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The cost and burden of schizophrenia in Portugal in 2015

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Abstract

Introduction: Schizophrenia is an important cause of disability and consumption of economic resources. This study aims to estimate the costs and the burden of schizophrenia in mainland Portugal in 2015.

Methods: The burden of disease was measured through disability-adjusted life years (DALY), a metric adopted by the World Health Organisation. The cost of illness was estimated based on the prevalence and adopting a comprehensive perspective of society. Costs included direct consumption of resources and indirect costs of patients and caregivers (loss of productivity). The main sources of cost data were: Diagnosis Related Groups (DRG), healthcare delivery contracts, drug consumption, and expert opinion.

Results: The prevalence of schizophrenia is approximately 48,000 patients, and approximately 41,000 patients are followed in the healthcare system (both public and private units). In 2015, 28,588 DALYs were lost (84% due to disability; 16% due to premature death). At 2015 prices, estimated direct costs totalled €96.1 million, while indirect costs totalled €340.3 million; 97% of the indirect costs were generated by patients, the remaining by the caregivers.

Conclusion: Schizophrenia has an important social impact in Portugal due to the associated morbidity, with a total estimated cost in 2015 of €436.3 million, approximately 0.24% of the Gross Domestic Product. Direct costs represent 0.6% of all healthcare expenditures during 2015, while total costs (direct and indirect) represent 2.7% of healthcare expenditures.

Keywords: Schizophrenia, Cost of illness, Burden of Disease, Disability-adjusted life years.

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Introduction

Schizophrenia is a chronic, clinically diagnosed disease that presents at young age. Despite the heterogeneous course of disease, the evolution of schizophrenia is described as favourable in about 20% of individuals and complete recovery is rare. Most patients remain chronically ill, with exacerbations and remissions of active symptoms, while others have a course of progressive deterioration [1]. Schizophrenia has a significant impact on different domains of human life, namely those related to work, education, interpersonal relationships, ability to live independently, and self-care [2].

Cost of illness studies aim to measure and evaluate the impact of a disease in terms of consumption of economic resources, as well as the impact on economic activity generated by the associated disability [3]. On the other hand, disease burden studies aim to quantify, in a general index, the effects of illness on the health level of a given population [4]. Together, these studies aim to establish a rigorous picture of a given health condition and its magnitude, thus contributing to the definition of priority areas that may need resources, and to establish research and intervention plans within healthcare systems.

Schizophrenia was ranked as the 11th most important cause of disease burden globally in 2015 when measured by total years of disability [5]. According to studies conducted in other countries, schizophrenia is also associated with direct costs (including consumption of healthcare resources) and indirect costs (generated, for example, by the loss of labour productivity) that have relevant societal impact [6, 7].

Despite this international recognition that schizophrenia is an important cause of disability and is characterised by high consumption of economic resources, detailed and updated data for the Portuguese population are not available. In this context, this study aims to estimate the cost and burden of schizophrenia in mainland Portugal in 2015.

Methods

The burden of disease was estimated through disability-adjusted life years (DALY), a metric introduced by the World Bank and the World Health Organisation (WHO), which has now been used in disease burden studies conducted since 1990 [8]. This methodology uses epidemiological data, in particular the incidence of the disease by severity stages, the duration of each stage, and the patient mortality patterns.

The cost of illness was estimated based on the prevalence and adopting a comprehensive perspective of society (not only the perspectives of patients, healthcare systems, hospitals, etc.) [9]. This method considers the number of patients with schizophrenia in the year of analysis and their annual direct and indirect costs associated with the disease.

It should be noted that this type of study uses a wide variety of data sources, both in the types of sources and in the period of reference. In the absence of national data, epidemiological parameters retrieved from the international scientific literature are used. In this context, to estimate the cost and burden of schizophrenia, it was necessary, in the first phase, to obtain estimates of the prevalence, incidence, and mortality of schizophrenia in mainland Portugal.

Estimates of prevalence, incidence, and mortality of schizophrenia in mainland Portugal

According to a recent systematic review that included 65 observational studies, the median lifetime prevalence of schizophrenia in the European general population was estimated at 0.52% (IQR: 0.39–0.87%). Estimates were, nonetheless, heterogeneous between studies (variation: 0.21% to 1.3%) [10]. In Portugal, there are no studies on the prevalence of schizophrenia. Therefore, to estimate the prevalence in Portugal, we used data on the consumption of antipsychotics.

First, the number of patients receiving antipsychotic drugs was estimated based on official drug consumption data from the outpatient clinic of the Regional Health Administration of Lisbon and Tagus Valley (ARSLVT) (which includes a population of over 3.6 million individuals) and sales data provided by IMS Health (2016). Drug consumption in terms of packages was converted into the number of patients under treatment considering the daily defined dose (DDD) of each active ingredient. In the case of antipsychotic drugs with approved therapeutic indications beyond schizophrenia, the proportion of sales attributable to schizophrenia was estimated. This proportion was calculated using the distribution of pathology groups as reported in the 3rd Portuguese Psychiatric Census [11]. It was also considered that a proportion of patients is under treatment with more than one antipsychotic drug. The proportion of patients on concomitant injectable and oral therapy and the proportion of patients on two concomitant oral therapies were estimated on the basis of expert opinion at 35% and 50%, respectively. Secondly, it was necessary to assume that, at any moment, only a proportion of patients adhere to antipsychotic therapy. Based on expert opinion, an average rate of adherence of 75% was considered. Finally, to estimate the prevalence rates of schizophrenia by gender and age group in mainland Portugal in 2015, the results of the 3rd Psychiatric Census [11] were considered.

Regard mortality due to schizophrenia, in 2014, the disease was identified as the cause of death in only 14 deaths reports in Portugal [12]. For the 2010-2014 period, the average annual number of deaths due to schizophrenia is less than 18. However, there is solid evidence that patients with schizophrenia have an increased mortality risk compared to the general population, with a standardised mortality ratio of 2.50 (95% CI: 2.18 to 2.43), as estimated in the systematic review by Saha et al. (2007) [13]. These two outcomes (near-zero schizophrenia mortality and increased mortality risk) are, however, compatible since

deaths in patients with schizophrenia can be attributed to causes other than schizophrenia *per se* (e.g. self-inflicted lesions, unintentional, infectious diseases, substance abuse, cardiovascular disease, and neoplasms) [14].

According to an overview of three systematic reviews of the literature on the incidence, prevalence, and mortality associated with schizophrenia, including 158 studies in 32 countries, the overall incidence of schizophrenia in 2008 was estimated at 15.2/100,000 individuals, but there is a significant variability between studies and countries (interquartile range [IQR]: 10.2 to 22.0/100.000 individuals) [15]. As with prevalence, no data are available on the incidence of schizophrenia in Portugal.

To estimate the incidence and duration of the disease in Portugal, the DISMOD II model was used, which is a tool developed by the WHO [16]. This model ensures internal consistency between epidemiological parameters of the disease: incidence rates, prevalence, remission, lethality, mortality or relative risk (RR) of mortality, and durations. The model requires a minimum of three inputs, which in this case were the prevalence (estimated by the authors using the described methodology), the relative risk of death (as estimated by Saha et al.) [13], and the remission of the disease (here defined as cure of the disease and assumed to be zero as there are no curative treatments for the disease) [17].

Burden of disease

The burden of disease was estimated through DALYs, a measure, expressed in time, of the amount of health lost due to disability generated by the disease or premature death. It includes two components: 1) years of life lost (YLL) due to premature death, with time lost estimated as the difference between age at death and standard life expectancy for that age; and 2) Years lost due to disability (YLD), which considers time spent suffering from disability [4].

Standard life expectancy was obtained from the mortality tables adopted as standard of reference [4]. Disability was measured by a coefficient with scores between 0 (without any disability, perfect health) and 1 (total disability or death). To estimate the number of DALYs lost by an individual, the following equation was used:
where:

$$DALY = \int_{a}^{a+L} DCxe^{-\beta x}e^{-r(x-a)}dx$$

a - initial age.
L - length of disability or years of life lost due to premature death.
D - coefficient of disability, between 0 e 1.
C - constant - correction for age (0.04).
X - age, varies between *a* and *a+L*.
β - parameter from the rule for age correction (0.1658) [18].
r - rate of time discount (3%).

In the calculation of the DALYs, a discount rate of 3% and an age-differentiated weighting were used, in which intermediate age groups (between 20 and 50 were given more weight than the younger and older groups) [4] (**Figure 1, supplementary material**). It was considered that all prevalent patients, even without diagnosis, and therefore without follow-up, contribute to the burden associated with the disease.

Years of life lost (YLL) due to premature death

As mentioned previously, deaths due to schizophrenia in Portugal [12] are not the most adequate source to estimate YLLs due to schizophrenia. In this context, YLLs were estimated considering that a fraction of the overall mortality in patients with schizophrenia may be attributable to the disease. In this case, following the approach that uses the concept of attributable fraction [19], the fraction of total mortality attributable to schizophrenia was determined by the equation:

$$\text{Attributable Fraction} = (RR-1)/RR$$

where RR is the relative risk of death in patients with schizophrenia. The RR of mortality in schizophrenia considered was estimated by Saha et al. (2007) (2.50) [13], whereby the attributable fraction is 60%.

The number of deaths, by sex and age group, to which the fraction attributable to schizophrenia was later applied, was estimated from the DISMOD II model, in accordance with the previously described calibration assumptions.

Years lost due to disability (YLD)

To estimate YLDs, the methodology and disability weights applied in the Global Burden of Disease 2015 study [5] were used. For schizophrenia, this study considers two stages, acute and residual, whose disability weights were estimated at 0.778 and 0.588, respectively.

To apply these disability weights, the overall incidence of schizophrenia needs to be distributed for each of the stages, which was done in the Global Burden of Disease 2015 study based on the results of the systematic review by Ferrari et al. (2012) [20]. The parameters used are summarised in **Table 1**.

Given the lack of more detailed information in the literature, it was considered that the distribution of incident cases for the two stages (according to **Table 1**) was independent of the age of onset and duration of the disease.

Cost of illness

Cost of illness was estimated from the prevalence perspective. Conservatively, it was assumed that only follow-up patients generate costs. Direct costs (healthcare consumption of the patients themselves) and indirect costs (productivity losses of patients and caregivers) were considered.

Table 1. Disability weighting factors and distribution by schizophrenia stages.

Stage	Disability weights (IC 95%)	Description	Proportion (IC 95%)
Acute	0.778 (0.61-0.90)	Hears and sees things that are not real and is afraid, confused, and sometimes violent. Has difficulty in communication and activities of daily living and sometimes wants to self-harm or commit suicide.	63% (29%-91%)
Residual	0.588 (0.41-0.75)	Hears and sees things that are not real and has communication problems. May have forgetfulness, has difficulties in activities of daily living, and thinks about self-harm.	37% (9%-71%)

95% CI: 95% confidence interval.
Source: Adaptated from GBD 2015 Disease and Injury Incidence and Prevalence Collaborators (2016) [5] e de Ferrari et al. (2012) [20].

Direct costs

The direct costs considered were: 1) hospitalisation, ambulatory hospital visits, and others; 2) emergency department visits without hospitalisation; 3) outpatient visits of psychiatry, mental health, and general and family medicine (GFM); 4) pharmacological therapy; and 5) transport.

Costs of hospitalisation, ambulatory hospital visits, and others

Consumption of resources for hospitalisations and ambulatory hospital visits was assessed using the Diagnosis Related Groups (DRG) database of the 2015 National Health Service[i]. In the DRG database, episodes of patients over the age of 15 and with the main diagnosis of schizophrenia (International Classification of Diseases 9, Clinical Modification, ICD 9-CM equals 295.XX)[ii] were identified. The unit cost of hospitalisation episodes was estimated based on the prices of Ordinance No. 234/2015 of August 7 (https://dre.pt/application/file/a/69965783, accessed in July 2017), which approves the regulation and the price lists of institutions and services integrated in the national health service.

Resource consumption, and their respective costs, generated in the context of the hospitalisation of chronic patients, rehabilitation, ambulatory hospital, and home psychiatry visits was estimated using a top-down methodology [21]. Initially, the overall costs associated with psychiatric patients was estimated and, then, the proportion of these costs specifically associated with schizophrenia patients was estimated. The overall psychiatry costs were estimated based on the prices and consumptions reported in the 2015 healthcare delivery contracts (signed between national health service hospitals and entities that represent the national health service) and the 2015 "Reports and Accounts" documents of each psychiatric hospital (Hospital Magalhães Lemos, EPE and Psychiatric Hospital Center of Lisbon) (**Table 2**).

The proportion of consumption presented in **Table 2** that is specifically attributable to schizophrenia patients was estimated based on the results of a panel of 3 experts (Delphi methodology) with national representativeness.

Costs of emergency department visits

The use of the emergency department (without subsequent hospitalisation) was estimated based on the results of the panel of experts and by searching the DRG database. According to expert opinion, on average, 70% of patients who go to the emergency department of psychiatry due to schizophrenia are not hospitalised. The number of emergency visits without hospitalisation was estimated based on this proportion as well as the number of hospitalisation episodes due to schizophrenia with urgent admission (by consulting the DRG database).

The unit cost of emergencies without hospitalisation was calculated as the weighted average of the prices of hospital emergency department visits reported in healthcare delivery contracts of the national health services hospitals. The weighting was performed according to the distribution of the number of hospitalisation episodes for schizophrenia with urgent admission in the national health service hospitals.

Costs of ambulatory hospital visits

Consumption of ambulatory psychiatric and mental health visits in the community was estimated from the total number of visits reported in the annual report on access to healthcare in the national health service and contracted entities in 2014, and in healthcare delivery contracts, respectively. The proportion of visits attributable to schizophrenia (12.4%) was estimated based on the results of the 3rd Psychiatric Census [11]. Ambulatory psychiatric visits in the public sector were increased by 28.8% to include the contribution of the private sector; according to the proportion of antipsychotics with exclusive therapeutic indication for the treatment of schizophrenia prescribed in the private sector. Based on the number of ambulatory visits of psychiatry and considering an average of three follow-up visits per patient per year (expert opinion), it was possible to estimate the number of patients in follow-up (in the public and private sector).

The unit cost of psychiatric and mental health visits in the community was estimated through the healthcare delivery contracts of national health service hospitals for 2015, assuming that this amount already includes the ex-

[i]Source: Administração Central do Sistema de Saúde ACSS, I.P.
[ii]It should be noted that, in the case of schizophrenia, there is a substantial proportion of long-term hospitalisations, that is, beyond the maximum duration threshold contemplated in the DRG. In these cases, costing rules were applied evaluating the days in excess of the daily rate indicated in the legislation.

Table 2. Estimate of resource consumption and respective price for psychiatric patients in national health service hospitals.

	Psychiatric Hospitals[a]			Other Hospitals		
	No days / sessions	**Value (€)**	**Unit cost**	**No days / sessions**	**Value (€)**	**Unit cost**
Hospitalisation of chronic patients						
Hospital	71,038	5,025,939	70.75	65.554	2,597,023	39.62
External (religious orders)	294,491	11,535,212	39.17	607.601	23,785,107	39.15
External (other institutions)	58,321	2,282,014	39.13	49.331	1,932,295	39.17
Psychosocial Rehabilitation	48,374	3,422,461	70.75	2.500	176,875	70.75
Ambulatory hospital						
Psychiatry	54,620	1,665,364	30.49	133.367	4,085,512	30.63
Psychology – socio-occupational	26,904	820,303	30.49	11.840	361,002	30.49
Rehabilitation structures[b]						
Psychiatry	31,312	954,703	30.49	-	-	-
Home visits (Psychiatry)						
Psychiatry	9,035	299,059	33.1	-	-	-

[a]Hospital de Magalhães Lemos, E.P.E. e o Centro Hospitalar Psiquiátrico de Lisboa.
[b]This section is only completed in the healthcare delivery contract for Hospital de Magalhães Lemos, E.P.E., thus the number of sessions corresponds only to the production of this hospital.
Source: healthcare delivery contracts of national health service hospitals e "Report and Accounts" documents of Hospital de Magalhães Lemos, E.P.E. and Centro Hospitalar Psiquiátrico de Lisboa.

penses with the visits itself and with the possible use of complementary means of diagnosis.

To estimate the number of GFM visits, the proportion of psychiatric visits with primary care referral reported in the healthcare delivery contracts (9.6%) was considered and it was assumed that, for each patient referred, two GFM visits would occur.

The unit cost of the consultation considered was €31.00, according to the price defined in Ordinance No. 234/2015 of August 7.

Costs of pharmacological therapy

To estimate the cost of antipsychotic pharmacological therapy in the ambulatory setting, the same sources and assumptions used to estimate the prevalence of patients with schizophrenia in Portugal were applied. In addition, the cost of other pharmacological therapies with action on the central nervous system (Anatomical Therapeutic Chemical [22] codes N05B, N05C, N044AA01 N04AA02 N06A and N03) were also considered. These ATC classes were selected based on the national study by Simões do Couto et al. (2011) [23] in which the demographic and clinical characteristics of 474 patients with schizophrenia were monitored between 2004 and 2005. The proportion of non-institutionalised patients treated with each class was estimated by the panel of experts. Unit prices for non-antipsychotic drugs with central nervous system action result from the weighted average prices per mg (http://app7.infarmed.pt/infomed/inicio.php, Infomed - IINFARMED, IP, accessed in June 2017) and market shares (IMS Health 2012). The annual price was calculated based on the DDD (https://www.whocc.no/atc_ddd_index/, accessed July 2017).

Costs of transport

Direct costs also included travel costs associated with urgent transport (to travel to the emergency department) and non-urgent transport (to travel to visits). The details of the estimated transport costs are presented in supplementary material (**Table 1, supplementary material**).

Indirect costs

Indirect costs included the costs of patients and their caregivers of working age, that is, under 65 years of age.

Patient costs

Patients were distributed in four mutually exclusive groups: 1) those who work with an unprotected job; 2) those who have protected jobs [24]; 3) those who would work if they did not have the disease; and 4) those who would be unemployed even if they did not have the disease. Groups 1 and 2 generate absenteeism costs. Group 2 generates costs associated with lost production by reduced productivity of patients with schizophrenia. Group 3 generates costs associated with lost production due to the disease because of non-participation in the labour market. The last group does not generate indirect costs.

To estimate the average productivity of workers, the Human Capital theory [25] was adopted. According to this theory, indirect costs—measuring the lost production due to the disease—are estimated based on the costs for employees incurred by the employer. The information considered to estimate indirect costs is summarised in **Table 3**.

Table 3. Information considered to estimate the indirect costs associated with schizophrenia patients.

No	Information	Estimate	Source
1	No of patients in follow-up under 65 years of age	32,568	Authors estimate
2	Proportion of patients with unprotected job	10.35%	Expert panel
3	Proportion of patients with protected job	4.65%	Expert panel
4	Proportion of patients that are not involved in the labour market	85.0%	Calculated from inputs no 2 and 3
5	Rate of employment of the overall population[a]	67.7%	Rate of employment in the 4th trimester of 2015 (INE 2016)
6	Ratio of the productivity of patients with protected job vs. the overall population	80.0%	Ratio of the average salary of patients with disability compared to the overall population (OECD) 2009
7	Daily income per worker[b] per work day	87.99€	Employment statistics from March 2016 referring to April 2015 and authors estimates
8	Annual income per worker[b]	20,238.82€	Employment statistics from March 2016 referring to April 2015 and authors estimates
9	No of work days lost per consultation	0.5	Assumption
10	No of work days lost per emergency episode (without hospitalisation)[c]	1	Assumption

INE – National Statistics Institute; OECD - Organisation for Economic Co-operation and Development.
[a]General population with the same distribution of schizophrenia patients by age group and gender.
[b]Using a gender distribution similar to that of schizophrenia patients.
[c]Travel to the emergency department due to schizophrenia during working hours estimated at 50% of total.

Caregivers costs

Based on expert opinion, it was estimated that 14.9% of patients in follow-up have an employed caregiver. The annual cost per caregiver in Portugal was estimated based on the results of the study by Gupta et al. (2015) [26]. This study estimates the annual indirect costs of caregivers of patients with schizophrenia, compared to non-caregivers, using the results of national health surveys from 5 European countries (EU5). The difference in annual indirect costs between the two groups (€ 2,872) was adjusted by the ratio (53%) between Portuguese GDP and the EU5 weighted average of GDP [27] to reflect lower productivity in Portugal.

Ethical responsibilities

This research did not use human participants and no patient data are presented.

Results

Burden of disease

Prevalence estimates

The number of patients receiving antipsychotic drugs in mainland Portugal during 2015 was estimated at 36,032 based on drug consumption data. When applying a 75% adherence rate, the number of prevalent patients was estimated at 48,042, corresponding to a crude prevalence rate in the population >15 years old of 0.57%. This estimate is in line with the results of the systematic review by Simeone et al. (2015) [10] (0.52% in the European population in general).

Years of life lost (YLL) due to premature death

The distribution of deaths from all causes and for schizophrenia, by age groups and gender, is presented in supplementary material (**Table 2, supplementary material**). The total number of deaths attributable to schizophrenia during 2015 was 223 in men and 180 in women, respectively, which in aggregate corresponds to 0.39% of overall mortality. Based on these results and the standard life expectancy, we estimated that in Continental Portugal in 2015, there were 4,041 YLLs lost due to schizophrenia (62% in men), which corresponds to 0.81% of total YLLs lost due to overall mortality.

Figure 1 shows the distribution of YLLs due to schizophrenia, by gender and age groups. The distribution by age group is slightly different between genders. The loss of YLLs is greater between 55 and 59 years in men and between 65 and 69 years in women.

Years lost due to disability (YLD)

Epidemiological data estimated in DISMOD II and used in the calculation of YLDs are summarised in **Figure 2** and supplementary material (**Table 3, supplementary material**).

Based on these data and considering the disability weights and distribution among severity stages (**Table 1**), we estimated 24,547 YLDs due to schizophrenia in mainland Portugal in 2015, 62% of which in men.

Figure 3 shows the distribution of YLDs due to schizophrenia, by gender and age groups. Most of the burden (74%) falls in the age groups between 15 and 34 years. These age groups present the highest disability weights (**Figure 1, supplementary material**) and the highest incidence rate of schizophrenia (**Figure 2**).

Disability-adjusted life years (DALY)

The sum of YLLs and YLDs results in a total burden of schizophrenia of 28,588 DALYs in 2015 (**Table 4**).

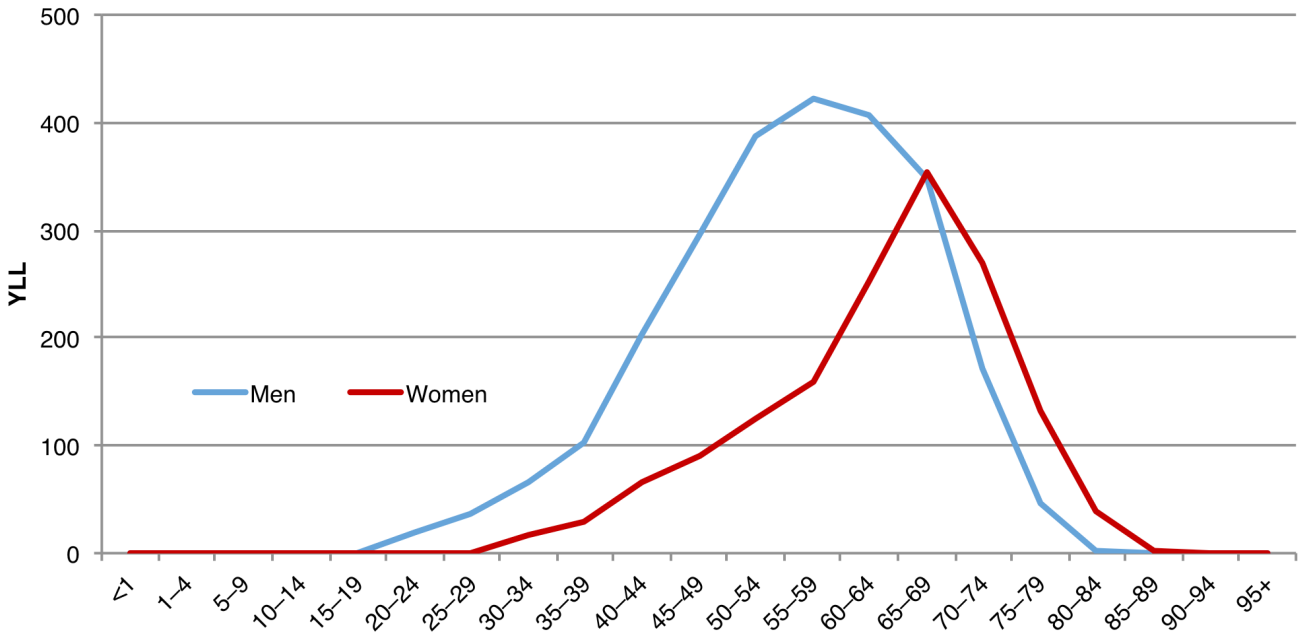

Figure 1. Years of life lost (YLL) due to premature death attributable to schizophrenia in mainland Portugal, by age groups and gender, 2015.

Direct, indirect, and total costs

In the 2015 DRG database, there were 3,124 inpatient episodes with the main diagnosis of schizophrenia, corresponding to the hospitalisation of 2,429 patients. Most of the episodes (92%) corresponded to emergency admissions. The average price per episode was estimated at €3,722.5. The total cost related to hospitalisation episodes was estimated at €11,629,215. There were no ambulatory episodes in the DRG database with the main diagnosis of schizophrenia.

Table 5 summarises the consumptions, unit prices, and estimated total costs of the remaining sources of direct costs considered in the analysis. The calculation of costs with pharmacological therapy (antipsychotic and other) is summarised in the supplementary material (**Table 4, supplementary material**). The total direct cost associated with schizophrenia in mainland Portugal in 2015 was €96,075,590.

Indirect costs generated by patients and caregivers totalled €340,273,639 (**Table 5**). The vast majority of indirect costs (95%) are associated with non-participation of patients in the labour market.

The overall costs attributable to schizophrenia in 2015 in mainland Portugal totalled €436,349,229, 78% of which are indirect.

Discussion

Schizophrenia, as other areas of mental health, is a poorly captured in health information systems. This problem is particularly striking in Portugal, where any research of an epidemiological or economic nature encounters enormous obstacles due to the difficulties in accessing the necessary data, and in some cases, due to lack of such data.

During the execution of this study, we found an substantial lack of epidemiological data for the Portuguese population, with no information on the prevalence, incidence, or even mortality patterns of patients with schizophrenia. The lack of epidemiological data is exacerbated by the lack of data on resource consumption beyond what is listed in the DRG database. These problems are worsened by the specificities of the care provided to these patients, including long-term hospitalisations, use of providers in the social system, etc. Finally, data on indirect costs, both for patients and caregivers, is scarce or non-existent, including studies on the effects of early exit from the labour market on caregivers' lives.

Despite these difficulties, or perhaps because of them, schizophrenia is an area where improvements in knowledge can be extremely relevant to better manage the healthcare system, and to improve policies and optimise the use of resources. For example, the recent effort of Perelman et al. (2017) [28] containing proposals for improving the model of mental health care financing in Portugal.

The study of the costs and burden of disease in a pathology with a human dimension as relevant as schizophrenia has a high potential to leverage improvements in the health of a group of Portuguese people deserving our full attention.

The present work attempted to overcome the above mentioned problems by relying mostly on what we can call indirect estimation techniques. Thus, the few but precious epidemiological data were complemented with epidemiological information inferred from the patterns of drug consumption. In some cases, information on studies in other countries was used to obtain estimates of variables in the Portuguese context. We needed to make use of hospital

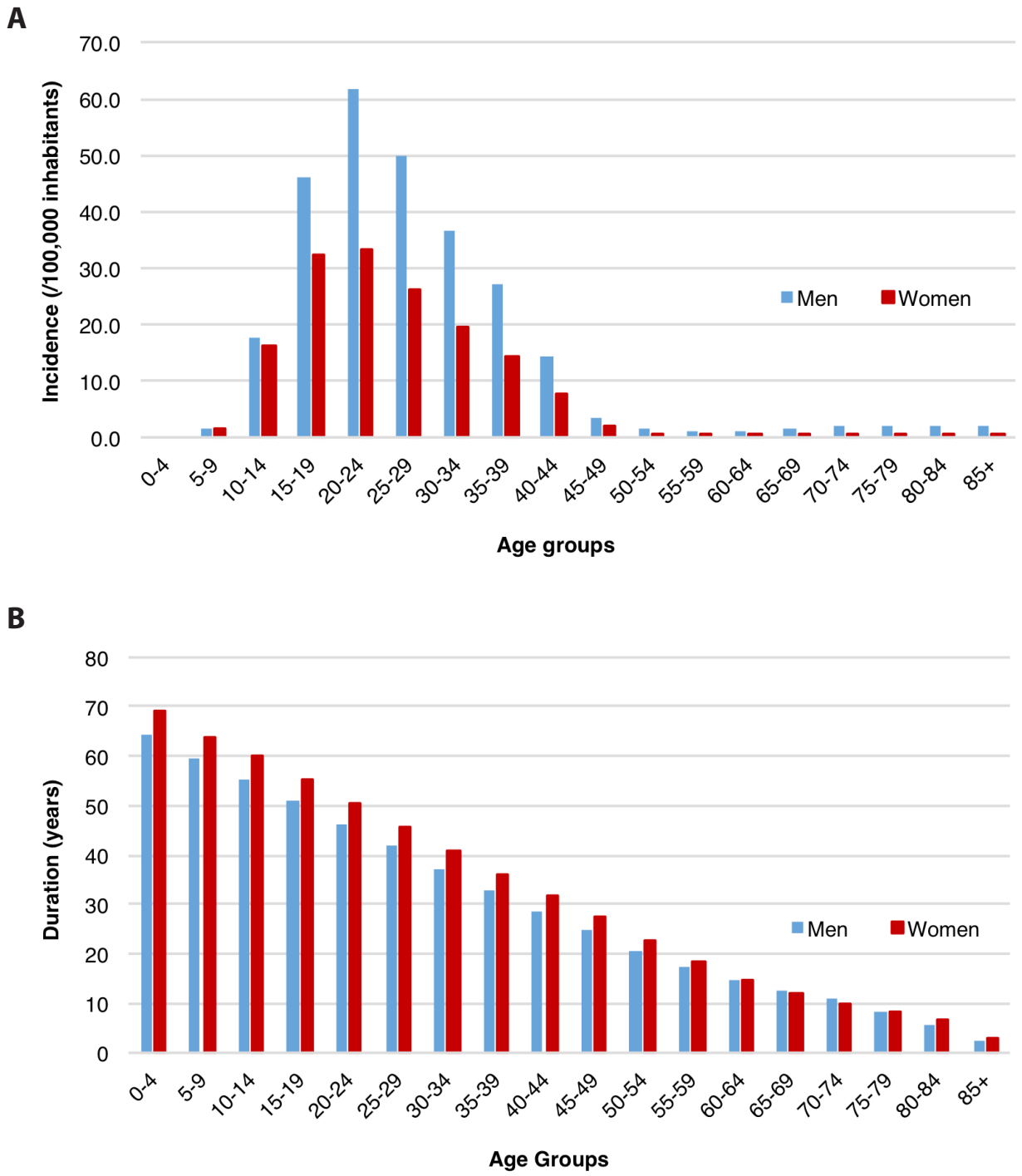

Figure 2. Incidence (A) and estimated duration (B) of schizophrenia in mainland Portugal, 2015.

contract data to fill many statistical gaps, a strategy that is not usually required in the cost and burden studies of other pathologies. In many cases, the informed opinion of experts was the only available information. Although the use of several estimates may be fragile and inaccurate, we believe that the aggregate quantities estimated in this work are reliable estimates of the amounts involved.

The final results show that there should be almost 50,000 patients with schizophrenia in Portugal and that of these more than 40,000 are being followed in the health-care system.

Regarding the burden of disease in 2015, it is estimated that 24,547 years of life have been lost due to disability attributable to schizophrenia. As for the burden generated by mortality, 403 deaths were attributed to schizophrenia, resulting in a total of 4,041 years lost due to premature death. When comparing mortality and YLLs generated by schizophrenia with mortality and YLLs from all causes, YLLs for schizophrenia correspond to 0.81% of total YLL for overall mortality. This percentage is more than double the percentage of deaths due to schizophrenia (compared to total deaths), which can be explained by the fact that

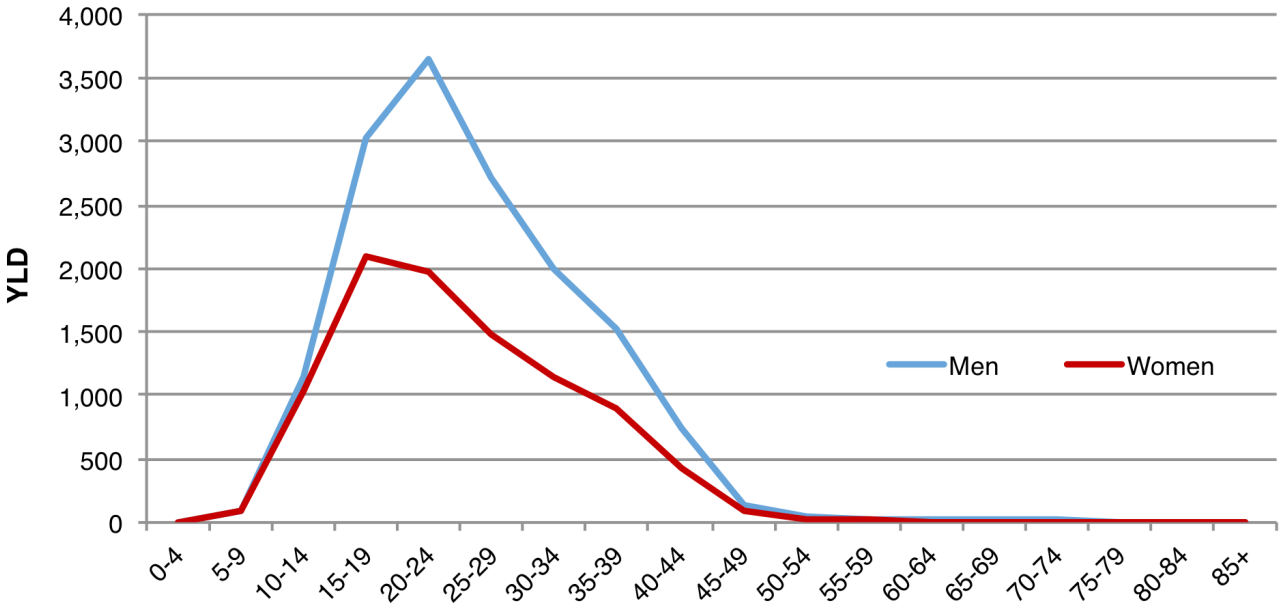

Figura 3. Years lost due to disability (YLD) attributable to schizophrenia in mainland Portugal, 2015.

deaths in schizophrenia occur, on average, at an earlier age than overall deaths.

Overall, the burden of schizophrenia was estimated at 28,588 DALYs. As might be expected, although the disease burden due to premature death is not zero, the burden due to disability is the most relevant, accounting for 86% of the total DALYs.

Regarding the cost of disease in 2015 prices, the estimated total direct cost associated with schizophrenia was €96.1 million. To these direct cost we have to add the indirect cost generated by the patients (absenteeism, non-participation in the labour market, reduced productivity), and by caregivers, respectively, €331.0 million and €9.3 million. This result is very different from what is usually estimated for other diseases, since indirect costs account for 78% of total cost. In other diseases, indirect costs are almost always a minority of total cost [29-32].

The total cost of schizophrenia was estimated at €436.3 million, approximately 0.24% of GDP in 2015. Direct costs account for 0.6% of all healthcare expenditure in 2015, while total costs (direct and indirect) represent 2.7% of healthcare expenditure.

Another recent study used similar methodologies to evaluate the cost and burden of atrial fibrillation in Portugal [30]. The costs and burden associated with schizophrenia are approximately 3.1 and 1.23 times higher than atrial fibrillation, respectively. Despite the limitations of this type of indirect comparisons, the results of the present study document the high socio-economic impact that schizophrenia has in Portugal and at the same time indicate that schizophrenia is an area where significant health gains can be obtained. Therefore, schizophrenia should be a priority area for the healthcare system.

Table 4. Disability-adjusted life years (DALY) attributable to schizophrenia in mainland Portugal, 2015.

	YLL	YLD	DALY
Men	2,511	15,215	17,726
Women	1,531	9,332	10,863
Total	4,041	24,547	28,588

YLL - Years of Life Lost; YLD - Years Lost due to Disability

Supplementary Material

Supplementary material available at http://ijcnmh.arc-publishing.org.

Abbreviations

ARSLVT: Regional Health Administration of Lisbon and Tagus Valley; ATC : Anatomical Therapeutic Chemical; CI: Confidence interval; DALY: Disability-adjusted life years; DDD: Daily defined dose; DRG: Diagnosis Related Groups; EU5: European Union 5 (France, Germany, Italy, Spain, and United Kingdom); GDP: Gross Domestic Product; GFM: General and family medicine; ICD: International Classification of Diseases; IQR: Interquartile range; RR: Relative risk; WHO: World Health Organisation; YLD: Years Lost due to Disability; YLL: Years of Life Lost

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Competing interests

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Table 5. Total annual cost of schizophrenia in mainland Portugal, 2015.

Type	Units	Cost per patient per year[f]	Total annual cost[f]
Direct costs			**96,075,590 €**
Hospitalisation of acute patients (DRG database)	3,124	3,723 €	11,629,215 €
Hospitalisation of chronic patients	495,210[a]	43 €	21,468,365 €
Ambulatory hospital	43,832[b]	50 €	2,197,099 €
Rehabilitation structures (psychiatry)	NA	NA	556,910 €
Home visits (psychiatry)	NA	NA	234,262 €
Emergency episodes without hospitalisation	9,567	85 €	812,076 €
Ambulatory psychiatry visits	122,742	65 €	8,038,010 €
Mental health visits in the community	10,801	85 €	917,214 €
General and family medicine visits	18,868	31 €	584,914 €
Antipsychotic treatment	36,032[c]	1,204 €[d]	43,376,304 €
Other treatment	40,914	127 €	5,206,917 €
Non-urgent travel	152,411	4 €[e]	624,362 €
Urgent travel	9,567	45 €[e]	429,941 €
Indirect costs			**340,273,639 €**
Patient absenteeism	6,137	163 €	1,002,716 €
Patient non-participation in the labour market	15,926	20,239 €	322,317,422 €
Patient reduced productivity	1,903	4,048 €	7,700,876 €
Indirect costs of caregivers	6,089	1,519 €	9,252,625 €
Total cost			**436,349,229 €**

NA – Not available (only the total is available, contracts do not specify quantities).
[a]In days; [b]No of sesions; [c]No of patients in follow-up and with antipsychotic treatment; [d]Each patient may be under more than one antipsychotic treatment at the same time; [e]Two-way travel; [f]Rounded to the unit.

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