Lung cancer 1997: Lung cancer	1987: Other heart diseases 1997: Other heart diseases
Jané et al., 2003	Barcelona	1983-1998	1983: 9.6% 1998: 13.8%	1998: 25.1%	1998: 2.9%	1983: CVD 1998: Tumours	1983: CVD 1998: Tumours	1983: CVD 1998: CVD	1998: Lung cancer	Lung cancer	COPD
Zorrilla Torras et al., 2005	Madrid	1992-1998	1998: 15.9%	1998: 28.4%	1998: 2.8%	1998: Tumours	1998: Tumours	1998: CVD	1998: Lung cancer	1998: Lung cancer	1998: Lung cancer
Pérez Ríos et al., 2009	Galicia	2001-2006	12.5%	22.4%	2.2%	Tumours	Tumours	Tumours	Lung cancer	Lung cancer	COPD
Pérez Ríos et al., 2011	Galicia	1980-2007	12.6%	23.5%	1.5%	Tumours	Tumours	CVD and respiratory disease	Lung cancer	Lung cancer	–

Note. AM: attributed mortality. COPD: chronic obstructive pulmonary disease. CVA: cerebrovascular accident. CVD: cardiovascular disease.

rheumatic heart disease, cardiopulmonary disease, atherosclerosis, aortic aneurysm and other vascular diseases (classified as I72-I78 in ICD-10)) (U.S. Department of Health and Human Services, 1989). The third report, published in 2004, added causal relationships with stomach cancer, acute myeloid leukaemia, and pneumonia and influenza (U.S. Department of Health and Human Services, 2004). In the most recent report, published in 2014, new causal relationships with colorectal cancer, liver cell cancer, tuberculosis and diabetes mellitus were established. At present, different causes of death such as breast cancer continue to be studied (U.S. Department of Health and Human Services, 2014). Some of the estimation studies carried out in Spain failed to include all the pathologies with a causal relationship established at the time of research (González Enríquez et al., 1997; Rodriguez Tapioles et al., 1997; Santana Armas et al., 1998; Santos Zarza et al., 2001; Valero Juan et al., 1999) or included more causas (Banegas et al., 2001; Banegas et al., 2003; Banegas et al., 2005; Banegas et al., 2011; Bello Luján et al., 2001; Criado-Álvarez et al., 2002; González Enríquez et al., 1989a; González Enríquez et al., 1989b; González Enríquez et al., 1997; Gutiérrez-Abejón et al., 2015; Hernández-García et al., 2010; Jané et al., 2003; Montes et al., 2004; Santana Armas et al., 1998; Zorrilla-Torras et al., 2005). The latter may be due to the fact that several studies incorporated pathologies for which the available evidence suggested a possible link to smoking, although not enough evidence was available at the time to establish a causal relationship.

To date, the age at which mortality should be attributed to smoking has not been established, although most studies take 35 years as the lower limit. Estimating AM at an early age conflicts with the temporal precedence criterion of causality, according to which a risk factor causes illness or death after being exposed to it long enough to cause harm. This limitation can also be applied to prevalence data, since in several studies the prevalence used is close to OM in terms of time and does not take into account the time lapse between exposure and effect. Following methodological criteria, for example based on STROBE guidelines, would improve communication and standardize the publication of results and thus make it easier to carry out these analyses.

Since the first estimate of SAM in 1978, different studies conducted at the national level reflect an increase in the burden of SAM until 2001, when a decrease was observed for the first time in men. Direct comparison of estimates is complicated by differences across studies regarding changes in the age structure of the population from 1978 to 2017, the causes studied, or the risks used. Nevertheless, it can be highlighted that a comparison of SAM in men and women shows that SAM increased in the latter; in the latest estimates of 2016 and 2017, around 84%-85 % of deaths attributed to smoking occurred in men (Pérez-Ríos et al., 2020; Rey et al., 2021) compared to 96.6% observed in the first estimate in 1978 (González Enríquez et al., 1997). In countries such as the United States of America (USA) or the United Kingdom, where the tobacco epidemic has evolved further, the increase in SAM levels in women began to be observed decades before being seen in Spanish women. In the case of the United States, the impact of smoking on female mortality began to be detected towards the end of the 1950s, since when the figures for SAM increased until reaching the same level as those for men in the period 2005-2010 (Peto, Lopez, Boreham & Thun, 2011). In the case of the United Kingdom, the increase of SAM in women began before 1950 and, as in the United States, the percentage continued to rise until practically equalling that of men between 2005-2010 (Peto et al., 2011). In comparison to the United Kingdom and the United States, women in Spain started smoking later, and the decrease observed in the prevalence of smoking in men since 1987 was not observed in women until 2006. Thus, in the period 1987-2005, the absolute average annual decrease in the prevalence of male smokers was 1%, and 0.7% in the period 2006-2014. In women, the average annual decrease in the 2006-2014 period was 0.5% (Fernández et al., 2017). This means that men and women are in different stages of the tobacco epidemic model. Men are in stage IV, marked by the steady decline in the prevalence of smoking and AM among the population aged 35 to 69 years, and women could still be at late stage III, characterized by stabilizing prevalence and increased AM (Lopez, Collishaw & Piha, 1994; Thun, Peto, Boreham & Lopez, 2012).

Over the years, a decline has been observed in deaths from cardiovascular/cardiometabolic diseases attributed to smoking. This can be explained both by better control of the main risk factors for cardiovascular diseases, such as hypertension, hypercholesterolemia and sedentary lifestyle, as well as by the development of new medical treatments (Flores-Mateo et al., 2011). This decrease in AM to cardiovascular/cardiometabolic diseases means that tumours are the group of causes with the greatest burden of mortality. To interpret these changes, it is necessary to consider the large differences in time elapsing between exposure to the risk factor and the outcome in these groups of diseases, which is much longer in the case of tumours than in cardiovascular/cardiometabolic diseases, where the effects are observed in a shorter period.

Regarding specific causes of death, it can be observed how lung cancer became the main cause of death in men due to smoking in the early 1990s (González Enríquez et al., 1997). In women, the increase in the number of deaths from lung cancer was slower, and the disease did not become the leading cause of smoking-related death in Spanish women until the latest estimates of 2016 and 2017, and those made in the five-year period 2010-2014 (Ministerio de Sanidad, Consumo & Bienestar Social, 2016; Pérez-Ríos

et al., 2020; Rey et al., 2021). However, in countries like the USA and Canada, where women started smoking earlier, lung cancer was already the main cause of death in women in 1990 and 1991, respectively (Centers for Disease Control and Prevention, 1993; Illing & Kaiserman, 1995).

The most important limitation of this study is linked to the occasional difficulty in summarizing the information from the different studies included, given the heterogeneity in the presentation of results. The advantages are its systematic review design and thoroughness in the gathering of information.

In conclusion, there are different estimates in Spain of AM at the national level, but they are not regular in terms of the time periods involved. Although the tobacco epidemic is developing differently in terms of smoking prevalence across the constituent regions of Spain, there are few studies assessing the varying impact of smoking on mortality in smaller regional areas such as autonomous communities, provinces or cities. The age at which AM is estimated, and the data sources or the causes for which mortality is estimated are not homogeneous across the studies. Updating the causes of mortality linked to smoking, or smokers' and ex-smokers' current level of excess risk of death compared to that of never-smokers make it difficult to accurately assess the changes in the SAM estimates. In general, it can be affirmed that SAM increased in Spanish women from the first estimates to the most recent, while in men, it decreased after 2001. In Spain, lung cancer is currently the cause of death with the highest SAM in both sexes. Having periodic estimates at global and disaggregated levels, such as autonomous communities, would be necessary to correctly monitor the tobacco epidemic in Spain and assess the impact of the different tobacco control measures, both clinical and legislative, which have been implemented in Spain in recent years. Although this review shows that, overall, SAM is decreasing in Spain, the most recent estimates still have smoking as the risk factor that causes the greatest number of deaths. There is, therefore, an indisputable need to implement comprehensive tobacco control measures and primary and secondary prevention measures to enable progress towards a tobacco-free society.

Conflicts of interest

All authors declare no conflicts of interest.

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