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# Original article

# The burden of disease in Spain: Results from the Global Burden of Disease 2016<sup>★</sup>



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### ABSTRACT

Background and objectives: The global burden of disease (GBD) project measures the health of populations worldwide on an annual basis, and results are available by country. We used the estimates of the GBD to summarise the state of health in Spain in 2016 and report trends in mortality and morbidity from 1990 to 2016.

Material and methods: GBD 2016 estimated disease burden due to 333 diseases and injuries, and 84 risk factors. The GBD list of causes is hierarchical and includes 3 top level categories, namely: (1) communicable, maternal, neonatal, and nutritional diseases; (2) non-communicable diseases (NCDs), and (3) injuries. Mortality and disability-adjusted life-years (DALYs), risk factors, and progress towards the sustainable development goals (SDGs) are presented based on the GBD 2016 data in Spain.

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Results: There were 418,516 deaths in Spain in 2016, from a total population of 46.5 million, and 80.5% of them occurred in those aged 70 years and older. Overall, NCDs were the main cause of death: 388,617 (95% uncertainty interval 374,959–402,486), corresponding to 92.8% of all deaths. They were followed by 3.6% due to injuries with 15,052 (13,902-17,107) deaths, and 3.5% communicable diseases with 14,847 (13,208-16,482) deaths. The 5 leading specific causes of death were ischaemic heart disease (IHD, 14.6% of all deaths), Alzheimer disease and other dementias (13.6%), stroke (7.1%), chronic obstructive pulmonary disease (6.9%), and lung cancer (5.0%). Remarkable increases in mortality from 1990 to 2016 were observed in other cancers, lower respiratory infections, chronic kidney disease, and other cardiovascular disease, among others. On the contrary, road injuries moved down from 8th to 32nd position, and diabetes from 6th to 10th. Low back and neck pain became the number one cause of DALYs in Spain in 2016, just surpassing IHD, while Alzheimer disease moved from 9th to 3rd position. The greatest changes in DALYs were observed for road injuries dropping from 4th to 16th position, and congenital disorders from 17th to 35th; conversely, oral disorders rose from 25th to 17th. Overall, smoking is by far the most relevant risk factor in Spain, followed by high blood pressure, high body mass index, alcohol use, and high fasting plasma glucose. Finally, Spain scored 74.3 of 100 points in the SDG index classification in 2016, and the main national drivers of detrimental health in SDGs were alcohol consumption, smoking and child obesity. An increase to 80.3 points is projected in 2030.

Conclusion: Low back and neck pain was the most important contributor of disability in Spain in 2016. There has seen a remarkable increase in the burden due to Alzheimer disease and other dementias. Tobacco remains the most important health issue to address in Spain.

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# La carga de enfermedad en España: resultados del Estudio de la Carga Global de las Enfermedades 2016

RESUMEN

Antecedentes y objetivo: El estudio de la carga global de las enfermedades, conocido como GBD por sus siglas en inglés (global burden of disease), mide la salud poblacional en todo el mundo de forma anual y sus resultados están disponibles por país. Utilizamos las estimaciones GBD para resumir el estado de salud poblacional en España en 2016 y describir las tendencias en morbimortalidad de 1990 a 2016.

Material y métodos: GBD 2016 estima la carga debida a 333 enfermedades y lesiones, y a 84 factores de riesgo. La lista de causas de GBD es jerárquica e incluye 3 categorías de nivel superior: 1) enfermedades transmisibles, maternas, neonatales y nutricionales; 2) enfermedades no transmisibles (ENT), y 3) accidentes. Se presentan la mortalidad, los años de vida ajustados por discapacidad (AVAD), los factores de riesgo y el progreso hacia los objetivos de desarrollo sostenible (ODS) a partir de los datos de GBD 2016 en España.

Resultados: En 2016 en España hubo 418.516 muertes, de una población total de 46,5 millones, y el 80,5% de ellas ocurrieron en personas de 70 años o más. Las ENT fueron la principal causa de muerte (92,8%), con 388.617 (intervalo de incertidumbre del 95% 374.959-402.486), seguidas de los accidentes (3,6%), con 15.052 (13.902-17.107), y de las enfermedades transmisibles (3,5%), con 14.847 (13.208-16.482) muertes. Las 5 principales causas específicas de muerte fueron la cardiopatía isquémica (CI), con el 14,6% de todas las muertes, la enfermedad de Alzheimer y otras demencias (13,6%), el accidente cerebrovascular (7,1%), la enfermedad pulmonar obstructiva crónica (6,9%) y el cáncer de pulmón (5,0%). Se observaron incrementos notables en la mortalidad de 1990 a 2016 en otros cánceres, infecciones respiratorias del tracto inferior, enfermedad renal crónica y otras enfermedades cardiovasculares, entre otros. Por el contrario, los accidentes de tráfico bajaron del puesto 8 al 32 y la diabetes del 6 al 10. Los dolores de espalda y cervicales se convirtieron en la causa principal de AVAD en España en 2016, superando a la CI, mientras que la enfermedad de Alzheimer pasó del puesto 9 al 3. Los mayores cambios en AVAD se observaron para accidentes de tráfico, que cayeron de la posición 4 a la posición 16, y los trastornos congénitos, de la 17 a la 35; por el contrario, los trastornos orales aumentaron, pasando del puesto 25 al 17. En general, fumar es, con mucho, el factor de riesgo más relevante en España, seguido de presión arterial alta, índice de masa corporal alto, consumo de alcohol y glucemia alta en ayunas. Finalmente, España obtuvo 74,3 sobre 100 puntos en la clasificación del índice ODS en 2016, y los principales determinantes de salud nacionales relacionados con los ODS fueron el consumo de alcohol, el tabaquismo y la obesidad infantil. Se proyecta un aumento a 80,3 puntos en 2030.

Conclusión: Los dolores de espalda y cervical fueron el contribuyente más importante de discapacidad en España en 2016. Hubo un aumento notable de la carga poblacional debida a la enfermedad de Alzheimer y otras demencias. El tabaco sigue siendo el riesgo para la salud más importante que debe abordarse en España.

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Palabras clave:
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# Introduction

The first Global Burden of Disease (GBD) report was published in 1997, and it now measures the health of populations worldwide on an annual basis. GBD produces age-, sex-, and country-specific

estimates (including selected subnational units) of cause-specific mortality and morbidity, risk factor exposure, mortality and morbidity attributable to these risks, and a range of health system characteristics, from 1990 to the most recent year available. Various summary measures are computed, including disability-adjusted

life-years (DALYs) and healthy life expectancy (see Box for related terms and their definitions). GBD uses highly standardised, validated approaches, which are applied to all available data sources and adjusted for major sources of bias. Further details on GBD 2016, which covers 1990–2016, are available elsewhere.<sup>3</sup> As with all iterations of the GBD study, GBD 2016 provides an update of the full-time series based on methodological improvements and newly identified data sources. Further information on recent changes and future improvements of the GBD initiative are available elsewhere.<sup>4</sup>

The GBD 2016 report, published in September 2017, represents a unique opportunity for studies addressing health metrics and their determinants in a given country, using a standardised methodology for the correction of contextual issues at the national level, depending on the quality of available statistics. Although the GBD initiative constitutes a source of internationally comparable information on the burden of disease and its determinants, the availability of such information at the national level with a greater degree of geographic disaggregation is an important asset for the development and implementation of health policies. In recent years, countries such as Brazil, Ethiopia, Japan, India, England, Mexico, Sweden, the USA, and others have developed the GBD nationally and subnationally, and their experience provides a useful basis to extend this practice to other countries. Elsewhere, there are already several GBD national-specific papers, 5-9 including some focused on specific diseases. 10,11 that already provided relevant insights of health states and changes over time.

Spain does not yet have a national burden of disease initiative, but there are other sources of information that provide similar information. Regarding morbidity, since 1987, and every five years since, the Ministry of Health in Spain comprehensively surveys health indicators through the *Encuesta Nacional de Salud* (The National Health Interview Survey of Spain). The latest available is the 2011/12 report, which collected health information relative to the population resident in Spain from a representative sampling of 21,508 households. Several of the 17 autonomous communities of Spain also produce comprehensive regional reports, available elsewhere. In addition, the European Health Interview Surveys (EHIS), coordinated by EUROSTAT, was updated in 2014 with health information on Spain. However, none of these morbidity data comprehensively covers all health conditions.

Assessment of attributable risk factors is an important component of public health policies. However, the information is much more scarce and partial regarding risk factors in Spain, only available for some periods and areas. <sup>16</sup> Indeed, the current information systems in Spain do not provide systematic comparative risk assessment of the main health determinants, which is an important limitation.

A previous analysis, based on GBD 2010, was reported of Spain in 2014, <sup>17</sup> and the country profile of Spain has been updated with GBD 2016 data. <sup>18</sup> To date, there are also two additional Spain reports using GBD methodology, <sup>19,20</sup> and one reporting disease burden in the autonomous region of Comunidad Valenciana. <sup>21</sup>

This study presents GBD 2016 results focused on Spain, mirroring the template of the recent GBD 2016 capstone papers.<sup>3,22</sup> In particular, we further explored Spain's performance on the Sustainable Development Goals (SDGs).<sup>23</sup> The SDGs were established by the United Nations (UN) General Assembly on September 2015, including 17 universal goals, 169 targets, and 230 indicators leading up to 2030.<sup>24</sup>

The main objectives of this paper are to use the estimates of the GBD 2016 study to provide an updated description of the current state of health in Spain, and to report trends in mortality and morbidity from 1990 to 2016. Ultimately, it should contribute to set up and prioritise public health interventions, including current and future unmet needs in the country.

#### Methods

Before the GBD project was initiated in 1991, no comprehensive assessments of human health had been carried out. GBD is a global comparative risk assessment exercise, with the first preliminary results (for base year 1990) published in the World Development Report 1993. This international collaborative effort is currently led by the Institute for Health Metrics and Evaluation (IHME) in Seattle, Washington, USA. This analysis complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER). The GBD 2016 initiative includes 400.8 million condition-age-sex-location-years data points, which produce more than 3.5 billion estimated quantities. Although most of them are available from the IHME website, this information needs to be filtered and interpreted in a coherent, consistent way, for its presentation and eventual use and implementation, at its global, national and other granularity levels.

In Spain, the main source of mortality data is the Mortality Information System.<sup>27</sup> The GBD uses methodologies for correcting the underreporting of deaths and garbage codes. Correction of the codes uses evidence from the medical literature, expert opinions and statistical techniques to designate each item to the most probable causes of death.<sup>22</sup>

After addressing data quality issues, the GBD 2016 study employed a variety of statistical models to determine the number of deaths from each cause, through the cause of death ensemble model (CODEm) algorithm. To ensure that the number of deaths per cause did not exceed the total number of estimated deaths, a correction technique called CoCorrect was used. This technique ensures that estimates of the number of deaths from each cause do not total more than 100% of deaths in a given year, age band, and sex strata.<sup>28</sup> After producing estimates for the number of deaths from each of the 264 fatal outcomes included in the list of causes of the GBD 2016 study, the years of life lost (YLLs) due to premature death were calculated. For every death due to a particular cause, the number of years lost was estimated based on the highest life expectancy in the deceased individual's age group.<sup>29,30</sup> The GBD study used a list of causes that placed 333 causes of death within a four-level hierarchy. The first level divided causes into three groups: communicable, maternal, neonatal, and nutritional diseases (CMNNDs); non-communicable diseases (NCDs), and injuries. The second level consisted of 20 major causes of diseases such as neonatal disorders, cardiovascular diseases and traffic injuries. The third level subdivided level 2 into types such as neonatal preterm birth complications, cerebrovascular disease and traffic injuries; and the fourth level further subdivided those types in some cases, for example: ischaemic stroke and haemorrhagic stroke; and pedestrian road injuries, cyclist road injuries, motorcyclist road injuries, motor vehicle road injuries and other road injuries. All specific GBD codes in ICD9 and/or ICD10 for each disease and condition are available http://www.healthdata.org/sites/default/files/files/data\_for\_ download/2012/IHME\_GBD2010\_CauseListandICD.pdf. Just as a token, there are 194 data sources on neck pain http://www.ghdx. healthdata.org/keyword/neck-pain and 730 data sources on back pain http://www.ghdx.healthdata.org/keyword/back-pain.

The redistribution of impossible or non-underlying causes of death (so-called "garbage codes"), was conducted according GBD methodology, as explained elsewhere.<sup>3</sup> Uncertainty in GBD estimates is attributable to cause-specific model specifications; varied availability of data by age, sex, location, or year; and variability of sample size within data sources. Therefore, this uncertainty estimation considers time lags in some data, the absence of data from specific conditions, age groups, or time periods, or unreliability in the data that are available.

The study used the concept of premature mortality, as previously employed by the World Health Organization (WHO) and the UN, respectively in the Global Plan for NCDs (2013) and in the SDGs for NCDs (2015). Although there is no consensus on the definitions of preventable versus premature death, the WHO proposes using premature deaths to define those that occur before age 70, or deaths that occur before the average age of death in a population. As the World population is taken as a GBD reference, and its life expectancy was 71.4 years in 2016, it could be approximated that premature deaths worldwide and in Spain are those that occur at age 70 years or younger. A full explanation is available via these links: https://www.cancer.gov/publications/dictionaries/cancer-terms/ def/premature-death and http://www.who.int/gho/mortality\_ burden\_disease/life\_tables/situation\_trends/en. The 20 leading causes of death were analysed using the level 3 aggregation of causes of death from the GBD 2016 study, in the age group from 30 to 69 years. The results were compared between the years 1990, 2006 and 2016.

Information on risk factors and their attributable DALYs can be found elsewhere.<sup>31</sup> Briefly, GBD uses the comparative risk assessment framework developed for previous iterations to estimate levels and trends in exposure, attributable deaths, and attributable DALYs, by age group, sex, year, and location for 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks from 1990 to 2016. The GBD study included 481 risk-outcome pairs that met the GBD study criteria for convincing or probable evidence of causation. The IHME extracted relative risk (RR) and exposure estimates from 22,717 randomised controlled trials, cohorts, pooled cohorts, household surveys, census data, satellite data, and other sources, according to the GBD 2016 source counting methods. Using the counterfactual scenario of theoretical minimum risk exposure level, the portion of deaths and DALYs that could be attributed to a given risk were estimated.

SDGs were further explored in Spain, both in GBD 2015,<sup>32</sup> and also in GBD 2016.<sup>33</sup> The 17 SDGs and their 169 targets were formally adopted by all UN member states in September 2015. There are 50 health-related indicators (i.e.: indicators that directly involve health services, health outcomes, and risk factors with well-established causal connections to health). They are part of the 29 health-related targets and 11 goals, including SDG 3, which aims to "ensure healthy lives and promote wellbeing for all at all ages".

All GBD research is conducted on a public-domain secondary database, without nominal identification, in accordance with US Decree No. 7724 of May 16, 2012, and Resolution No. 510 of April 7, 2016; thus, there was no need to submit this study to a research ethics committee, neither in the USA nor in Spain, as no ethics approval was required.

# Statistical analysis

Information about the data sources, estimation methods, computational tools, and statistical analysis used in the derivation of GBD estimates are available elsewhere.<sup>3</sup> All calculations are presented with 95% bootstrapped uncertainty intervals (UI), modelled by resampling the sample data and performing inference about a sample from resampled data, calculated using the R boot package (with 1000 iterations) which is implemented in R, <sup>34</sup> an open-source statistical software.<sup>35</sup> The 95% UIs were calculated using the 2.5th and 97.5th percentiles, and point estimates were calculated from the mean of the draws; they take into account the uncertainty in the epidemiological parameters used to estimate YLLs, YLDs and DALYs.

#### Results

In 2016, the total population of Spain was 46.5 million (23.7) million women, and 22.8 million men). The distribution by age and sex of the Spanish population (Fig. 1) has shifted from 1990 to 2006 and then to 2016, to substantially older age groups in both women and men, with significant population ageing accordingly, particularly in women. These changes in size, sex and age distribution, and other demographic trends, affect the health burden and determine health-related trends, as reported below by mortality and DALYs; risk factors; and the SDGs. To facilitate comparison, some estimates are reported as age-standardised. Assessing trends in any health indicator based on absolute, relative, or adjusted data by age and other variables, often produces different, even opposite results, which require careful interpretation. Commonly, the use and users of each of these trends are diverse: for practicing physicians, especially in Primary Care, the absolute and crude number of cases of any given disease helps to determine the volume of work needed now and in the future; on the contrary, percentages and relative rates are very useful for managers, health administrators and politicians, to allocate resources, always limited, and distribute them by specialty, level of care, and interventions/programmes; finally, epidemiologists use standardised rates by age (and by sex, comorbidities, geography,...) to explore the causes and determinants of disease, and establishing trends taking into account any changes in the structure of the population pyramid, migration, and other factors.

#### Mortality and DALYs

The main causes of death and YLLs in Spain in 2016 by age group and by sex are shown in Table 1. Overall, it is estimated that there were 418,516 deaths in Spain in 2016; 80.5% of all deaths occurred in those aged 70 years and older. NCDs were the main cause of death: 388,617, 95% UI (374,959–402,486), with 92.8%. They were followed by 3.6% due to injuries with 15,052 (13,902–17,107) deaths, and 3.5% CMNNDs with 14,847 (13,208–16,482) deaths.

The ranking of specific causes of death was led by ischaemic heart disease (IHD) 60,983 (57,094–65,803), second Alzheimer's disease and other dementias with 57,098 (49,114–65,392), third cerebrovascular disease 29,646 (26,209–33,330), and fourth chronic obstructive pulmonary disease (COPD) 28,945 (26,786–31,071). Within communicable diseases, diarrhoea, lower respiratory, and other common infectious disease accounted for 12,203 (10,612–13,860) deaths, while HIV/AIDS and tuberculosis totalled 1091 (1028–1156). Overall, lung cancer (plus tracheal and bronchus) were the most frequent in cancer deaths with 20,891 (19,418–22,539), followed by colon and rectum cancers with 15,984 (14,712–17,503). By sex, breast cancer accounted for 6949 (6291–7661) deaths, with 6793 (6125–7496) deaths in women and 156 (96–188) deaths in men; and, there were 7355 (6272–10,647) prostate cancer deaths.

Similarly expressed as before, total YLLs were 5,428,970, made of 3,188,866 in men and 2,240,104 in women. Of them, 88.9% of YLLs were due to NCDs, that is 4,826,975 (4,628,334–5,032,975), followed by 6.8% due to injuries with 368,761 (339,861–419,015), and by 4.3% due to CMNNDs with 233,235 (210,259–259,358) YLLs. YLLs due to injury were nearly double in men than in women, 8.4% vs 4.5%, respectively, being YLLs for females were 1.8% of total YLLs or 27.1% of YLLs due to injuries, while YLLs for males were 4.9% of total YLLs or 72.9% of YLLs due to injuries.

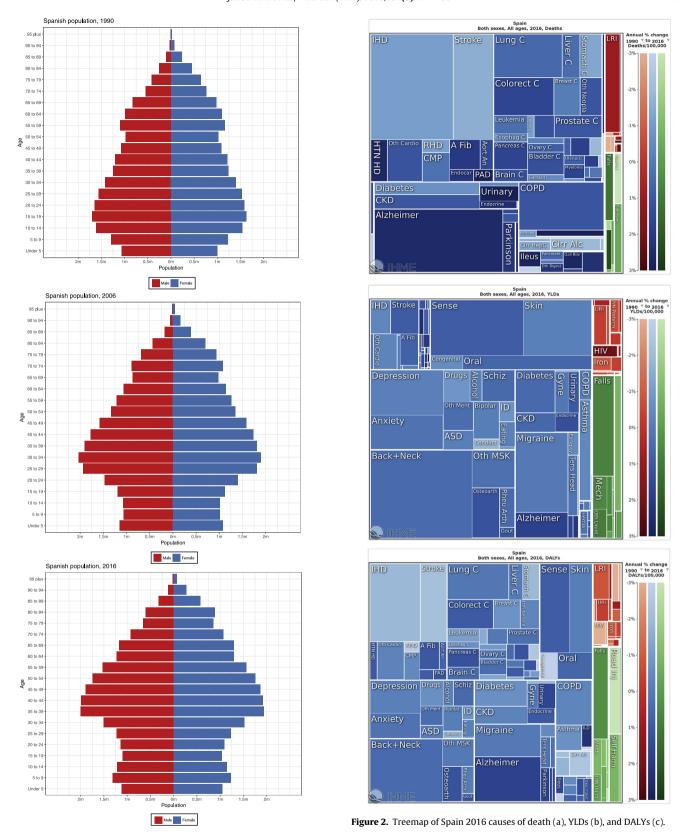
Further to Table 1, a graphical treemap presentation of causes of death in 2016 can be seen in Fig. 2a. The five leading specific causes of death were: 1. IHD with 14.6% (13.8-15.5%) of all deaths and with an annual change of -1.1% from 1990; 2. Alzheimer disease and other dementias with 13.6% (11.8-15.6%) of all deaths and

**Table 1**Main causes of death and years of life lost (YLLs) by age groups and by sex, in Spain in 2016.

		I	Deaths								
	Both Sexes,	< 5	5-14	15-49	50-69	70 +	Males,	Females,	Both Sexes,	Males,	Females,
	All ages	years	years	years	years	years	All ages	All ages	All ages	All ages	All ages
All causes	418516	1396	414	15782	64056	336868	208900	209616	5428970	3188866	2240104
Communicable, maternal, neonatal, and nutritional	14847 (13208 – 16482)	685	29	883	1513	11737	7788 (6800 – 8940)	7059 (6061–8185)	233235 (210259 – 259358)	140268 (125142 – 157848)	92967 (82259 – 10514
HIV/AIDS and tuberculosis	1091 (1028 – 1156)	5	4	491	288	303	784 (740 – 834)	307 (273 – 337)	34388 (32686 - 36187)	25968 (24551 - 27531)	8420 (7782 - 9064)
Diarrhea, lower respiratory, and other common infectious lisease	12203 (10612 -13860)	75	21	307	1052	10748	6221 (5280 – 7323)	5982 (5010 – 7084)	131757 (117866 – 147122)	77034 (67187 - 89627)	54723 (47470 - 63224
Neglected tropical diseases and malaria	31 (24 – 43)	0	1	6	9	15	16 (12 – 22)	15 (11 – 22)	799 (614- 1070)	421 (308 - 561)	378 (260- 542)
Aaternal disorders	21 (18 – 25)	0	0	20	í	0	.*	21 (18 – 25)	1053 (908 - 1219)	-*	1053 (908 - 1219)
Neonatal disorders	593 (428-809)	593	0	0	0	0	336 (232-467)	257 (188–342)	51256 (36975 - 69962)	29018 (20095 - 40415)	22238 (16244 - 2960
Nutritional deficiencies	455 (406 - 508)	1	1	7	27	419	187 (157 – 218)	268 (229 - 312)	4056 (3672 - 4470)	2082 (1734 - 2390)	1974 (1740 - 2235)
Other communicable, maternal, neonatal, and nutritional liseases	453 (389 – 495)	11	3	51	136	252	245 (217 – 274)	208 (147 – 240)	9927 (8553 - 10907)	5746 (5065 - 6445)	4181 (2927 - 4806)
Non-communicable diseases	388617 (374959 – 402486)	611	270	11139	59242	317355	191629 (181793 – 202370)	196988 (187222 – 206970)	4826975 (4628334 - 5032975)	2779890 (2614812 – 2956977)	2047085 (1933030 - 2165066)
Neoplasms	111958 (106818 – 117522)	69	150	5747	33659	72333	68662 (64360 – 73519)	43296 (40547 – 46191)	1921873 (1833785 – 2021015)	1201005 (1119572 – 1287570)	720868 (673770 - 770423)
Esophageal cancer	2050 (1785– 2331)	0	0	116	905	1029	1700 (1427–1979)	350 (310-390)	41226 (35261 - 47341)	35800 (29750 - 41925)	5426 (4818 - 6061)
	1								110451 (102533 -		`
Stomach cancer	7026 (6519 – 7544)	0	0	306	1805	4915	4223 (3845–4652)	2803 (2519–3091)	118675)	71460 (65253 - 78810)	38991 (35171 - 4310
Liver cancer	5256 (4652 - 5782)	0	2	205	1651	3398	3519 (2966 – 3998)	1737 (1496 – 2030)	90398 (78973 – 100176)	66347 (55666 - 75383)	24051 (20948 - 2753
Larynx cancer	1501 (1354 – 1651)	0	0	68	691	742	1425 (1279 – 1571)	76 (67 – 85)	30252 (27142 - 33303)	28734 (25644 - 31835)	1518 (1338 - 1708)
Tracheal, bronchus, and lung cancer	20891 (19418 – 22539)	0	0	980	8827	11084	16788 (15396 – 18395)	4103 (3708 – 4520)	408238 (378730 – 441212)	324645 (297004 – 356838)	83593 (75551 - 9211
Breast cancer	6949 (6291 – 7661)	0	0	799	2237	3913	156 (96 – 188)	6793 (6125 – 7496)	134788 (122486 - 148381)	2689 (1551 – 3281)	132099 (119728 – 145662)
Cervical cancer	1038 (935 - 1159)	0	0	166	345	527	_*	1038 (935 - 1159)	22254 (19830 - 25124)	_*	22254 (19830 - 2512
Uterine cancer	1302 (1150- 1498)	0	0	36	372	894	_*	1302 (1150-1498)	20413 (18083 - 23213)	_*	20413 (18083 - 232)
Prostate cancer	7355 (6272-10646)	0	0	17	834	6504	7355 (6272-10647)	_*	81883 (69432 – 126246)	81883 (69432 - 126246)	_*
Colon and rectum cancers	15984 (14712– 17503)	0	0	478	3902	11604	9285 (8265–10452)	6699 (6055– 7413)	238137 (218235 – 260846)	146021 (129190 – 164924)	92116 (83589 – 1018
Lip and oral cavity cancer	1440 (1310 - 1571)	0	0	99	592	749	1003 (881 – 1138)	437 (392 – 485)	28435 (25611 - 31499)	21598 (18775 - 24607)	6837 (6137 - 7619)
Nasopharynx cancer	448 (406 – 498)	0	1	43	184	220	385 (343 - 437)	63 (56 – 70)	9445 (8471 - 10642)	8021 (7066 - 9229)	1424 (1270 - 1600)
Other pharynx cancer	853 (767 – 940)	0	0	79	530	244	735 (649 – 818)	118 (105 – 133)	21305 (19062 - 23523)	18442 (16222 - 20712)	2863 (2527 - 3245)
Gallbladder and biliary tract cancer	1785 (1650 – 1950)	0	0	40	392	1353	804 (700 – 927)	981 (891–1081)	25262 (23251 - 27979) 110425 (100077 -	12582 (10930 - 14735)	12680 (11514 - 1396
Pancreatic cancer	6466 (5888 –7018)	0	0	262	2062	4142	3296 (2898 – 3690)	3170 (2837 –3549)	120330)	62715 (54992 - 70718)	47710 (42492 - 5317
Malignant skin melanoma	1150 (926 -1302)	0	0	152	362	636	608 (484 – 702)	542 (365 – 664)	23403 (18766- 27036)	13263 (10454- 15513)	10140 (6742- 1269
Non-melanoma skin cancer	856 (791 – 934)	0	0	21	129	706	572 (520 – 636)	284 (246 – 327)	10004 (9180 - 11017)	7733 (6961 - 8676)	2271 (1990 - 2575)
Ovarian cancer Testicular cancer	2225 (1884 – 2588) 50 (42 – 60)	0	0	183 21	833 10	1209 19	-* 50 (42 – 60)	2225 (1884 – 2588)	43789 (37015 - 51048) 1554 (1241 - 1917)	_* 1554 (1241 - 1917)	43789 (37015 - 5104 -*
Kidney cancer	2427 (2171 – 2686)	4	4	123	736	1560	1630 (1407 – 1848)	797 (710 – 889)	42225 (37632 - 46841)	29692 (25557 - 34079)	12533 (11141 - 1390
Bladder cancer	5764 (5240 - 6341)	0	0	62	1094	4608	4692 (4173 – 5225)	1072 (925 – 1236)	75488 (68381 - 82990)	63853 (57027 - 71119)	11635 (10159 - 1320
Brain and nervous system cancer	2901 (2100 – 3272)	15	37	414	1239	1196	1632 (1119- 1999)	1269 (776- 1457)	71638 (57056 – 86826)	41854 (31116 - 55594)	29784 (20561 - 3389
Thyroid cancer	358 (323 – 399)	0	0	21	104	233	160 (135 – 188)	198 (174 – 227)	6146 (5555 - 6864)	3034 (2544 - 3639)	3112 (2712 - 3545
Hodgkin lymphoma	240 (220 - 269)	0	1	49	79	111	148 (131 - 183)	92 (78- 105)	5931 (5448 - 6856)	3880 (3390-4807)	2051 (1786- 2298)
Non-Hodgkin lymphoma	3166 (2776 - 4151)	4	11	222	836	2093	1726 (1430-2707)	1440 (1248- 1720)	56051 (48536 - 74892)	33186 (27057 - 52313)	22865 (20017 - 2762
Multiple myeloma	2003 (1727 - 2522)	0	0	48	493	1462	1033 (774 - 1352)	970 (804 - 1321)	30284 (26051 - 39158)	16513 (12647 - 22621)	13771 (11343 - 1913
Leukemia	4284 (3961 – 4615)	20	47	281	966	2970	2508 (2230 – 2779)	1776 (1593 – 1978)	74753 (68523 - 80659)	45273 (39534 - 50408)	29480 (26642 - 327)
Other neoplasms	5676 (5039 – 6237)	26	47	433	1259	3911	2840 (2344 - 3230)	2836 (2520 – 3167)	98152 (87089 – 107151)	52918 (44267 - 59822)	45234 (40830 - 497
Cardiovascular diseases	126864 (120400 – 133080)	27	19	2524	13383	110911	57590 (54124 – 61532)	69274 (64966 – 73804)	1349501 (1280088 – 1418083)	762167 (710602 – 819982)	587334 (548966 - 627598)
Rheumatic heart disease	2507 (2236 - 2760)	0	1	47	322	2137	896 (792 – 1013)	1611 (1388 – 1836)	29131 (26133 - 32384)	11605 (10317 - 13256)	17526 (15271 - 200
Ischemic heart disease	60983 (57094 – 65803)	0	1	1361	7292	52329	30220 (27942 – 32757)	30763 (28042 – 33985)	668369 (626032 – 712494)	415574 (383372 – 449507)	252795 (230573 - 277443)
Cerebrovascular disease	29646 (26209— 33330)	7	7	489	2559	26584	12858 (11374 – 14487)	16788 (14360 – 19516)	299838 (271681 – 329403)	155449 (139680 – 173001)	144389 (126464 - 163784)
Hypertensive heart disease	4883 (2003 – 6751)	0	1	42	297	4543	1473 (656 – 1922)	3410 (1135 – 5065)	42363 (22522 - 54116)	16467 (9652 - 24542)	25896 (9981 - 3725
Cardiomyopathy and myocarditis	5583 (3622 - 6621)	10	5	212	779	4577	2621 (1432 – 3240)	2962 (1941 – 3615)	68332 (46236 - 79108)	41942 (25736 - 50227)	26390 (18194 - 316
Atrial fibrillation and flutter	6393 (4962 – 8162)	0	0	11	178	6204	2194 (1651 –2842)	4199 (3205 – 5366)	50810 (39610 - 64019)	19964 (15454 - 25520)	30846 (23646 - 391
Aortic aneurysm	2760 (2519 - 3036)	0	0	67	519	2174	1911 (1681 – 2167)	849 (746 – 959)	37085 (33621 - 40832)	28317 (25043 - 32063)	8768 (7704 - 9961
Peripheral artery disease	1718 (1006 – 2495)	0	0	4	106	1608	771 (446 – 1038)	947 (383 – 1697)	14877 (9431 - 21656)	8216 (5212 - 11670)	6661 (2735 - 1242)
Endocarditis	2083 (1606 – 3013)	2	1	66	285	1729	715 (552 – 1126)	1368 (903 – 2122)	25893 (20955 - 38151)	11410 (8975 - 18497)	14483 (10173 - 236)
Other cardiovascular and circulatory diseases	10309 (9361 – 11354)	7	4	226	1046	9026	3932 (3479 – 4415)	6377 (5546 – 7296)	112803 (103458	53223 (47355	59580 (52299
and the same of the sam	(		151	2,000				(	- 123697)	- 59746)	- 67248)

# Table 1 (Continued)

Control   Cont												
Personal Processor   1965	Chronic respiratory diseases		3	6	245	2591	30579		14278 (12907 – 15678)			
Second   Properties   Propert	Chronic obstructive pulmonary disease	28945 (26786 -	1	1	152	1999	26792	17026 (15484 -	11919 (10573 – 13455)	268928 (250339 -	177872 (160710 -	
March   1997   1998			0	0	2	20	240					
Control of the cont				2								
Control control and control			- 0	2								
Content and contained contained and contai			1	2								
Communication flowers for a few part with a communication of the communication flowers and the segment at the signature of the communication flowers and the segment at the signature of the communication of the communi			2							159350 (145749-	114370 (101247-	
Control and includes best about 1   1711												
Center and efficiency for contents for contents for contents of				0								
Control and that chemis but disness de solutions   15 (141 - 159)   2   2   2   2   3   3   3   3   3   3												
			-	-								
Page   1867   1879		12847 (10313 -								140553 (116593-	1	· · · · · · · · · · · · · · · · · · ·
Communication devolution												
Public bits of missent personal perso												
Penthis plane infected debendered   \$400 (1985) 200   \$   \$   \$   \$   \$   \$   \$   \$   \$												
Pages   Page	Appendicus  Pombatic ilore and intestinal abstraction			1								
Information bereficied (2006-23)				1								
Marche content desiration   1916/209-1079   1				_								
Company   Comp			- 0									
Processing   148   118 - 118   2			1									
Company   Comp			-	-								
Marcingroal devoletes				1								7428 (6072 9626)
Second color of the color of	Other digestive diseases			1								
Post	Neurological disorders	72186)	34	19	344	2334	61233	24500)	42535 (36970 – 48083)	596722)	235350)	365328)
Part	Alzheimer's disease and other dementias		0	0	34	1234	55830		39379 (34033 – 45008)			
Mary	Parkinson's disease		0	0	8	220	4135		1961 (1467 – 2612)			
Minisple selection		452 (405 - 515)	8	7	83	95	259	227 (197 – 268)	225 (196- 259)	10399 (9313 - 12013)	5899 (5116 - 7033)	4500 (3966 - 5257)
Manual malamane we denote   199 (113-148)   0   0   0   0   0   0   0   0   0		215 (166 - 280)	0	0	47	111	57	91 (72 - 125)		5932 (4517 - 7587)	2533 (2003 - 3431)	3399 (2351 - 4419)
Part	Other neurological disorders	931 (798 - 1034)	21	10	110	289	501	506 (389 - 592)	425 (374 - 481)	21206 (17710 - 23790)	12508 (9326 - 14655)	8698 (7684 - 9816)
Page	Mental and substance use disorders	1299 (1153 - 1436)	0	0	591	334	374	958 (818- 1082)	341 (304 - 377)	41900 (35998 - 46875)	33499 (27761 - 38398)	8401 (7380 - 9411)
Part	Alcohol use disorders	399 (355 - 448)	0	0	89	197	113	338 (293 - 386)	61 (55 - 69)	10952 (9651 - 12380)	9246 (7916 - 10616)	1706 (1514 - 1926)
Diabetes uniform of the series   1708 (25500-28911)   52   30   409   2277   2440   11755 (10864- 12702)   15455 (1075-1083)   278785 (26506- 1 1997) (27788- 11595)   15959 (12778-	Drug use disorders	896 (766-1008)	0	0	499	137	260	620 (493-721)	276 (241-310)	30749 (25415 - 35204)	24230 (18962 - 28522)	6519 (5587 - 7427)
Part	Eating disorders	4 (3 - 5)	0	0	4	0	0	0 (0 - 1)	4 (3 - 4)	198 (156 - 243)	22 (16 - 28)	176 (135 - 220)
Property of the Composition of	Diabetes, urogenital, blood, and endocrine diseases	27208 (25500- 28911)	52	30	409	2277	24440		15453 (14075 - 16833)			
Chronic kidney diseases   1000 (1998-1153)   4   3   11   700   9882   4992 (4375-5314)   5708 (5116-5385)   9942 (9245-10527)   222 (4270-5077)   4722 (4270-5077)	Diabetes mellitus	9176 (8331 - 10111)	1	1	86	864	8224	3791 (3293-4314)	5385 (4637-6154)	94132 (85610 - 103625)	47071 (40666 - 53913)	47061 (40557 - 54319)
Property	Acute glomerulonephritis	7 (6 - 8)	0	1	2	1	3	4 (4 - 5)	3 (3 - 3)	224 (209 - 241)	120 (108 - 134)	104 (97 - 112)
Marcolabinesing   Marcolabin	Chronic kidney diseases	10700 (9908- 11533)	4	3	111	700	9882	4992 (4517-5514)	5708 (5119-6358)	99423 (92645 - 106527)	52202 (47310 - 57571)	47221 (42720 - 52077)
Hemoglobinopathies and Inemolyte ammules   1018 (828 - 1318)   2	Urinary diseases and male infertility	4244 (3843 - 4708)	3	1	29	214	3997	1727 (1526- 1957)	2517 (2176- 2910)	36872 (33821 - 40418)	16406 (14602 - 18410)	20466 (17972 - 23322)
Endocrinc, metholic, blood, and immune disorders   2043 (986-2416)   42   22   149   402   1428   889 (471-1044)   1714 (420-1451)   36334 (20241-4201)   1836 (1185-22211)   17804 (758-21148)   1840 (129-1377)   1840 (129-1377)   17804 (758-21148)   1840 (129-1377)   1840 (129-13	Gynecological diseases	21 (10 - 27)	0	0	2	4	15	_*	21 (10 - 27)	346 (178 - 435)	_*	346 (178 - 435)
Endocrine, metabolic, blood, and immune disorders   2043 (956-2416)   42   22   149   402   1428   809 (471-1034)   1714 (420-1451)   36334 (20241-4200)   1850 (1155-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22231)   1780 (1755-22331)   1780 (175	Hemoglobinopathies and hemolytic anemias	1018 (828 - 1318)	2	3	29	93	891	372 (321 - 451)	646 (476 - 968)	11047 (9645 - 15509)	4811 (4167 - 6168)	6236 (5093 - 10617)
Miscokeleal disorders   1064 (291-177)   0		2043 (956 - 2416)	42	22	149	402	1428	869 (471 - 1034)	1174 (420 - 1451)	36334 (20241 - 42401)	18530 (11555 - 22231)	17804 (7538 - 21483)
Remainded arthritis	Musculoskeletal disorders		0	1	33	135	895	307 (259- 382)		12775 (11197 - 16860)	3986 (3373 - 5433)	8789 (7432 - 12481)
Other muscuokscleat disorders   76 (1888-89)   0   0   27   76   658   218 (162-26)   43 (395-634)   8500 (6319-1062)   0221 (1963-3397)   8579 (1327-7327)	Rheumatoid arthritis	303 (246- 494)	0	0	7	59	237	89 (69 - 144)	214 (164- 370)	4276 (3516 - 6836)	1366 (1032 - 2098)	
Differ non-communicable diseases   2236 (1588-3065)   416   40   171   241   1368   931 (638-1365)   1305 (716-1980)   64841 (22938-80612)   33165 (2891-42643)   3105 (24983-4196)   246 (1688-12648)   246 (1891-1264)   246 (18		761 (585- 891)	0	0	27		658	218 (162-262)	543 (395-684)	8500 (6519 - 10621)	2621 (1963 - 3397)	5879 (4152 - 7527)
Skin and subcutaneous diseases   1503 (784 - 12289)   2	Other non-communicable diseases	2236 (1538-3065)	416	40	171	241	1368	931 (638- 1363)	1305 (716- 1980)	64841 (52938 - 80612)	33146 (25801 - 42643)	
Marie   Mari	Congenital birth defects	689 (553 - 870)	369	39	150	131	0	365 (273 - 477)	324 (250 - 425)	46265 (36301 - 58770)	24560 (18054 - 32640)	21705 (16588 - 28648)
Marie   Mari				1								
Page				0								
Transport injuries		15052 (13902 -		115				<u> </u>	1	368761 (339861 -	268709 (242021 -	100052 (91969 -
Road injuries 2632 (2415-2891) 24 49 1137 667 755 1933 (1723-2158) 699 (625-788) 29903 (82785 - 101785) 7136 (61605 - 80703) 21567 (19371 - 24276) (19371 - 24	Transport injuries		25	53	1241	756	828	2162 (1938- 2402)	741 (662- 833)	101998 (91308 -		
Chimtentional injuries   Continuent of the	procedura de contrata de contr	DESCRIPTION OF THE RESIDENCE	1000	6900	10.0000014	860780	27(932)23	Surfer Day Color of Colors	AN ANY ANDRONE CONVOCA			POST-STATE CONTROL POST STATE OF THE STATE O
Substitute												
Falls		8057 (7312 - 9870)	68	50	804	1240	5895	4228 (3799 - 5115)	3829 (3334 - 5053)		86590 (77581 – 100485)	44743 (40289 - 55026)
Drowning   454 (418 - 49)   15   14   139   148   138   354 (321 - 391)   100 (90 - 111)   15184 (13779 - 16590)   12153 (10819 - 13509)   3031 (2703 - 3432)   19   19   1715 - 242   151 (116 - 203)   6511 (5725 - 7715)   4347 (370 - 5369)   2164 (1806 - 3665)   18   18   18   18   18   18   18   1	Falls	4083 (3568 - 5886)	8	9	261	534	3271	2066 (1768 - 2952)	2017 (1668 - 3205)		35248 (30587 - 48038)	19441 (16686 - 27950)
Fire, heat, and hot substances   350 (296 - 149)   5   3   44   59   239   199 (173 - 242)   151 (116 - 203)   6511 (5725 - 7715)   4347 (3730 - 5369)   2164 (1806 - 3063)			- 0	-								
Poisonings   79 (67 - 136)   1   2   23   19   34   45 (35 - 90)   34 (27 - 54)   2277 (1863 - 4399)   1457 (1048 - 3190)   820 (633 - 1451)												
Exposure to mechanical forces 354 (314 - 446) 6 7 95 87 159 222 (169 - 267) 132 (106 - 202) 9637 (7682) 7203 (5315) 2434 (2082 - 3082) 14170 (10880 - 2255) 786 (5513 - 14649) 6274 (4082 - 3082) 14170 (10880 - 2255) 786 (5513 - 14649) 6274 (4094 - 10204) 14170 (10880 - 2255) 786 (5513 - 14649) 6274 (4094 - 10204) 14170 (10880 - 2255) 14170 (108			1									
Adverse effects of medical treatment 1009 (735 - 1655) 5 3 55 152 794 461 (309 - 865) 548 (397 - 954) 14170 (10880 - 22655) 786 (5513 - 14649) 6274 (4094 - 10204) 1470 (10880 - 10205) 1470 (10880 -			6	7					1	9637 (7682	7203 (5315	2434 (2082
Animal contact 31 (25 -46) 0 1 7 11 12 22 (16 -36) 9 (8 -11) 866 (666 -1224) 630 (412 -991) 236 (204 -310) Other unimentional injuries 57 (50 -64) 1 2 30 13 11 49 (43 -56) 8 (7 -9) 2230 (1927 -2550) 2028 (173 - 2348) 202 (178 -228) Self-ham and interpersonal violence 4087 (3469 -4887) 6 12 1712 1304 1053 3092 (2501 -3903) 995 (902 -1102) 135228 (117678 - 177150) 103097 (86101 -146895) 3213 (28790 -36088) Self-ham and interpersonal violence 4087 (3469 -4887) 0 6 1546 1217 992 2890 (2313 -3757) 871 (778 -971) 122521 (105138 - 182		2000 0000000 0000000	-	2	55	150	704	100000000000000000000000000000000000000				
Other unintentional injuries         57 (50-64)         1         2         30         13         11         49 (43-56)         8 (7-9)         2230 (1927-2550)         2028 (1732-2348)         202 (178-228)           Self-harm and interpersonal violence         4087 (3469-4887)         6         12         1712         1304         1053         3092 (2501-3903)         995 (902-1102)         135228 (117678 – 177150)         103097 (86101 - 146895)         32131 (28790 - 36058)           Self-harm         3761 (3194-4625)         0         6         1546         1217         992         2890 (2313-3757)         871 (778-971)         122521 (105138 – 167886)         94884 (78421 - 140290)         27637 (24489 - 31215)				3								
Self-harm and interpersonal violence         4087 (3469-4887)         6         12         1712         1304         1053         3092 (2501-3903)         995 (902-1102)         135228 (117678-177150)         103097 (86101-146895)         32131 (28790-36058)           Self-harm         3761 (3194-4625)         0         6         1546         1217         992         2890 (2313-3757)         871 (778-971)         122521 (105138-167886)         94884 (78421-140290)         27637 (24489-31215)			0	1								
Self-harm and interpersonal violence 408 / (3409-488) 6 12 1/12 1.904 1055 3092 (2201-3903) 995 (902-1102) 1771.50 103097 (86101-140895) 32131 (28790-36088) 1 1771.50 103097 (86101-140895) 32131 (28790-36088) 1 1771.50 103097 (86101-140895) 1 1771.50 103	Oiner unimentional injuries	37 (30-64)	1	2	30	13	- 11	49 (43- 36)	8 (7-9)		2028 (1/32 - 2348)	202 (178 - 228)
Self-harm 3761 (3194-4625) 0 6 1546 1217 992 2890 (2313-3757) 871 (778-971) 122521 (105138 - 167886) 94884 (78421 - 140290) 27637 (24489 - 31215)	Self-harm and interpersonal violence	4087 (3469- 4887)	6	12	1712	1304	1053	3092 (2501- 3903)	995 (902-1102)		103097 (86101 - 146895)	32131 (28790 - 36058)
	Self-harm	3761 (3194- 4625)	0	6	1546	1217	992	2890 (2313- 3757)	871 (778- 971)	122521 (105138 -	94884 (78421 – 140290)	27637 (24489 - 31215)
	Interpersonal violence	326 (194 - 396)	6	6	167	86	61	202 (99- 278)	124 (66 - 155)		8213 (4131 - 11652)	4494 (2428 - 5744)



**Figure 1.** Age- and sex-pyramid of the Spanish population (millions) in 1990, 2006 and 2016.

with a highly positive annual increase of 2.6%; 3. stroke with 7.1% (6.3-7.9%) of all deaths and with an annual change of -1.6%; 4. COPD with 6.9% (6.5-7.4%) of all deaths and with an annual change of 1.1%; and 5. lung cancer (5.0% (4.7-5.3%)) of all deaths and with an annual change of 0.6%. Diseases are also represented as YLDs (Fig. 2b), and as DALYs (Fig. 2c), where % change is shown in for both measures too.

Changes in ranking of causes of death from 1990 to 2006 to 2016 for both age-standardised and all ages are explored in Fig. 3, where no changes were observed in the top five causes of deaths per 100,000 rates since 1990 as IHD, stroke, Alzheimer disease, COPD and lung cancer, except from a switch of positions in 2006 in Alzheimer disease per stroke. The most remarkable increase in ranking was atrial fibrillation (from 1990 to 2016), pancreatic cancer, and Parkinson's disease. Remarkable increases in the ranking of causes of death were also observed in other cancers, lower respiratory infections, chronic kidney disease (CKD), and other CVD, among others. The main communicable cause of death, lower respiratory tract infection moved up in this ranking from 10th to 7th already from 2006, and CKD disease climbed to the top ten causes of death, from 11th to 8th. On the opposite trend, road injuries moved down from position 8th to 32nd, and diabetes from 6th to 10th

As compared to crude deaths, YLD and DALYS show a very different picture of the disease burden. Change in trends in YLDs and DALYs from 1990 to 2006 to 2016 are also presented in Figs. 4 and 5. In Fig. 4, it can be seen that low back and neck pain remained the number one cause of YLDs in Spain during the entire period, while sense organ diseases overcame migraine as the second most frequent cause of YLDs from 2006. Completing the top 5 causes of YLDs from 1990 to 2016 were in 4th position skin diseases and 5th depressive disorders. It can be seen in Fig. 5 that low back and neck pain became the number one cause of DALYs in Spain from 2006, just surpassing IHD in the ranking, while Alzheimer disease moved from 9th to 3rd position. The greatest changes were observed in DALYs for road injuries dropping from 4th to 16th position, and congenital disorders from 17th to 35th; on an opposite trend, oral disorders raised from 25th to 17th.

In Fig. 6, the sex differences in YLD rates per 100,000 for 21 Level 2 causes by age for 2016 are compared. Apart from differences in sex-specific disorders, like prostate or breast cancers, there were no large differences in the distribution of male and female YLDs.

The relationship of global age-standardised YLD rates per 100,000 in 2016 and the annualised rate of change in age-standardised YLD rates for each Level 3 cause, from 2006 to 2016 in Spain for both sexes is presented in Fig. 7. It indicates that the conditions with the largest YLD rates per 100,000 in 2016, such as back and neck disorders, migraine, skin disorders, depression and anxiety increased in burden from 2006, while sense disorders and migraine did not materially change. Other musculoskeletal conditions, and other cancers also increased, although with less YLD burden in 2016. Significant decreases were observed for a number of infectious diseases (leishmaniosis, whooping cough, tuberculosis, diphtheria and other neglected tropical diseases) as well as for epilepsy and road injuries.

Finally, in Fig. 8 DALYs by sex in all ages for Spain in 2016, are compared with Western Europe and the World. While the total number of DALYs was lower for Spain, their overall distribution in Spain mirrors the one of Western Europe by sex, particularly for the low rates of communicable diseases and also injuries in both males and females, which are disproportionally greater globally; also transport injuries in males appear to be much lower in Western Europe and Spain compared with global rates. *Au contraire*, DALYs by sex in Spain due to NCDs appear equally distributed as it happens at the global level.

Risk factors

Standardised rates of DALYs (Level 3) attributable to major risk factors in Spain in 2016 are shown in Fig. 9. Overall, smoking is the most relevant risk factor in Spain contributing to 2363.96 (2161.83–2569.73) DALYs per 100,000, mostly due to cancer, CVD and then chronic respiratory diseases. Next in the ranking of risk factors were high blood pressure, high body mass index (BMI), alcohol use, high fasting plasma glucose, high total cholesterol, impaired kidney function, low nuts and seeds, low whole grains and ambient particulate matter. Among the environmental risk factors included in GBD 2016, ambient particulate matter (10th), occupational carcinogens (12th), low physical activity (13th) and occupational, ergonomic risk factors (20th) were among the top 20.

The top risk factors contributing to DALYs in percentage in 2016, by sex are presented in Fig. 10A and B. In Spanish males, smoking continues to be the leading risk factor followed by alcohol and drug use, high-systolic blood pressure and then dietary risks. In females, high BMI comes as the first risk factor, followed by high-systolic blood pressure, dietary risks, high fasting plasma glucose, alcohol and drug use, and tobacco; air pollution appears in the 10th position of risk factors in both genders. In Fig. 11, changes in mortality attributable to major risk factors according to population-level determinants from 1990, 2006 to 2016 were relatively minor, with behavioural and metabolic risk factors dominating the rankings with few changes from 2006 to 2016. Smoking was the number one risk factor in this regard, and high blood pressure was second from 1990 to 2016, while high BMI switched with alcohol from 4th to 3rd cause of DALYs since 2006.

Finally, Fig. 12 shows several estimators of smoking in Spain. Historically, the percentage of daily smokers declined from 1980 to 2016, with a higher decline in men (from 41% to 26%) than in women (from 21% to 17%), in whom there is an apparent stagnation from 2005 onwards. Interestingly, in 2015 the prevalence of daily smoking is higher in men than in women in all ages, except the younger. Namely, for adolescents they are nearly even: 19% (95%UI: 13–28%) in young females and 18% (95%UI: 12–26%) in young males. And most worryingly, smoking prevalence in children (10-14years) is already higher in girls 4.5% (2.5–7.7%) than in boys 2.6% (1.4–4.4%).

# Sustainable Development Goals

In 2016, Spain scored 74.3 (UI 67.9-81.3) of 100 points in the SDG index classification, ranking 23rd globally,<sup>33</sup> and with a significant decline from its 7th position in 2015.<sup>32</sup> From 2016 a further (but slow) increase to 80.3 points (70.5-86.7) in 2030 is projected (Fig. 13). An analysis of the components of the SDG index in Spain based upon GBD 2016 (Fig. 14) indicates that the main national drivers of detrimental health in SDGs were alcohol consumption, as measured by the health indicator summary exposure value (SEV) for alcohol use, with only 10.1 (UI 0.0-34.9) points out of 100; 24.9 (UI 20.2.-29.5) points for smoking (age-standardised prevalence of daily smoking among those aged 10 years and older); and 35.7 (UI 19.6–31.2) points for child obesity (prevalence of overweight among children 2 to 4 years). Further, with a score of 48.9 (UI 39.7-59.0), sexual violence in adults 18-29 yrs who experienced sexual violence by age 18 did not pass. Finally, the rate per 1000 of reported new HIV infections, with 51.0 (UI 44.3-58.7) points, was borderline no-pass. Historically, the health indicators of Spain in the SDG index have had upward trends, increasing from 51.8 points (48.6–54.1) in 1990 to the current estimate of 74.3 points (67.9–81.3). In spite of this increases, it is projected that in 2030 alcohol use with 21 (UI 0.0-54.6) points, child overweight with 28 points (UI 0.0–55.7), smoking prevalence with 36 (UI 27.3–44.1)

Stocke	Leading causes 1990			Mean % change number of Deaths 1990-2006	Mean % change all-age Death rate 1990-2006	Mean % change age- standardized Death rate 1990-2006		Leading causes 2016	Mean % change number of Deaths 2006-2016	Mean % change all-age Death rate 2006-2016	Mean % change age- standardized Death rate 2006-2016
Schemen   1,9% 1,97 to 1,47	1 Ischemic heart disease		1 Ischemic heart disease	-6.6% (-10.4 to -2.3%)	-18.1% (-21.4 to -14.4%)	-41.3% (-43.5 to -38.9%)	<del> </del>	1 Ischemic heart disease	-2.9% (-8.6 to 3.1%)	-7.3% (-12.8 to -1.5%)	-29.6% (-33.7 to -25.1%)
## 4.0PD ## 4.0PD ## 4.0PD ## 4.0PD ## 4.0PD ## 1.5% (+17.9 to -5.0%) ## 4.0PD ## 1.5% (+17.9 to -5.0%) ## 5.5 Lung canner ## 5.5% (+2.20 to 5.0%) ## 5.5% (+2.20	2 Stroke		2 Alzheimer disease	76.0% (65.5 to 88.5%)	54.2% (45.1 to 65.2%)	-0.7% (-6.3 to 5.2%)		2 Alzheimer disease	33.6% (22.1 to 45.3%)	27.5% (16.6 to 38.7%)	-8.9% (-16.2 to -1.6%)
Stung cancer   96.4% (27.0 to 56.9%)   1.96% (11.3 to 27.9%)   2.1% (4.5.9 to 8.9%)   2.1% (4.5.9 to 8.9%)   1.0% (6.5 to 13.7%)	3 Alzheimer disease		3 Stroke	-19.4% (-24.7 to -14.1%)	-29.4% (-34.0 to -24.7%)	-49.8% (-52.8 to -46.7%)		3 Stroke	-1.3% (-10.7 to 8.6%)	-5.7% (-14.8 to 3.6%)	-28.9% (-35.4 to -22.5%)
Colorectal cancer	4 COPD		4 COPD	42.8% (32.1 to 53.6%)	25.2% (15.8 to 34.6%)	-11.5% (-17.9 to -5.0%)	<del> </del>	4 COPD	11.9% (3.8 to 20.2%)	6.8% (-0.9 to 14.8%)	-20.1% (-25.7 to -14.1%)
Tower respiratory infect   South (2.20 to 50.8%)   18.6% (6.9 to 32.2%)   1.15 (5.5 to 9.8%)   7.00 (1.72 to 4.8%)   7.6% (1.72 to	5 Lung cancer		5 Lung cancer	36.4% (27.0 to 45.6%)	19.6% (11.3 to 27.6%)	2.1% (-4.5 to 8.9%)		5 Lung cancer	1.5% (-6.7 to 10.9%)	-3.1% (-10.9 to 5.8%)	-15.9% (-22.5 to -8.5%)
Blackers   Stompton (according disease   2.0% (13.0 3.0%)   3.0% (13	6 Diabetes		6 Colorectal cancer	62.9% (53.7 to 72.5%)	42.8% (34.7 to 51.2%)	11.9% (5.6 to 18.1%)	<del> </del>	6 Colorectal cancer	12.9% (3.4 to 24.1%)	7.8% (-1.3 to 18.4%)	-10.8% (-18.6 to -2.0%)
9 Strench cancer 10 Cower registratory infact 11 Chronic kidney disease 12 Chronic kidney disease 13 Other cardiovascular 11 Stomach cancer 13 Other cardiovascular 11 Stomach cancer 14 Strench cardiovascular 12 Strench cancer 15 Strench cancer 16 Strench cancer 16 Strench cancer 17 Strench cancer 18 Strench cancer 19	7 Colorectal cancer		7 Lower respiratory infect	35.4% (22.0 to 50.8%)	18.6% (6.9 to 32.2%)	-18.1% (-25.7 to -9.8%)	<del> </del>	7 Lower respiratory infect	12.7% (-2.8 to 30.4%)	7.6% (-7.2 to 24.5%)	-20.2% (-30.1 to -8.7%)
10 Other cardiovascular   10 Other cardiovascular   15.0% (c.0.0.1 to 2.4%)   14.3% (c.5.1.5 to 2.4%)   14.0% (c.5.1.5 to 2.3%)   17.0% (c.0.0.1 to 10.0.5%)   2.5% (c.0.0.1 to 2.5%)   2.5% (c.0.	8 Road injuries		8 Diabetes	1.7% (-5.5 to 9.0%)	-10.9% (-17.2 to -4.4%)	-35.1% (-39.3 to -30.8%)	人	8 Chronic kidney disease	28.8% (18.5 to 40.0%)	23.0% (13.1 to 33.6%)	-9.6% (-16.5 to -2.1%)
11 Stomack cancer 1.52% (20.3 to 9.6%) 2.55% (20.1 to 1-20.8%) 4.1.0% (44.5 to 9.73%) 11 Prestate cancer 1.57% (3.9 to 15.6%) 4.5% (4.1 to 3.8%) 12 Common cancer 1.57% (3.9 to 15.6%) 12 Stomack cancer 2.534% (42.9 to 6.5.9%) 16.5% (5.6 to 17.1%) 1.35% (2.2 to 1.6.7%) 15 Beast cancer 7.1% (3.9 to 16.4%) 2.2% (62.2 to 1.5.0%) 15 Brostate cancer 7.1% (3.9 to 16.4%) 2.2% (62.2 to 1.5.0%) 15 Beast cancer 7.1% (3.9 to 16.4%) 2.2% (62.2 to 1.5.0%) 15 Brostate cancer 7.1% (3.9 to 16.4%) 2.2% (62.2 to 15.0%) 15 Brostate cancer 7.1% (3.9 to 16.4%) 2.2% (62.2 to 15.0%) 15 Brostate cancer 7.1% (3.9 to 16.4%) 2.2% (62.2 to 15.0%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 2.2% (62.2 to 15.0%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 2.2% (62.2 to 15.0%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 2.2% (62.2 to 15.0%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 1.5% (6.1 to 2.7%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 1.5% (6.1 to 2.7%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 1.5% (6.1 to 2.7%) 1.5% (6.1 to 2.7%) 15 Brostate cancer 1.5% (3.9 to 16.4%) 1.5% (6.1 to 2.7%) 1.	9 Stomach cancer		9 Chronic kidney disease	22.0% (13.9 to 30.8%)	6.9% (-0.2 to 14.6%)	-25.4% (-30.3 to -20.5%)		9 Other cardiovascular	24.9% (12.4 to 39.1%)	19.2% (7.3 to 32.8%)	-8.8% (-17.3 to 0.8%)
12 Dene cardiovascular 12 Breast cancer 10,7% (3,3 to 10,0%) 4.0% (24,0 to 4,3%) 15 prostate cancer 22,0% (62,2 to 16,7%) 16 prostate cancer 32,0% (18,2 to 68,5%) 16,8% (3,6 to 97,7%) 16,9% (22,7 to 1,7%) 17,9% (22,7 to 1,7%) 17,9% (22,7 to 1,7%) 17,9% (23,1 to 1,2%) 18 prostate cancer 22,2% (10,4 to 3,3%) 16,5% (22,0 to 1,3%) 19 prostate cancer 32,5% (42,2 to 1,6,3%) 34,5% (22,2 to 4,3%) 10,1% (2,8 to 1,7,5%) 14 Pancreatic cancer 21,2% (10,4 to 3,3%) 15,7% (6,4 to 2,7,%) 16,6% (6,5 to 3,0,7,%) 16,6% (6,5 to 3,0,7,%) 16,6% (6,5 to 3,0,7,%) 16,6% (6,5 to 3,0,7,%) 17,1% (23,0 to 1,4,7,%) 17,1% (23,0 to 1,4,7,4,1,4,4,1,4,1	10 Lower respiratory infect		10 Other cardiovascular	30.4% (20.4 to 41.8%)	14.3% (5.5 to 24.2%)	-18.6% (-24.7 to -11.9%)		10 Diabetes	-1.0% (-10.8 to 10.2%)	-5.4% (-14.9 to 5.2%)	-27.6% (-34.9 to -19.7%)
13 Crimosis alcohol 18 Prostate cancer 22.9% (18.2 to 56.5%) 16.5% (3.6 to 37.1%) -13.6% (22.7 to 1.6%) 14 Pancreatic cancer 53.4% (42.9 to 63.9%) 34.5% (25.2 to 43.7%) 10.1% (2.8 to 17.5%) 14 Pancreatic cancer 21.2% (10.4 to 33.7%) 15.7% (5.4 to 27.7%) 1-1.3% (10.2 to 6.3%) 15 Prostate cancer 34.9% (31.5 to 57.0%) 22.5% (5.6 to 37.6%) 22.5% (6.6 to 77.8%) 15.5% (6.5 to 57.6%) 15 Afrial fibrillation 35.1% (18.4 to 52.2%) 29.0% (13.0 to 45.9%) -7.5% (14.2 to 40.3%) 15 Cardiomyopathy 16 Cardiomyopathy 16 Cardiomyopathy 18 Cardiomy	11 Chronic kidney disease		11 Stomach cancer	-15.2% (-20.3 to -9.6%)	-25.6% (-30.1 to -20.8%)	-41.0% (-44.5 to -37.3%)	}	11 Prostate cancer	18.9% (3.8 to 35.6%)	13.5% (-0.9 to 29.5%)	-9.5% (-21.5 to 3.8%)
14 Pencreatic cancer 15 Prostate	12 Other cardiovascular		12 Breast cancer	10.7% (3.3 to 19.0%)	-3.0% (-9.4 to 4.3%)	-22.0% (-27.0 to -16.7%)		12 Stomach cancer	0.1% (-7.6 to 8.1%)	-4.5% (-11.8 to 3.2%)	-20.4% (-26.2 to -13.7%)
15 Bladder cancer 16 Cardiomyopathy 16 Cirrhosis lackohol 17 Liver cancer 17 Almal fibrillation 18,8% (3.2 to 68,4%) 18 Cirrhosis lackohol 17 Liver cancer 18 Cardiomyopathy 18 Cardiomyopathy 18 Cardiomyopathy 18 Cardiomyopathy 19 Self-harm 10 Self-harm	13 Cirrhosis alcohol		13 Prostate cancer	32.9% (18.2 to 56.5%)	16.5% (3.6 to 37.1%)	-13.6% (-22.7 to 1.6%)		13 Breast cancer	7.1% (-3.9 to 18.4%)	2.2% (-8.2 to 13.0%)	-15.2% (-23.9 to -6.0%)
16 Cardiomyopathy 16 Cirrhosis alcohol 22,6% (-27,6 to -17,6%) 32,2% (-36,6 to -27,8%) 43,8% (-47,4 to -40,3%) 47 Afrial fibrilation 51,8% (-37,2 to 66,4%) 33,0% (-20,3 to 47,6%) 41 Cardiomyopathy 48,6% (-5,6 to 30,5%) 41 Cardiomyopathy 48,6% (-5,6 to 30,5%) 41 Cardiomyopathy 48,6% (-5,6 to 30,5%) 41 Cardiomyopathy 41,6% (-47,7 to -41,2%) 42 Parkinson disease 42,2% (11,6 to 36,2%) 41 Cardiomyopathy 48,6% (-5,6 to 30,5%) 41 Cardiomyopathy 48,6% (-5,6 to 30,5%) 41 Cardiomyopathy 48,6% (-5,6 to 45,5%) 41 Cardiomyopathy 48,6% (-5,6 to 45,5%) 41 Cardiomyopathy 48,6% (-6,6 to -5,1%) 42 Unicardiomyopathy 48,6% (-6,6 to -5,1%) 42 Leukemia 42 Leukemia 43 Safrial fibrilation 44 Parkinson disease 45 Falls 47 Purpetnesive heart disease 49 Phypertensive heart disease 49 Phypertensive heart disease 49 Phypertensive heart disease 49 Vascular intestinal 40 Unicardiomed 40 Unicardio	14 Breast cancer	X/ /	14 Pancreatic cancer	53.4% (42.9 to 63.9%)	34.5% (25.2 to 43.7%)	10.1% (2.8 to 17.5%)		14 Pancreatic cancer	21.2% (10.4 to 33.7%)	15.7% (5.4 to 27.7%)	-1.3% (-10.2 to 8.3%)
17 Liver cancer 18 Other neoplasms 18 Cardiomyopathy 8, 8% (9,3 to 9,3%) 19 Self-harm 19 Road injunes 44,6% (47,7 to 41,2%) 19 Self-harm 19 Road injunes 44,6% (47,7 to 41,2%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 19 Liver cancer 20 Other neoplasms 28,8% (20,7 to 37,6%) 10,9% (5,7 to 20,8%) 11,0% (5,7 to 20,8%) 11,0% (5,7 to 20,8%) 12 Bladder cancer 20 Univer selection of the selection of th	15 Prostate cancer		15 Bladder cancer	43.9% (31.5 to 57.0%)	26.1% (15.3 to 37.6%)	-2.2% (-10.5 to 6.4%)	· /	15 Atrial fibri∎ation	35.1% (18.4 to 52.9%)	29.0% (13.0 to 45.9%)	-7.5% (-18.2 to 4.0%)
18 Cher neoplasms 18 Cher neoplasms 19 Self-harm 19 Fload injunes 4.46,% (47,7 to -41,2%) 5.14,% (54,2 to -48,5%) 19 Fload injunes 4.46,% (47,7 to -41,2%) 5.14,% (54,2 to -48,5%) 19 Fload injunes 4.46,% (47,7 to -41,2%) 5.14,% (54,2 to -48,5%) 19 Fload injunes 4.46,% (47,7 to -41,2%) 19 Fload injunes 11,4% (43,1 to 23,5%) 19 Fload injunes 11,4% (43,1 to 34,3%) 19 Fload injunes 11,4% (43,1 to 34,3%) 10 Fload injunes 12 Fload injunes 12 Fload injunes 13 Fload injunes 14,4% (43,1 to -44,3%) 14	16 Cardiomyopathy		16 Cirrhosis alcohol	-22.6% (-27.6 to -17.6%)	-32.2% (-36.6 to -27.8%)	-43.8% (-47.4 to -40.3%)	1	16 Bladder cancer	16.5% (4.8 to 30.5%)	11.2% (0.0 to 24.6%)	-10.0% (-18.8 to 0.3%)
19 Self-harm 19 Road injuries 44,6% (-47,7 to -41,2%) 20 Pancreatic cancer 20 Other neoplasms 28,6% (20,7 to 37,6%) 21 Liver cancer 21 Bladder cancer 22 Leukemia 22 Leukemia 22 Leukemia 22 Leukemia 23 Self-harm 24 Rheumatic heart disease 24 Parkinson disease 25 Cirrhosis hepatitis C 26 Falls 27 Liver cancer 27 Liver cancer 28 Falls 27 Liver cancer 28 Falls 27 Liver cancer 29 Falls 29 Eypertensive heart disease 21 Sind (-44,0 to 21,5%) 20 Eypertensive heart disease 22 Leukemia 21 Liver cancer 22 Leukemia 22 Leukemia 23 Self-harm 24 Parkinson disease 25 Liver cancer 26 Falls 27 Liver cancer 27 Liver cancer 28 Falls 27 Liver cancer 29 Leukemia 29 Self-harm 20 Liver cancer 20 Liver cancer 20 Chrys (-56,9 to -51,4%) 20 Parkinson disease 20 Chrys (-56,5 to -10,1%) 20 Leukemia 20 Chrys (-56,5 to -10,1%) 21 Liver cancer 22 Leukemia 22 Leukemia 23 Self-harm 24 Parkinson disease 24 Parkinson disease 25 Liver cancer 25 Liver cancer 25 Liver cancer 26 Liver cancer 27 Liver cancer 27 Liver cancer 28 Liver cancer 29 Liver cancer 29 Liver cancer 20 Chrys (-56,9 to -51,4%) 20 Hypertensive heart disease 36,4% (-7, to 64,7%) 30,2% (-2,9 to 57,2%) 21 Liver cancer 29 Liver cancer 29 Liver cancer 20 Chrys (-56,9 to -15,5%) 20 Liver cancer 20 Chrys (-56,10 to -10,5%) 21 Liver cancer 20 Liver cancer 20 Liver cancer 20 Chrys (-56,10 to -10,5%) 22 Leukemia 23 Liver cancer 24 Daylor cancer 25 Liver cancer 25 Liver cancer 25 Liver cancer 26 Liver cancer 26 Liver cancer 27 Liver (-16,5 to -25,7%) 28 Liver cancer 29 Liver cancer 20 Liver	17 Liver cancer	7-2/	17 Atrial fibrilation	51.8% (37.2 to 68.4%)	33.0% (20.3 to 47.6%)	-12.7% (-20.7 to -3.5%)	$\times$	17 Other neoplasms	24.2% (11.6 to 36.2%)	18.6% (6.6 to 30.0%)	-1.9% (-11.9 to 6.8%)
20 Other neoplasms	18 Other neoplasms	$\times/\times$	18 Cardiomyopathy	8.8% (-3.8 to 43.7%)	-4.7% (-15.7 to 26.0%)	-31.7% (-39.9 to -7.8%)	$\vdash$	18 Cardiomyopathy	18.8% (7.0 to 35.8%)	13.4% (2.2 to 29.6%)	-13.2% (-21.6 to 0.1%)
21 Eladder cancer  21 Liver cancer  13.5% (4.3 to 23.5%)  -0.6% (-8.6 to 8.2%)  -18.6% (-25.2 to -11.5%)  22 Leukemia  22 Leukemia  22 Leukemia  23 Self-harm  23 Self-harm  23 Self-harm  24 Parkinson disease  77.2% (6.6.5 to 100.1%)  24 Parkinson disease  77.2% (56.5 to 100.1%)  25 Falls  26 Falls  27 Urinary diseases  27 Urinary diseases  27 Urinary diseases  28 Lymphoma  49.9% (31.8 to 62.7%)  30 Brain cancer  49 Interstitial lung disease  49 Urinary diseases  47 HIV/AIDS  21 Liver cancer  13.5% (4.3 to 23.5%)  -0.6% (-8.6 to 8.2%)  -0.6% (-8.6 to 8.2%)  -1.8% (-25.2 to -11.5%)  21 Liver cancer  13.5% (4.3 to 23.5%)  -0.6% (-8.6 to 8.2%)  -1.8% (-25.2 to -11.5%)  22 Leukemia  22 Leukemia  23 Self-harm  24 Parkinson disease  77.2% (65.6 to 100.1%)  55.3% (37.1 to 75.3%)  9.5% (-2.9 to 22.9%)  25 Falls  27 Living diseases  34.5% (20.1 to 51.0%)  28 Laweria  27.5% (17.7 to 14.4%)  29 Lymphoma  49.9% (31.8 to 62.7%)  30 Brain cancer  31 Interstitial lung disease  32 Road injuries  33 Rineumatic heart disease  49 Urinary diseases  47 HIV/AIDS  21 Cirrhosis alcohol  -6.5% (-14.2 to 13.3%)  -10.7% (-18.1 to -3.3%)  -10.7% (-18.1 to -3.3%)  -10.7% (-18.1 to -13.5%)  -10.7% (-15.0 to 15.6%)  22 Parkinson disease  20.7% (9.7 to 16.6%)  23 Leukemia  77.2% (60.5 to 100.1%)  55.3% (37.1 to 75.3%)  9.5% (-2.9 to 22.9%)  24 Urinary diseases  34.5% (20.1 to 51.0%)  24 Urinary diseases  34.5% (20.1 to 51.0%)  24 Urinary diseases  34.5% (20.1 to 51.0%)  25 Falls  27.5% (17.7 to 41.4%)  27 Vascular intestinal  17.4% (3.1 to 34.0%)  11.4% (-4.0 to 15.5%)  11.4% (-4.0 to 15.5%)  11.4% (-4.0 to 15.5%)  11.4% (-4.0 to 15.5%)  12.5% (-2.4 to 24.5%)  12.5% (-2.4 to 24.5%)  13.8% (-25.2 to 1.1.3%)  24 Urinary diseases  34.5% (20.1 to 51.0%)  25 Falls  27.5% (17.7 to 41.4%)  27 Vascular intestinal  28 Lymphoma  39 Brain cancer  30 Brai	19 Self-harm	77m/	19 Road injuries	-44.6% (-47.7 to -41.2%)	-51.4% (-54.2 to -48.5%)	-54.2% (-56.9 to -51.4%)		19 Liver cancer	17.5% (3.2 to 30.6%)	12.2% (-1.5 to 24.7%)	-2.9% (-15.3 to 8.3%)
22 Leukemia 22 Leukemia 23.0% (15.1 to 31.5%) 7.8% (0.9 to 15.2%) -14.7% (-19.9 to -9.5%) 23 Atrial fibrillation 23 Self-harm 9.4% (-6.6 to 19.0%) -4.1% (-18.2 to 4.3%) -14.9% (-26.7 to -7.3%) 23 Leukemia 7.7% (-0.7 to 16.6%) 2.8% (-5.2 to 11.3%) -14.0% (-21.0 to -7.1%) 24 Rheumatic heart disease 24 Parkinson disease 77.2% (56.5 to 100.1%) 55.3% (37.1 to 75.3%) 9.5% (-2.9 to 22.9%) 25 Cirrhosis hepatitis C 25 Cirrhosis hepatitis C 25 Cirrhosis hepatitis C 26 Falls 27.1% (9.5 to 38.6%) 11.4% (-4.0 to 21.5%) -17.9% (-31.5 to -9.9%) 26 Falls 27.1% (12.2 to 35.0%) 27 Larynx cancer 28 Parkinson disease 151.1% (128.4 to 176.4%) 120.1% (100.1 to 142.3%) 49.9% (37.1 to 63.3%) 28 Lymphoma 29 Hypertensive heart disease 30 Vascular intestinal 90.4% (62.4 to 115.0%) 66.9% (42.3 to 88.4%) 19.5% (36.1 to 33.7%) 29 Interstitial lung disease 30 Vascular intestinal 49 Interstitial lung disease 47 HIV/AIDS 15.0% (100.1 to 142.3%) 41.4% (-20.8 to 21.9%) 30 Parain cancer 46 Larynx	20 Pancreatic cancer		20 Other neoplasms	28.8% (20.7 to 37.6%)	12.9% (5.7 to 20.6%)	-10.8% (-16.3 to -5.1%)		20 Hypertensive heart disease	36.4% (1.7 to 64.7%)	30.2% (-2.9 to 57.2%)	-5.5% (-25.4 to 11.6%)
23 Atrial fibrillation 24 Parkinson disease 25 Cirrhosis hepatitis C 25 Cirrhosis hepatitis C 26 Falls 27.7% (5.5.5 to 10.1%) 26 Falls 27.1% (9.5 to 38.6%) 28 Parkinson disease 28 Parkinson disease 29 Typertensive heart disease 28 Elymphoma 49.9% (37.1 to 63.3%) 29 Hypertensive heart disease 30 Five disease 31.5% (27.5% (17.7 to 41.1%) 20 Falls 20 F	21 Bladder cancer	X	21 Liver cancer	13.5% (4.3 to 23.5%)	-0.6% (-8.6 to 8.2%)	-18.6% (-25.2 to -11.5%)	K /	21 Cirrhosis alcohol	-6.5% (-14.2 to 1.3%)	-10.7% (-18.1 to -3.3%)	-24.4% (-31.0 to -17.6%)
24 Pheumatic heart disease 24 Parkinson disease 77.2% (56.5 to 100.1%) 55.3% (37.1 to 75.3%) 9.5% (-2.9 to 22.9%) 25 Cirrhosis hepatitis C 25 Etypertensive heart disease 76.7% (2.9 to 10.00%) 56.9% (-9.8 to 101.6%) 56.3% (-9.9 to 22.9%) 26 Falls 27.1% (9.5 to 38.6%) 17.1% (-9.5 to 38.6%) 19.1% (-9.5 to 38.6%) 19.1% (-9.5 to 38.6%) 19.1% (-9.5 to 38.6	22 Leukemia	$\leftarrow$	22 Leukemia	23.0% (15.1 to 31.5%)	7.8% (0.9 to 15.2%)	-14.7% (-19.9 to -9.5%)	1-1/	22 Parkinson disease	20.7% (9.5 to 31.9%)	15.2% (4.6 to 25.9%)	-8.1% (-15.9 to -0.3%)
25 Cirrhosis hepatitis C 25 Hypertensive heart disease 76.7% (2.9 to 130.0%) 54.9% (-9.8 to 101.6%) 6.3% (-35.1 to 35.7%) 26 Falls 27 Larynx cancer 26 Falls 27 Urinary diseases 27 Urinary diseases 27 Urinary diseases 28 Hypertensive heart disease 39 Vascular intestinal 49 Interstitial lung disease 47 HIV/AIDS 25 Falls 27.5% (17.7 to 41.4%) 21.7% (12.4 to 35.0%) 21.2% (-16.4 to 1.7%) 22 Earlyn (15.5 to 36.6%) 21.2% (-9.8 to 101.6%) 22 Earlyn (10.0.1 to 142.3%) 24 Earlyn (10.0.1 to 142.3%) 25 Eyphoma 26 Self-harm -1.2% (-16.7 to 11.8%) -5.7% (-20.4 to 6.7%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-24.8 to 17.5%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-1.5 to 27.9%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-1.5 to 27.9%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-1.5 to 27.9%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-1.5 to 27.9%) -1.1.2% (-24.8 to 0.9.4%) -1.1.2% (-1.5 to 27.9%) -1.1.2% (-2.4 to 24.5%) -1.2.2% (-1.5 to 27.9%) -1.2.2% (-1.5 to 27	23 Atrial fibrillation	Y	23 Self-harm	9.4% (-6.6 to 19.0%)	-4.1% (-18.2 to 4.3%)	-14.9% (-26.7 to -7.3%)	1	23 Leukemia	7.7% (-0.7 to 16.6%)	2.8% (-5.2 to 11.3%)	-14.0% (-21.0 to -7.1%)
26 Falls 26 Falls 27.1% (9.5 to 38.6%) 11.4% (-4.0 to 21.5%) -17.9% (-31.5 to -9.9%) 27 Larynx cancer 27 Urinary diseases 151.1% (128.4 to 176.4%) 120.1% (100.1 to 142.3%) 49.9% (37.1 to 63.3%) 27 Vascular intestinal 17.4% (3.1 to 34.0%) 12.1% (-1.5 to 27.9%) 13.6% (-2.4 to 6.7%) -11.2% (-24.8 to 0.9%) 27 Larynx cancer 28 Parkinson disease 28 Lymphoma 49.9% (37.1 to 63.3%) 28 Lymphoma 49.9% (37.1 to 63.3%) 29 Vascular intestinal 90.4% (62.2 to 115.0%) 66.9% (42.3 to 88.4%) 19.5% (3.6 to 33.7%) 29 Interstitial lung disease 30 Parin cancer 30 Parin cance	24 Rheumatic heart disease	1	24 Parkinson disease	77.2% (56.5 to 100.1%)	55.3% (37.1 to 75.3%)	9.5% (-2.9 to 22.9%)		24 Urinary diseases	34.5% (20.1 to 51.0%)	28.4% (14.7 to 44.1%)	-6.4% (-15.8 to 4.2%)
27 Larynx cancer   27 Urinary diseases   151.1% (128.4 to 176.4%)   120.1% (100.1 to 142.3%)   49.9% (37.1 to 63.3%)   27 Vascular intestinal   17.4% (3.1 to 34.0%)   12.1% (-1.5 to 27.9%)   -13.8% (-24.7 to -1.4%)   28 Lymphoma   49.9% (31.8 to 62.7%)   31.4% (15.5 to 42.6%)   51.1% (-5.7 to 13.4%)   28 Lymphoma   11.4% (-0.1 to 23.4%)   6.3% (-4.6 to 17.8%)   -9.7% (-19.6 to 0.2%)   29 Vascular intestinal   90.4% (62.4 to 115.0%)   66.9% (42.3 to 88.4%)   19.5% (3.6 to 33.7%)   29 Hierestitial lung disease   30 Brain cancer   46.6% (1.5 to 63.3%)   28.5% (-11.1 to 43.1%)   10.7% (-20.8 to 21.9%)   30 Brain cancer   31 Interstitial lung disease   33 Interstitial lung disease   34 Cirrhosis hepatitis C   42 Larynx cancer   46 Larynx cancer   46 Larynx cancer   46 Larynx cancer   46 Larynx cancer   47 HIV/AIDS   47 HIV/AIDS   49.9% (37.1 to 63.3%)   49.9% (37.1 to 63.3%)   28.5% (-7.1 to 14.4%)   28 Lymphoma   11.4% (-0.1 to 23.4%)   6.3% (-4.6 to 17.8%)   6.3% (-4.6 to 17	25 Cirrhosis hepatitis C		25 Hypertensive heart disease	76.7% (2.9 to 130.0%)	54.9% (-9.8 to 101.6%)	6.3% (-35.1 to 35.7%)		25 Falls	27.5% (17.7 to 41.4%)	21.7% (12.4 to 35.0%)	-8.2% (-16.4 to 1.7%)
28 Lymphoma	26 Falls		26 Falls	27.1% (9.5 to 38.6%)	11.4% (-4.0 to 21.5%)	-17.9% (-31.5 to -9.9%)		26 Self-harm	-1.2% (-16.7 to 11.8%)	-5.7% (-20.4 to 6.7%)	-11.2% (-24.8 to 0.9%)
29 Hypertensive heart disease 30 HIV/AIDS 30 Brain cancer 31 Lymphoma 31 Lymphoma 32 Rheumatic heart disease 33 Rheumatic heart disease 34 Cirrhosis hepatitis C 42 Urinary disease 49 Interstitial lung disease 40 Interstitial lung disease 41 Interstitial lung disease 42 Interstitial lung disease 43 Interstitial lung disease 44 Interstitial lung disease 45 Interstitial lung disease 46 Interstitial lung disease 46 Interstitial lung disease 47 Interstitial lung disease 48 Interstitial lung disease 49 Interstitial lung disease 40 Interstitial lung disease 41 Interstitial lung disease 42 Interstitial lung disease 43 Interstitial lung disease 44 Interstitial lung disease 45 Interstitial lung disease 46 Interstitial lung disease 47 Interst	27 Larynx cancer	$\times \times 1$	27 Urinary diseases	151.1% (128.4 to 176.4%)	120.1% (100.1 to 142.3%)	49.9% (37.1 to 63.3%)		27 Vascular intestinal	17.4% (3.1 to 34.0%)	12.1% (-1.5 to 27.9%)	-13.8% (-24.7 to -1.4%)
30 HIV/AIDS   30 Brain cancer   46,6% (1,5 to 63,3%)   28,5% (-11,1 to 43,1%)   10,7% (-20,8 to 21,9%)   30 Brain cancer   12,5% (-2,4 to 24,5%)   7,4% (-6,9 to 18,8%)   -4,4% (-17,3 to 5,7%)   31 Lymphoma   32 Rheumatic heart disease   33 Interstitial lung disease   33 Interstitial lung disease   34 Cirrhosis hepatitis C   Legend:   42 Linynx cancer   46 Larynx cancer   46 Larynx cancer   46 Larynx cancer   47 HIV/AIDS   47 HIV/AIDS   48,6% (1,5 to 63,3%)   28,5% (-11,1 to 43,1%)   10,7% (-20,8 to 21,9%)   30 Brain cancer   12,5% (-2,4 to 24,5%)   7,4% (-6,9 to 18,8%)   -4,4% (-17,3 to 5,7%)   32 Rheumatic heart disease   33 Interstitial lung disease   34 Cirrhosis hepatitis C   Legend:   42 Larynx cancer   46 Larynx cancer   47 HIV/AIDS   47 HIV/AIDS   48 HIV/AIDS	28 Parkinson disease	$X \setminus A$	28 Lymphoma	49.9% (31.8 to 62.7%)	31.4% (15.5 to 42.6%)	5.1% (-5.7 to 13.4%)		28 Lymphoma	11.4% (-0.1 to 23.4%)	6.3% (-4.6 to 17.8%)	-9.7% (-19.6 to 0.2%)
31 Lymphoma 32 Rheumatic heart disease 33 Road injuries 34 Brain cancer 33 Interstitial lung disease 33 Rheumatic heart disease 33 Rheumatic heart disease 34 Cirrhosis hepatitis C Legend: 42 Urinary disease 42 Larynx cancer 46 Larynx cancer Communicable, maternal, neonatal and nutritional 49 Interstitial lung disease 47 HIV/AIDS 66 HIV/AIDS Non-communicable	29 Hypertensive heart disease	\\X	29 Vascular intestinal	90.4% (62.4 to 115.0%)	66.9% (42.3 to 88.4%)	19.5% (3.6 to 33.7%)		29 Interstitial lung disease	29.7% (8.0 to 50.3%)	23.8% (3.1 to 43.5%)	0.8% (-15.2 to 16.1%)
34 Brain cancer 39 Vascular intestinal 42 Urinary diseases 49 Interstitial lung disease 33 Interstitial lung disease 33 Rheumatic heart disease 34 Cirrhosis hepatitis C 38 Cirrhosis hepatitis C 20 Communicable, maternal, neonatal and nutritional hon-communicable. 49 Interstitial lung disease 47 HIV/AIDS 48 Communicable 48 Interstitial lung disease	30 HIV/AIDS	XXX	30 Brain cancer	46.6% (1.5 to 63.3%)	28.5% (-11.1 to 43.1%)	10.7% (-20.8 to 21.9%)	$\overline{}$	30 Brain cancer	12.5% (-2.4 to 24.5%)	7.4% (-6.9 to 18.8%)	-4.4% (-17.3 to 5.7%)
39 Vascular intestinal 42 Urinary diseases 42 Urinary diseases 49 Interstitial lung disease 47 HIV/AIDS 42 Cirrhosis hepatitis C 42 Larynx cancer 46 Larynx cancer 46 Larynx cancer 66 HIV/AIDS 48 Cirrhosis hepatitis C 49 Legend: Communicable, maternal, neonatal and nutritional Non-communicable	31 Lymphoma	ATI	32 Rheumatic heart disease	·			/-	32 Road injuries			
42 Urinary diseases 42 Larynx cancer 49 Interstitial lung disease 47 HIV/AIDS 42 Urinary disease 48 Larynx cancer 49 Interstitial lung disease 48 Larynx cancer 49 Interstitial lung disease 47 HIV/AIDS 48 Interstitial lung disease 48 Larynx cancer 66 HIV/AIDS 66 HIV/AIDS 66 Non-communicable	34 Brain cancer	XIV	33 Interstitial lung disease				/	33 Rheumatic heart disease			
49 Interstitial lung disease 47 HIV/AIDS neonatal and nutritional Non-communicable	39 Vascular intestinal		34 Cirrhosis hepatitis C					38 Cirrhosis hepatitis C		Legend:	
The final facility disease 47 mV/ADS 00 mV/ADS Non-communicable	42 Urinary diseases	///	42 Larynx cancer					- 46 Larynx cancer		Communicable, maternal,	
Non-communicable Non-communication	· · · · · · · · · · · · · · · · · · ·							•			
Injuries	ů -									Non-communicable	
										Injuries	

Figure 3. Arrow diagram of causes of death ranks for the top 20 main causes in 1990, 2006 and 2016, and the percentage change between time points.

Non-communicable

Leading causes 1990		Leading causes 2006	Mean % change number of YLDs 1990-2006	Mean % change all-age YLD rate 1990-2006	Mean % change age- standardized YLD rate 1990-2006		Leading causes 2016	Mean % change number of YLDs 2006-2016	Mean % change a <b>ll-</b> age YLD rate 2006-2016	Mean % change age- standardized YLD rate 2006-2016
1 Low back & neck pain		1 Low back & neck pain	21.0% (15.3 to 26.8%)	6.0% (1.1 to 11.2%)	-5.7% (-10.1 to -1.2%)		1 Low back & neck pain	12.1% (6.6 to 17.5%)	7.0% (1.8 to 12.2%)	2.8% (-2.0 to 7.8%)
2 Migraine		2 Sense organ diseases	29.4% (26.0 to 33.0%)	13.4% (10.4 to 16.6%)	-3.8% (-5.8 to -1.7%)	Ī	2 Sense organ diseases	17.2% (14.9 to 19.8%)	11.9% (9.7 to 14.4%)	-0.3% (-2.2 to 1.6%)
3 Sense organ diseases		3 Migraine	19.5% (15.6 to 23.6%)	4.7% (1.3 to 8.4%)	-0.6% (-3.5 to 2.6%)	Ī	3 Migraine	2.3% (-0.9 to 5.3%)	-2.4% (-5.4 to 0.5%)	0.0% (-3.0 to 3.3%)
4 Skin diseases	i	4 Skin diseases	10.7% (8.0 to 13.3%)	-3.0% (-5.3 to -0.7%)	3.9% (1.9 to 5.9%)	Ī	4 Skin diseases	4.3% (2.4 to 6.3%)	-0.4% (-2.2 to 1.5%)	1.3% (-0.5 to 3.1%)
5 Depressive disorders	i	5 Depressive disorders	6.1% (1.0 to 12.1%)	-7.0% (-11.5 to -1.8%)	-13.2% (-18.1 to -8.2%)	Ī	5 Depressive disorders	9.4% (4.3 to 14.8%)	4.4% (-0.5 to 9.6%)	4.3% (0.0 to 9.1%)
6 Anxiety disorders		6 Fa∎s	51.1% (47.4 to 55.1%)	32.4% (29.2 to 36.0%)	17.9% (15.1 to 20.8%)		6 Anxiety disorders	10.4% (3.6 to 17.4%)	5.4% (-1.1 to 12.1%)	5.8% (-0.6 to 12.2%)
7 Falls		7 Anxiety disorders	16.0% (8.9 to 24.4%)	1.7% (-4.6 to 9.0%)	1.3% (-5.0 to 8.5%)		7 Falls	-2.8% (-4.7 to -0.6%)	-7.2% (-9.0 to -5.1%)	-14.2% (-16.0 to -12.3%)
8 Oral disorders		8 Diabetes	30.2% (19.6 to 43.4%)	14.1% (4.8 to 25.7%)	-0.6% (-8.9 to 9.3%)		8 Oral disorders	16.2% (12.7 to 20.8%)	10.9% (7.5 to 15.3%)	3.0% (0.4 to 6.4%)
9 Diabetes		9 Oral disorders	21.8% (17.3 to 26.1%)	6.7% (2.8 to 10.5%)	-4.7% (-7.7 to -2.1%)		9 Diabetes	4.7% (-5.2 to 15.1%)	0.0% (-9.5 to 9.9%)	-10.8% (-19.2 to -2.1%)
10 Other musculoskeletal		10 Other musculoskeletal	3.4% (-8.8 to 17.0%)	-9.4% (-20.1 to 2.5%)	-15.8% (-25.3 to -5.8%)		10 Other musculoskeletal	26.4% (12.8 to 42.8%)	20.6% (7.7 to 36.3%)	17.3% (5.8 to 31.4%)
11 Asthma		11 Road injuries	22.6% (20.2 to 25.0%)	7.5% (5.4 to 9.5%)	-3.8% (-5.7 to -1.9%)		11 Osteoarthritis	16.1% (11.8 to 20.1%)	10.8% (6.7 to 14.6%)	-2.2% (-6.0 to 1.2%)
12 Road injuries		12 Osteoarthritis	41.0% (35.9 to 46.1%)	23.6% (19.1 to 28.1%)	5.7% (1.9 to 9.6%)		12 Alzheimer disease	22.5% (12.9 to 32.2%)	16.9% (7.8 to 26.2%)	-8.5% (-15.4 to -1.8%)
13 Drug use disorders		13 Asthma	5.1% (1.0 to 9.4%)	-7.9% (-11.4 to -4.1%)	-4.4% (-7.9 to -0.5%)		13 Asthma	4.0% (0.0 to 8.0%)	-0.7% (-4.5 to 3.1%)	-1.3% (-5.4 to 2.8%)
14 Osteoarthritis		14 Alzheimer disease	55.9% (45.5 to 67.6%)	36.7% (27.5 to 46.9%)	-3.5% (-9.5 to 3.3%)		14 Schizophrenia	6.1% (-1.8 to 13.7%)	1.3% (-6.3 to 8.6%)	0.4% (-6.7 to 7.9%)
15 Bipolar disorder		15 Drug use disorders	14.1% (2.1 to 27.3%)	0.0% (-10.5 to 11.6%)	-1.9% (-12.1 to 9.7%)		15 Bipolar disorder	1.5% (-3.7 to 6.7%)	-3.1% (-8.1 to 1.9%)	0.2% (-4.7 to 5.4%)
16 Other cardiovascular	X	16 Schizophrenia	30.3% (21.6 to 40.0%)	14.2% (6.6 to 22.7%)	0.7% (-6.2 to 8.3%)		16 Road injuries	-20.7% (-22.2 to -19.2%)	-24.3% (-25.8 to -22.8%)	-28.2% (-29.8 to -26.6%)
17 Schizophrenia	X	17 Bipolar disorder	16.0% (7.9 to 24.6%)	1.7% (-5.4 to 9.2%)	-1.0% (-8.1 to 6.7%)		17 Stroke	13.2% (4.2 to 24.1%)	8.1% (-0.5 to 18.4%)	-6.1% (-13.3 to 2.6%)
18 Alzheimer disease		18 Other mental & substance	27.8% (22.1 to 34.1%)	12.0% (7.0 to 17.5%)	0.7% (-4.0 to 5.8%)		18 Other mental & substance	4.4% (-0.1 to 9.5%)	-0.4% (-4.7 to 4.5%)	0.0% (-4.4 to 5.0%)
19 Other mental & substance		19 Stroke	34.3% (24.7 to 46.3%)	17.7% (9.3 to 28.3%)	-5.1% (-11.4 to 2.8%)		19 Other cardiovascular	6.0% (-3.3 to 14.9%)	1.2% (-7.7 to 9.7%)	-8.2% (-15.4 to -0.7%)
20 Ischemic heart disease		20 Other cardiovascular	5.5% (-2.0 to 14.3%)	-7.5% (-14.1 to 0.1%)	-21.7% (-27.2 to -15.5%)	`	20 Drug use disorders	-14.9% (-23.7 to -3.5%)	-18.7% (-27.1 to -7.8%)	-8.2% (-17.3 to 2.6%)
21 Stroke	$\overline{}$	21 Chronic kidney disease	22.0% (11.8 to 33.6%)	6.9% (-2.0 to 17.1%)	-11.7% (-18.8 to -4.0%)		21 Chronic kidney disease	14.5% (4.7 to 24.7%)	9.3% (0.0 to 19.1%)	-4.0% (-11.4 to 3.6%)
22 Chronic kidney disease		22 Ischemic heart disease	-2.4% (-6.8 to 2.7%)	-14.4% (-18.3 to -10.0%)	-28.2% (-31.6 to -24.4%)		22 Ischemic heart disease	13.1% (7.8 to 19.0%)	8.0% (3.0 to 13.6%)	-5.3% (-9.7 to -0.6%)
23 Autistic spectrum		23 Autistic spectrum	12.6% (7.1 to 18.3%)	-1.3% (-6.1 to 3.7%)	0.8% (-4.3 to 6.2%)	<b>.</b> _	23 Rheumatoid arthritis	8.8% (0.9 to 16.9%)	3.9% (-3.6 to 11.6%)	-4.2% (-10.9 to 3.2%)
24 Upper respiratory infect		24 Tension headache	21.9% (15.7 to 29.6%)	6.8% (1.4 to 13.6%)	0.2% (-4.5 to 6.3%)		24 Atrial fibrillation	10.0% (1.0 to 18.1%)	5.0% (-3.6 to 12.7%)	-9.8% (-17.4 to -2.4%)
25 Tension headache		25 Rheumatoid arthritis	25.0% (16.8 to 34.7%)	9.6% (2.3 to 18.1%)	-2.5% (-8.9 to 5.3%)		25 Tension headache	4.8% (-0.6 to 10.7%)	0.1% (-5.1 to 5.6%)	0.3% (-4.4 to 5.4%)
26 Rheumatoid arthritis		26 Gynecological diseases	24.0% (17.9 to 30.3%)	8.7% (3.4 to 14.2%)	-1.5% (-6.1 to 3.5%)	]/_ ``	26 Autistic spectrum	3.2% (-2.3 to 8.9%)	-1.5% (-6.7 to 4.0%)	-0.1% (-5.2 to 5.4%)
27 Gynecological diseases		27 Atrial fibrillation	32.8% (23.6 to 43.0%)	16.4% (8.3 to 25.3%)	-7.3% (-13.5 to -0.3%)		27 Gynecological diseases	0.3% (-5.1 to 5.0%)	-4.3% (-9.4 to 0.3%)	-0.1% (-5.3 to 4.8%)
28 Congenital defects		28 Upper respiratory infect	8.7% (3.3 to 15.0%)	-4.7% (-9.5 to 0.8%)	-0.6% (-4.7 to 3.9%)		28 Upper respiratory infect	3.4% (-1.5 to 8.8%)	-1.3% (-6.0 to 3.9%)	0.3% (-4.0 to 4.7%)
29 Atrial fibrillation	$^{\sim}$ $^{\prime}$	29 Eating disorders	27.7% (15.2 to 41.0%)	11.9% (1.0 to 23.6%)	17.1% (6.5 to 27.6%)	<b>-</b>	29 Mechanical forces	15.8% (13.7 to 18.0%)	10.5% (8.5 to 12.6%)	5.6% (3.7 to 7.6%)
30 Conduct disorder	$\sim$	30 Mechanical forces	20.6% (18.6 to 22.7%)	5.7% (3.9 to 7.6%)	-4.3% (-6.1 to -2.5%)		30 Endo/metab/blood/immune	18.8% (12.5 to 25.8%)	13.4% (7.4 to 20.1%)	1.6% (-3.6 to 7.5%)
31 Mechanical forces	X	31 Congenital defects					-32 Congenital defects			
32 Eating disorders		32 Endo/metab/blood/immune					34 Eating disorders			
39 Endo/metab/blood/immune -		42 Conduct disorder					-40 Conduct disorder		Legend:	
									Communicable, maternal, neonatal and nutritional	

Figure 4. Arrow diagram of YLDs ranks for the top 20 main causes in 1990, 2006 and 2016, and the percentage change between time points.

Leading causes 1990		Leading causes 2006	Mean % change number of DALYs 1990-2006	Mean % change all-age DALY rate 1990-2006	Mean % change age- standardized DALY rate 1990-2006		Leading causes 2016	Mean % change number of DALYs 2006-2016	Mean % change all-age DALY rate 2006-2016	Mean % change age- standardized DALY rate 2006-2016
1 Ischemic heart disease		1 Ischemic heart disease	-16.9% (-20.0 to -13.4%)	-27.1% (-29.9 to -24.1%)	-40.8% (-43.0 to -38.4%)		1 Low back & neck pain	12.1% (6.6 to 17.5%)	7.0% (1.8 to 12.2%)	2.8% (-2.0 to 7.8%)
2 Low back & neck pain		2 Low back & neck pain	21.1% (15.3 to 26.8%)	6.1% (1.1 to 11.2%)	-5.7% (-10.1 to -1.2%)		2 Ischemic heart disease	-12.5% (-17.4 to -6.9%)	-16.5% (-21.1 to -11.1%)	-29.5% (-33.6 to -24.9%)
3 Stroke		3 Alzheimer disease	57.0% (49.5 to 66.4%)	37.6% (31.0 to 45.8%)	-3.0% (-7.4 to 1.9%)		3 Alzheimer disease	21.0% (11.3 to 30.4%)	15.5% (6.2 to 24.5%)	-9.6% (-16.6 to -3.0%)
4 Road injuries	1	4 Stroke	-25.2% (-29.3 to -21.2%)	-34.4% (-38.0 to -30.9%)	-48.3% (-51.0 to -45.6%)		4 Sense organ diseases	17.3% (14.9 to 19.8%)	12.0% (9.7 to 14.4%)	-0.3% (-2.2 to 1.6%)
5 Lung cancer	<del>\                                    </del>	5 Lung cancer	27.8% (19.0 to 36.0%)	12.0% (4.3 to 19.2%)	0.5% (-6.6 to 6.9%)		5 Lung cancer	-2.5% (-10.4 to 6.4%)	-6.9% (-14.4 to 1.5%)	-18.2% (-24.6 to -10.6%)
6 Migraine	-1/_	6 Sense organ diseases	29.4% (26.0 to 33.0%)	13.4% (10.4 to 16.6%)	-3.8% (-5.8 to -1.7%)		6 Migraine	2.3% (-0.9 to 5.3%)	-2.3% (-5.4 to 0.5%)	0.1% (-3.0 to 3.3%)
7 Sense organ diseases	1	7 Migraine	19.5% (15.6 to 23.6%)	4.7% (1.3 to 8.4%)	-0.5% (-3.5 to 2.6%)		7 Stroke	9.3% (-15.9 to -2.7%)	-13.4% (-19.7 to -7.1%)	-27.1% (-32.1 to -22.2%)
8 Skin diseases		8 Skin diseases	12.1% (9.4 to 15.0%)	-1.7% (-4.1 to 0.8%)	4.2% (2.2 to 6.2%)	<u> </u>	8 Skin diseases	4.9% (2.9 to 6.9%)	0.1% (-1.8 to 2.0%)	1.1% (-0.6 to 2.9%)
9 Alzheimer disease		9 COPD	14.9% (5.9 to 23.0%)	0.7% (-7.2 to 7.8%)	-21.0% (-27.3 to -15.4%)		9 Depressive disorders	9.4% (4.3 to 14.8%)	4.4% (-0.5 to 9.6%)	4.4% (0.0 to 9.1%)
10 COPD	\	10 Road injuries	-37.6% (-42.5 to -31.8%)	-45.3% (-49.6 to -40.2%)	-47.2% (-51.0 to -42.9%)		- 10 COPD	-2.8% (-9.5 to 4.6%)	-7.2% (-13.6 to -0.2%)	-23.0% (-28.3 to -17.1%)
11 Depressive disorders		11 Depressive disorders	6.1% (1.0 to 12.1%)	-7.0% (-11.5 to -1.8%)	-13.2% (-18.1 to -8.2%)		11 Falls	-2.4% (-4.9 to 0.5%)	-6.9% (-9.2 to -4.1%)	-15.2% (-17.5 to -12.8%)
12 Diabetes		12 Falls	35.9% (28.3 to 41.0%)	19.1% (12.5 to 23.5%)	4.8% (-1.6 to 9.2%)	1	12 Diabetes	-2.4% (-9.6 to 5.1%)	-6.8% (-13.7 to 0.3%)	-18.0% (-23.9 to -11.4%)
13 Falls		13 Diabetes	4.4% (-2.7 to 12.4%)	-8.5% (-14.8 to -1.5%)	-22.6% (-28.4 to -16.6%)		13 Colorectal cancer	5.4% (-4.0 to 15.9%)	0.6% (-8.4 to 10.6%)	-12.2% (-20.2 to -3.4%)
14 Anxiety disorders	ļ.,	14 Colorectal cancer	46.4% (37.5 to 55.0%)	28.3% (20.5 to 35.8%)	8.9% (2.4 to 15.5%)		14 Anxiety disorders	10.4% (3.6 to 17.4%)	5.4% (-1.1 to 12.1%)	5.8% (-0.6 to 12.2%)
15 Other cardiovascular	-	15 Anxiety disorders	16.1% (8.9 to 24.4%)	1.8% (-4.6 to 9.0%)	1.4% (-5.0 to 8.5%)		15 Other cardiovascular	7.3% (0.4 to 14.7%)	2.4% (-4.1 to 9.5%)	-10.9% (-16.3 to -4.8%)
16 Colorectal cancer		16 Other cardiovascular	5.1% (-0.5 to 10.9%)	-7.9% (-12.8 to -2.8%)	-25.0% (-28.8 to -21.2%)		16 Road injuries	-40.7% (-44.7 to -36.2%)	-43.3% (-47.2 to -39.1%)	-44.9% (-48.8 to -40.5%)
17 Congenital defects		17 Chronic kidney disease	3.0% (-2.6 to 8.9%)	9.8% (-14.7 to -4.5%)	28.5% (-32.4 to -24.7%)	<b>-</b>	17 Oral disorders	16.2% (12.7 to 20.8%)	11.0% (7.5 to 15.3%)	3.0% (0.4 to 6.4%)
18 Stomach cancer	1\	18 Oral disorders	21.8% (17.3 to 26.1%)	6.8% (2.8 to 10.5%)	-4.7% (-7.7 to -2.1%)		- 18 Chronic kidney disease	10.1% (3.6 to 16.8%)	5.1% (-1.1 to 11.5%)	-11.8% (-16.9 to -6.5%)
19 Cirrhosis alcohol	1	19 Breast cancer	-1.9% (-8.6 to 5.0%)	-14.0% (-19.9 to -8.0%)	-26.7% (-31.8 to -21.4%)		19 Other musculoskeletal	25.9% (12.8 to 40.5%)	20.2% (7.7 to 34.1%)	16.5% (5.0 to 29.1%)
20 Chronic kidney disease		20 Self-harm	5.8% (-14.2 to 16.0%)	-7.3% (-24.8 to 1.7%)	-14.1% (-30.8 to -5.6%)	-	20 Breast cancer	0.7% (-9.5 to 11.1%)	-3.9% (-13.6 to 6.1%)	-15.7% (-24.2 to -6.6%)
21 Breast cancer	111/	21 Drug use disorders	20.6% (10.0 to 31.9%)	5.7% (-3.6 to 15.6%)	1,3% (-8,0 to 11,1%)		21 Osteoarthritis	16.1% (11.8 to 20.1%)	10.8% (6.7 to 14.6%)	2.3% (-6.0 to 1.2%)
22 Other musculoskeletal		22 Other musculoskeletal	-2.5% (-13.8 to 10.9%)	-14.6% (-24.5 to -2.8%)	-20.8% (-29.7 to -10.7%)	-X	22 Asthma	2.7% (-1.2 to 6.3%)	-2.0% (-5.7 to 1.5%)	3.1% (-7.2 to 0.9%)
23 Self-harm	/\\X	23 Asthma	-2.4% (-7.2 to 2.7%)	-14.5% (-18.7 to -10.0%)	-11.8% (-16.2 to -7.4%)		23 Self-harm	-8.7% (-24.7 to 4.5%)	-12.9% (-28.1 to -0.2%)	-12.6% (-27.4 to 0.1%)
24 Asthma	1	24 Stomach cancer	-22.2% (-27.1 to -17.4%)	-31.8% (-36.1 to -27.6%)	-41.4% (-45.0 to -37.9%)	<b>—X</b>	24 Stomach cancer	-6.6% (-13.4 to 1.7%)	-10.8% (-17.3 to -2.9%)	-21.8% (-27.7 to -14.5%)
25 Oral disorders		25 Lower respiratory infect	1.3% (-7.6 to 10.6%)	-11.2% (-19.1 to -3.0%)	-33.6% (-39.0 to -28.1%)		25 Lower respiratory infect	-4.4% (-15.7 to 8.2%)	-8.8% (-19.5 to 3.3%)	-24.4% (-33.0 to -14.9%)
26 HIV/AIDS	1/1	26 Osteoarthritis	41.1% (35.9 to 46.1%)	23.6% (19.1 to 28.1%)	5.7% (1.9 to 9.6%)	<b>■</b> / `	26 Drug use disorders	-15.6% (-23.2 to -6.4%)	-19.4% (-26.7 to -10.7%)	-11.0% (-18.6 to -2.1%)
27 Lower respiratory infect	X	27 Cirrhosis alcohol	-27.7% (-32.7 to -22.7%)	-36.6% (-41.0 to -32.3%)	-44.6% (-48.4 to -40.8%)		27 Pancreatic cancer	15.6% (4.6 to 26.7%)	10.3% (-0.2 to 20.9%)	-2.9% (-11.8 to 6.7%)
28 Drug use disorders	/\ /\	28 Congenital defects	-35.1% (-41.8 to -12.6%)	-43.1% (-49.0 to -23.4%)	-47.0% (-53.2 to -24.9%)	1	28 Atrial fibrillation	15.6% (5.2 to 25.3%)	10.4% (0.4 to 19.7%)	-9.4% (-17.2 to -1.8%)
29 Neonatal preterm birth	X	29 Pancreatic cancer	43.6% (33.7 to 53.3%)	25.9% (17.2 to 34.4%)	10.6% (2.9 to 18.0%)		29 Other neoplasms	10.1% (-1.2 to 19.6%)	5.1% (-5.6 to 14.2%)	-5.1% (-15.8 to 3.8%)
30 Other neoplasms		30 Atrial fibrillation	35.6% (27.0 to 44.3%)	18.8% (11.3 to 26.5%)	-9.7% (-15.1 to -3.9%)		30 Cirrhosis alcohol	-11.0% (-19.4 to -2.7%)	-15.1% (-23.1 to -7.1%)	-25.3% (-32.5 to -17.9%)
32 Osteoarthritis	1-4-	-31 Other neoplasms	001070 (271010 441070)	10.070 (11.0 to 20.070)	317 73 ( 1011 10 01070)		35 Congenital defects	111070 ( 1014 to 21770)	101170 ( 2011 to 71170)	251675 ( 52.15 10 17.1576)
38 Atrial fibrillation	1	35 HIV/AIDS					9			
39 Pancreatic cancer		44 Neonatal preterm birth					-54 Neonatal preterm birth		Legend:	
oo r androuilo danos.		Theoreta protein onto					o recondul poconi bini		Communicable, maternal, neonatal and nutritional Non-communicable Injuries	

Figure 5. Arrow diagram of DALYs ranks for the top 20 main causes in 1990, 2006 and 2016, and the percentage change between time points.

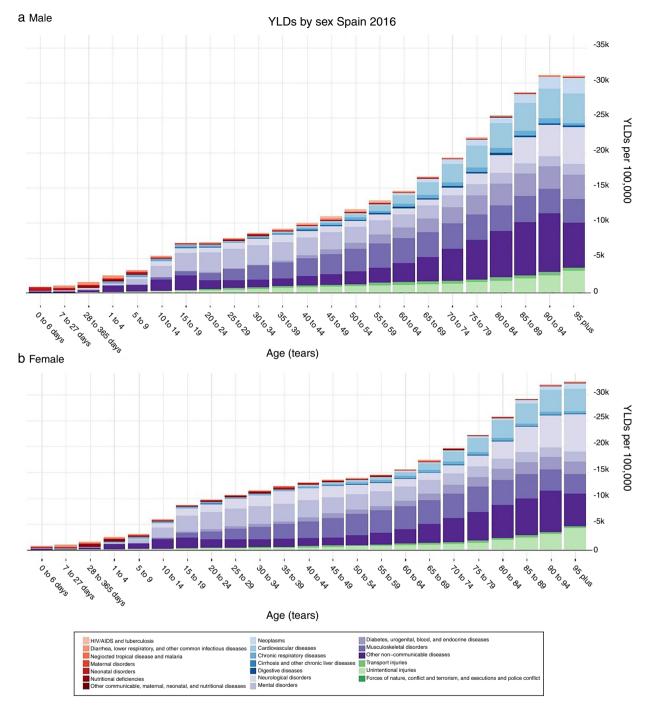


Figure 6. Sex difference in YLD rates per 100 000 for 21 Level 2 causes by age, 2016. (a) Male; (b) Female.

points), and child sex abuse with 49 (UI 38.8–59.6) points) will remain fails, well below 50 out of 100 points.

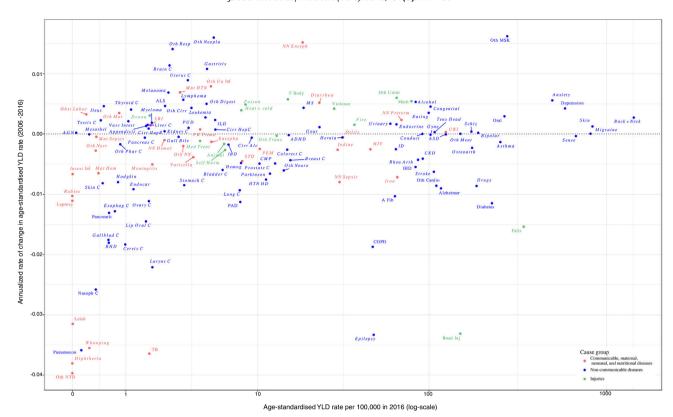
# Discussion

During the past 26 years, substantial changes have taken place in the burden of diseases in Spain. Low back and neck pain are the major driver of disability in Spain in 2016, while tobacco remains the most relevant risk factor overall. The country has seen a remarkable increase in the burden due to Alzheimer disease and other dementias. Overall, mortality and disability in Spain have become even more linked to non-communicable diseases over the last years, following worldwide trends. Cardiovascular and circulatory diseases, cancers, mental and behavioural disorders,

and neurological disorders are the leading causes of DALYs, as already observed in GBD 2010.  $^{17}$ 

Comparing the burden of disease in 2016 in Spain with neighbouring countries such as Portugal, France, and within Western Europe, the top 10 causes in DALYs per 100,000 are very similar, with the exception of neurological disorders that in Spain are listed as the 4th cause while in Western Europe, Portugal and France are the 6th cause. Actually, from 1990 and 2006 the top ten leading causes showed a similar trend in Spain, and the above mentioned countries. Globally the main risk factor is high blood pressure, followed by smoking, low birth weight, and short gestation, 31 this last one ranking number 29th as risk factor in Spain.

This analysis of Spain within the 2016 GBD study provides a detailed overall assessment of the main causes of death and



"Not shown in figure (YLD, ARC): Tetanus: (0.00005, -0.07), Measles: (0.001, 0.1), Chagas: (0.9, 0.04), Echino: (0.4, -0.06), Comp-Abort: (0.8, 0.04), Hep: (0.5, -0.07)

Figure 7. Relationship of global age-standardised YLD rates per 100,000 in 2016 and the annualised rate of change in age-standardised YLD rates for each Level 3 cause, 2006–2016. Spain both sexes.

For both sexes combined, Age-standardized YLD rates are represented on a logarithmic scale on the x-axis. Causes for which the annualised rate of change is not significant are listed in italics. Level 3 causes related to shocks (conflict and terrorism, state actor violence, and exposures to forces of nature) are excluded. A Fib: atrial fibrillation and flutter; ADHD: attention-deficit/hyperactivity disorder; AGN: acute glomerulonephritis; ALS: motor neuron disease; ASD: autistic spectrum disorders; Afr Tryp: African trypanosomiasis; Alcohol: alcohol use disorders; Alzheimer: Alzheimer disease and other dementias; Animal: animal contact; Anxiety: anxiety disorders; Appendicit: appendicitis; Asthma: asthma; Back + Neck: low back and neck pain; Bipolar: bipolar disorder; Bladder C: bladder cancer; Brain C: brain and nervous system cancer; Breast C: breast cancer; CKD: chronic kidney disease; CMP: cardiomyopathy and myocarditis; COPD: chronic obstructive pulmonary disease; Cervix C: cervical cancer; Chagas: Chagas disease; Cirr Alc: cirrhosis and other chronic liver diseases due to alcohol use; Cirr HepB: cirrhosis and other chronic liver diseases due to hepatitis B; Cirr HepC: cirrhosis and other chronic liver diseases due to hepatitis C; Colorect C: colon and rectum cancer; Comp Abort: maternal abortion, miscarriage, and ectopic pregnancy; Conduct: conduct disorder; Conflict Terror: conflict and terrorism; Congenital: congenital birth defects; Cysticer: cysticercosis; Dengue; dengue; Depression: depressive disorders; Diabetes: diabetes mellitus; Diarrhea: diarrheal diseases; Diphtheria; Disaster: exposure to forces of nature; Drown: drowning; Drugs: drug use disorders; Eating; eating disorders; Ebola: Ebola; Echino: cystic echinococcosis; Encepha: encephalitis; Endocar: endocarditis; Endocrine: endocrine, metabolic, blood, and immune disorders; Epilepsy: epilepsy; Esophag C: esophageal cancer; Exec & Police: executions and police conflict; F Body: foreign body; FB Trema: food-borne trematodiases; Falls: falls; Fire: fire, heat, and hot substances; GWD: Guinea worm disease; Gall Bile: gallbladder and biliary diseases; Gallbladder and biliary tract cancer; Gastritis: gastritis and duodenitis; Gout: gout; Gyne: gynecological diseases; HIV: HIV/AIDS; HTN HD: hypertensive heart disease; Heat + cold: environmental heat and cold exposure; Hemog: hemoglobinopathies and hemolytic anemias; Hep: acute hepatitis; Hernia: inguinal, femoral, and abdominal hernia; Hodgkin: Hodgkin lymphoma; IBD: inflammatory bowel disease; ID: idiopathic developmental intellectual disability; IHD: ischemic heart disease; ILD: interstitial lung disease and pulmonary sarcoidosis; Ileus: paralytic ileus and intestinal obstruction; Intest Inf: intestinal infectious diseases; Iodine: iodine deficiency; Iron: iron-deficiency anemia; Kidney C: kidney cancer; LF: lymphatic filariasis; LRI: lower respiratory infections; Larynx C: larynx cancer; Leish: leishmaniasis; Leprosy; leprosy; Leukemia; Lip Oral C: lip and oral cavity cancer; Liver C: liver cancer; Lung C: tracheal, bronchus, and lung cancer; Lymphoma: non-Hodgkin lymphoma; MS: multiple sclerosis; Malaria: malaria; Mat HTN: maternal hypertensive disorders; Mat Hem: maternal hemorrhage; Mat Sepsis: maternal sepsis and other maternal infections; Measles: measles; Mech: exposure to mechanical forces; Med Treat: adverse effects of medical treatment; Melanoma: malignant skin melanoma; Meningitis: meningitis; Mesothel: mesothelioma; Migraine: migraine; Myeloma: multiple myeloma; NN Enceph: neonatal encephalopathy due to birth asphyxia and trauma; NN Hemol; hemolytic disease and other neonatal jaundice; NN Preterm: neonatal preterm birth complications; NN Sepsis: neonatal sepsis and other neonatal infections; Nasoph C: nasopharynx cancer; Nematode: intestinal nematode infections; Obst Labor: maternal obstructed labor and uterine rupture; Oncho: onchocerciasis; Oral: oral disorders; Osteoarth: osteoarthritis; Oth Cardio: other cardiovascular and circulatory diseases; Oth Cirr: cirrhosis and other chronic liver diseases due to other causes; Oth Digest: other digestive diseases; Oth MSK: other musculoskeletal disorders; Oth Mat: other maternal disorders; Oth Ment: other mental and substance use disorders; Oth NN: other neonatal disorders; Oth NTD: other neglected tropical diseases; Oth Neopla: other neoplasms; Oth Neuro: other neurological disorders; Oth Nutr: other nutritional deficiencies; Oth Phar C: other pharynx cancer; Oth Resp: other chronic respiratory diseases; Oth Trans: other transport injuries; Oth Un Inf: other unspecified infectious diseases; Oth Unint: other unintentional injuries; Otitis: otitis media; Ovary C: ovarian cancer; PAD: peripheral artery disease; PEM: protein-energy malnutrition; PUD: peptic ulcer disease; Pancreas C: pancreatic cancer; Pancreatit: pancreatitis; Parkinson: Parkinson disease; Pneumocon: pneumoconiosis; Poison: poisonings; Prostate C: prostate cancer; RHD: rheumatic heart disease; Rabies: rabies; Rheu Arth: rheumatoid arthritis; Road Inj: road injuries; STD: sexually transmitted diseases excluding HIV; Schisto: schistosomiasis; Schiz: schizophrenia; Self Harm: self-harm; Sense: sense organ diseases; Skin: skin and subcutaneous diseases; Skin C: non-melanoma skin cancer; Stomach C: stomach cancer; Stroke: stroke; TB: tuberculosis; Tens Head: tension-type headache; Testis C: testicular cancer; Tetanus: tetanus; Thyroid C: thyroid cancer; Trachoma: trachoma; URI: upper respiratory infections; Urinary: urinary diseases and male infertility; Uterus C: uterine cancer; Varicella: varicella and herpes zoster; Vasc Intest: vascular intestinal disorders; Violence: interpersonal violence; Vit A: vitamin A deficiency; Whooping; whooping cough; Yellow Fev: yellow fever; Zika: zika virus.

disability, and its leading risk factors. Considering DALYS as the overarching marker of health burden, the five leading diseases were low back and neck pain, IHD, Alzheimer, sense organ diseases, and lung cancer, whereas the five leading risk factors were smoking,

alcohol & drug use, high blood pressure, high BMI, and dietary risks. As above mentioned, this pattern is again similar to Portugal and France, as well as to all Western Europe. This similarity has been maintained during the 26 years of the study period. One of the few

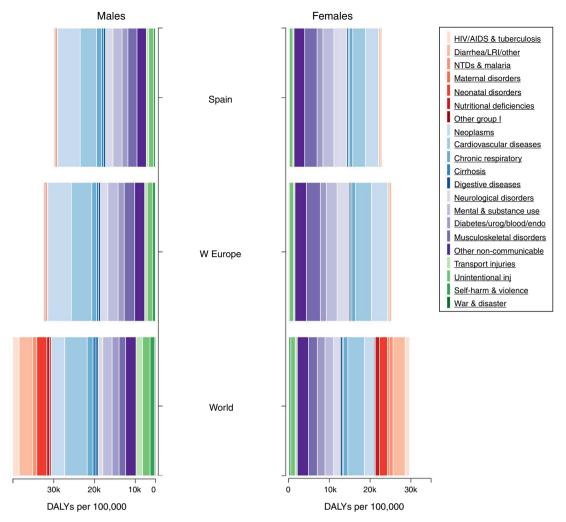


Figure 8. DALYs by sex in all ages in 2016, in Spain, Western Europe and the World.

significant differences is alcohol abuse, which ranks 1st in Portugal, but 4th in Spain.

There are some discrepancies between causes of death for Spain GBD 2016 and data from the Instituto Nacional de Estadística (INE, for National Institute of Statistics), 36 the official Spanish statistics organism, which is used to guide public policy, and follows the ICD-10 cause of death list. Top causes of death in 2016 (both sex combined) according to INE are shown in Online Table 1. Although definitions differ (e.g. IHD is represented by two different categories in INE, that is "Acute myocardial infarction" and "Other ischaemic heart diseases", hypertension is considered a garbage code in GBD and is redistributed to other causes of death. Several items labelled "other", representing several different conditions, made it into the top ten list in INE. Overall, all conditions except one in the top ten causes according to GBD 2016 can be recognised in the INE list, the sole exception being CKD. The discrepancies between INE and GBD may depend on the different definitions used. In INE, the closest term to CKD, at position seventeen, is a wider category of "diseases of the kidney and of the ureter". The fact that one of the top ten causes of death, according to the GBD 2016 methodology, is hidden from the view of policy makers may be considered room for improvement in the INE information system (Table 2).

The top ten leading risk factors in Spain in 2016 are smoking, high systolic blood pressure, high BMI, alcohol use, high fasting plasma glucose, high total cholesterol, impaired kidney function, diet low in seed, nuts and whole grains, and finally ambient air pollution. Among these top ten risk factors according to impact on

DALYs, seven, that is smoking, alcohol use, high blood pressure, high BMI, high fasting plasma glucose and high total cholesterol, are subject to lifestyle modifications.

All of them may be improved through public health and education campaigns in order to both decrease DALYs and achieve the SDG goals.<sup>37</sup> The implementation of tobacco control policies (mainly taxation, health warnings as plain packaging, and support for smoking cessation), food policies (taxation and availability), or physical activity (promotion) are key interventions to positively intervene the future burden of disease in Spain. Additionally, high blood pressure, high fasting plasma glucose and high total cholesterol, may be responsive to changes in weight and physical activity, and also to pharmacological intervention. There is also margin for improvement on this from the primary care point of view. In a recent study, undiagnosed hypertension was identified in 37% of patients and well-controlled blood pressure was found in only 24% of patients in Spain. 38 Impaired kidney function merits a specific comment. Despite its high prevalence, estimated as much as 10% of the adult population in Spain, as the GBD 2016 definition included both decreased glomerular filtration rate or the presence of pathological albuminuria,<sup>39</sup> impaired kidney function is not directly related to lifestyle changes. Further, there is little awareness of its risk factor consideration, both among the general population and among physicians, despite statements by scientific societies.<sup>40</sup> Together with its growing contribution to mortality, kidney disorders require a major focused effort on the part of health authorities.

Spain, Both sexes, all ages, 2016

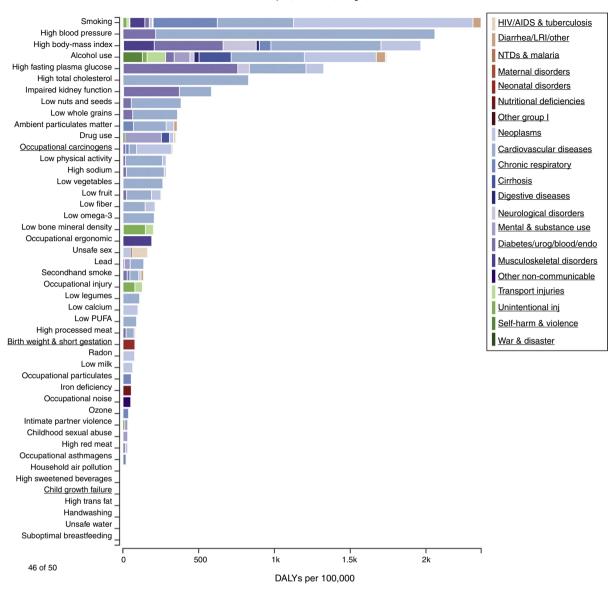
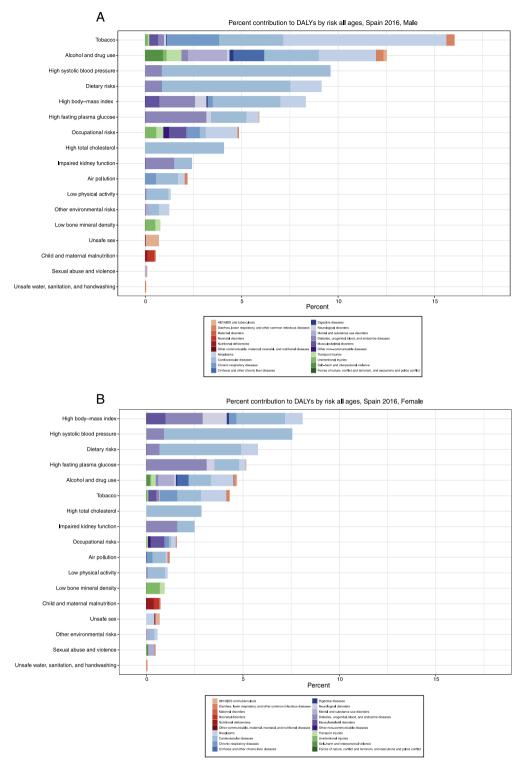


Figure 9. Standardised rates of DALYs (Level 3) attributable to major risk factors in Spain in 2016.

Table 2

Most common causes of death in Spain in 2016 according to Basic cause of death. INE-Instituto Nacional de Estadística [as per http://www.ine.es/dynt3/inebase/en/index.htm?padre=4321&capsel=4322 [accessed January 20, 2018].

	Condition	Both	Male	Female
1	Cerebrovascular diseases	66,053	28,143	37,909
2	Other heart diseases	56,642	25,260	31,383
3	Malignant tumour of the trachea, bronchial tube and lungs	54,034	42,921	11,113
4	Organic, senile and presenile mental disorders	49,227	16,300	32,927
5	Other diseases of the respiratory system	48,367	22,323	26,044
6	Heart failure	43,669	16,200	27,469
7	Other ischaemic heart diseases	41,762	24,505	17,257
8	Acute myocardial infarction	36,307	21,940	14,366
9	Alzheimer's disease	36,027	10,643	25,384
10	Chronic diseases of the lower respiratory tracts (except Asthma)	34,161	26,422	7740
11	Hypertension diseases	29,597	9518	20,080
12	Other diseases of the digestive system	29,042	13,594	15,448
13	Malignant tumour of the colon	28,691	16,785	11,907
14	Other diseases of the nervous system and sensory organs	25,177	13,039	12,138
15	Diabetes mellitus	22,674	9961	12,713
16	Pneumonia	22,308	11,610	10,699
17	Diseases of the kidney and of the ureter	16,641	7752	8889



**Figure 10.** Top risk factors contributing to DALYs in % in 2016, by sex. A-Male; B-Female.

Ambient air pollution is the only environmental risk factor within the top ten risk factors in Spain, which is also a leading risk factor globally. Policies and regulations to reduce main emission sources of ambient air pollution are also urgently needed. Specific interventions to reduce motorised transport use, with interventions such as reducing public parking space for cars, increasing the availability and efficiency of public transport, and promoting walking and cycling, are good examples for effective interventions in urban areas.

There were major sex differences on the impact of risk factors on DALYs, both in their ranking and percent contribution. In women, no single risk factor contributed more than 10% of DALYs, and only four contributed more than 5%. By contrast, in men six contributed more than 5% and two more than 15%, and the latter being behaviour-related (tobacco and alcohol/drug use). Moreover, with the exception of high BMI and impaired kidney function, the contribution to DALYS of the other ten leading risk factors in Spain was substantially larger in males than in females. The latter was

Leading causes 1990			Mean % change number of DALYs 1990-2006	Mean % change all-age DALY rate 1990-2006	Mean % change age- standardized DALY rate 1990-2006		Leading causes 2016	Mean % change number of DALYs 2006-2016	Mean % change all-age DALY rate 2006-2016	Mean % change age- standardized DALY rate 2006-2016
1 Smoking		1 Smoking	-0.7% (-5.0 to 3.8%)	-13.0% (-16.7 to -9.0%)	-24.0% (-27.1 to -20.6%)		1 Smoking	-8,5% (-15,2 to -1,2%)	-12.6% (-19.1 to -5.7%)	-22,8% (-28,4 to -16,9%)
2 High blood pressure		2 High blood pressure	-14.4% (-17.6 to -10.9%)	-24.9% (-27.8 to -21.9%)	-38,7% (-40,9 to -36,2%)		2 High blood pressure	-6.1% (-10.9 to -1.3%)	-10.3% (-14.9 to -5.7%)	-24,0% (-27,9 to -20,0%)
3 Alcohol use		3 High body-mass index	17,7% (7,1 to 33,4%)	3.2% (-6.1 to 16.9%)	-12.5% (-20.3 to -0.5%)		3 High body-mass index	-1,6% (-8,5 to 4,8%)	-6.1% (-12.7 to 0.1%)	-17,7% (-23,0 to -12,7%)
4 High body-mass index		4 Alcohol use	-22.7% (-33.8 to -13.3%)	32.3% (-42.0 to -24.0%)	-39.7% (-47.9 to -32.5%)	<del></del>	4 Alcohol use	-9.1% (-26.5 to 6.9%)	-13.2% (-29.8 to 2.1%)	-22.4% (-36.4 to -9.8%)
5 High fasting plasma glucose		5 High fasting plasma glucose	0.5% (-8.1 to 9.2%)	-11.9% (-19.5 to -4.3%)	-27.4% (-33.8 to -21.0%)		5 High fasting plasma glucose	-6.1% (-12.1 to 0.2%)	-10.4% (-16.1 to -4.4%)	-22.8% (-27.8 to -17.4%)
6 High total cholesterol		6 High total cholesterol	-22.2% (-26.4 to -17.9%)	-31.8% (-35.5 to -28.0%)	-43.3% (-45.9 to -40.6%)	<u> </u>	6 High total cholesterol	-15.2% (-21.1 to -9.6%)	-19.0% (-24.7 to -13.7%)	-31.3% (-35.8 to -26.9%)
7 Impaired kidney function		7 Impaired kidney function	-5.6% (-8.9 to -1.9%)	-17.3% (-20.2 to -14.0%)	-35.1% (-37.6 to -32.6%)		7 Impaired kidney function	-1.4% (-6.2 to 3.7%)	-5.9% (-10.4 to -1.0%)	-21.2% (-25.0 to -17.0%)
8 Low whole grains		8 Low nuts and seeds	-7.2% (-12.2 to -0.2%)	-18.7% (-23.1 to -12.6%)	-32.3% (-36.3 to -27.1%)		8 Low nuts and seeds	-14.9% (-20.1 to -9.6%)	-18.8% (-23.7 to -13.7%)	-29.8% (-34.3 to -24.9%)
9 Low nuts and seeds		9 Low whole grains	-21.5% (-32.4 to -12.3%)	-31.2% (-40.7 to -23.2%)	-41.8% (-49.5 to -35.0%)		9 Low whole grains	-18.0% (-28.2 to -9.8%)	-21.7% (-31.4 to -13.9%)	-31.2% (-39.2 to -24.1%)
10 Ambient particulate matter		10 Ambient particulate matter	-14.2% (-19.2 to -9.3%)	-24.8% (-29.2 to -20.5%)	-37.7% (-41.2 to -34.3%)		10 Ambient particulate matter	-11.1% (-16.5 to -5.6%)	-15.1% (-20.3 to -9.9%)	-27.1% (-31.4 to -22.5%)
11 Low fruit		11 Drug use	16.0% (7.4 to 24.8%)	1.6% (-5.9 to 9.3%)	-5.0% (-12.3 to 2.2%)	<del> </del>	11 Drug use	-9.7% (-16.8 to -2.0%)	-13.8% (-20.6 to -6.4%)	-9.9% (-16.4 to -2.3%)
12 Low physical activity	1	12 Occupational carcinogens	15.0% (9.1 to 21.1%)	0.8% (-4.4 to 6.2%)	-10.2% (-14.6 to -5.6%)		12 Occupational carcinogens	-6.6% (-12.8 to 0.5%)	-10.9% (-16.8 to -4.1%)	-21.0% (-26.3 to -15.0%)
13 Drug use	1	13 Low physical activity	-15.6% (-34.5 to 8.6%)	-26.0% (-42.6 to -4.9%)	-40.6% (-54.2 to -23.1%)	<del></del>	13 Low physical activity	-9.5% (-28.7 to 18.1%)	-13.6% (-32.0 to 12.7%)	-27.3% (-43.4 to -4.8%)
14 Low omega-3	X	14 High sodium	-14.7% (-64.9 to 129.5%)	-25.2% (-69.2 to 101.1%)	-37.2% (-70.5 to 71.5%)	<del></del>	14 High sodium	5.6% (-25.8 to 232.5%)	0.8% (-29.2 to 217.4%)	-14.1% (-39.3 to 168.1%)
15 High sodium	$\times$	15 Low vegetables	0.5% (-12.0 to 30.9%)	-11.9% (-22.8 to 14.7%)	-29.5% (-37.7 to -9.2%)	<del> </del>	15 Low vegetables	0.3% (-7.4 to 10.0%)	-4.2% (-11.6 to 5.0%)	-14.3% (-21.5 to -5.2%)
16 Occupational carcinogens	$\sim$	16 Low fruit	-42.4% (-62.4 to -30.4%)	-49.5% (-67.0 to -39.0%)	-57.2% (-72.1 to -48.1%)	<del>                                     </del>	16 Low fruit	-0.3% (-15.9 to 29.1%)	-4.9% (-19.8 to 23.3%)	-15.2% (-28.9 to 9.5%)
17 Occupational injury		17 Low omega-3	-24.4% (-28.4 to -20.6%)	-33.7% (-37.3 to -30.4%)	-44.4% (-47.5 to -41.5%)	·	17 Low fiber	7.2% (-1.2 to 19.8%)	2.4% (-5.7 to 14.3%)	-13.2% (-20.0 to -3.0%)
18 Unsafe sex	/	18 Unsafe sex	-22.7% (-29.5 to -13.8%)	-32.3% (-38.2 to -24.4%)	-42.4% (-47.6 to -35.6%)		18 Low omega-3	-16.7% (-22.6 to -10.3%)	-20.5% (-26.1 to -14.4%)	-31.1% (-36.3 to -25.6%)
19 Low vegetables		19 Low fiber	-1.1% (-8.4 to 9.3%)	-13.3% (-19.8 to -4.2%)	-26.6% (-32.2 to -18.7%)		19 Low bone mineral density	5.8% (3.0 to 9.0%)	1.0% (-1.7 to 4.0%)	-16.3% (-18.5 to -14.2%)
20 Secondhand smoke		20 Low bone mineral density	30.9% (22.7 to 35.7%)	14.7% (7.5 to 18.9%)	-5.6% (-12.8 to -1.7%)		20 Occupational ergonomic	7.5% (-1.1 to 17.0%)	2.6% (-5.6 to 11.7%)	2.5% (-4.8 to 10.4%)
21 Low birth weight & short gest.	$\times 1$	21 Occupational ergonomic	18.3% (9.9 to 27.6%)	3.7% (-3.7 to 11.8%)	-8.6% (-14.7 to -1.2%)	-	21 Unsafe sex	-24.1% (-30.9 to -17.2%)	-27.5% (-34.1 to -20.9%)	-32.7% (-38.8 to -26.8%)
22 Low fiber		22 Lead	-5.9% (-12.2 to 4.3%)	-17.5% (-23.0 to -8.6%)	-29.2% (-34.9 to -19.6%)		22 Lead	-17.5% (-24.1 to -12.3%)	-21.3% (-27.5 to -16.3%)	-29.7% (-36.3 to -24.3%)
23 Lead		23 Secondhand smoke	-32.5% (-36.8 to -28.3%)	-40.8% (-44.6 to -37.1%)	-50.9% (-54.2 to -47.7%)	<del></del>	23 Secondhand smoke	-17.7% (-24.9 to -9.9%)	-21.4% (-28.3 to -14.0%)	-31.9% (-37.4 to -26.3%)
24 Low PUFA		24 Occupational injury	-46.5% (-51.0 to -42.5%)	-53.1% (-57.1 to -49.6%)	-58.3% (-61.7 to -55.1%)		24 Occupational injury	-18.2% (-28.2 to -8.5%)	-21.9% (-31.5 to -12.6%)	-19.0% (-28.8 to -9.0%)
25 Low legumes		25 Low birth weight & short gest		-51.3% (-59.5 to -45.8%)	-54.7% (-62.4 to -49.6%)	<u>ا</u>	25 Low legumes	-5.9% (-14.8 to 8.4%)	-10.2% (-18.6 to 3.4%)	-23.7% (-31.4 to -11.0%)
26 Occupational ergonomic		26 Low legumes	-23.1% (-31.9 to -15.8%)	-32.6% (-40.3 to -26.2%)	-45.0% (-51.9 to -39.5%)	H /	26 Low calcium	8.0% (-2.0 to 20.5%)	3.1% (-6.4 to 15.0%)	-10.2% (-18.7 to 0.2%)
27 Low bone mineral density		27 Low PUFA	-34.0% (-37.8 to -30.5%)	-42.2% (-45.5 to -39.0%)	-52.5% (-55.3 to -49.8%)	$\rightarrow \leftarrow$	27 Low PUFA	-19.5% (-25.3 to -13.6%)	-23.2% (-28.7 to -17.6%)	-34.3% (-39.2 to -29.3%)
28 Household air pollution		28 Low calcium	53.9% (42.8 to 68.4%)	34.9% (25.2 to 47.6%)	14.3% (6.3 to 24.6%)		28 High processed meat	16.8% (0.8 to 47.6%)	11.5% (-3.8 to 40.9%)	-1.9% (-15.4 to 25.2%)
29 Radon		29 Radon	27.5% (16.9 to 40.3%)	11.8% (2.4 to 22.9%)	0.4% (-7.0 to 7.8%)		29 Low birth weight & short ges		-38.1% (-56.0 to -15.0%)	-25.7% (-47.2 to 2.0%)
30 Low calcium		30 High processed meat	30.2% (7.9 to 105.1%)	14.1% (-5.5 to 79.8%)	-2.4% (-19.6 to 54.3%)		30 Radon	-2.5% (-10.8 to 7.6%)	-6.9% (-14.9 to 2.7%)	-18.2% (-25.0 to -10.3%)
33 High processed meat -		38 Household air pollution					-40 Household air pollution			

Legend:
Environmental/occupational risks
Metabolic risks

Figure 11. Arrow diagram of changes in Risk Factors in 1990, 2006 and 2016 attributable to DALYs.

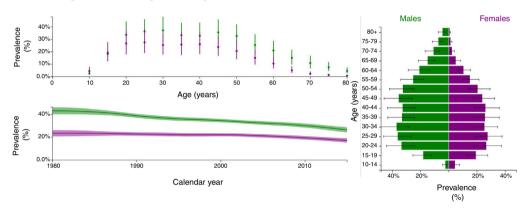
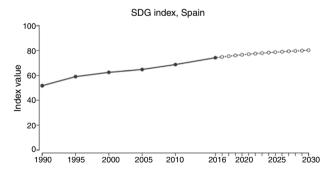


Figure 12. Tobacco trends in Spain, by year and sex (vizhub up to 2015 only).



**Figure 13.** Trends in SDG index scores for Spain from 1990 to 2016, and projections up to 2030.

particularly evident for tobacco (16% in male vs 4.5% in female) and alcohol and drug use (13% in male vs 5% in female). This finding suggests the need for targeting gender issues in any public health policies of the burden of health and its risk factors. Public policy campaigns should specifically target men, with the potential exception of tobacco use, since projected prevalence for 2025 indicate a decrease except for women aged 40–64 years. <sup>41</sup> Correction of these differences in risk behaviour may help further closing the gap in mortality between Spanish men and women. A better understanding of gender differences in the burden of diseases should also involve the identification and assessment of potential gender biases, both in the identification of risk factors and the assessment of their effects.

Occupational risk factors deserve particular attention, as causes of loss of productivity, frequent sickness absence and high economic cost, since they rank among the top-ten leading factors in both men and women, and there is a recognised deficit in occupational health policies in Spain. 42,43 Ongoing challenges are coordination within Autonomous Communities and centralised regulators, and wider collaboration of different institutes and administrations.

In terms of SDGs, the health-related index provided by GBD is a very useful tool to track advances and accomplishment of SDGs in Spain. Out of a total of 188 countries evaluated according to the SDGs, Spain fell from position 7th in 2015 to 23rd in 2016.<sup>32,33</sup> Spain achieved 74 points, eight less than in 2016, and the worst score, ten out of 100, was related with consumption of alcohol (the previous year it obtained a mere pass with 57 points, although the way of measuring this factor had been slightly modified.<sup>33</sup> The second and third worst scores referred to tobacco use (25 out of 100) and childhood obesity (36 out of 100). On incidence of HIV and child abuse, Spain barely reached a pass. The goals included in the index are based on the SDG agreements signed by individual countries (Spain included) to be achieved by 2030. The SDG index estimations forecast that, assuming current trends, Spain is not expected to achieve these goals by 2030, when is estimated to reach only 84 points out of 100. The top worse performing goals for Spain are alcohol use, smoking, childhood overweight, child health abuse, and HIV incidence. Stronger and effective interventions, and inter-sectorial policies to improve those health indicators are needed.

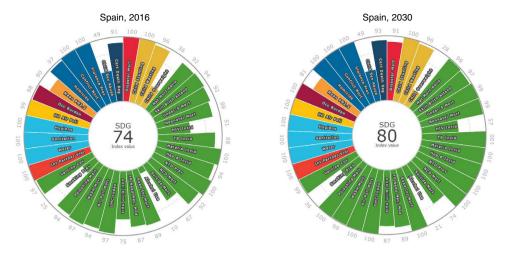


Figure 14. Components of SDG in 2016 and projected to 2030.

### Strengths and limitations

Among the many inherent strengths of this study are novelty, being the first, unique, comparable, consistent assessment of health, morbidity and mortality, and risk factors in Spain, and also comparable within our European neighbours and globally. The systematic, independent and regularly updated evaluation of the original information sources is one of the strengths of the GBD initiative. In addition, each of the new GBD iterations incorporates new sources and updates existing ones, and therefore substitutes previously published estimates. The list of original data sources for Spain on risk factors, demographics, morbidity-mortality, use of health services and other estimators is available on the server http://www.ghdx.healthdata.org. For example, as of April 11, 2017 GBD uses 1587 different sources of information on Spain, including sources from the Spanish National Institute of Statistics (INE), different Ministries, WHO-Europe, Autonomous Communities, and other (http://www.ghdx.healthdata.org/geography/spain).'

However, a number of limitations must be considered, perhaps in future iteration of GBD Spain. First, although Spain follows the European Statistics Code of Practice and data is collected in a consistent way across the country, there are a number of issues that should be considered when interpreting mortality results. The GBD project defined a number of garbage codes, which are causes of death that should not be identified as underlying causes of death on death certificates. Garbage codes were substituted by IHME with other underlying causes based on pathophysiology. The fraction of garbage codes in Spain was within the expected average, rated with four out of five stars.<sup>3</sup> Second, calculation of disability weights was based on surveys including several countries, and not just Spain. Third, demographic trends, especially of migrants on fertility and other epidemiological estimators, and global climate uncertainties,44 may significantly change current assumptions of SDGs in Spain up to 2030 and beyond. Given the decentralised health system in Spain, with most Medicine and Public Health budgets managed separately by the 17 different Autonomous Communities, there likely is great heterogeneity regionally and by smaller areas in many of the estimates presented only nationally in here. Accordingly, further efforts should be explored to perform a sub-national GBD study in Spain.

Modelling of data and extrapolation to the most recent years, overcoming the usual one- or two-year gap of data unavailability due to internal processing, could be considered one of the GBD strengths. As referred in all previous iterations of the GBD study,<sup>2</sup> Bayesian statistical models were used to estimate prevalence of conditions in each country by age, sex, and year. The nature of

this estimation process implies that, in some cases, depending on the covariates, the estimated variance might be smaller than the real variance across countries in a region, and in some other cases, uncertainty intervals for a specific estimate might be exaggerated. Furthermore, the calculation of uncertainty intervals throughout the Bayesian model analysis has provided some information on the extent of available information for Spain. However, the nature of the estimation process for causes of death and the prevalence of sequelae more generally may lead to exaggerated uncertainty intervals in a high-income country such as Spain.

# Impact of the economic crisis

Spain experienced a great economic crisis, which began in 2008 during the world financial crisis of 2007-2008. The main cause of Spain's crisis was the housing bubble and the accompanying unsustainably high GDP growth rate. Regidor et al.45 described that all-cause mortality in Spain decreased more during the economic crisis than before, especially in low socioeconomic groups, probably due to the decreased exposure to risk factors. It has been argued that this study oversimplified the economic crisis, which was a long-term occurrence, particularly given that austerity in Spain mostly started after a constitutional reform in 2011 to prioritise budget deficit control over social expenditures. 46 Additionally, children younger than 10 years and adults older than 74 years were excluded from that analysis, despite being highly susceptible social groups.<sup>47</sup> Similar to Regidor et al.,<sup>46</sup> others reported that in European countries in general and especially in those most affected by the crisis (i.e.: Greece, 48 and Iceland 49), general mortality also decreased and the health of the population improved in 2007–2010.<sup>50</sup> As compared to before the crisis, for adults 60 years and older the observed mortality seemed to be decreasing at a slower rate than what would have been expected in the absence of the crisis, with an increase in winter mortality, and a greater impact for female than for male mortality.<sup>48</sup> These results suggest sizable effects of the economic crisis on the mortality of older adults and argue for research done using more detailed analyses integrating economic indicators. On the negative side, the economic crisis in the above three countries negatively impacted mental health and some other population health indicators. 51,52 Overall, within a universal, health-for-all society, any economic recession will produce changes on use of and access to health services: it is more likely detrimental to low-income groups regarding specialist appointments and hospitalisations, whereas it works to their advantage in the case of emergency services and family doctor appointments. Future studies might investigate further the role of the Spanish Welfare State, consolidated in recent decades, because through various mechanisms of social protection, such as pensions, unemployment insurance, work disability, and else, it could have acted as a buffer against the negative effects of the economic crisis.<sup>44</sup>

Success stories: road accidents, self-harm and tobacco

In the GBD 2016 study, road injuries as cause of death fell from the 8th position in 1990 to 32nd in 2016. This success could be attributable to a number of factors, including the obligatory enforcement of fastened seat belts; fastening while driving was compulsory in roads from1974, and in urban areas from 1992,<sup>53</sup> plus the compulsory helmet for motorbike riders of >125 cc, and of <125 in roads but not cities from 1982; tax incentives for the renovation of the oldest automobiles; major road work improvements; and last but not least, less traffic because of the impact of the economic crisis from 2008.<sup>46</sup>

Deaths attributable to self-harm went down from position 19th to 26th. Contrary, Alvarez-Galvez et al.<sup>54</sup> reported that suicide deaths decreased during the first period of the economic recession (2007–2011), but there was a positive and significant relationship between the crisis and suicide rates during the second period (2011–2014). This difference could be explained by a delayed effect of personal economic problems due to initial protection policies.

Following the WHO Framework Convention for Tobacco Control, tobacco control policies fuelled smoke-free legislation (Law 28/2005 and Law 42/2010) to further protect non-smokers and implemented MPOWER recommendations. 55,56 Close attention to monitoring all tobacco trends, implementing and strengthening tobacco control, and limiting vaping of e-cigarettes, particularly in the youngest, are fundamental for widening long-term Public Health goals in most/all diseases. Moreover, among other risk factors, reductions in most urban air pollution exposures will have massive beneficial long-term health effects.

# A sub-national GBD study in Spain

The GBD 2016 Study provides a global assessment of the health-related burden and its determinants in an international comparative risk assessment framework. This information is important and useful to inform health policy managers, and the society in general. The present GBD 2016 Spain report shows important unmet needs, and opportunities to improve the public health and health care systems. The GBD international comparative framework offers an uncanny opportunity to explore appropriate benchmarking, and to identify the best policies and practices that proved successful in other countries, to be adapted and implemented in Spain. So far, no other source of health information in Spain offers this type of international comparative risk assessment. Unfortunately, the information is only provided at the national level, a limitation that other countries have approached and overcome by extending the GBD at the sub-national level (state, counties, districts and cities).5-11 In these sub-national GBD studies, the improved granularity of the information allows to assess social inequalities, and to extend the opportunities for learning from others at the regional level, health planning, and provision of public health and health care services, which in Spain belong to the Autonomous Communities. Therefore, such further exploitation of GBD tools would further reinforce the GBD contribution to health policy in Spain.

### **Conclusions**

To conclude, given stagnation of population growth and generalised ageing, in a country with high quality Public Medicine and Preventive services and systems, the burden of disease in Spain

is rapidly evolving within the well-known epidemiological transition to chronic, non-communicable diseases.<sup>57</sup> Low back and neck pain became the major driver of disability in Spain in 2016, while tobacco remains the most relevant risk factor overall to be tackled, and we observe a remarkable increase in the burden due to Alzheimer disease and other dementias. Close monitoring of these trends is fundamental to set up and prioritise effective health interventions in Spain.

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# **Conflict of interests**

The authors declare no conflict of interest.

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# Appendix A.

List of GBD collaborators in Spain, that includes:

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# References

- Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet. 1997;349:1269–76.
- Institute for Health Metrics and Evaluation. Global Burden of Disease. Available from: http://www.healthdata.org/gbd [accessed 01.12.17].

- GBD 2016 Mortality Collaborators. Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970–2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390:1084–150.
- 4. Murray CJL, Lopez AD. Measuring global health: motivation and evolution of the Global Burden of Disease Study. Lancet. 2017;390:1460-4.
- Newton JN, Briggs AD, Murray CJ, Dicker D, Foreman KJ, Wang H, et al. Changes in health in England, with analysis by English regions and areas of deprivation, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386:2257–74.
- Zhou M, Wang H, Zhu J, Chen W, Wang L, Liu S, et al. Cause-specific mortality for 240 causes in China during 1990–2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. Lancet. 2016;387:251–72.
- Nomura S, Sakamoto H, Glenn S, Tsugawa Y, Abe SK, Rahman MM, et al. Population health and regional variations of disease burden in Japan, 1990–2015: a systematic subnational analysis for the Global Burden of Disease Study 2015. Lancet. 2017;390:1521–38.
- 8. Misganaw A, Melaku YA, Tessema GA, Deribew A, Deribe K, Abera SF, et al. National disability-adjusted life years (DALYs) for 257 diseases and injuries in Ethiopia, 1990–2015: findings from the global burden of disease study 2015. Popul Health Metr. 2017;15:28.
- Souza MFM, França EB, Cavalcante A. Burden of disease and health situation analysis: results of the Global Burden of Disease (GBD) Brazil network. Rev Bras Epidemiol. 2017;20 suppl. 1:1–3.
- Yin P, Wang H, Vos T, Li Y, Liu S, Liu Y, et al. A subnational analysis of mortality and prevalence of COPD in China from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Chest. 2016;150:1269–80.
- Corrêa RA, José BPS, Malta DC, Passos VMA, França EB, Teixeira RA, et al. Burden
  of disease by lower respiratory tract infections in Brazil, 1990 to 2015: estimates
  of the Global Burden of Disease 2015 study. Rev Bras Epidemiol. 2017;20 suppl.
  1:171–81.
- Ministerio de Sanidad, Servicios Sociales e Igualdad. Encuesta Nacional de Salud de España. Available from: https://www.msssi.gob.es/estadEstudios/ estadisticas/encuestaNacional/ [accessed 30.01.18].
- Ministerio de Sanidad, Seguridad Social e Igualdad. Encuesta Nacional de Salud de España 2017. Madrid: MSSSI; 2018.
- 14. Requena ML, Suárez M, Pérez Ó, Grupo Técnico de Encuestas de Salud de la Subcomisión de Sistemas de Información Consejo Interterritorial del Sistema Nacional de Salud. Encuestas de salud en España: situación actual. Rev Esp Salud Publica. 2013;87:549–73.
- EUROSTAT. European Health Interview Survey (EHIS). Available from: http://www.ec.europa.eu/eurostat/web/microdata/european-health-interview-survey [accessed 10.01.18].
- Mueller N, Rojas-Rueda D, Basagaña X, Cirach M, Cole-Hunter T, Dadvand P, et al. Health impacts related to urban and transport planning: a burden of disease assessment. Environ Int. 2017;107:243–57.
- Haro JM, Tyrovolas S, Garin N, Diaz-Torne C, Carmona L, Sanchez-Riera L, et al. The burden of disease in Spain: results from the global burden of disease study 2010. BMC Med. 2014:12:236.
- Institute for Health Metrics and Evaluation. Spain. Available from: http://www.healthdata.org/spain [accessed 11.10.17].
- Genova-Maleras R, Álvarez-Martín E, Morant-Ginestar C, Fernández de Larrea-Baz N, Catalá-López F. Measuring the burden of disease and injury in Spain using disability-adjusted life years: an updated and policy-oriented overview. Public Health. 2012;126:1024–31.
- 20. Catalá-López F, Fernández de Larrea-Baz N, Morant-Ginestar C, Álvarez-Martín E, Díaz-Guzmán J, Gènova-Maleras R. The national burden of cerebrovascular diseases in Spain: a population-based study using disability-adjusted life years. Med Clin (Barc). 2015;144:353–9.
- 21. Catalá-López F, Gènova-Maleras R, Ridao M, Álvarez E, Sanfélix-Gimeno G, Morant C, et al. Burden of disease assessment with summary measures of population health for the Region of Valencia, Spain: a population-based study. Med Clin (Barc). 2013;140:343–50.
- GBD 2016 Causes of Death Collaborators. Global, regional, and national agesex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390: 1151–210.
- United Nations. Sustainable development knowledge platform. Transforming our world: The 2030 agenda for sustainable development. New York: United Nations; 2015. Available from: https://www.sustainabledevelopment.un.org/ post2015/transformingourworld [accessed 30.01.18].
- Yamey G, Shretta R, Binka FN. The 2030 sustainable development goal for health. BMJ. 2014;349:g5295.
- Open knowledge repository. World development report 1993: Investing in health. World Bank; 1993.
- Stevens GA, Alkema L, Black RE, Boerma JT, Collins GS, Ezzati M, et al. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. Lancet. 2016;388:e19–23.
- 27. Instituto Nacional de Estadística. Estadística de defunciones según la causa de muerte. Available from: http://www.ine.es/ [accessed 29.01.18].
- Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C, et al. GBD 2010 design, definitions, and metrics. Lancet. 2012;380:2063–6.

- 29. GBD 2016 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390:1260–344.
- **30.** GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390:1211–59.
- **31.** GBD 2016 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390:1345–422.
- GBD 2015 SDG Collaborators. Measuring the health-related Sustainable Development Goals in 188 countries: a baseline analysis from the Global Burden of Disease Study 2015. Lancet. 2016;388:1813–50.
- 33. GBD 2016 SDG Collaborators. Measuring progress and projecting attainment on the basis of past trends of the health-related Sustainable Development Goals in 188 countries: an analysis from the Global Burden of Disease Study 2016. Lancet. 2017: 390
- **34.** Davison A, Hinkley D. Bootstrap methods and their application. Cambridge: Cambridge University Press; 1977.
- 35. The R Development Core Team. R: A language and environment for statistical computing. Version 2.6.2. R Foundation fos Statistical Computing; 2008.
- Instituto Nacional de Estadística. Basic cause of death. Available from: http://www.ine.es/dynt3/inebase/en/index.htm?padre=4321&capsel=4322 [accessed 20.01.18].
- Fuster V. Global burden of cardiovascular disease: time to implement feasible strategies and to monitor results. J Am Coll Cardiol. 2014;64:520–2.
- 38. Menéndez E, Delgado E, Fernández-Vega F, Prieto MA, Bordiú E, Calle A, et al. Prevalence, diagnosis, treatment, and control of hypertension in Spain. Results of the Di@bet.es Study. Rev Esp Cardiol (Engl Ed). 2016;69:572–8.
- Otero A, de Francisco A, Gayoso P, García F, EPIRCE Study Group. Prevalence of chronic renal disease in Spain: results of the EPIRCE study. Nefrologia. 2010:30:78–86.
- 40. Jellinger PS, Handelsman Y, Rosenblit PD, Bloomgarden ZT, Fonseca VA, Garber AJ, et al. American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract. 2017;23 suppl. 2:1–87.
- 41. Martín-Sánchez JC, Martinez-Sanchez JM, Bilal U, Cleries R, Fu M, Lidón-Moyano C, et al. Sex and age specific projections of smoking prevalence in Spain: a Bayesian approach. Nicotine Tob Res. 2018;20:725–30.
- 42. Instituto Nacional de Seguridad e Higiene en el Trabajo. Informe sobre el estado de la seguridad y salud laboral en España 2015. Madrid: INSHT; 2016.
- Benavides FG, Delclós J, Serra C. [Welfare State and public health: The role of occupational health] Spanish. Gac Sanit. 2017;32:377–80.
   Soriano JB, Soriano C, Fernández E. Respiratory planetary medicine. Arch Bron-
- Soriano JB, Soriano C, Fernández E. Respiratory planetary medicine. Arch Bronconeumol. 2017;53:297–9.
- **45.** Regidor E, Vallejo F, Granados JAT, Viciana-Fernández FJ, de la Fuente L, Barrio G. Mortality decrease according to socioeconomic groups during the economic crisis in Spain: a cohort study of 36 million people. Lancet. 2016;388:2642–52.
- **46.** Urbanos Garrido R, Puig-Junoy J. [Austerity policies and changes in healthcare use patterns. SESPAS report 2014] Spanish. Gac Sanit. 2014;28 supl. 1:81–8.
- Benmarhnia T, Zunzunegui MV, Llácer A, Béland F. [Impact of the economic crisis on the health of older persons in Spain: Research clues based on an analysis of mortality. SESPAS report 2014] Spanish. Gac Sanit. 2014;28 supl. 1:137–41.
- 48. Laliotis I, Ioannidis JPA, Stavropoulou C. Total and cause-specific mortality before and after the onset of the Greek economic crisis: an interrupted time-series analysis. Lancet Public Health. 2016;1:e56–65.
- Asgeirsdottir TL, Olafsdottir T, Ragnarsdottir DO. Business cycles, hypertension and cardiovascular disease: evidence from the Icelandic economic collapse. Blood Press. 2014;23:213–21.
- 50. Tapia Granados JA. [The economic crisis and health in Spain and Europe: Is mortality increasing?] Spanish. Salud Colect. 2014;10:81–91.
- 51. Bacigalupe A, Shahidi FV, Muntaner C, Martín U, Borrell C. Why is there so much controversy regarding the population health impact of the great recession? Reflections on three case studies. Int J Health Serv. 2016;46:5–35.
- 52. Gili M, García Campayo J, Roca M. [Economic crisis and mental health SESPAS report 2014] Spanish. Gac Sanit. 2014;28 supl. 1:104–8.
- 53. Ministerio del Interior. Cinturón de seguridad. Sistemas de retención infantil. Madrid: Dirección General de Tráfico; 2014.
- 54. Alvarez-Galvez J, Salinas-Perez JA, Rodero-Cosano ML, Salvador-Carulla L. Methodological barriers to studying the association between the economic crisis and suicide in Spain. BMC Public Health. 2017;17:694.
- 55. Jiménez Ruiz CA, Riesco Miranda JA, Altet Gómez N, Costa-Miñana JS, Lorza Blasco JJ, Ruiz Manzano J, et al. Impact of legislation on passive smoking in Spain. Respiration. 2014;87:190–5.
- **56.** Fernandez E, Nebot M. Spain: Beyond the 'Spanish model' to a total ban. Tob Control. 2011;20:6–7.
- Van der Zee S, Fuster V. [Cardiovascular disease and chronic kidney disease: From treatment to promoting health] Spanish. Med Clin (Barc). 2009;132 supl. 1:33–7.