ORIGINAL RESEARCH ARTICLE

The Economic Burden of Depression in Switzerland

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Abstract

Background Despite the high prevalence of depression,
information about the burden of this disease in Switzerland
is scarce. A better knowledge of the costs of depression
may provide important information for future national
preventive programmes, optimizing cost-effective budget-
ing. The estimates of national costs may improve the
public's awareness of depression and depression-related
costs, breaking down the taboo of depression as an illness.

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Objectives The aims of this study were to analyse the annual
cost for different levels of depression and to investigate the
annual economic burden of depression in Switzerland.
Methods A retrospective, multicentre, non-interventional
study in psychiatrist practices was carried out. Outpatients
who had been diagnosed with depression in the last 3 years
were included. Patient demographics and information on
clinical characteristics and resource utilization in the first
12 months after diagnosis were collected. Costs analysis,
subdivided into direct and indirect costs, was performed for
three depression severity classes (mild, moderate and
severe), according to the 17-item Hamilton Depression
Rating Scale (HDRS-17). Costs were also extrapolated to a
national level. Regression analysis was performed to control
for factors that may have an impact on the cost of depression.
Results A total of 556 patients were included. Hospital-
ization and hospitalization days were directly correlated
with disease severity ($p < 0.001$). Medical resource utili-
zation linked to depression and antidepressant treatments
was also correlated to the disease status. Severely depressed
patients reported a significantly higher number of workdays
lost and were significantly more often on disability insur-
ance. The mean total direct costs per person per year,
mainly due to hospitalization costs, were €3,561 for mild,
€9,744 for moderate and €16,240 for severe depression. The
mean indirect costs per person per year, mainly due to
workdays lost, were €8,730 for mild, €12,675 for moderate
and €16,669 for severe depression (year 2007/2008 values).
Regression analysis showed that hospitalization days,
psychiatrist visits in hospital, disability insurance, work-
days lost and the HDRS-17 score were significantly corre-
lated to the total costs. Extrapolation at a national level
resulted in a total burden of about €8.1–8.3 billion per year.
Conclusions The burden of depression in Switzerland
was estimated to be about €8 billion per year. The costs of

depression were directly related to disease severity. However, since many cases of depression remain unreported and since this analysis only included individuals between 18 and 65 years of age, it is reasonable to suppose that the total burden of depression may be even higher.

Key Points for Decision Makers

- Despite the high prevalence of depression, information about the burden of this disease in Switzerland is scarce. A better knowledge of the costs of depression may provide important information for future national preventive programmes, optimizing the resource allocation process
- In this study, we estimated that the mean total direct costs of depression per person per year, mainly due to hospitalization costs, were €3,561 for mild, €9,744 for moderate and €16,240 for severe illness. The mean indirect costs per person per year, mainly due to workdays lost, were €8,730 for mild, €12,675 for moderate and €16,669 for severe depression
- The economic burden of depression in Switzerland was estimated to be about €8 billion per year

1 Introduction

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide, a tragic fatality associated with the loss of nearly 1 million lives annually worldwide [1].

Depression may occur at almost any stage of life, from childhood to old age. While influenced by genetic predisposition, common triggers for depression are chronic stress, emotional loss, social isolation, dysfunctional interpersonal relationships, traumatic experiences, aging, and physical stress situations such as severe diseases. The World Health Organization (WHO) estimates that depression affects about 350 million people worldwide, and is the leading cause of disability [1].

Depression is diagnosed on the basis of the symptoms reported, biographical and family history, and the patient's current circumstances. The most widely used criteria for diagnosing depressive conditions are found in the American Psychiatric Association's revised fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) [2], and the WHO's *International Classification of Diseases* (ICD-10) [3, 4]. However, even if depression can be reliably diagnosed and treated, it is estimated that fewer than half of those affected (in some countries fewer than 10 %) receive adequate treatment [1].

About 50 % of the citizens in Switzerland will suffer from psychiatric problems requiring treatment during their lives [5]. Fifteen per cent of the Swiss population suffers from mild depression and more than 3 % suffer from moderate to severe depression [6]. More than 1,000 suicides (723 males, 281 females) were recorded in Switzerland in 2010 [7]. About 90 % of these fatalities were related to depression or other psychiatric problems [8]. Switzerland presents a higher rate of suicide per inhabitant compared with the average rate in Europe (19.3 suicides/100,000 inhabitants in Switzerland vs. 10.4 suicides/100,000 inhabitants in Europe in 2009) [9, 10]. There are more than 10,000 suicide attempts in Switzerland annually that are medically treated (approximately 4,000 males and 6,000 females). However, the estimated number of unreported suicide attempts is around 15,000–25,000. It is also estimated that 10 % of the Swiss population will attempt suicide during their lifetime [6].

Although a high percentage of the population in Switzerland suffers from psychiatric problems, it is estimated that only about 5–6 % of the population received adequate treatment for depression in 2007 [11]. In 2004, psychiatric hospitals registered 47,555 new admissions, corresponding to an average of eight inpatient episodes per 1,000 inhabitants [6]. Depression leads to the highest number of hospitalizations in psychiatric institutions. In 2004, almost 3 million hospitalization days in Swiss psychiatric hospitals were due to psychiatric disorders, corresponding to 471 hospitalization days per 1,000 inhabitants [6]. Data about psychiatric ambulatory structures and their admission rate are sporadic in Switzerland [6].

The costs of psychiatric structures in Switzerland have been estimated to total €1,553 million for the year 2000, and represent about 5 % of the total healthcare expenditure in Switzerland [12–14]. The economic burden of psychiatric problems is estimated to represent 4 % of the Swiss gross domestic product (GDP), and is mainly due to loss of productivity and prolonged absence from work [6, 15].

So far there have been very few data [16, 17] available regarding the costs of depression in Switzerland. Jäger et al. [17], in their publication derived from the Costs of Disorders of the Brain in Europe study of the European Brain Council (EBC), have estimated that the annual costs of disorders of the brain in Switzerland in 2004 may have amounted to €8.9 billion, with €2.6 billion due to affective disorders (i.e. depression and bipolar disorder). However, as remarked by the authors, these results "probably underestimate the full economic burden of brain and especially mental disorders in Switzerland".

Thus, the purpose of this study was to provide a new estimation of the financial burden of depression to the Swiss population. The costs for the management of depressive patients were analysed during an observational period of 12 months following diagnosis for different severity classes of the disease (mild, moderate and severe), based on the 17-item Hamilton Depression Rating Scale (HDRS-17; also known as the HAMD-17).

The results of this study and, in particular, the analysis of the costs of depression for different depression severities may provide important information for future national preventive programmes, optimizing the resource allocation process. The estimations of national costs may improve the public's awareness of depression and depression-related costs, breaking down the taboo of depression as an illness.

2 Methods

2.1 Study Design

A retrospective, multicentre, non-interventional survey in psychiatric practices and clinics was carried out between June 2009 and September 2009. Twenty-three psychiatrists in seven Swiss cantons volunteered to participate in the study. Fifteen of them were working in medical offices, seven in clinics (two university and five private clinics) and one worked in an ambulant psychiatric service. In five clinics and the ambulant psychiatric service, chief physicians were responsible for the data sampling. In one university clinic, the Vice-Director, who is also a psychiatrist, was involved. All psychiatrists were directly involved in the diagnosis and treatment of the study subjects. In the psychiatric clinics, several patients were admitted after receiving a working diagnosis of depression from an external practitioner; in these cases, the patients were newly diagnosed and subsequently treated.

2.2 Participants

Outpatients who had been diagnosed with major depressive disorders within the last 3 years and for whom records for the initial 12 months were available were included. The criteria from the WHO's ICD-10 [3] was used for diagnosing depression (ICD-10 codes: F30–F39). Only outpatients aged between 18 and 65 years were included. Schizophrenic patients, patients with psychosis or other major psychiatric disorders were excluded (ICD-10 codes: F20–F29). All data were extracted from the patients' medical records. The study received approval from the cantonal ethics committees of Basel and Geneva ("Ethikkommission beider Basel" and "Commission d'éthique pour la recherche clinique dans le Canton de Genève"), in line with the *Declaration of Helsinki*. The ethics committees responsible for other Cantons (Aargau, Graubünden, Schaffhausen, Ticino and Zurich) decided that it was not necessary to ask for approval since the study was non-interventional, and since all data were anonymized.

2.3 Measures

Patient demographics and clinical characteristics included sex, age, body mass index (kg/m^2), co-morbidities, and depression classification based on the HDRS-17 [18–20]. In order to evaluate the burden of depression, only the first 12 months after diagnosis were taken into account for each patient.

The following variables linked to depression were collected for the direct costs evaluation: number of hospitalizations and hospitalization days, physician's visits (subdivided into general practitioners [GPs], psychiatrists in primary care and psychiatrists in hospitals), medical resource utilization (electrocardiogram [ECG], electroencephalogram [EEG], computed tomography [CT], magnetic resonance imaging [MRI] and laboratory tests), psychotherapy (defined as antidepressant treatment through personal counselling with a trained psychotherapist, a non-medical psychotherapist or a qualified GP), antidepressant treatment (selective serotonin reuptake inhibitors [SSRIs], serotonin–norepinephrine reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs], monoamine oxidase inhibitors, trazodone, mirtazapine, lithium, and St. John's wort), and additional medication (hypnotics, neuroleptics/antipsychotics, etc.). It is necessary to specify that in the case report form concerning the total number of physician's visits and medical resource utilization during the first 12 months after diagnosis, all numbers of visits/tests above three were equally reported (i.e. as >3), even if the visits/tests were four, five or many more. We were strictly conservative when calculating the average number of visits/tests for each patient, calculating four visits/tests for all patients with more than three consultations/tests.

Disability insurance and workdays lost because of depression were taken into account for the indirect costs evaluation. The psychiatrists extracted the information from the medical records where the start and the end dates of the rest/invalidity period of the patients are reported. In order to calculate the workdays lost, 5 workdays per week were assumed and festive days were excluded.

All measures were reported on a questionnaire, which was developed based on the literature (in particular, for co-morbidities) and expert opinion [21–23].

2.4 Statistical Analyses and Cost Estimations

Data were analysed with IBM SPSS® Statistics 19.0 (IBM Corporation, Somers, NY, USA) and Microsoft Office

Excel 2007 (Microsoft Corporation, Redmond, WA, USA). Chi-square tests and *t* tests were used for categorical and continuous variables, respectively. A two-tailed *p* value of <0.05 was considered statistically significant.

Severity classes, based on HDRS-17 scores, were defined as follows: 0–7 = no depression (patient in remission), 8–14 = mild depression, 15–22 = moderate depression and >22 = severe depression [22, 23].

The costs analysis was performed from a societal perspective with a bottom-up approach. The reference years, especially for the extrapolation to a national level, were 2007 and 2008. All reference prices come from Swiss publications or national databases. The costs of hospitalization were calculated using the running costs for a hospitalization day in a psychiatric clinic in 2005 (i.e. €430). Costs related to medical resource utilization (i.e. for ECG, EEG, etc.) are already included in these cost estimations [25]. We assumed average costs per session of €81 and €110 for primary care and psychiatrist visits, respectively, as reported by Beeler et al [13]. We used a mean yearly cost (in 2007) per patient of €1,222, as reported by the Swiss Health Observatory [26], to evaluate the costs of psychotherapy.

The costs of the most frequently used treatments were estimated by calculating a mean of the costs of some of the most common medications on the market in 2009. Product costs were based on pharmacy retail prices in Switzerland, as mainly pharmacies are authorized to sell drugs to outpatients [27]. Minimal dosages were used in the absence of recommendations. The following mean treatment costs per year were calculated: €363 for SSRIs, €507 for SNRIs, €726 for mirtazapine, €178 for trazodone, €192 for TCAs, €149 for lithium, €231 for St. John's wort, €145 for hypnotics and €480 for neuroleptics/antipsychotics.

We assumed €1,054 per month for patients with 100 % disability for the disability insurance costs, as reported by the Federal Social Insurance Office (FSIO) in 2008 [24]. Since it was possible in the questionnaire to indicate the degree (%) of disability insurance, the €1,054 cost was divided depending on the degree of disability (e.g. €527 per month for a 50 % disability). The cost of a single workday lost was calculated by dividing the mean GDP per person in 2008 (i.e. €51,602) by 220 workdays per year.

The costs analysis was subdivided into direct and indirect costs. The exchange rate as at 25 October 2010 was used (European Central Bank: €1 = 1.3618 Swiss Francs).

Concerning the extrapolation to a national level, we firstly calculated that there were about 311,170 Swiss patients between 15 and 65 years of age who received a medical treatment because of depression (i.e. about 6.1 % of the Swiss population) in 2007, as reported by the Federal Statistical Office (FSO) [11]. In order to take into account the distribution of these patients in different severity classes, we used the results of two published studies [29, 30]. Kessler et al. [29], in a study showing the results from the National Comorbidity Survey Replication (NCS-R), which included 9,090 participants 18 years of age or older, reported that the depression prevalence for a 12-month period was 6.6 %, with 10.4 % of cases of depression classified as mild, 38.6 % as moderate and 50.9 % as severe or very severe. In a more recent study, also based on the NCS-R, Birnbaum et al. [30] reported that in a sample of 539 US workforce respondents with depression, 13.8 % were classified as mild, 38.5 % as moderate and 47.7 % as severe.

A sensitivity analysis was performed to investigate the robustness of the cost predictions. The costs of hospitalization days, the costs of physician visits, the medication costs, the costs for a workday lost and the costs for disability insurance varied by ±20 %.

Generalized linear models were fitted to control for factors that may have an impact on the cost of depression. In the first model, age, sex, physician visits, hospitalization days, workdays lost, disability insurance and HDRS-17 score were entered. In the second model, psychotherapy, antidepressant medication and additional medication were used. In a third model, all co-morbidities were entered. The variables showing significant results in the first three analyses were then combined in a fourth model. Since the generalized linear model does not allow a direct representation of a cost equation, the significant variables in the fourth model were used to perform a simple linear regression analysis. Finally, assuming that the cost variable was right skewed (i.e. was not normally distributed), a similar linear regression using the logarithm of the costs as a dependent variable was performed. Significant variables were tested for multicollinearity by calculating the variance inflation factors (VIFs).

3 Results

3.1 Demographic and Clinical Characteristics

Table 1 provides demographic and clinical characteristics of the patients. Depression classification at time of diagnosis was available for 554 of the 556 patients recruited; 119 (21.5 %), 260 (46.9 %) and 175 (31.6 %) reported having mild, moderate or severe depression, respectively. All diagnoses were made between September 2005 and September 2008. A mean (± SD) of 24 ± 15 patients per psychiatrist were recruited (95 % CI 17.6–30.8). The sex distribution was similar for all the depression severity

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Table 1 Demographic and clinical characteristics of the patients

Characteristic	Depression severity [n (%) or mean ± SD]				p value
	Mild	Moderate	Severe	All	
Number of subjects	119 (21.5)	260 (46.9)	175 (31.6)	554 (31.6)	
Female	67 (56.3)	153 (58.8)	109 (62.3)	329 (59.4)	0.574
Age (years)	41.4 ± 10.9	43.7 ± 9.9	44.6 ± 11.0	43.5 ± 10.5	0.031
BMI (kg/m^2)	24.5 ± 3.9	25.7 ± 5.8	25.3 ± 5.1	25.3 ± 5.2	0.372
Cardiovascular disease					
MI, angina, CAD	3 (2.5)	1 (0.4)	6 (3.4)	10 (1.8)	0.052
Cardiac arrhythmias	1 (0.8)	6 (2.3)	3 (1.7)	10 (1.8)	0.605
Mitral valve prolapse	0	1 (0.4)	0	1 (0.2)	0.568
Pulmonary disease					
Asthma	2 (1.7)	8 (3.1)	2 (1.1)	12 (2.2)	0.365
COPD	0	1 (0.4)	7 (4.0)	8 (1.4)	0.003
Pneumonia	0	1 (0.4)	0	1 (0.2)	0.568
Pulmonary embolus	0	1 (0.4)	2 (1.1)	3 (0.5)	0.319
Pneumothorax	1 (0.8)	0	0	1 (0.2)	0.160
Neurological disease					
HIV/AIDS dementia	0	2 (0.8)	0	2 (0.4)	0.321
Cerebrovascular accident	1 (0.8)	1 (0.4)	3 (1.7)	5 (0.9)	0.354
Chronic pain	17 (14.3)	54 (20.8)	27 (15.4)	98 (17.7)	0.196
CNS tumour	0	2 (0.8)	0	2 (0.4)	0.321
Complex partial seizures	0	1 (0.4)	2 (1.1)	3 (0.5)	0.379
Encephalopathy	0	2 (0.8)	0	2 (0.4)	0.321
Encephalitis	1 (0.8)	1 (0.4)	1 (0.6)	3 (0.5)	0.853
Endocrine disease					
Diabetes mellitus	2 (1.7)	7 (2.7)	1 (0.6)	10 (1.8)	0.263
Carcinoid syndrome	1 (0.8)	2 (0.8)	0	3 (0.5)	0.496
Hypo- and hyperthyroid states	2 (1.7)	5 (1.9)	8 (4.6)	15 (2.7)	0.183
Gastrointestinal disease					
GERD	5 (4.2)	12 (4.6)	8 (4.6)	25 (4.5)	0.983
Irritable bowel syndrome	5 (4.2)	8 (3.1)	15 (8.6)	28 (5.1)	0.033
Metabolic disease					
Anaemia	6 (5.0)	19 (7.3)	11 (6.3)	36 (6.5)	0.702
Dehydration	0	0	2 (1.1)	2 (0.4)	0.114
Electrolyte imbalance	0	1 (0.4)	1 (0.6)	2 (0.4)	0.722
Hepatic failure	0	2 (0.8)	2 (1.1)	4 (0.7)	0.521
Miscellaneous					
Rheumatoid arthritis	1 (0.8)	5 (1.9)	1 (0.6)	7 (1.3)	0.417
SLE	1 (0.8)	0	0	1 (0.2)	0.160
Chronic fatigue syndrome	5 (4.2)	6 (2.3)	19 (10.9)	30 (5.4)	<0.001
Vitamin B$_{12}$ deficiency	1 (0.8)	3 (1.2)	6 (3.4)	10 (1.8)	0.146
Sleep disturbances	24 (20.2)	62 (23.8)	46 (26.3)	132 (23.8)	0.482

BMI body mass index, *CAD* coronary artery disease, *CNS* central nervous system, *COPD* chronic obstructive pulmonary disease, *GERD* gastroesophageal reflux disorder, *MI* myocardial infarction, *SD* standard deviation, *SLE* systemic lupus erythematosus

classes. The age at the time of diagnosis was significantly and directly related to the depression severity ($p = 0.031$). The most frequent co-morbidities were chronic pain and sleep disturbances, which affected 17.7 % and 23.8 %, respectively, of the study population. Chronic obstructive pulmonary disease, irritable bowel syndrome and chronic fatigue syndrome seemed to be significantly associated with disease severity.

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3.2 Resource Utilization

The number of hospitalizations and the mean hospitalization days per patient were strongly associated with the depression severity, as shown in Table 2

Concerning the total number of physician visits, severely depressed patients reported significantly more visits than mildly or moderately depressed patients did ($p < 0.001$).

Regarding medical resource utilization, we could generally observe that EEG, CT and MRI were rarely performed. In contrast, more than 40 % of the patients received at least an ECG, and about 75 % of the patients received at least one laboratory test.

Table 2 shows the percentage of patients who received psychotherapy and antidepressant medication. Psychotherapy prevalence was high for all the depression severity classes. Interestingly, the comparison between the levels of depression suggests that mildly depressed patients undertook psychotherapy significantly more often than moderately and severely depressed patients ($p = 0.025$). In contrast, we observed a direct association between the prescription and disease severity for almost all antidepressant medications, hypnotics and neuroleptics/antipsychotics. For other medications (e.g. antihypertensive or lipid-lowering drugs), there was generally no difference between the levels of depression.

3.3 Occupational Status, Disability Insurance and Workdays Lost

In general, mildly and severely depressed patients showed an inverse tendency concerning occupational status (Table 3); almost three-quarters of the mildly depressed patients were employed and less than 6 % were receiving disability insurance, whereas only about half of the severely depressed patients worked and 19 % received disability insurance.

The mean workdays lost of all patients included in this study was about 50 days and was directly correlated with the disease severity. Every mildly depressed patient had lost about 34 (95 % CI 22.3–46.6) workdays in 1 year, compared with 48 (95 % CI 39.3–57.0) and 62 (95 % CI 50.3–74.4) workdays lost for moderately and severely depressed patients, respectively.

3.4 Costs

3.4.1 Direct Costs

As expected, the great differences in the number of hospitalization days per patient for the different levels of depression strongly influenced the costs outcomes. The mean hospitalization cost for mild depression was €1,352, i.e. about one-fifth and one-tenth of the cost for moderate and severe depression, respectively (Table 4) (year 2007/2008 values). In contrast, the differences in the costs of physician visits between the levels of depression were less pronounced. Psychotherapy was the most common and expensive treatment for depression, with an average cost of €1,070 per patient per year (year 2007/2008 values). Concerning the medication costs, hypnotics and neuroleptics/antipsychotics costs were added to the antidepressant costs since they seemed to be directly related to the disease. Other additional medications (e.g. anticoagulants, antidiabetic drugs, antihypertensives and non-steroidal anti-inflammatory drugs) were not considered cost-relevant (rare) and/or were considered to be related to other disorders, and were, therefore, excluded from the cost analysis.

3.4.2 Indirect Costs

In this study, the mean disability insurance costs per patient per year showed a linear tendency between the levels of depression, with about €660 for a mild depression, double for a moderate depression and triple for a severe depression (year 2007/2008 values). Concerning the mean costs per patient due to workdays lost, we observed that severe depression caused about double the costs when compared with mild depression (Table 4).

3.4.3 Total Costs

Fig. 1 shows the direct and indirect costs for mild, moderate and severe depression. We can observe for mildly depressed patients that indirect costs represent more than two-thirds of the total expenses (i.e. 71 %). Indirect costs for moderately depressed patients accounted for about 57 % of the costs. Finally, severely depressed patients show a balance between direct and indirect costs. The difference between mild and severe depression was principally due to the greater number of hospitalization days recorded for severely depressed patients.

3.5 Regression Analysis

In the first generalized linear model, hospitalization days ($p < 0.001$), GP visits ($p < 0.001$), psychiatrist visits in hospital ($p = 0.002$), workdays lost ($p < 0.001$), disability insurance ($p < 0.001$) and HDRS-17 score ($p = 0.002$) showed significant results. In the second model, the following medications were significantly related to the costs: TCAs ($p = 0.002$), SSRIs ($p = 0.022$), SNRIs ($p < 0.001$), trazodone ($p = 0.028$), lithium ($p = 0.040$), hypnotics ($p < 0.001$) and neuroleptics/antipsychotics ($p < 0.001$). In the third model, including all co-morbidities, HIV/AIDS

Table 2 Resource utilization: hospitalizations, physician visits, medical resource utilization, psychotherapy, antidepressant and additional medication

Resource	Depression severity [n (%) or mean ± SD]				p value
	Mild	Moderate	Severe	All	
Hospitalization	11 (9.2)	80 (30.8)	86 (49.1)	177 (31.9)	<0.001
Hospitalization days	3.1 ± 12.1	16.9 ± 35.5	31.1 ± 47.1	18.4 ± 37.7	<0.001
Physician visits[a]	5.81 ± 2.12	6.52 ± 2.52	7.39 ± 2.83	6.64 ± 2.60	<0.001
GP	1.82 ± 1.70	2.10 ± 1.70	2.34 ± 1.75	2.11 ± 1.72	0.042
Psychiatrist in primary care	3.34 ± 1.44	3.22 ± 1.43	3.45 ± 1.25	3.32 ± 1.38	0.234
Psychiatrist in hospitals	0.64 ± 1.33	1.18 ± 1.68	1.54 ± 1.76	1.18 ± 1.67	<0.001
Medical[a]					
ECG	0.50 ± 1.01	0.50 ± 0.89	1.13 ± 1.22	0.70 ± 1.07	<0.001
EEG	0.08 ± 0.47	0.12 ± 0.34	0.34 ± 0.70	0.18 ± 0.52	<0.001
CT	0.03 ± 0.16	0.02 ± 0.14	0.08 ± 0.35	0.04 ± 0.23	0.019
MRI	0.09 ± 0.45	0.08 ± 0.30	0.20 ± 0.43	0.12 ± 0.38	0.004
Laboratory test	1.24 ± 1.41	1.82 ± 1.55	2.47 ± 1.50	1.90 ± 1.56	<0.001
Psychotherapy	112 (94.1)	219 (84.2)	154 (88.0)	485 (87.5)	0.025
Antidepressant treatment					
SSRIs	53 (44.5)	130 (50.0)	106 (60.6)	289 (52.2)	0.016
SNRIs	26 (21.8)	96 (36.9)	82 (46.9)	204 (36.8)	<0.001
Mirtazapine	9 (7.6)	57 (21.9)	52 (29.7)	118 (21.3)	<0.001
Trazodone	13 (10.9)	46 (17.7)	50 (28.6)	109 (19.7)	0.001
TCAs	15 (12.6)	50 (19.2)	34 (19.4)	99 (17.9)	0.239
Lithium	0 (0)	4 (1.5)	12 (6.9)	16 (2.9)	0.001
St. John's wort	13 (10.9)	17 (6.5)	8 (4.6)	38 (6.9)	0.103
Additional medication					
Hypnotics	38 (31.9)	123 (47.3)	111 (63.4)	272 (49.1)	<0.001
Neuroleptics/antipsychotics	8 (6.7)	52 (20.0)	69 (39.4)	129 (23.3)	<0.001
Antihypertensive drugs	16 (13.4)	29 (11.2)	25 (14.3)	70 (12.6)	0.601
NSAIDs	12 (10.1)	35 (13.5)	20 (11.4)	67 (12.1)	0.612
Lipid lowering medication	4 (3.4)	9 (3.5)	9 (5.1)	22 (4.0)	0.630
Ritalin	2 (1.7)	8 (3.1)	5 (2.9)	15 (2.7)	0.731
Anticoagulation drugs	3 (2.5)	2 (0.8)	9 (5.1)	14 (2.5)	0.017
Antidiabetic drugs	2 (1.7)	7 (2.7)	1 (0.6)	10 (1.8)	0.263
Other	12 (10.1)	25 (9.6)	18 (10.3)	55 (9.9)	0.972

CT computed tomography, ECG electrocardiogram, EEG electroencephalogram, GP general practitioner, MRI magnetic resonance imaging, NSAIDs non-steroidal anti-inflammatory drugs, SD standard deviation, SNRIs serotonin–norepinephrine reuptake inhibitors, SSRIs selective serotonin reuptake inhibitors, TCAs tricyclic antidepressants

[a] p values may be biased because of truncation of maximal number of visits reported (see Sect. 2.3)

dementia ($p = 0.021$), central nervous system tumours ($p = 0.048$) and systemic lupus erythematosus ($p = 0.046$) showed significant results. In the final generalized linear model, including all significant variables in models 1–3, only hospitalization days ($p < 0.001$), psychiatrist visits in hospital ($p < 0.001$), workdays lost ($p < 0.001$), disability insurance ($p < 0.001$) and depression severity ($p = 0.002$) confirmed the significant results.

These variables were combined in a simple linear regression model in order to obtain a direct representation of a cost equation: €1,725 + (€432 × hospitalization days) + (€127 × disability insurance) + (€236 × workdays lost) + (€36 × HDRS-17 score). Psychiatrist visits in hospital showed a non-significant relationship to the total costs and were, therefore, excluded from the equation. Since the cost variable was right skewed (i.e. was not normally distributed), a similar linear regression using the logarithm of the costs was performed in order to check the goodness of fit of the model. The results indicate a strong relationship (R = 896, adjusted R-square = 0.801), with

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Table 3 Occupational status, disability insurance and workdays lost

	Depression severity [n (%) or mean ± SD]				p value
	Mild	Moderate	Severe	All	
Occupational status					0.001
Employed[a]	86 (72.3)	149 (57.3)	93 (53.1)	328 (59.2)	
Unemployed	26 (21.8)	75 (28.8)	42 (23.4)	143 (25.8)	
Retired	0	6 (2.3)	7 (4.0)	13 (2.3)	
Disability insurance[b]	7 (5.9)	30 (11.5)	34 (19.4)	71 (12.8)	
Workdays lost	34.4 ± 67.0	48.2 ± 72.5	62.4 ± 80.9	49.7 ± 74.7	0.006

[a] One mildly depressed patient, three moderately depressed patients and one severely depressed patient were working despite disability insurance and were, therefore, classified in the employed group

[b] Two mildly, four moderately and three severely depressed patients who were unemployed and had contemporaneous disability insurance were classified in the disability insurance group. The same applied to one patient who was retired and on disability insurance

Table 4 Direct and indirect costs per patient per year

Cost category	Depression severity (€; mean [95 % CI])				p value
	Mild	Moderate	Severe	All	
Direct costs					
Hospitalization	1,352 [405–2,299]	7,286 [5,421–9,150]	13,369 [10,345–16,393]	7,932 [6,579–9,286]	<0.001
Physician visits	586 [551–621]	654 [624–289]	736 [694–779]	665 [644–687]	<0.001
Psychotherapy	1,150 [1,098–1,202]	1,029 [975–1,084]	1,075 [1,016–1,135]	1,070 [1,036–1,103]	0.025
Medication[a]	473 [411–535]	775 [716–834]	1,059 [983–1,136]	800 [757–843]	<0.001
Total	3,561 [2,601–4,521]	9,744 [7,856–11,632]	16,240 [13,203–19,277]	10,468 [9,098–11,838]	<0.001
Indirect costs					
Disability insurance	664 [180–1,148]	1,374 [917–1,831]	2,040 [1,392–2,687]	1,432 [1,117–1,747]	0.008
Workdays lost costs	8,066 [5,213–10,918]	11,301 [9,224–13,378]	14,630 [11,798–17,461]	11,658 [10,195–13,120]	0.006
Total	8,730 [5,883–11,577]	12,675 [10,602–14,748]	16,669 [13,884–19,455]	13,089 [11,631–14,547]	0.001
Total costs	12,291 [9,142–15,440]	22,419 [19,329–25,509]	32,909 [28,527–37,292]	23,557 [21,363–25,751]	<0.001

Costs are presented in €, year 2007/2008 values

CI confidence interval

[a] Medication includes antidepressant medication, hypnotics and neuroleptics/antipsychotics
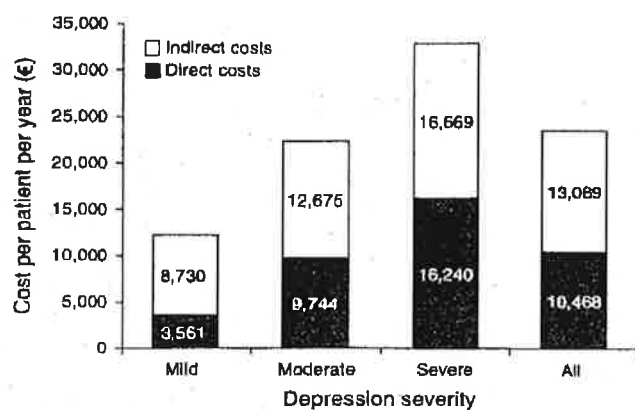

Fig. 1 Mean direct and indirect costs of depression per patient per year (€; year 2007/2008 values)

the following Pearson correlation coefficients: 0.573 for hospitalization days, 0.257 for disability insurance, 0.464 for psychiatrist visits in hospital, 0.701 for workdays lost and 0.346 for HDRS-17 score. No multicollinearity problems were found (hospitalization days: VIF = 1.771; disability insurance: VIF = 1.057; psychiatrist visits in hospital: VIF = 1.633; workdays lost: VIF = 1.069; and HDRS-17 score: VIF = 1.124).

3.6 Economic Burden of Depression in Switzerland

Table 5 shows the calculation of the economic burden of depression at a national level utilizing the percentages reported by Kessler et al. [29] and Birnbaum et al. [30]. The results indicate that the annual costs of depression in

△ **Adis**

Table 5 Yearly burden of depression in Switzerland

Reference	Parameter	Depression severity			
		Mild	Moderate	Severe	All
Kessler et al. [29]	Severity distribution (%)	10.4	38.6	50.9	
	Estimated number of patients	32,465	120,215	158,489	311,170
	Total direct costs (billion €)	0.116	1.171	2.574	3.861
	Total indirect costs (billion €)	0.283	1.524	2.642	4.449
	Total costs (billion €)	0.399	2.695	5.216	8.310
Birnbaum et al. [30]	Severity distribution (%)	13.8	38.5	47.7	
	Estimated number of patients	42,941	119,800	148,428	311,170
	Total direct costs (billion €)	0.153	1.167	2.410	3.731
	Total indirect costs (billion €)	0.375	1.518	2.474	4.368
	Total costs (billion €)	0.528	2.686	4.885	8.098

Costs are presented in billion €, year 2007/2008 values. The disease severity distributions (percentage of patients with mild, moderate and severe depression) reported in two different studies were utilized for the cost estimations. See Sect. 2.4 for further information

Switzerland are about €8.1–8.3 billion. Severe depression accounts for more than 60 % of the total costs, whereas cases of moderate and mild depression account for about 32–33 % and 5–7 % of the total costs, respectively.

3.7 Sensitivity Analysis

The sensitivity analysis (Fig. 2) showed that the factors that cause the costs to vary are the cost of workdays lost and the costs of hospitalization, which decrease/increase by 20 %, resulting in a variation of the total cost of depression of about 10 % and 7 %, respectively. The effect of the other cost variables (disability costs: ±1.2 %; medication costs: ±0.7 %; and physician visit costs: ±0.5 %) was less pronounced. Because of the truncation of the maximal number of physician visits, we also performed a sensitivity analysis by doubling the mean number of visits; in this case, the total costs would increase by about €0.2 billion (i.e. ±2.6 %).

4 Discussion

In our study, 21.5 %, 46.9 % and 31.6 % of the patients had mild, moderate or severe depression, respectively. When compared with the results of the studies of Kessler et al. [29] (10.4 %, 38.6 % and 50.9 %, respectively) and Birnbaum et al. [30] (13.8 %, 38.5 % and 47.7 %, respectively), we found a higher prevalence of mild and moderate depression, whereas severe depression was less frequent. This difference may be due to the study design, as discussed later in this section.

The costs analysis emphasizes a strong relationship between the severity of depression and mean costs per patient. Both direct and indirect costs are directly correlated with the level of depression. Similar to the results seen in the study of Birnbaum et al. [30] about the employer burden of major depressive disorders, the severity of depression was significantly associated with increased treatment usage and costs, increased unemployment and disability, and reduced work performance (in terms of workdays lost). The unemployment rate in Switzerland in 2009, according to the FSO and the FSIO [31], was 3.7 %, whereas 82.5 % of the population between 15 and 64 years of age was employed. Disability insurance was received by 5.0 % of the Swiss population under 65 years of age [32]. The mean number of workdays lost for a full-time worker in Switzerland in 2008 was about 8 (the mean annual number of hours of time off work for full-time employees was 67, with a mean duration of the normal working week of 41.6 hours) [33]. The results of our study emphasize the enormous impact of depression on patients' ability to work, with unemployment and employment rates of 25.8 % and 59.2 %, respectively, with 12.8 % disability insurance, and with almost 50 workdays lost per year.

Interestingly, we observed that the proportions for direct and indirect costs for the three levels of depression were different. While the costs of mild depression were mainly due to indirect factors, in particular, to the loss of productivity, the costs of moderate and, especially, severe depression showed a more balanced cost distribution. The direct costs accounted for about 29 % of the total costs of mild depression, whereas they accounted for about 43 % and 49 % of the total costs of moderate and severe depression, respectively.

Both the moderate and severe depression cost subdivisions reflect the percentages calculated by Johnston et al. [34] in a recent study about the direct and indirect costs of employee depression, anxiety and emotional disorders. In their study involving 4,152 employees, the direct costs accounted for 47 % of the total costs of depression.

Fig. 2 Sensitivity analysis. The costs of the selected variables were varied by ±20 % (billion €; year 2007/2008 values). The disease severity distributions (percentage of patients with mild, moderate and severe depression) reported in two different studies were utilized for the cost estimations [29, 30]. See Sect. 2.4 for further information
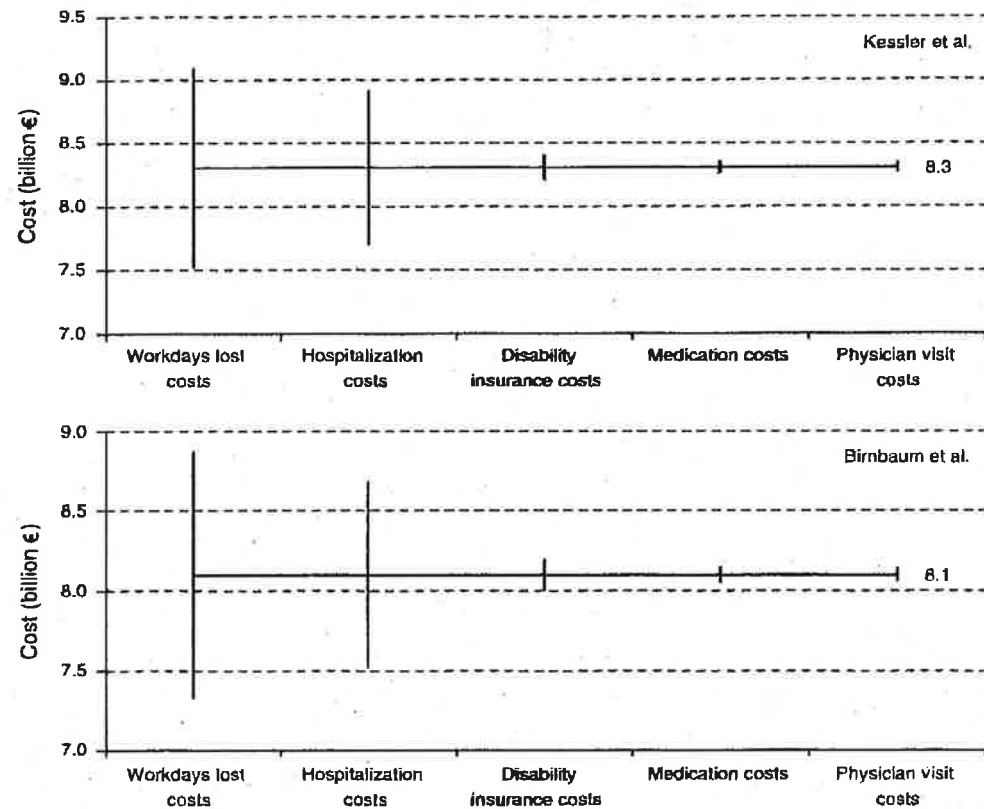
Some additional remarks may be helpful to better characterize the differences in cost share of total cost between mild and more severe depression. Firstly, as has already been mentioned in the Sect. 3, the hospitalization rates and days were strongly associated with depression severity. Patients with mild depression were admitted less frequently (9.2 %) than patients with moderate (30.8 %) or severe depression (49.1 %). The mean number of hospitalization days, calculated by dividing the total number of hospitalization days by all patients in each group, was also clearly different between study groups (3.1, 16.9 and 31.1 inpatient days for patients with mild, moderate and severe depression, respectively). Moreover, it is interesting to calculate the mean length of stay for the hospitalized patient only. Patients admitted with mild depression reported a mean of 34 hospitalization days, whereas patients with moderate and severe depression reported a mean of 55 and 63 hospitalization days, respectively. These calculations confirm the correlation between the length of stay in hospital and disease severity.

Secondly, it should be noted that the difference in workdays lost between the groups, although highly significant, was less pronounced when compared with the difference in hospitalization rates and days (34, 48 and 62 workdays lost for mild, moderate and severe depressions,

respectively). Moreover, it is intriguing to compare the mean number of workdays lost for hospitalized versus non-hospitalized patients: patients with mild depression reported 78 workdays lost if hospitalized, and 30 workdays lost if not; patients with moderate depression reported 58 workdays lost if hospitalized, and 44 workdays lost if not; and patients with severe depression reported 69 and 56 workdays lost if hospitalized or not, respectively.

These data highlight that the number of workdays lost for non-hospitalized patients, although lower than that for hospitalized patients, is conspicuous. Interestingly, the biggest difference of workdays lost between hospitalized and non-hospitalized patients was found in cases of mild depression. However, because of the limited number of hospitalized patients in this group, it may be inappropriate to draw a conclusion from this observation.

It is important to remark on indirect costs, that in Switzerland, in addition to disability insurance, which is part of the basic first pillar of the AHV/IV/EO system (insurance for old age, disability, loss of income), there is the occupational pension fund, also called the 'second pillar.' Together, these two insurance systems should ensure that retired people maintain their former standard of living to a large extent. In this study, it was not possible to evaluate which patients benefited from this second pillar.

However, it is reasonable to think that some anticipated retirement because of developing depression, meaning that the indirect cost may be higher.

The results of the regression analyses merit some discussion. Strong correlation was confirmed for hospitalization days and workdays lost (Pearson correlation coefficients of 0.573 and 0.701, respectively), which are responsible for more than 80 % of the total costs. Disability insurance, psychiatrist visits in hospital and HDRS-17 score showed less pronounced but still significant correlations. In contrast, age, sex, medication and co-morbidities showed no direct relationship with the total costs.

We have estimated at a national level that 311,170 patients (about 6.1 % of the Swiss population between 15 and 65 years of age) received medical treatment because of depression in 2007 [11]. These data are comparable to the data used by Andlin-Sobocki et al. [16] in their evaluation of the cost of disorders of the brain in Europe, and to the prevalence data calculated by Angst et al. [35] in the Zurich Cohort Study. Andlin-Sobocki et al. [16] reported a prevalence of 370,860 patients with affective disorders (i.e. depression or bipolar disorders) in Switzerland in 2004. On the other hand, in the Zurich Cohort Study, Angst et al. [35] reported a 6 % weighted prevalence rate of long-term depression, specifying that there was also about 21 % of the population reporting episodic (non-chronic) major depression episodes and 18 % reporting episodic milder depression. Similarly, Eaton et al. [28] observed in a prospective population-based cohort study with 23 years of follow-up that major depressive disorder was unremitting in 15 % of cases and recurrent in 35 %.

We have calculated that depression may cause costs at a national level of about €8.1–8.3 billion. These results strongly overtake the data derived from the Costs of Disorders of the Brain in Europe study of the EBC reported by Jäger et al. [17]; the annual costs of all brain disorders in Switzerland in 2004 were estimated to be about €8.9 billion, with €2.6 billion due to affective disorders (i.e. depression and bipolar disorder). This difference is mainly due to different cost estimations: the cost per case of depression in Switzerland in the EBC Study was estimated to be €6,622, whereas the mean costs per patient in our study were over €12,000 for mild depression, over €22,000 for moderate depression and almost €33,000 for severe depression. This difference is probably due to the paucity of good studies in Switzerland and Europe at the time of the EBC study. In fact, Jäger et al. [17] emphasized that their extrapolation was relatively uncertain. Therefore, the calculations were particularly conservative. In contrast, the new data collected in our study permit a more detailed and audacious cost estimation.

An additional factor influencing the cost estimation is the exchange rate; we used a relatively recent exchange rate (European Central Bank exchange rate as at 25 October 2010: €1 = 1.3618 Swiss francs) in our calculations. Using the mean exchange rate in 2004–2005 (€1 = 1.5460 Swiss francs), the total costs would have been €7.1–7.3 billion.

To put these numbers in context, note that the total healthcare cost in Switzerland in 2008 was about €42.9 billion (i.e. 10.7 % of GDP), with a mean cost of €5,573 per inhabitant [56]. Therefore, with a cost of €8.1–8.3 billion, depression may be responsible for about 19 % of the total healthcare expenditure, i.e. about 2.0 % of the Swiss GDP.

Although our results have already largely overtaken previous estimations, many factors suggest that the real costs of depression may be even higher. We should be aware, for example, that the majority of cases of mild depression and a portion of the cases of moderate depression remain unreported and untreated, which will also cause significant cost, particularly related to workdays lost or productivity reduced. Cuijpers et al. [36], supporting this hypothesis, although using a different depression classification (minor vs. major depression) and different diagnostic criteria (one mainly based on the DSM-III-R), reported in a population-based study performed in The Netherlands that the annual costs associated with minor depression approach those of major depression.

Furthermore, it must be remembered that this study and the subsequent analyses only included the patients/population between 18 and 65 years of age, i.e. the potential workforce in Switzerland. However, it is well known that depression is highly prevalent throughout the whole population, including minors and the elderly (>65 years of age) [37–43]. If depression in younger people is often unsuspected or ignored, depression in elderly is often more evident and requires treatment and support from the family and/or external caregivers. Luppa et al. [44], in a recent study analysing the direct costs associated with depression in old age (>75 years of age) in Germany, have calculated that the mean annual direct costs of depressed people clearly exceed the mean costs of non-depressive individuals (€5,141 vs. €3,648, $p < 0.01$). In another study, Katon et al. [45] have also concluded that "depressive disorders in elderly patients are associated with significantly higher health care costs, even after adjustment for chronic medical illness" (the costs were about 50 % higher in depressive patients than in non-depressed patients).

Finally, it is important to mention how the co-occurrence of depression and other diseases may result in an even higher financial burden. Some studies [46, 47] have, for example, reported that co-morbid sleep disturbances exacerbate the adverse effect of depression (e.g. lowering of work performance) and, if not treated, may contribute to a future relapse of the depressive disorder. Co-morbid

chronic pain, which is also highly prevalent in depressed patients, may also be responsible for significantly longer periods of depressed mood [48]. Other examples are the significantly higher mean number of emergency department visits reported by patients with substance use disorders (SUD) and psychiatric co-morbidity (5.2 visits vs. 2.5 visits for SUD patients without psychiatric problems), and the increased number of medical and psychiatric inpatients' days of care, as well as the increased number of psychiatric outpatients' visits reported by dementia patients with psychiatric co-morbidity [49, 50]. Concerning cardiovascular problems, the authors in the WISE (Women's Ischemia Syndrome Evaluation) study [51] reported that depression was associated with 15–53 % increases in 5-year cardiovascular costs. In another study [52], the researchers found that older adults with heart failure showed additional hospitalization costs of US$3,816 in cases of co-morbid depression in 1999. Similarly, several studies [53, 54] have reported that depressive patients with diabetes have significantly higher diabetes-related medical costs than diabetes patients without depression.

The sensitivity analysis confirmed that the costs of workdays lost and the costs of hospitalizations were the most influencing variables in the calculation of the total financial burden of depression in Switzerland. However, even with a probably unrealistic 20 % reduction of the costs of workdays lost or hospitalizations, the financial burden at a national level was enormous (~€7.3 billion).

Some limitations of the study require discussion. We excluded, for example, from this analysis the costs due to depression-related suicides; however, it is known that there are about 1,000 suicides in Switzerland yearly [7]. Even if the causes of these suicides are not made public, it is reasonable to suppose that depression plays a main role [8]. The indirect costs (loss of work) due to these deaths may be considerably high, especially for suicides in the young (10 % of male and female individuals who commit suicide are younger than 26 and 31 years, respectively) [55]. Additionally, as has already been mentioned, there are a lot of suicide attempts every year. Unfortunately, it is actually very difficult to evaluate the direct and indirect costs of these attempts.

A second limitation concerns the potential indirect cost due to loss of work of the patient's caregivers (in particular parents), which is very difficult to estimate; it is dependent on the patient's personality, disease severity, family structure, religion, work status, etc. A depressed patient may require sporadic to constant care from parents or professional caregivers.

A third limitation concerns the hospitalization costs: we assumed in our analysis that the patients were hospitalized in a psychiatric clinic. However, it is also possible that some of them were hospitalized in a general hospital or clinic, in particular, for emergency cases (e.g. suicide attempts). Since the costs for a hospitalization day in a general hospital or clinic is higher than that for a day in a psychiatric clinic (€966 vs. €430), we can suppose that the real hospitalization costs may be higher [25].

A fourth limitation concerns the psychotherapy costs: it was only reported on the questionnaire if the patients did or did not receive psychotherapy during the first 12 months after diagnosis. We used the mean costs per patient per year for a psychiatrist in 2007 to evaluate the economic impact of psychotherapy for all depression groups. However, since the consultation frequency may vary substantially depending on depression severity, this might lead to a significant bias, with a systematic overestimation of the psychotherapy costs for mild depression and an underestimation of those for severe depression. Furthermore, as has been mentioned in Sect. 3, we calculated four visits for all patients with more than three consultations to estimate the average number of visits per patient (on the case report forms, there was no possibility to indicate the exact number of visits if there were more than three). This may have systematically reduced the variation in the data, causing an underestimation of the real costs related to physician visits. However, as shown in the sensitivity analysis, the costs of physician visits have little influence on total depression costs.

Other limitations concern the study design. On one hand, the fact that we included only outpatients probably influenced the percentage distribution of the patients in the severity classes; our sample showed a relatively high prevalence of mild depression compared with the studies performed by Kessler et al. [29] and Birnbaum et al. [30]. Our choice was based on the assumption that this was the simplest way to recruit enough patients with mild depression, allowing the subclasses analysis. On the other hand, it is known that depressive disorders have the tendency to get worse over time; the inclusion of outpatients who have been diagnosed with depression only within the last 3 years may have caused a selection bias and, consequently, an underestimation of the costs, particularly for severe depression. Moreover, the fact that we only used the first 12 months after diagnosis for our analysis might also be a source of bias; however, the hospitalization rates during the first months are usually higher, with a longer length of stay and, consequently, higher direct costs. In addition, chronic patients with a longer disease history will report a higher loss of productivity and, therefore, higher indirect costs. These factors may have been responsible for the relatively low percentage of cases of severe depression. In addition, every retrospective study is subjected to a certain risk of recall bias. However, the majority of the data collected (e.g. depression diagnoses, hospitalization days and workdays lost) are usually reported in official documents of psychiatrists, hospitals and health insurance companies.

5 Conclusions

The burden of depression in Switzerland was estimated to be around €8.1–8.3 billion per year. The costs of depression were directly related to disease severity. However, whereas the majority of the costs of mild depression were due to indirect causes (i.e. workdays lost), severe depression showed a balance between direct and indirect costs. Since many cases of depression remain unreported and since this analysis only included individuals between 18 and 65 years of age, it is reasonable to suppose that the total burden of depression in Switzerland may be even higher.

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