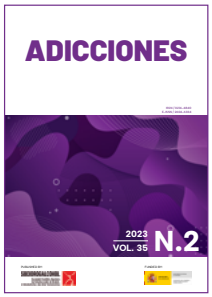
SOCIDROGALCOHOL
Sociedad Científica Española de Estudios sobre el Alcohol, el Alcoholismo y las otras Toxicomanías

ADICCIONES
2023 ■ VOL. 35 ■ N. 2 ■ PAGES 165–176
www.adicciones.es



ORIGINAL

Evolution of mortality attributable to alcohol in Spain according to age, sex, cause of death and type of drinker (2001-2017)

Evolución de la mortalidad atribuible al alcohol en España según edad, sexo, causa de muerte y tipo de bebedor (2001-2017)

Marta Donat*,**, Luis Sordo**,***, María José Belza*,**, Juan Hoyos***, Enrique Regidor**,***, Gregorio Barrio *,**.

* Escuela Nacional de Sanidad. Instituto de Salud Carlos III, Madrid.

** Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP).

*** Departamento de Salud Pública y Materno-infantil, Facultad de Medicina, Universidad Complutense de Madrid.

Abstract

There are no recent estimates of alcohol-attributable mortality in Spain with Spanish alcohol consumption data. The objective is to estimate it and know its evolution between 2001 and 2017 in people ≥15 years, according to sex, age, period, cause of death and type of drinker. The cause-specific approach and Levin's equation were used. Survey consumption was corrected for underestimation with respect to sales statistics, and past consumption and binge drinking were considered. The average annual number of deaths attributable to alcohol in 2010-2017 was 14,927, 58.6% of which were premature (<75 years). The age-standardized alcohol-attributable mortality rate was 39.4/100,000 inhabitants, representing 3.9% of overall mortality. Using standardized percentages, 68.7% corresponded to heavy drinkers. The most frequent causes of alcohol-attributable mortality were cancer (44.7%) and digestive diseases (33.2%). The rate of alcohol-attributable mortality was 3.5 times higher in men than in women (with higher ratios for young people and external causes). Between 2001-2009 and 2010-2017, the average annual rate decreased 16.8% (60.7% in 15-34 years; 19.4% in men and 9.8% in women). The contribution of heavy drinkers, digestive diseases and external causes to the risk of alcohol-attributable mortality decreased slightly between the two periods, while the contribution of cancer and circulatory diseases increased. These estimates are conservative. The contribution of alcohol to overall mortality is significant in Spain, requiring collective action to reduce it.

Key words: alcohol, attributable mortality, Spain, type of consumption, cause of death

Resumen

En España no hay estimaciones recientes de la mortalidad atribuible a alcohol con datos de consumo de alcohol españoles. El objetivo es estimarla y conocer la evolución entre 2001 y 2017 en personas ≥15 años, según sexo, edad, periodo, causa de muerte y tipo de bebedor. Se utilizó el enfoque causa específico y la ecuación de Levin. El consumo de las encuestas se corrigió por subestimación con respecto a las estadísticas de ventas y se consideró el consumo pasado y los atracones de alcohol. El número medio anual de muertes atribuibles a alcohol en 2010-2017 fue 14.927, un 58,6% prematuras (<75 años). La tasa de mortalidad atribuible a alcohol estandarizada por edad fue 39,4/ 100.000 habitantes, representando un 3,9% de la mortalidad general. Usando porcentajes estandarizados un 68,7% correspondió a bebedores de alto riesgo. Las causas de mortalidad atribuible a alcohol más frecuentes fueron cáncer (43,8%) y enfermedades digestivas (32,9%). La tasa de mortalidad atribuible a alcohol fue 3,5 veces mayor en hombres que en mujeres (con cocientes más elevados para jóvenes y causas externas). Entre 2001-2009 y 2010-2017 la tasa media anual disminuyó un 16,8% (60,7% en 15-34 años; 19,4% en hombres y 9,8% en mujeres). La contribución de los bebedores de alto riesgo y de las enfermedades digestivas y causas externas al riesgo de mortalidad atribuible a alcohol disminuyó ligeramente entre los dos períodos, mientras que aumentó la contribución del cáncer y enfermedades circulatorias. Estas estimaciones son conservadoras. La contribución del alcohol a la mortalidad general es importante en España, requiriendo medidas colectivas para reducirla.

Palabras clave: alcohol, mortalidad atribuible, España, tipo de consumo, causa de muerte

■ *Received: August 2020; Accepted: March 2021.*

■ ISSN: 0214-4840 / E-ISSN: 2604-6334

■ **Send correspondence to:**
Luis Sordo. Departamento de Salud Pública y Materno-Infantil. Facultad de Medicina. Universidad Complutense de Madrid.
E-mail: lsordo@ucm.es

Alcohol use is one of the main preventable risk factors for morbidity, mortality and disability in the world. Alcohol-attributable mortality (AAM) is perhaps the main indicator of the damage caused by alcohol in population health, and its periodic or routine estimation should serve to guide and assess the efforts of a country or region to prevent it. It is estimated that in 2017, 5.1% of all deaths worldwide were due to alcohol use, with important differences between countries (Institute for Health Metrics and Evaluation [IHME], 2019). The damage caused by alcohol to population health in a given region or subgroup depends above all on the amount of alcohol consumed by each individual in a given time interval (for example, one year), but also on consumption guidelines and patterns (distribution of that amount over time) (Rehm et al., 2017).

Regarding average consumption, alcohol begins to cause harm and increase the risk of illness, injury or death at fairly low average levels of use (Di Castelnuovo et al., 2006; Rehm et al., 2017). The risk curves for most chronic diseases are exponential, so that the greatest contribution of alcohol to mortality risk in many countries is concentrated in high-risk drinkers (those with an average consumption ≥ 60 g/day of pure alcohol in men or ≥ 40 g/day in women), who often show signs of addiction or alcohol use disorder. However, the contribution of drinkers with a lower average consumption may be substantial in some regions or subgroups (Corrao, Bagnardi, Zambon & Arico, 1999; Corrao, Bagnardi, Zambron & La Vecchia, 2004; Rehm, Rehm, Shield, Gmel & Gual, 2013; Rehm, Shield, Gmel, Rehm & Frick, 2013). It would thus be interesting to disaggregate AAM according to the average consumption level (for example, for high and medium/low risk drinkers). In addition, taking into account that some negative effects of alcohol persist after stopping drinking, it would also be relevant to consider the contribution of ex-drinkers to AAM.

In recent years, evidence has been found that heavy episodic drinking (binge drinking) is linked to an increased risk of general mortality, and from specific causes (mainly cardiovascular diseases and external causes) regardless of average consumption (Graff-Iversen et al., 2013; Murray et al., 2002; Plunk, Syed-Mohammed, Cavazos-Rehg, Bierut & Grucza, 2014; Roerecke & Rehm, 2011); not considering the contribution of this pattern of consumption could therefore distort the AAM estimates, especially in the comparison between sociodemographic subgroups (for example, age and sex).

Despite the existence of a certain methodological consensus in AAM estimation (Rehm et al., 2009), the estimations made in Spain are quite disparate (Pulido et al., 2014). Thus, for example, figures have been published on the contribution of AAM to general mortality in the population aged 15 years and over of 2.1% (Fierro, Ochoa, Yánez, Valderrama & Álvarez, 2008) for 1999-2004, of 4.3% (World Health Organization [WHO], 2019) and 7.5% (IHME, 2019; Global Burden of Disease [GBD], 2018) for 2016, and in the population aged 15-64 years of 12.3% in men, and 8.4% in women for 2004 (Rehm et al., 2013a). The main reason for these discrepancies probably lies in the way population-attributable fractions for alcohol use were calculated; this is often based on data on consumption distribution by quantity consumed from other countries or on Spanish data without taking into account the underestimation of consumption in the surveys. Given the spatial variability of the population distribution of the quantities consumed and the consumption patterns over time, the use of valid data on these aspects from the country to which the estimate refers should in principle increase the validity of the AAM estimates.

The purpose of this study was thus to estimate AAM in Spain and ascertain how it evolved between 2001 and 2017 by sex, age group, cause of death and type of drinker, using consumption estimates made with empirical data obtained almost entirely from the Spanish population.

Method

The methodology for estimating AAM was set out in detail in the recently published AAM Report for Spain (Donat, Sordo, Belza & Barrio, 2020) and in a previous methodological article, published in this journal. The total AAM is the sum of AAM from different causes partially or completely attributable to alcohol. The AAM for each cause was estimated by multiplying the number of deaths from that cause by its corresponding population attributable fraction (PAF). Completely attributable deaths, such as those from alcohol use disorder, have a PAF of 1, while the PAF of each partially attributable cause was estimated using a formula which includes the relative risks (RRs) with regard to abstainers and the population prevalences of different categories of alcohol use (ex-drinkers and various ranges of average daily amount consumed). Thus, for 1,000 deaths from a selected cause with a FAP of 0.45, 450 would be considered attributable to alcohol.

FAPs were calculated using eight categories of alcohol use (ex-drinkers, ≤19, 20-39, 40-49, 50-59, 60-79, 80-99, and ≥ 100 grams of pure alcohol/day). The RRs for each of the selected diseases were obtained from different recent international meta-analyses on the subject (Corrao et al., 1999; Rehm et al., 2017; Samokhvalov, Irving & Rehm, 2010). The calculation of prevalences was carried out on the basis of self-reported consumption in the National Health Survey and the European Health Survey in Spain (Instituto Nacional de Estadística [INE], 2019), corrected for underestimation by weighting the quantities consumed with sales statistics (Sordo et al., 2016).

The results were stratified by periods (2001-2009 and 2010-2017), age, sex, cause of death and type of drinker,

with ex-drinkers considered to be those who had not drunk alcohol in the last year, but who had consumed it at least 12 times in any given year in their life, with high-risk drinkers being individuals consuming ≥ 60 g of pure alcohol (men) or ≥ 40 g of pure alcohol (women) daily in the last year, and medium-low-risk drinkers those who had consumed less. Absolute AAM figures were calculated, as were age-standardized AAM rates calculated by five-year age groups, and various age-standardized AAM percentages such as the percentage of AAM over total mortality, the percentage of AAM due to various groups of defined causes over total AAM, and for current drinkers, the percentage of AAM corresponding to high-risk drinkers. The comparison of rates between groups and periods was measured with the rate ratio that measures relative disparity and the difference in rates that measures absolute disparity.

Results

Evolution of the number of deaths attributable to alcohol

During the period 2010-2017 in Spain, an annual average of 14,927 alcohol-attributable deaths occurred among people aged over 15 years, 72.6% in men and 58.6% in those under 75 years of age (premature). Regarding the basic cause of death, 76.7% were due to cancer or digestive diseases and 68.7% occurred in high-risk drinkers.

During 2001-2009, the annual average number of these deaths had been 15,420, of which 76.0% were men, 68.2% premature, 78.1% due to cancer or digestive diseases, 72.7% were high-risk drinkers (Table 1). Focusing on more specific causes, calculations based on Table 1 in the appendix reveal that cirrhosis/chronic liver disease was the partially attributable cause contributing the most to AAM, both in 2010-2017 (36.1%) and in 2001-2009 (42.7%).

Most alcohol-attributable deaths corresponded to causes partially attributable to alcohol (FAP < 1), both in 2010-2017 (84.0%) and in 2001-2009 (80.9%).

For more detail, Table 2 in the appendix includes the average annual number of deaths totally and partially attributable to alcohol by age group and sex for the two periods considered.

Evolution of alcohol-attributable mortality rates

During 2010-2017, the average annual rate of AAM standardized by age per 100,000 inhabitants was 39.4 (65.0

Table 1. ***Evolution of the average annual number of deaths attributable to alcohol by cause, type of drinker, sex and age, in the population aged 15 years and over. Spain, 2001-2017.***

	PERIOD	TOTAL	MEN	WOMEN	AGE GROUPS (years)						
					15-34	35-44	45-54	55-64	65-74	75-84	>=85
TOTAL	**2001-09**	15,420	11,724	3,697	815	1,059	2,127	2,891	3,621	3,401	1,505
	2010-17	14,927	10,844	4,083	268	518	1,878	2,726	3,354	3,511	2,672
CAUSE OF DEATH											
Cancer	**2001-09**	6,314	4,979	1,336	31	187	808	1,420	1,798	1,510	561
	2010-17	6,534	4,995	1,539	20	110	694	1,429	1,809	1,596	877
Circulatory diseases	**2001-09**	653	-291	944	4	-16	-25	-81	-51	359	464
	2010-17	1,229	-16	1,245	-1	-26	-56	-125	16	436	984
Infectious diseases	**2001-09**	193	147	46	6	14	22	28	47	35	41
	2010-17	222	169	53	3	6	17	23	31	60	83
Metabolic diseases	**2001-09**	-476	-43	-433	-2	-4	-8	-30	-85	-161	-187
	2010-17	-471	-49	-422	-1	-2	-9	-26	-55	-135	-243
Digestive diseases	**2001-09**	5,725	4,273	1,452	56	406	897	1,176	1,533	1,276	380
	2010-17	4,918	3,668	1,250	17	160	826	1,091	1,195	1,122	506
Neurological/mental diseases	**2001-09**	89	69	20	11	10	12	11	15	19	11
	2010-17	140	101	39	8	8	14	18	26	35	32
External causes	**2001-09**	2,922	2,590	332	710	462	421	367	364	363	235
	2010-17	2,356	1,977	379	223	262	392	316	332	397	433
TYPE OF DRINKER											
High risk drinkers	**2001-09**	11,210	9,521	1,689	430	705	1,623	2,315	2,845	2,254	1,039
	2010-17	10,248	8,401	1,847	111	264	1,381	2,099	2,651	2,116	1,625
Medium-low risk drinkers	**2001-09**	1,535	906	629	379	326	422	424	332	30	-379
	2010-17	1,729	937	792	153	231	411	462	345	320	-193
Regular ex-drinkers	**2001-09**	2,676	1,297	1,378	6	27	83	154	446	1116	844
	2010-17	2,951	1,507	1,444	4	21	85	164	359	1,074	1,243

Note. The category "other diseases" is not included among the causes of death because no cases are registered.

in men and 18.3 in women). Between 2001-2009 and 2010-2017, this rate saw an absolute change of -7.9/100,000 inhabitants, representing a change of -16.8% in relative terms. The decrease was more pronounced in men (-15.6/100,000 inhabitants and -19.4%) than in women (-2.0/100,000 inhabitants and -9.8%). Furthermore, the relative decline in rates decreased with age, from -60.7% in young people aged 15-34 years to only -11.3% in those older than >= 75 years. In the elderly >= 85 years, the relative decrease was positive (16.6%) (Table 2).

Figure 1 shows the standardized rates of AAM by combined age and sex groups. The rates decreased in all groups, except in men and women >= 85 years, where they increased. The decrease, both in absolute and relative terms, was in general greater in men than in women in all age groups. The strongest relative decline was observed in men aged 15-34 years, with a rate ratio between periods of 2.72.

By type of drinker, the highest rates in both periods corresponded to high-risk drinkers, followed by ex-drinkers and medium-low risk drinkers. Across time periods, rates decreased in high-risk drinkers and former drinkers and increased in medium-low risk drinkers (4.0 and 4.6/100,000 inhabitants) (Table 3, appendix).

Evolution of the contribution of alcohol-attributable mortality to total mortality

This was measured by the percentage of the age-standardized AAM rate over the age-standardized all-cause mortality rate. The contribution of AAM to total mortality did not vary between 2001-2009 and 2010-2017; for both periods it was 3.9%. By age, however, the contribution of AAM decreased very sharply in young people aged 15-34 years (12.4% and 8.6%), and increased for those over 65 years of age (Table 2). Regarding mortality in those aged under 75 years, this percentage stood at 8.3% in the 2001-

Table 2. ***Evolution of the alcohol-attributable mortality rate (AAM) and the contribution of AAM to total mortality, by sex and age, in the population aged 15 years and over. Spain, 2001-2017.***

	2001-2009	2010-2017	Difference between periods[3]	Relative change between periods (%)[4]
			Average annual rates of AAM standardized by age per 100,000 inhabitants[1]	
Total	47.3	39.4	-7.9	-16.8
Men	80.6	65.0	-15.6	-19.4
Women	20.3	18.3	-2.0	-9.8
15-34	6.1	2.4	-3.7	-60.7
35-44	15.2	6.6	-8.6	-56.6
45-54	37.9	27.1	-13.8	-28.5
55-64	63.8	50.5	-13.3	-20.8
65-74	93.9	81.6	-12.3	-13.1
75-84	128.6	114.1	-14.5	-11.3
>=85	186.3	217.3	31.0	16.6
			Contribution of AAM to total mortality (%)[2]	
Total	3.9	3.9	0.0	0.0
Men	5.2	5.0	-0.2	-3.8
Women	2.2	2.3	0.1	4.5
15-34	12.4	8.6	-3.8	-30.6
35-44	12.1	8.5	-3.6	-29.8
45-54	13.7	11.4	-2.3	-16.8
55-64	9.8	8.8	-1.0	-10.2
65-74	5.8	6.3	0.5	8.6
75-84	2.8	3.0	0.2	7.1
>=85	1.2	1.6	0.4	33.3

Note. [1]Average annual rates of AAM standardized by age per 100,000 inhabitants aged 15 years and over. To calculate these, the population figures of residents in Spain on July 1 of each year and the European Standard Population of 2013 were used. [2]This is interpreted as the percentage weight of AAM in all-cause mortality, calculated as follows: (age-standardized alcohol-attributable mortality rate / age-standardized all-cause mortality rate) x 100. [3]Difference between the mean annual mortality rates attributable to alcohol standardized by age for the period 2010-2017 and the corresponding rates for the period 2001-2009. It is expressed in deaths per 100,000 inhabitants and indicates the absolute change in risk or mortality rate between the two periods. Negative and positive values indicate decreases and increases in risk, respectively. The same applies to the percentage of AAM over all-cause mortality standardized by age. [4]The percentage of change (PC) between periods was calculated by subtracting one from the ratio of average annual mortality rates attributable to alcohol standardized by age between the periods 2010-2017 and the period 2001-2009 (RR) and multiplying the result by 100 [PC = (RR-1)*100]. It is unitless and indicates the relative change in risk or mortality rate attributable to alcohol between the two periods. Negative and positive values indicate decreases and increases in risk, respectively. The same applies to the percentage of AAM over all-cause mortality standardized by age.

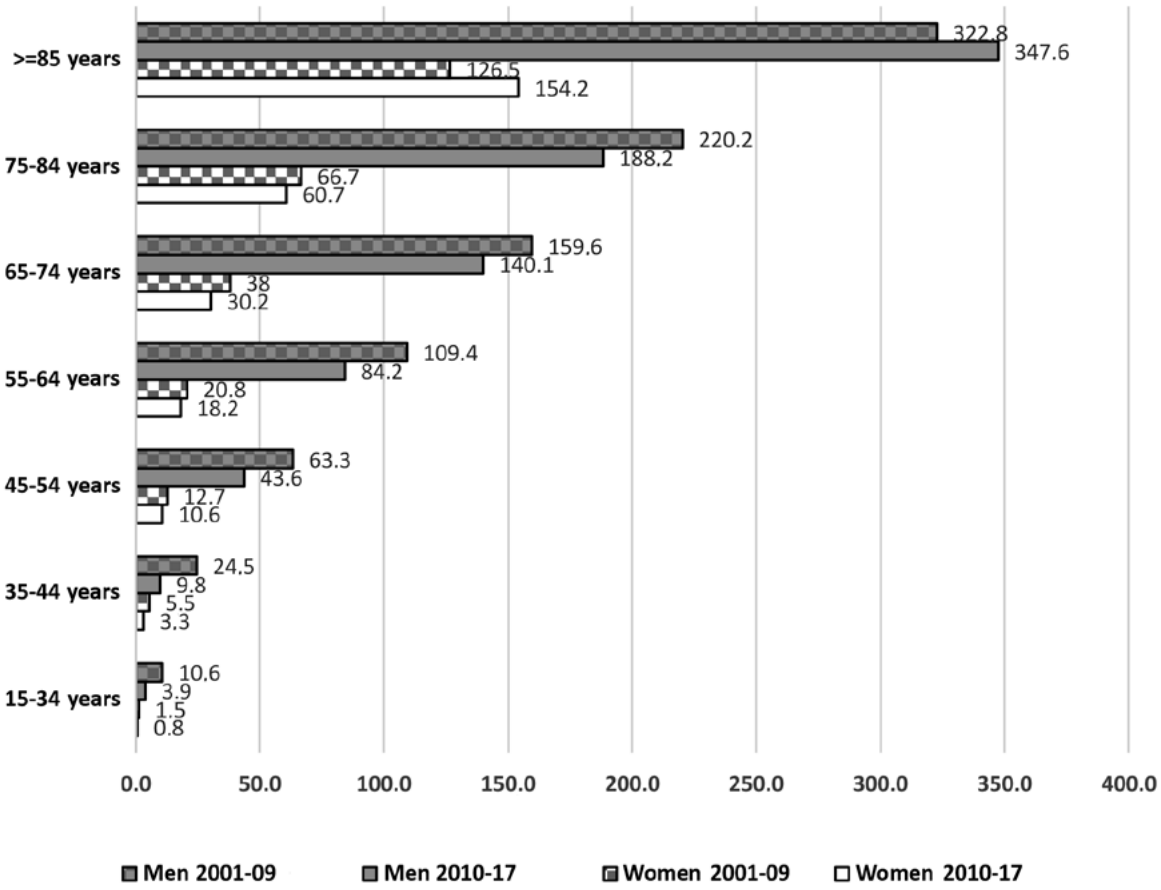


Figure 1. **Average annual mortality rates attributable to alcohol standardized by age1 according to age group, sex and period. Spain, 2001-2017.**

Note. [1] Average annual mortality rates attributable to alcohol standardized by age per 100,000 inhabitants, calculated by five-year age groups. To calculate these, the figures for the population of residents in Spain on July 1 of each year and the European Standard Population for 2013 were used. P1: refers to the period 2001-2009. P2: refers to the period 2010-2017.

2009 period (9.8% in men and 4.9% in women); there was a slight decrease in the following period (2010-2017) to 7.8% (9.2% in men and 4.7% in women).

Evolution of the distribution of alcohol-attributable mortality according to basic cause

During 2010-2017, the four groups of causes contributing most to total AAM were cancer, digestive diseases, injuries from external causes, and circulatory diseases. Between the periods 2001-09 and 2010-17, there were increases in the contributions of cancer (42.1% and 44.7% of AAM) and circulatory diseases (4.7% and 7.4%), while those of digestive diseases (37.4% and 33.2%) and external causes (17.3% and 15.2%) decreased. Some heterogeneity in sex was observed in the temporal changes of these contributions. Thus, for example, the decrease in the contribution of external causes was exclusively due to changes in men, and the decrease in the contribution of digestive diseases was more notable in women than in men. Regarding heterogeneity in terms of age, the contribution of cancer to the total AAM increased across all ages, except in the range of 45-54 years and in ≥ 85 years, that of circulatory diseases increased especially in those aged ≥ 65 years, that of digestive diseases decreased across all ages, except in the 45-54-year group and those aged ≥ 75 years. In the case of external causes, there was an increase in the 35-54-year range and those aged ≥ 75 years (Table 3). For more detail, the evolution of the AAM rates for the different basic causes can be observed in Table 4 of the appendix, stratified simultaneously by age groups and sex.

Evolution of the distribution of alcohol-attributable mortality by type of drinker

In 2010-2017, the majority of AAM occurred in high-risk drinkers (> 2/3), followed by ex-drinkers and medium-low risk drinkers. The contribution of high-risk drinkers to total AAM was significantly higher in men than in women, while the opposite was true for the other types of drinkers.

Table 3. ***Evolution of the distribution by cause and type of drinker of total alcohol-attributable deaths, by sex and age in the population aged 15 years and over (%). Spain, 2001-2017[1].***

	PERIOD	TOTAL	MEN	WOMEN	AGE GROUPS (years)						
					15-34	35-44	45-54	55-64	65-74	75-84	>=85
CAUSE OF DEATH	**Percentage of total deaths attributable to alcohol standardized by age**										
Cancer	**2001-09**	42.1	44.3	36.9	3.3	17.8	38.3	49.2	49.7	44.4	37.3
	2010-17	44.7	46.8	39.0	8.3	19.7	37.2	52.4	53.9	45.8	32.8
Circulatory diseases	**2001-09**	4.7	-2.0	24.6	0.0	-1.3	-1.2	-2.8	-1.5	10.4	30.9
	2010-17	7.4	0.6	27.0	0.0	-4.5	-3.0	-4.6	0.6	11.8	36.8
Infectious diseases	**2001-09**	1.3	1.4	1.0	0.0	1.3	1.0	1.0	1.3	1.0	2.7
	2010-17	1.5	1.7	1.2	0.0	1.5	0.9	0.8	0.9	1.7	3.1
Metabolic diseases	**2001-09**	-3.4	-0.4	-11.3	0.0	-0.7	-0.4	-1.0	-2.3	-4.7	-12.4
	2010-17	-3.0	-0.5	-9.4	0.0	0.0	-0.5	-1.0	-1.7	-3.7	-9.1
Digestive diseases	**2001-09**	37.4	36.5	39.4	6.6	38.2	42.1	40.7	42.3	37.7	25.3
	2010-17	33.2	33.1	32.1	4.2	31.8	44.1	40.0	35.6	32.3	18.9
Neurological/mental diseases	**2001-09**	0.6	0.6	0.5	1.6	0.7	0.6	0.4	0.4	0.5	0.7
	2010-17	1.0	0.9	0.9	4.2	1.5	0.8	0.6	0.8	1.0	1.2
External causes	**2001-09**	17.3	19.6	8.9	88.5	44.1	19.6	12.7	10.0	10.6	15.6
	2010-17	15.2	17.4	9.2	83.3	50.0	20.7	11.6	9.9	11.2	16.2
TYPE OF DRINKER	**Percentage of all deaths attributable to alcohol standardized by age**										
High risk drinkers	**2001-09**	73.4	82.0	45.8	52.5	66.4	76.3	80.1	78.5	66.3	69.1
	2010-17	69.3	77.5	44.8	41.7	50.0	73.8	77.0	79.0	60.4	60.7
Medium-low risk drinkers	**2001-09**	8.5	4.6	18.2	47.5	30.9	19.8	14.6	9.3	1.1	-25.2
	2010-17	11.7	7.4	22.4	58.3	45.5	21.8	16.8	10.2	9.6	-7.2
Regular ex-drinkers	**2001-09**	18.2	13.4	36.0	0.0	2.6	4.0	5.3	12.2	32.7	56.1
	2010-17	19.0	15.1	32.8	0.0	4.5	4.4	6.1	10.8	30.1	46.4

Note. [1]Percentages were calculated by dividing the age-standardized AAM rate for each cause of death by the age-standardized total alcohol-attributable death rate and multiplying the result by 100. The category "other diseases" is not included among the causes of death because no cases are registered.

By age, the high-risk drinker group contributing the most to AAM was the 65-74-year group, while in medium-low-risk drinkers this was the case in the 15-34-year group, and the ≥ 85-year group took this role in ex-drinkers. Between the periods 2001-2009 and 2010-2017, the percentage of AAM decreased in high-risk drinkers (73.4% and 69.3%) and increased in ex-drinkers (18.2% and 19.0%) and in moderate-low-risk drinkers (8.5% and 11.7%).

Some heterogeneity in sex was observed in the temporal changes of this contribution. Thus, the decrease in the contribution of high-risk drinkers and the increase in that of ex-drinkers was due to respective changes in men, given that the contribution of women high-risk drinkers barely varied and that of women ex-drinkers decreased. By age, the contribution of high-risk drinkers decreased except in the 65-74 age group, and that of medium-low risk drinkers increased in all ages, especially in the 15-34 and ≥ 75-year groups. The contribution of ex-drinkers increased in the group aged 35-64 years and decreased in those aged ≥ 65 years (Table 3).

For more detail, Table 4 of the appendix shows the evolution of the AAM rates for the three types of drinkers, simultaneously stratified by age groups and sex.

Evolution of the disparity by sex in alcohol-attributable mortality

During 2010-2017, the male/female ratio of age-standardized AAM rates was 3.5, with the highest disparity among young people aged 15-34 years (4.8) and the lowest in ≥ 85-year group (2.3). By cause of death, the highest disparity was observed in the group of external causes (6.7), followed by infectious diseases (4.9) and cancer (4.3). Between 2001-2009 and 2010-2017, the male/female rate ratio decreased, from 4.0 to 3.5, with the decrease particularly pronounced in young people aged 15-34 years (7.0 and 4.8). In terms of evolution by cause, the ratio decreased in cancer, neurological/mental diseases and especially in external causes, while it increased in circulatory and infectious diseases. Considering the difference in rates between men and women, a large increase was observed

Table 4. ***Evolution of sex diversity in alcohol-attributable mortality by age and by basic cause in the population aged 15 years and over. Spain, 2001-2017.***

	Male-female rate ratio[1]			Difference in male-female rates[2]		
	2001-17	2001-09	2010-17	2001-17	2001-09	2010-17
TOTAL	3.8	4.0	3.5	53.5	60.3	46.7
15-34 years	6.4	7.0	4.8	6.5	9.1	3.1
35-44 years	3.9	4.4	3.0	12.8	19.0	6.6
45-54 years	4.6	5.0	4.1	41.3	50.5	33.0
55-64 years	5.0	5.3	4.6	77.0	88.7	66.1
65-74 years	4.4	4.2	4.6	115.7	121.6	110.0
75-84 years	3.2	3.3	3.1	140.1	153.5	127.4
>=85 years	2.4	2.6	2.3	195.3	196.3	193.5
Cancer	4.5	4.8	4.3	25.7	28.3	23.3
Circulatory diseases	-0.1	-0.3	0.1	-5.5	-6.5	-4.5
Infectious diseases	4.7	4.4	4.9	0.9	0.8	0.8
Metabolic diseases	0.2	0.1	0.2	1.7	2.0	1.4
Digestive diseases	3.7	3.7	3.7	18.4	21.3	15.6
Neurological / mental diseases	3.9	4.4	3.6	0.4	0.4	0.4
Other diseases	0.0	0.0	0.0	0.0	0.0	0.0
External causes	7.9	9.0	6.7	11.9	14.1	9.6

Note. [1] Rate ratio: ratio of the age-standardized mortality rate in men and women, unitless. [2] Difference in rates2: Difference of standardized rates by age in men and women. It is expressed as the number of deaths attributable to alcohol per 100,000 inhabitants.

with age. By cause, the largest differences during 2010-2017 were seen in cancer and external causes. Between the periods, a decrease in the differences was observed in all ages and causes, except in the 65-74-year-old group and in the case of circulatory, infectious and metabolic diseases (Table 4).

Discussion

Main findings

In the period 2010-2017, an annual average of 14,927 deaths attributable to alcohol occurred in Spain in the population aged 15 years and over, 58.6% of which were premature. AAM represented 3.9% of total mortality. The most frequent causes of AAM were cancer (43.8%), digestive diseases (32.9%) and external causes (15.8%). High-risk drinkers contributed the most to AAM (68.7%), followed by ex-drinkers (19.8%). The age-standardized AAM rate was 3.5 times higher in men than in women, with higher rates for young people and external causes. Between 2001-2009 and 2010-2017, the standardized AAM rate decreased by 16.8%, with a greater decrease in men (19.4%) than in women (9.8%), and in the 15-34-year group (60.7%) than in the 75-84-year group (11.3%),and there was an increase of 16.6% in the group aged 85 and over. In addition, between both periods, the contribution to AAM of high-risk drinkers, digestive diseases and external causes decreased slightly, while that of ex-drinkers, medium-low risk drinkers, cancer and circulatory diseases increased.

Comparison with other estimates of alcohol-attributable mortality

The magnitude of such AAM estimates strongly depends on the methodological options selected; in our study, these were aimed at avoiding overestimation, so the estimates can be considered conservative. The main methodological options leading to a somewhat conservative estimate here are the following: 1) including in the calculations only those causes of death in which there is clear evidence of their relationship with alcohol and valid estimates of the relative risk function according to quantity consumed; 2) attributing ≥ 100 g of pure alcohol/day to consumers with an RR corresponding to 130 g/day; 3) not considering the latency period between alcohol consumption and death in a context in which per capita alcohol consumption is falling; 4) using RR functions usually affected by biases that tend to underestimate the number of deaths attributable to alcohol in some cases by not excluding the ex-drinkers who stopped drinking due to health problems from the category of lifetime abstainers; 5) applying an alcohol content to wine (11.5% ABV) which may be low in the current Spanish context; 6) not taking the risk associated with binge drinking into account in the calculations. Some authors point out that this may cause an underestimation of deaths attributable to alcohol due to cardiomyopathy and ischemic strokes and external causes (Connor, Kydd,

Rehm & Shield, 2013; Roerecke & Rehm, 2010; Sherk, Stockwell, Rehm, Dorocicz & Shield, 2017). However, this would only be the case if the average consumption for said conditions were adjusted for binge drinking, something that was possibly not done in the RRs used.

Focusing on the population aged 15 years and over, the annual estimate obtained for 2010-2017 (14,927) was higher than that of Fierro et al. for 2001-2004 (5,136) (Fierro et al., 2008), which did not correct for underestimation of alcohol consumption in surveys, and lower than that of the WHO study for 2016 (WHO, 2019) (17,828) or the Global Burden of Disease (CBD) for 2017 (32,003) (GBD, 2018; IHME, 2019). This last study reports very high AAM estimates and it would be desirable to know the specific sources from which the empirical data on alcohol consumption in Spain were extracted, but identifying them from the extensive list of sources that the IHME provides on its website is very difficult. In any case, both the prevalence of current drinkers and the daily average amount of alcohol consumed by them seem significantly higher than those estimated in the framework of our study. And high levels of consumption may also have been favoured in the GBD with respect to our study when distributing average consumption among drinkers. Regarding the population aged 15-64 years, the estimate for 2004 (7,585) (Rehm et al., 2013a) is somewhat higher than that obtained in the present study for the same year (6,762). Comparing our estimates with those of other developed countries is a delicate matter. Taking as a reference the WHO study, which estimates the contribution of AAM to general mortality in Spain in 2016 as 4.3%, close to that of this study (3.9% in 2010-2017), it can be seen that both estimates would be below those of countries such as Portugal (5.9%), France (5.8%), Germany (5.2%), United Kingdom (4.6%) or Switzerland (4.5%), and closer to those of Italy (3.6%) or Greece (4.0%) (Rehm et al., 2013b).

Alcohol-attributable mortality by cause of death and type of drinker

In 2001-2017, the causes of death responsible for the highest AAM were, in this order, cancer, digestive diseases, external causes and circulatory diseases, which is consistent with previous studies (IHME, 2019; Shield, Rylett & Rehm, 2016). In international studies, the contribution of the different groups of causes to total AAM is variable. Thus, the figures for cancer, circulatory and digestive diseases and external causes were, respectively, 31%, 21%, 16% and 17% in France in 2009 (Guerin, Laplanche, Dunant & Hill, 2013); 30%, 8%, 21% and 32% in Switzerland in 2011 (Marmet, Rehm & Gmel, 2016); and 36%, 17%, 17% and 17% in Australia in 2015 (National Drug Research Institute [NDRI], 2019). There are also differences between studies regarding disparities by sex in the contribution of the different causes (Guerin et al., 2013). In both our study and GBD-2017 (GBD, 2018; IHME, 2019), the contribution of circulatory diseases increased with age, that of cancer and digestive diseases increased, reaching a peak in 65-74 years and 45-54 years, respectively, and then decreased, and that of external causes was highest in the 15-34-year group (≈80%) and then decreased.

In 2010-2017, 69.3% of AAM in the population aged ≥ 15 years (77.5% in men and 44.8% in women) occurred in high-risk drinkers. This percentage increased with age, peaking at 65-74 years (79.0%). Although there are almost no studies on this topic, those available coincide in indicating a concentration of AAM in high-risk drinkers. Thus, in the 15-64-year group in 2004, 72.2% of deaths attributable to alcohol occurred in high-risk drinkers (76.1% in men and 57.6% in women) in Spain (Rehm et al., 2013a), 74.5% in Italia (Shield, Rehm, Gmel, Rehm & Allamani, 2013), and 77% in the European Union as a whole (Rehm et al., 2013a). In the Swiss population aged 15-74 years in 2011, the percentage was 67% in men and 48% in women (Marmet, Rehm, Gmel, Frick & Gmel, 2014).

Disparities in alcohol-attributable mortality by sex and age

Our results indicate that AAM in Spain during 2010-2017 was 3.5 times higher in men than in women, in line with the GBD-2017 (IHME, 2019; GBD, 2018) and WHO-2016 (WHO, 2019) studies. These estimates are also quite consistent with the male/female ratio of the number admitted to treatment for alcohol abuse/addiction in Spain in 2016 (3.3) (Delegación del Gobierno para el Plan Nacional Sobre Drogas [DGPNSD], 2018), of the prevalence of daily alcohol use in 2017 (3.1) (Ministerio de Sanidad, Consumo & Bienestar Social [MSCBS], 2019) and high-risk alcohol use in 2017 (2.9) (DGPNSD, 2018). The contribution of alcohol to total mortality was also considerably higher in men (5.0%) than in women (2.3%), but sex disparity was less pronounced, as was also the case in GBD-2017 and WHO-2016 (GBD, 2018; IHME, 2019; WHO, 2019). This suggests that sex disparity is greater in AAM than in non-attributable mortality. As in other studies (Guerin et al., 2013), the contribution of cancer and external causes to the total AAM risk was greater in men than in women, while the opposite was the case with circulatory and digestive diseases. Finally, it is also consistent with the aforementioned studies that the increase in the rate of AAM increases greatly with age, although the contribution of alcohol to total mortality is greater in those under 55 years of age (> 8%).

Evolution of alcohol-attributable mortality

In Spain between 2001-2009 and 2010-2017, the average annual rate of AAM fell by almost 8%, a decrease also seen in many European countries, including Mediterranean ones (Shield et al., 2016; WHO, 2019; World Health Organization-Europe [WHO-Europe], 2019). Many

causes of AAM are determined by several factors, including exposure to alcohol, which sometimes interact with each other. Additionally, changes in alcohol exposure can take decades to manifest in mortality. Therefore, in a context of decreasing mortality from many causes, it is possible that part of the decrease in AAM is due to favourable changes in other determinants of the causes of AAM, including improvements in the treatment of underlying diseases. For example, liver cirrhosis can be caused by alcohol and other agents, such as the hepatitis C virus, so the introduction of effective treatments against this virus as of 2014 may have contributed to the decrease in AAM due to digestive diseases. However, most of the decrease in AAM is probably due to the decrease in per capita alcohol consumption, influenced by multiple factors, such as the economic crisis that began in 2008 and subsequent budget cuts, effective road safety interventions or even the greater number of immigrants, with per capita consumption lower than the Spanish-born population (Alonso et al., 2017). In addition, AAM had already been decreasing in Spain before 2001, as evidenced by comparing 1981-1990 and 1999-2004 (Fierro et al., 2008), which is consistent with the decrease in per capita alcohol consumption since the mid-1970s (Ministerio de Sanidad, Servicios Sociales e Igualdad [MSSSI], 2017). Finally, the stability of the contribution of alcohol to general mortality between 2001-2009 and 2010-2017 indicates that the decrease in AAM was similar to that in non-attributable mortality.

The relative decrease in AAM was much stronger in men (-19.4%) than in women (-9.8%), and in the population aged 15-54 years than in the elderly, findings which are corroborated by other earlier results on alcohol-related mortality (MSSSI, 2018) and are consistent with international studies (Marmet et al., 2016; WHO-Europe, 2019). Furthermore, the decline was much greater for external causes and digestive diseases than for cancer. The decrease in AAM due to external causes is consistent with other studies (IHME, 2019) and is probably explained by a decrease in alcohol use, but also by reduced exposure to road traffic and occupational hazards during the economic crisis and the period of cuts in public spending, as well as by the effectiveness of road safety interventions (points-based driving licence, speed controls and penalties for reckless driving). The significant decrease in AAM due to digestive diseases surely reflects the context of declining alcohol use in Spain, since liver cirrhosis, which predominates in these causes, quickly reveals changes in alcohol use (Shield et al., 2016). However, it cannot be ruled out that part of the decline in recent years was due to the control of chronic liver disease linked to hepatitis B and C viruses.

Implications for public health

The almost 15,000 deaths attributable to alcohol in Spain (approximately 4% of total mortality) represent a considerable burden of disease, especially if one takes into account that most are premature and that the estimate is conservative. Thus, premature mortality attributable to alcohol in turn accounts for around 8% of all premature deaths in the period as a whole. While low levels of alcohol consumption in adults may reduce mortality from diabetes or ischemic circulatory diseases, it is clear that at the population level, alcohol use causes many more deaths than it prevents. Many interventions have been shown to be effective in reducing the burden of disease attributable to alcohol, such as pricing and tax policies, restriction of access to alcohol, limitation of advertising and sponsorship, drink-driving controls, educational measures and campaigns, including those involving healthcare professionals, widely available and accessible treatments for alcohol use disorders, etc. Given the concentration of AAM in high-risk drinkers, it is essential to focus interventions on this type of consumption. To this end, however, the most effective in population terms would surely be to develop wide-ranging and efficacious strategies aimed at reducing average consumption in the population as a whole or in all drinkers because this will simultaneously succeed in reducing in high- and medium-low risk consumption.

Acknowledgments

This article is a product of work carried out within the framework of a research project funded by the Government Delegation for the National Plan on Drugs (Delegación del Gobierno para el Plan Nacional sobre Drogas, DGPNSD) [Nº Exp: 2015I040] and the support of the human resources department of the Carlos III Health Institute (Instituto de Salud Carlos III) (ISCIII-PFIS contract, Nº Exp: ENPY-397/18-PFIS). We also wish to thank Cristina Ortiz from the ISCIII for her collaboration in carrying out the analysis of alcohol consumption from some of the population surveys used for the estimates, and the Alcohol Group of the Spanish Epidemiology Society for their support in the completion of this study.

Conflict of interests

The authors declare no conflict of interest related to aspects discussed in this article.

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